Patient Blood Management Guidelines: Module 2

Perioperative

Technical Report

Volume 2a

Appendixes (questions 1, 2 and 4–9)

Note

This volume presents the appendixes to *Technical report on perioperative patient blood management.* Volume I a presents the review of the evidence. These two volumes cover the background, foreground and generic research questions developed for this topic, with the exception of question 3, which is presented in Volumes 1b and 2b.

Contents

Figures

Appendix A: Literature searches

A1 Literature searches, Question 1

In patients undergoing surgery, what is the effect of a multidisciplinary, multimodal, programmatic approach to perioperative patient blood management on patient outcomes?

EMBASE.com: search conducted 4 June 2009

Blood management

No.	Query	Results
#1	'blood *1 management':ab,ti	553
#2	'management of blood loss':ab,ti OR 'blood loss management':ab,ti	27
#3	'transfusion practice':ab,ti OR 'transfusion practices':ab,ti	915
#4	'transfusion strategy':ab,ti OR 'transfusion strategies':ab,ti	179
#5	'transfusion management':ab,ti	75
#6	#1 OR #2 OR #3 OR #4 OR #5	1677

Blood transfusion/bleeding

No.	Query	Results
#1	'blood transfusion'/exp	107916
#2	'bleeding'/exp	353682
#3	#1 OR #2	443100

Blood loss

No.	Query	Results
#1	'transfusion *1 technique':ab,ti OR 'transfusion *1 techniques':ab,ti	124
#2	minimis*:ab,ti AND ('blood loss':ab,ti OR transfusion*:ab,ti)	182
#3	minimis* AND ('blood loss' OR transfusion*)	213
#4	minimiz*:ab,ti AND ('blood loss':ab,ti OR transfusion*:ab,ti)	1,680
#5	minimiz*:ab,ti AND ('blood loss':ab,ti OR transfusion*:ab,ti)	1,680
#6	#1 OR #2 OR #3 OR #4 OR #5	2,009

Guidelines

No.	Query	Results
#1	'health program'/exp	58,557
#2	'patient care planning'/exp	2,792
#3	'treatment planning'/exp	70,098
#4	'clinical practice'/exp	94,187
#5	'practice guideline'/exp	205,463
#6	'perioperative plan':ab,ti OR 'perioperative planning':ab,ti	34
#7	'preoperative plan':ab,ti OR 'preoperative planning':ab,ti	2,277
#8	'best practice':ab,ti OR 'best practices':ab,ti	5,635
#9	guideline*:ab,ti	139,794
#10	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9	473,799

Multidisciplinary

No.	Query	Results
#1	'patient care'/exp	376,841
#2	'teamwork'/exp	7,851
#3	'coordinated approach':ab,ti OR 'co ordinated approach':ab,ti	375
#4	interdisciplinary:ab,ti OR 'inter disciplinary':ab,ti	17,616
#5	multidisciplinary:ab,ti OR 'multi disciplinary':ab,ti	34,171
#6	multimodal:ab,ti OR 'multi modal':ab,ti	8,949
#7	multipronged:ab,ti OR 'multi pronged':ab,ti	296
#8	'multi team':ab,ti OR 'team approach':ab,ti	3,892
#9	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8	433,735

Elective surgery

No.	Query	Results
#1	'elective surgery'/exp	12,473
#2	'surgical patient'/exp	11,151
#3	'elective *1 surgery':ab,ti OR 'elective *1 surgeries':ab,ti	9,182
#4	'elective *1 procedure':ab,ti OR 'elective *1 procedures':ab,ti	1,812
#5	#1 OR #2 OR #3 OR #4	30,113

Emergency

No.	Query	Results
#1	'emergency surgery'/exp	8,133
#2	'emergency health service'/exp	45,989
#3	'emergency'/exp	21,395
#4	'emergency care'/exp	6,118
#5	'emergency treatment'/exp	102,279
#6	'emergency ward'/exp	23,394
#7	'emergency patient'/exp	255
#8	'emergency physician'/exp	922
#9	'emergency nursing'/exp	943
#10	'emergency nurse practitioner'/exp	84
#11	emergency:ab,ti	124,049
#12	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11	250,102

Disseminated search

No.	Query	Results
#1	'disseminated intravascular clotting'/exp	14,584
#2	'consumption coagulopathy':ab,ti OR 'consumptive coagulopathy':ab,ti	1,262
#3	'defibrination syndrome':ab,ti OR 'sanarelli shwartzman syndrome':ab,ti	120
#4	'disseminated fibrin thromboembolism':ab,ti	3
#5	'disseminated intravasal thromboembolism':ab,ti	0
#6	'intravasal agglutination':ab,ti OR 'intravasal *1 clotting':ab,ti	5
#7	'intravascular *1 clotting':ab,ti OR 'intravascular *1 coagulation':ab,ti	10,140
#8	'intravascular *1 coagulopathy':ab,ti OR 'intravenous *1 coagulation':ab,ti	670
#9	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8	18,468

Final search strategy

No.	Query	Results
#1	(('perioperative period'/exp) OR ('perioperative nursing'/exp) OR ('perioperative complication'/exp) OR ('preoperative period'/exp) OR ('preoperative complication'/exp) OR ('intraoperative period'/exp) OR (perioperative:ab,ti OR 'peri operative':ab,ti) OR (preoperative:ab,ti OR 'pre operative':ab,ti) OR (intraoperative:ab,ti OR 'intra operative':ab,ti) OR (peroperative:ab,ti OR 'per operative':ab,ti)) OR ('postoperative period'/exp) OR ('postoperative complication'/exp) OR (postoperative:ab,ti OR 'post operative':ab,ti)	866,452
#2	('blood *1 management':ab,ti) OR ('management of blood loss':ab,ti OR 'blood loss management':ab,ti) OR ('transfusion practice':ab,ti OR 'transfusion practices':ab,ti) OR ('transfusion strategy':ab,ti OR 'transfusion strategies':ab,ti) OR ('transfusion management':ab,ti)	1,677
#3	#1 AND #2	456
#4	('blood transfusion'/exp) OR ('bleeding'/exp)	443,100
#5	#1 AND #4	74,059
#6	('health program'/exp) OR ('patient care planning'/exp) OR ('treatment planning'/exp) OR ('clinical practice'/exp) OR ('practice guideline'/exp) OR ('perioperative plan':ab,ti OR 'perioperative planning':ab,ti) OR ('preoperative plan':ab,ti OR 'preoperative planning':ab,ti) OR ('best practice':ab,ti OR 'best practices':ab,ti) OR (guideline*:ab,ti)	473,799
#7	#5 AND #6	4,272
#8	('patient care'/exp) OR ('teamwork'/exp) OR ('coordinated approach':ab,ti OR 'co ordinated approach':ab,ti) OR (interdisciplinary:ab,ti OR 'inter disciplinary':ab,ti) OR (multidisciplinary:ab,ti OR 'multi disciplinary':ab,ti) OR (multimodal:ab,ti OR 'multi modal':ab,ti) OR (multipronged:ab,ti OR 'multi pronged':ab,ti) OR ('multi team':ab,ti OR 'team approach':ab,ti)	433,735
#9	#5 AND #8	5,877
#10	('emergency surgery'/exp) OR ('emergency health service'/exp) OR ('emergency'/exp) OR ('emergency care'/exp) OR ('emergency treatment'/exp) OR ('emergency ward'/exp) OR ('emergency patient'/exp) OR ('emergency physician'/exp) OR ('emergency nursing'/exp) OR ('emergency nurse practitioner'/exp) OR (emergency:ab,ti)	250,102
#11	#5 AND #10	4,055
#12	('elective surgery'/exp) OR ('surgical patient'/exp) OR ('elective *1 surgery':ab,ti OR 'elective *1 surgeries':ab,ti) OR ('elective *1 procedure':ab,ti OR 'elective *1 procedures':ab,ti)	30,113
#13	#5 AND #12	2,842
#14	'anemia'/exp	145,885
#15	anaemia:ab,ti OR anemia:ab,ti	85,334
#16	#14 OR #15	171,004
#17	#5 AND #16	3,586
#18	#11 OR #13 OR #17	9,732
#19	'risk management'/exp	19,412
#20	'risk management':ab,ti	5,735
#21	#19 OR #20	21,371

No.	Query	Results
#22	#18 AND #21	27
#23	('adverse outcome'/exp) OR ('outcome assessment'/exp) OR ('morbidity'/exp) OR ('mortality'/exp) OR (morbidity:ab,ti OR incidence:ab,ti OR prevalence:ab,ti OR occurrence:ab,ti) OR (mortality:ab,ti OR death:ab,ti OR survival:ab,ti)	1,929,304
#24	#18 AND #23	3,835
#25	('quality of life'/exp) OR (qol:ab,ti OR 'quality of life':ab,ti OR 'quality of wellbeing':ab,ti) OR ('health related quality':ab,ti OR hrqol:ab,ti) OR (qaly*:ab,ti OR 'quality adjusted':ab,ti OR 'adjusted life':ab,ti)	160,131
#26	#18 AND #25	233
#27	(('blood component therapy'/exp) AND (('dose response'/exp) OR ('drug dose'/exp))) OR ('fresh frozen plasma'/exp/dd_do) OR ('recombinant erythropoietin'/exp/dd_do) OR ('transfusion frequency':ab,ti) OR ('frequency *5 transfusion':ab,ti OR 'frequency *5 transfusions':ab,ti) OR ('transfusion rate':ab,ti OR 'transfusion rates':ab,ti) OR ('rate *5 transfusion':ab,ti OR 'rates *5 transfusion':ab,ti) OR ('transfusion requirement':ab,ti OR 'transfusion requirements':ab,ti) OR ('transfusion indication':ab,ti OR 'transfusion indications':ab,ti) OR ('indications *5 transfusion':ab,ti OR 'indications *5 transfusions':ab,ti) OR ('indication *5 transfusion':ab,ti OR 'indication *5 transfusions':ab,ti) OR ('transfusion interval':ab,ti OR 'transfusion intervals':ab,ti) OR ('need *3 transfusion':ab,ti OR 'need *3 transfusions':ab,ti) OR ('transfusion need':ab,ti OR 'transfusion needs':ab,ti) OR ('dose *3 transfusion':ab,ti OR 'dose *3 transfusions':ab,ti) OR ('dose *3 transfused':ab,ti OR 'transfusions *3 dose':ab,ti) OR ('transfusion dose':ab,ti OR 'transfused *3 dose':ab,ti) OR ('platelet dose':ab,ti OR 'dose *3 platelets':ab,ti) OR (dose:ab,ti AND transfus*:ab,ti)	17,414
#28	#18 AND #27	931
#29	('transfusion *1 technique':ab,ti OR 'transfusion *1 techniques':ab,ti) OR (minimis*:ab,ti AND ('blood loss':ab,ti OR transfusion*:ab,ti)) OR (minimis* AND ('blood loss' OR transfusion*)) OR (minimiz*:ab,ti AND ('blood loss':ab,ti OR transfusion*:ab,ti)) OR (minimiz*:ab,ti AND ('blood loss':ab,ti OR transfusion*:ab,ti))	2,009
#30	#18 AND #29	177
#31	('hemoglobin'/de) OR ('hemoglobin determination'/de) OR ('hemoglobin blood level'/de) OR ('mean corpuscular volume'/de) OR ('blood haemoglobin':ab,ti OR 'blood hemoglobin':ab,ti) OR ('haemoglobin *1 level':ab,ti OR 'hemoglobin *1 level':ab,ti) OR ('haemoglobin *1 levels':ab,ti OR 'hemoglobin *1 levels':ab,ti) OR ('hb level':ab,ti OR 'hb levels':ab,ti) OR ('haemoglobin determination':ab,ti OR 'hemoglobin determination':ab,ti) OR ('hemoglobin assay':ab,ti OR 'haemoglobin assay':ab,ti) OR ('hemoglobin estimation':ab,ti OR 'haemoglobin estimation':ab,ti) OR ('hb determination':ab,ti OR 'hb estimation':ab,ti OR 'hb assay':ab,ti) OR ('hemoglobin *1 content':ab,ti OR 'hemoglobin *1 concentration':ab,ti) OR ('haemoglobin *1 content':ti,ab OR 'haemoglobin *1 concentration':ti,ab) OR ('hb content':ab,ti OR 'hb concentration':ab,ti) OR (hemoglobinometry:ab,ti OR haemoglobinometry:ab,ti) OR ('plasma haemoglobin':ab,ti OR 'plasma hemoglobin':ab,ti) OR ('serum haemoglobin':ab,ti OR 'serum hemoglobin':ab,ti) OR ('mean corpuscular haemoglobin':ab,ti OR 'mean corpuscular hemoglobin':ab,ti) OR ('mean cell *1 haemoglobin':ab,ti OR 'mean cell *1 hemoglobin':ab,ti) OR ('erythrocyte indices':ti,ab OR 'erythrocyte index':ti,ab OR 'erythrocyte indexes':ti,ab) OR ('red *1 cell indices':ab,ti OR 'red *1 cell index':ab,ti OR 'red *1 cell indexes':ab,ti) OR ('rbc indices':ab,ti OR 'rbc index':ab,ti OR 'rbc indexes':ab,ti)	86,926
#32	#18 AND #31	1,049

No.	Query	Results
#33	('re-operation'/de) OR ('bleeding'/de) OR ('postoperative hemorrhage'/de) OR (('bleeding'/de) OR ('postoperative hemorrhage'/de)) OR (('re-operation'/de) OR ('postoperative hemorrhage'/de)) OR (re-operation*:ti AND (bleeding:ti OR 'blood loss':ti)) OR (re-operation*:ti AND (hemorrhag*:ti OR haemorrhag*:ti)) OR (('re operation':ti OR 're operations':ti) AND bleeding:ti) OR (('re operation':ti OR 're operations':ti) AND 'blood loss':ti) OR (('re operation':ti OR 're operations':ti) AND hemorrhag*:ti) OR (('re operation':ti OR 're operations':ti) AND haemorrhag*:ti) OR (re-operation*:ab AND (bleeding:ab OR 'blood loss':ab)) OR (re-operation*:ab AND (hemorrhag*:ab OR haemorrhag*:ab)) OR (('re operation':ab OR 're operations':ab) AND bleeding:ab) OR (('re operation':ab OR 're operations':ab) AND 'blood loss':ab) OR (('re operation':ab OR 're operations':ab) AND hemorrhag*:ab) OR (('re operation':ab OR 're operations':ab) AND haemorrhag*:ab) OR ('repeat surgery':ab,ti OR 'surgical revision':ab,ti)	135,002
#34	#18 AND #33	4,086
#35	('disseminated intravascular clotting'/exp) OR ('consumption coagulopathy':ab,ti OR 'consumptive coagulopathy':ab,ti) OR ('defibrination syndrome':ab,ti OR 'sanarelli shwartzman syndrome':ab,ti) OR ('disseminated fibrin thromboembolism':ab,ti) OR ('disseminated intravasal thromboembolism':ab,ti) OR ('intravasal agglutination':ab,ti OR 'intravasal *1 clotting':ab,ti) OR ('intravascular *1 clotting':ab,ti OR 'intravascular *1 coagulation':ab,ti) OR ('intravascular *1 coagulopathy':ab,ti OR 'intravenous *1 coagulation':ab,ti)	18,468
#36	#18 AND #35	131
#37	('health economics'/exp) OR ('economic aspect'/exp) OR ('economics'/exp) OR ('finance'/exp) OR ('biomedical technology assessment'/exp) OR ('economic evaluation'/exp) OR ('health care cost'/exp) OR (economic*:ab,ti OR pharmacoeconomic*:ab,ti) OR (cost*:ab,ti OR price*:ab,ti OR pricing:ab,ti) OR ('burden of illness':ab,ti OR 'value *1 money':ab,ti) OR (resource*:ab,ti AND utili*:ab,ti) OR (resource*:ab,ti AND utili*:ab,ti) OR ('technology assessment':ab,ti OR 'technology assessments':ab,ti) OR ('technology appraisal':ab,ti OR 'technology appraisals':ab,ti)	997,535
#38	#18 AND #37	814
#39	('hospitalization'/exp) OR ('length of stay'/exp) OR (hospitaliz*:ab,ti OR hospitalis*:ab,ti) OR ('length *3 stay':ab,ti OR 'hospital stay':ab,ti)	244,973
#40	#18 AND #39	1,113
#41	('intensive care unit'/exp) OR ('intensive care unit':ab,ti OR icu:ab,ti OR 'intensive care units':ab,ti) OR ('close attention unit':ab,ti OR 'close attention units':ab,ti) OR ('intensive care department':ab,ti OR 'intensive care departments':ab,ti) OR ('special care unit':ab,ti OR 'special care units':ab,ti) OR ('critical care unit':ab,ti OR 'critical care units':ab,ti)	76,826
#42	#18 AND #41	510
#43	('hospital admission'/exp) OR ('hospital readmission'/exp) OR ('hospital admission':ab,ti OR 'hospital admittance':ab,ti) OR ('patient admission':ab,ti OR readmission:ab,ti) OR (rehospitalization:ab,ti OR rehospitalisation:ab,ti)	77,727
#44	#18 AND #43	394
#45	#3 OR #7 OR #9 OR #22 OR #24 OR #26 OR #28 OR #30 OR #32 OR #34 OR #36 OR #38 OR #40 OR #42 OR #44	15,279

Cochrane Library Database: search conducted 12 June 2009

No.	Query	Results
#1	MeSH descriptor Perioperative Care explode all trees	4254
#2	MeSH descriptor Preoperative Care explode all trees	4098
#3	MeSH descriptor Postoperative Complications explode all trees	21418
#4	MeSH descriptor Postoperative Period explode all trees	3483
#5	MeSH descriptor Intraoperative Complications explode all trees	2476
#6	MeSH descriptor Intraoperative Period, this term only	919
#7	(perioperative OR "peri operative")	5196
#8	(preoperative OR "pre operative")	11093
#9	(intraoperative OR "intra operative")	8039
#10	(peroperative OR "per operative")	474
#11	(postoperative OR "post operative")	40236
#12	(#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11)	52453
#13	(blood NEAR/1 management)	22
#14	"management of blood loss" OR "blood loss management"	0
#15	"transfusion practice" OR "transfusion practices"	48
#16	"transfusion strategy" OR "transfusion strategies"	24
#17	"transfusion management"	4
#18	(#13 OR #14 OR #15 OR #16 OR #17)	92
#19	(#12 AND #18)	40
#20	MeSH descriptor Blood Transfusion explode all trees	2628
#21	MeSH descriptor Blood Loss, Surgical, this term only	1399
#22	(#20 OR #21)	3547
#23	(#12 AND #22)	2098
#24	(#19 OR #23)	2110
#25	MeSH descriptor Patient Care Planning explode all trees	1200
#26	MeSH descriptor Practice Guidelines as Topic, this term only	1272
#27	MeSH descriptor Physician's Practice Patterns, this term only	1047
#28	Any MeSH descriptor with qualifier: BL	64174
#29	"perioperative plan" OR "perioperative planning"	0
#30	"preoperative plan" OR "preoperative planning"	19
#31	"best practice" OR "best practices"	330
#32	(guideline*)	15591
#33	(#25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32)	80854
#34	(#24 AND #33)	444
#35	MeSH descriptor Patient Care Team explode all trees	1101

No.	Query	Results
#36	MeSH descriptor Health Personnel explode all trees	3996
#37	"coordinated approach" OR "co ordinated approach"	14
#38	(interdisciplinary OR "inter disciplinary")	552
#39	(multidisciplinary OR "multi disciplinary")	1661
#40	(multimodal* OR "multi modal" OR "multi modality")	870
#41	(multipronged OR "multi pronged")	10
#42	"multi team" OR "team approach"	66
#43	(#35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42)	7597
#44	(#24 AND #43)	11
#45	(#34 OR #44)	451
#46	MeSH descriptor Emergency Medical Services explode all trees	2146
#47	MeSH descriptor Emergency Service, Hospital explode all trees	1300
#48	MeSH descriptor Emergencies, this term only	569
#49	MeSH descriptor Emergency Medicine, this term only	132
#50	MeSH descriptor Emergency Medical Technicians, this term only	80
#51	MeSH descriptor Emergency Nursing, this term only	47
#52	MeSH descriptor Evidence-Based Emergency Medicine, this term only	0
#53	(emergency OR emergent)	9724
#54	(#46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52 OR #53)	9979
#55	(#45 AND #54)	13
#56	MeSH descriptor Surgical Procedures, Elective, this term only	1001
#57	MeSH descriptor Surgery Department, Hospital, this term only	68
#58	(elective NEAR/1 surger*)	1531
#59	(elective NEAR/1 procedure*)	1108
#60	(#56 OR #57 OR #58 OR #59)	2506
#61	(#45 AND #60)	32
#62	(#55 OR #61)	44
#63	MeSH descriptor Anemia explode all trees	2505
#64	(anaemia OR anemia)	5050
#65	(#63 OR #64)	5273
#66	(#45 AND #65)	31
#67	MeSH descriptor Orthopedic Procedures explode all trees	5335
#68	MeSH descriptor Orthopedics, this term only	272
#69	"orthopedic surgery" OR "orthopaedic surgery"	2339
#70	"bone surgery" OR orthopaedics or orthopedics	7975
#71	(orthopedic OR orthopaedic) NEAR/1 patient*	223

No.	Query	Results
#72	"orthopedic operation" OR "orthopaedic operation"	6
#73	(orthopedic OR orthopaedic) NEAR/1 procedure*	638
#74	(#67 OR #68 OR #69 OR #70 OR #71 OR #72 OR #73)	10914
#75	(#45 AND #74)	79
#76	(#66 AND #75)	9
#77	(#62 OR #76)	51

PreMedline: search conducted 15 June 2009

No.	Query	Results
#1	Search perioperative[tw] OR "peri operative"[tw]	42963
#2	Search preoperative[tw] OR "pre operative"[tw]	149752
#3	Search intraoperative[tw] OR "intra operative"[tw]	88318
#4	Search peroperative[tw] OR "per operative"[tw]	3710
#5	Search postoperative[tw] OR "post operative"[tw]	468760
#6	Search #1 OR #2 OR #3 OR #4 OR #5	612719
#7	Search "blood management"[tw]	134
#8	Search "management of blood loss"[tw] OR "blood loss management"[tw]	7
#9	Search "transfusion practice"[tw] OR "transfusion practices"[tw]	822
#10	Search "transfusion practice"[tw] OR "transfusion practices"[tw]"transfusion strategy"[tw] OR "transfusion strategies"[tw]	97
#11	Search "transfusion management"[tw]	76
#12	Search #7 OR #8 OR #9 OR #10 OR #11	1088
#13	Search #6 AND #12	314
#14	Search "blood transfusion"[tw]	61621
#15	Search bleeding[tw]	100172
#16	Search #14 OR #15	158228
#17	Search #6 AND #16	29517
#18	Search #13 OR #17	29556
#19	Search "perioperative plan"[tw] OR "perioperative planning"[tw]	35
#20	Search "preoperative plan"[tw] OR "preoperative planning"[tw]	1976
#21	Search "best practice"[tw] OR "best practices"[tw]	4804
#22	Search guideline*[tw]	175541
#23	Search #19 OR #20 OR #21 OR #22	180830
#24	Search #18 AND #23	609
#25	Search "coordinated approach"[tw] OR "co ordinated approach"[tw]	328

No.	Query	Results
#26	Search interdisciplinary[tw] OR "inter disciplinary"[tw]	17338
#27	Search multidisciplinary[tw] OR "multi disciplinary"[tw]	27954
#28	Search multimodal*[tw] OR "multi modal"[tw] OR "multi modality"[tw]	12461
#29	Search multipronged[tw] OR "multi pronged"[tw]	273
#30	Search "multi team"[tw] OR "team approach"[tw]	3281
#31	Search #25 OR #26 OR #27 OR #28 OR #29 OR #30	59061
#32	Search #18 AND #31	223
#33	Search #24 OR #32	807
#34	Search #33 NOT (medline[SB] OR oldmedline[sb])	36
#35	Search #33 AND in process[sb]	21
#36	Search #33 AND pubmednotmedline[sb]	8
#37	Search #34 OR #35 OR #36	36
#38	Search emergency[tw] OR emergent[tw]	149139
#39	Search #37 AND #38	3
#40	Search "elective surgery"[tw] OR "elective surgeries"[tw]	5105
#41	Search "elective procedure"[tw] OR "elective procedures"[tw]	773
#42	Search #40 OR #41	5825
#43	Search #37 AND #42	0
#44	Search #39 OR #43	3
#45	Search anaemia[tw] OR anemia [tw]	126122
#46	Search #37 AND #45	2
#47	Search "orthopedic surgery"[tw] OR "orthopaedic surgery"[tw]	6018
#48	Search "bone surgery"[tw] OR orthopaedics[tw] or orthopedics[tw]	17651
#49	Search orthopedic[tw] AND patient*[tw]	15165
#50	Search orthopaedic[tw] AND patient*[tw]	8148
#51	Search "orthopedic operation"[tw] OR "orthopaedic operation"[tw]	75
#52	Search orthopaedic[tw] AND procedure*[tw]	3368
#53	Search orthopedic[tw] AND procedure*[tw]	11147
#54	Search #47 OR #48 OR #49 OR #50 OR #51 OR #52 OR #53	42963
#55	Search #37 AND #54	5
#56	Search #46 AND #55	1
#57	Search #44 OR #56	4

CINAHL: search conducted 11 June 2009

No.	Query	Results
#1	(MH "Perioperative Care+")	16170
#2	(MH "Perioperative Nursing")	8853
#3	(MH "Preoperative Period+")	725
#4	(MH "Intraoperative Complications+")	1817
#5	(MH "Intraoperative Period")	367
#6	(MH "Postoperative Complications+")	21425
#7	(MH "Postoperative Period")	1916
#8	TI (perioperative OR "peri operative") or AB (perioperative OR "peri operative")	5346
#9	TI (preoperative OR "pre operative") or AB (preoperative OR "pre operative")	7246
#10	TI (intraoperative OR "intra operative") or AB (intraoperative OR "intra operative")	2984
#11	TI (peroperative OR "per operative") or AB (peroperative OR "per operative")	51
#12	TI (postoperative OR "post operative") or AB (postoperative OR "post operative")	14494
#13	S1 or S2 or S3 or S4 or S5 or S6 or S7 or S8 or S9 or S10 or S11 or S12	54689
#14	TI blood N1 management or AB blood N1 management	212
#15	TI ("management of blood loss" OR "blood loss management") or AB ("management of blood loss" OR "blood loss management")	4
#16	TI ("transfusion practice" OR "transfusion practices") or AB ("transfusion practice" OR "transfusion practices")	127
#17	TI ("transfusion strategy" OR "transfusion strategies") or AB ("transfusion strategy" OR "transfusion strategies")	34
#18	TI "transfusion management" or AB "transfusion management"	9
#19	S14 or S15 or S16 or S17 or S18	370
#20	S13 and S19	64
#21	(MH "Blood Transfusion+")	5055
#22	(MH "Blood Loss, Surgical")	616
#23	S21 or S22	5455
#24	S13 and S23	1142
#25	S20 or S24	1159
#26	(MH "Patient Care Plans+")	3571
#27	(MH "Practice Guidelines")	17946
#28	(MH "Practice Patterns")	1566
#29	TI ("perioperative plan" OR "perioperative planning") or AB ("perioperative plan" OR "perioperative planning")	5
#30	TI ("preoperative plan" OR "preoperative planning") or AB ("preoperative plan" OR "preoperative planning")	169
#31	TI ("best practice" OR "best practices") or AB ("best practice" OR "best practices")	4014

No.	Query	Results
#32	TI guideline* or AB guideline*	32632
#33	S26 or S27 or S28 or S29 or S30 or S31 or S32	50402
#34	S25 and S33	50
#35	(MH "Multidisciplinary Care Team+")	13911
#36	(MH "Health Personnel+")	207322
#37	TI ("coordinated approach" OR "co ordinated approach") or AB ("coordinated approach" OR "co ordinated approach")	121
#38	TI (interdisciplinary OR "inter disciplinary") or AB (interdisciplinary OR "inter disciplinary")	4766
#39	TI (multidisciplinary OR "multi disciplinary") or AB (multidisciplinary OR "multi disciplinary")	8504
#40	TI (multimodal* OR "multi modal" OR "multi modality") or AB (multimodal* OR "multi modal" OR "multi modality")	1160
#41	TI (multipronged OR "multi pronged") or AB (multipronged OR "multi pronged")	83
#42	TI ("multi team" OR "team approach") or AB ("multi team" OR "team approach")	1287
#43	S35 or S36 or S37 or S38 or S39 or S40 or S41 or S42	228142
#44	S25 and S43	54
#45	S34 or S44	97

AMI: search conducted 11 June 2009

No.	Query	Results
#1	TI=(blood %1 management) OR AB=(blood %1 management)	2
#2	TI=("management of blood loss" OR "blood loss management") OR AB=("management of blood loss" OR "blood loss management")	1
#3	TI=("transfusion practice" OR "transfusion practices") OR AB=("transfusion practice" OR "transfusion practices")	7
#4	TI=("transfusion strategy" OR "transfusion strategies") OR AB=("transfusion strategy" OR "transfusion strategies")	1
#5	TI=("transfusion management") OR AB=("transfusion management")	1
#6	(MH_PHRASE="Platelet Transfusion" OR MH_PHRASE="Erythrocyte Transfusion" OR MH_PHRASE="Leukocyte Transfusion" OR MH_PHRASE="Blood Transfusion, Autologous" OR MH_PHRASE="Lymphocyte Transfusion" OR MH_PHRASE="Blood Transfusion" OR MH_PHRASE="Blood Component Transfusion" OR MH_PHRASE="Exchange Transfusion, Whole Blood" OR MH_PHRASE="Plasma Exchange")	262
#7	(MH_PHRASE="Blood Loss, Surgical" OR MH_PHRASE="Postoperative Hemorrhage")	34

No.	Query	Results
#8	(((MH_PHRASE="Blood Loss, Surgical" OR MH_PHRASE="Postoperative Hemorrhage")) OR ((MH_PHRASE="Platelet Transfusion" OR MH_PHRASE="Erythrocyte Transfusion" OR MH_PHRASE="Leukocyte Transfusion" OR MH_PHRASE="Blood Transfusion, Autologous" OR MH_PHRASE="Lymphocyte Transfusion" OR MH_PHRASE="Blood Transfusion" OR MH_PHRASE="Blood Component Transfusion" OR MH_PHRASE="Exchange Transfusion, Whole Blood" OR MH_PHRASE="Plasma Exchange")) OR (TI=("transfusion management") OR AB=("transfusion management")) OR (TI=("transfusion strategy" OR "transfusion strategies") OR AB=("transfusion strategy" OR "transfusion strategies")) OR (TI=("transfusion practice" OR "transfusion practices") OR AB=("transfusion practice" OR "transfusion practices")) OR (TI=("management of blood loss" OR "blood loss management") OR AB=("management of blood loss" OR "blood loss management")) OR (TI=(blood %1 management) OR AB=(blood %1 management)))	290
#9	(MH_PHRASE="Patient Care Planning")	832
#10	(MH_PHRASE="Practice Guidelines")	619
#11	(MH_PHRASE="Physician's Practice Patterns")	365
#12	TI=("perioperative plan" OR "perioperative planning") OR AB=("perioperative plan" OR "perioperative planning")	1
#13	TI=("preoperative plan" OR "preoperative planning") OR AB=("preoperative plan" OR "preoperative planning")	7
#14	TI=("best practice" OR "best practices") OR AB=("best practice" OR "best practices")	450
#15	TI=(guideline*) OR AB=(guideline*)	3365
#16	((TI=(guideline*) OR AB=(guideline*)) OR (TI=("best practice" OR "best practices") OR AB=("best practice" OR "best practices")) OR (TI=("preoperative plan" OR "preoperative planning") OR AB=("preoperative plan" OR "preoperative planning")) OR (TI=("perioperative plan" OR "perioperative planning") OR AB=("perioperative plan" OR "perioperative planning")) OR ((MH_PHRASE="Physician's Practice Patterns")) OR ((MH_PHRASE="Practice Guidelines")) OR ((MH_PHRASE="Patient Care Planning")))	5036
#17	((((TI=(guideline*) OR AB=(guideline*)) OR (TI=("best practice" OR "best practices") OR AB=("best practice" OR "best practices")) OR (TI=("preoperative plan" OR "preoperative planning") OR AB=("preoperative plan" OR "preoperative planning")) OR (TI=("perioperative plan" OR "perioperative planning") OR AB=("perioperative plan" OR "perioperative planning")) OR ((MH_PHRASE="Physician's Practice Patterns")) OR ((MH_PHRASE="Practice Guidelines")) OR ((MH_PHRASE="Patient Care Planning")))) AND ((((MH_PHRASE="Blood Loss, Surgical" OR MH_PHRASE="Postoperative Hemorrhage")) OR ((MH_PHRASE="Platelet Transfusion" OR MH_PHRASE="Erythrocyte Transfusion" OR MH_PHRASE="Leukocyte Transfusion" OR MH_PHRASE="Blood Transfusion, Autologous" OR MH_PHRASE="Lymphocyte Transfusion" OR MH_PHRASE="Blood Transfusion" OR MH_PHRASE="Blood Component Transfusion" OR MH_PHRASE="Exchange Transfusion, Whole Blood" OR MH_PHRASE="Plasma Exchange")) OR (TI=("transfusion management") OR AB=("transfusion management")) OR (TI=("transfusion strategy" OR "transfusion strategies") OR AB=("transfusion strategy" OR "transfusion strategies")) OR (TI=("transfusion practice" OR "transfusion practices") OR AB=("transfusion practice" OR "transfusion practices")) OR (TI=("management of blood loss" OR "blood loss management") OR AB=("management of blood loss" OR "blood loss management")) OR (TI=(blood %1 management) OR AB=(blood %1 management)))))	23
#18	(MH_PHRASE="Patient Care Team")	927
#19	(MH_PHRASE="Health Personnel")	116

No.	Query	Results
#20	TI=("coordinated approach" OR "co ordinated approach") OR AB=("coordinated approach" OR "co ordinated approach")	47
#21	TI=(interdisciplinary OR "inter disciplinary") OR AB=(interdisciplinary OR "inter disciplinary")	167
#22	TI=(multidisciplinary OR "multi disciplinary") OR AB=(multidisciplinary OR "multi disciplinary")	905
#23	TI=(multimodal* OR "multi modal" OR "multi modality") OR AB=(multimodal* OR "multi modal" OR "multi modality")	86
#24	TI=(multipronged OR "multi pronged") OR AB=(multipronged OR "multi pronged")	7
#25	TI=("multi team" OR "team approach")	23
#26	((TI=("multi team" OR "team approach")) OR (TI=(multipronged OR "multi pronged") OR AB=(multipronged OR "multi pronged")) OR (TI=(multimodal* OR "multi modal" OR "multi modality") OR AB=(multimodal* OR "multi modal" OR "multi modality")) OR (TI=(multidisciplinary OR "multi disciplinary") OR AB=(multidisciplinary OR "multi disciplinary")) OR (TI=(interdisciplinary OR "inter disciplinary") OR AB=(interdisciplinary OR "inter disciplinary")) OR (TI=("coordinated approach" OR "co ordinated approach") OR AB=("coordinated approach" OR "co ordinated approach")) OR ((MH_PHRASE="Health Personnel")) OR ((MH_PHRASE="Patient Care Team")))	1989
#27	((((TI=("multi team" OR "team approach")) OR (TI=(multipronged OR "multi pronged") OR AB=(multipronged OR "multi pronged")) OR (TI=(multimodal* OR "multi modal" OR "multi modality") OR AB=(multimodal* OR "multi modal" OR "multi modality")) OR (TI=(multidisciplinary OR "multi disciplinary") OR AB=(multidisciplinary OR "multi disciplinary")) OR (TI=(interdisciplinary OR "inter disciplinary") OR AB=(interdisciplinary OR "inter disciplinary")) OR (TI=("coordinated approach" OR "co ordinated approach") OR AB=("coordinated approach" OR "co ordinated approach")) OR ((MH_PHRASE="Health Personnel")) OR ((MH_PHRASE="Patient Care Team")))) AND ((((MH_PHRASE="Blood Loss, Surgical" OR MH_PHRASE="Postoperative Hemorrhage")) OR ((MH_PHRASE="Platelet Transfusion" OR MH_PHRASE="Erythrocyte Transfusion" OR MH_PHRASE="Leukocyte Transfusion" OR MH_PHRASE="Blood Transfusion, Autologous" OR MH_PHRASE="Lymphocyte Transfusion" OR MH_PHRASE="Blood Transfusion" OR MH_PHRASE="Blood Component Transfusion" OR MH_PHRASE="Exchange Transfusion, Whole Blood" OR MH_PHRASE="Plasma Exchange")) OR (TI=("transfusion management") OR AB=("transfusion management")) OR (TI=("transfusion strategy" OR "transfusion strategies") OR AB=("transfusion strategy" OR "transfusion strategies")) OR (TI=("transfusion practice" OR "transfusion practices") OR AB=("transfusion practice" OR "transfusion practices")) OR (TI=("management of blood loss" OR "blood loss management") OR AB=("management of blood loss" OR "blood loss management")) OR (TI=(blood %1 management) OR AB=(blood %1 management)))))	11

No.	Query	Results
#28	((((((TI=("multi team" OR "team approach")) OR (TI=(multipronged OR "multi pronged") OR AB=(multipronged OR "multi pronged")) OR (TI=(multimodal* OR "multi modal" OR "multi modality") OR AB=(multimodal* OR "multi modal" OR "multi modality")) OR (TI=(multidisciplinary OR "multi disciplinary") OR AB=(multidisciplinary OR "multi disciplinary")) OR (TI=(interdisciplinary OR "inter disciplinary") OR AB=(interdisciplinary OR "inter disciplinary")) OR (TI=("coordinated approach" OR "co ordinated approach") OR AB=("coordinated approach" OR "co ordinated approach")) OR ((MH_PHRASE="Health Personnel")) OR ((MH_PHRASE="Patient Care Team")))) AND ((((MH_PHRASE="Blood Loss, Surgical" OR MH_PHRASE="Postoperative Hemorrhage")) OR ((MH_PHRASE="Platelet Transfusion" OR MH_PHRASE="Erythrocyte Transfusion" OR MH_PHRASE="Leukocyte Transfusion" OR MH_PHRASE="Blood Transfusion, Autologous" OR MH_PHRASE="Lymphocyte Transfusion" OR MH_PHRASE="Blood Transfusion" OR MH_PHRASE="Blood Component Transfusion" OR MH_PHRASE="Exchange Transfusion, Whole Blood" OR MH_PHRASE="Plasma Exchange")) OR (TI=("transfusion management") OR AB=("transfusion management")) OR (TI=("transfusion strategy" OR "transfusion strategies") OR AB=("transfusion strategy" OR "transfusion strategies")) OR (TI=("transfusion practice" OR "transfusion practices") OR AB=("transfusion practice" OR "transfusion practices")) OR (TI=("management of blood loss" OR "blood loss management") OR AB=("management of blood loss" OR "blood loss management")) OR (TI=(blood %1 management) OR AB=(blood %1 management)))))) OR (((((TI=(guideline*) OR AB=(guideline*)) OR (TI=("best practice" OR "best practices") OR AB=("best practice" OR "best practices")) OR (TI=("preoperative plan" OR "preoperative planning") OR AB=("preoperative plan" OR "preoperative planning")) OR (TI=("perioperative plan" OR "perioperative planning") OR AB=("perioperative plan" OR "perioperative planning")) OR ((MH_PHRASE="Physician's Practice Patterns")) OR ((MH_PHRASE="Practice Guidelines")) OR ((MH_PHRASE="Patient Care Planning")))) AND ((((MH_PHRASE="Blood Loss, Surgical" OR MH_PHRASE="Postoperative Hemorrhage")) OR ((MH_PHRASE="Platelet Transfusion" OR MH_PHRASE="Erythrocyte Transfusion" OR MH_PHRASE="Leukocyte Transfusion" OR MH_PHRASE="Blood Transfusion, Autologous" OR MH_PHRASE="Lymphocyte Transfusion" OR MH_PHRASE="Blood Transfusion" OR MH_PHRASE="Blood Component Transfusion" OR MH_PHRASE="Exchange Transfusion, Whole Blood" OR MH_PHRASE="Plasma Exchange")) OR (TI=("transfusion management") OR AB=("transfusion management")) OR (TI=("transfusion strategy" OR "transfusion strategies") OR AB=("transfusion strategy" OR "transfusion strategies")) OR (TI=("transfusion practice" OR "transfusion practices") OR AB=("transfusion practice" OR "transfusion practices")) OR (TI=("management of blood loss" OR "blood loss management") OR AB=("management of blood loss" OR "blood loss management")) OR (TI=(blood %1 management) OR AB=(blood %1 management)))))))	24

* The search was conducted using Informit online platform on 11 June 2009

BMJ Clinical Evidence: search conducted 18 June 2009

341 matches were found for the search 'preoperative OR "pre operative"perioperative OR "peri operative" OR preoperative OR "pre operative" OR intraoperative OR "intra operative" OR peroperative OR "per operative" OR postoperative OR "post operative"' [oper intraop postop periop per intra preoper perop post pre peri].

A2 Literature searches, Question 2

In patients undergoing surgery, what effect does the cessation and timing of cessation of medication that affects haemostasis have on morbidity, mortality and red blood cell (RBC) transfusion?

EMBASE.com: search conducted 12 June 2009

#	Search	Results
#1	(('perioperative period'/exp) OR ('perioperative nursing'/exp) OR ('perioperative complication'/exp) OR ('preoperative period'/exp) OR (perioperative:ab,ti OR 'peri operative':ab,ti) OR (preoperative:ab,ti OR 'pre operative':ab,ti) OR ('preoperative complication'/exp)) AND (('hemostatic agent'/exp) OR ('hemostatic agent':ab,ti OR 'hemostatic agents':ab,ti) OR ('hemostasis agent':ab,ti OR 'hemostasis agents':ab,ti) OR (hemostatics:ab,ti OR antihemorrhagics:ab,ti OR antihaemorrhagics:ab,ti) OR ('anti hemorrhagics':ab,ti OR 'anti haemorrhagics':ab,ti))	3,968
#2	(('perioperative period'/exp) OR ('perioperative nursing'/exp) OR ('perioperative complication'/exp) OR ('preoperative period'/exp) OR (perioperative:ab,ti OR 'peri operative':ab,ti) OR (preoperative:ab,ti OR 'pre operative':ab,ti) OR ('preoperative complication'/exp)) AND (('anticoagulant agent'/exp) OR ('anticoagulant therapy'/exp) OR ('anticoagulation'/exp) OR (anticoagulant*:ab,ti OR 'anti coagulant':ab,ti OR 'anti coagulants':ab,ti) OR ('anticoagulating agent':ab,ti OR 'anticoagulating agents':ab,ti) OR ('anti coagulating agent':ab,ti OR 'anti coagulating agents':ab,ti) OR ('anticoagulation agent':ab,ti OR 'anticoagulation agents':ab,ti) OR ('anti coagulation agent':ab,ti OR 'anti coagulation agents':ab,ti) OR ('anticoagulation therapy':ab,ti OR 'anti coagulation therapy':ab,ti) OR ('anticoagulative agent':ab,ti OR 'anticoagulative agents':ab,ti) OR ('anti coagulative agent':ab,ti OR 'anti coagulative agents':ab,ti) OR (antithrombotic*:ab,ti OR 'anti thrombotic':ab,ti OR 'anti thrombotics':ab,ti) OR ('hirudin therapy':ab,ti OR clopidogrel:ab,ti OR aspirin:ab,ti) OR (antithrombocytic*:ab,ti OR 'anti thrombocytic':ab,ti OR 'anti thrombocytics':ab,ti) OR ('antiplatelet therapy':ab,ti OR 'anti platelet therapy':ab,ti) OR ('antiplatelet agent':ab,ti OR 'antiplatelet agents':ab,ti) OR ('anti platelet agent':ab,ti OR 'anti platelet agents':ab,ti) OR ('antiplatelet drug':ab,ti OR 'antiplatelet drugs':ab,ti) OR ('platelet *1 inhibitor':ab,ti OR 'platelet *1 inhibitors':ab,ti) OR ('thrombocyte aggregation inhibiting agent':ab,ti) OR ('thrombocyte aggregation inhibiting agents':ab,ti) OR ('thrombocyte aggregation inhibitor':ab,ti OR 'thrombocyte aggregation inhibitors':ab,ti) OR ('platelet antagonist':ab,ti OR 'platelet antagonists':ab,ti) OR ('platelet antiaggregant':ab,ti OR 'platelet antiaggregants':ab,ti))	9,321

#	Search	Results
#3	(('perioperative period'/exp) OR ('perioperative nursing'/exp) OR ('perioperative complication'/exp) OR ('preoperative period'/exp) OR (perioperative:ab,ti OR 'peri operative':ab,ti) OR (preoperative:ab,ti OR 'pre operative':ab,ti) OR ('preoperative complication'/exp)) AND (('nonsteroid antiinflammatory agent'/exp) OR (nsaid*:ab,ti) OR ('non steroid antiinflammatory agent':ab,ti OR 'nonsteroid antiinflammatory agent':ab,ti) OR ('non steroid antiinflammatory agents':ab,ti OR 'nonsteroid antiinflammatory agents':ab,ti) OR ('non steroid anti inflammatory agent':ab,ti OR 'nonsteroid anti inflammatory agent':ab,ti) OR ('non steroid anti inflammatory agents':ab,ti OR 'nonsteroid anti inflammatory agents':ab,ti) OR ('non steroid antiinflammatory drug':ab,ti OR 'nonsteroid antiinflammatory drug':ab,ti) OR ('non steroid antiinflammatory drugs':ab,ti OR 'nonsteroid antiinflammatory drugs':ab,ti) OR ('non steroid anti inflammatory drug':ab,ti OR 'nonsteroid anti inflammatory drug':ab,ti) OR ('non steroid anti inflammatory drugs':ab,ti OR 'nonsteroid anti inflammatory drugs':ab,ti) OR ('non steroid antirheumatic agent':ab,ti OR 'nonsteroid antirheumatic agent':ab,ti) OR ('non steroid antirheumatic agents':ab,ti OR 'nonsteroid antirheumatic agents':ab,ti) OR ('non steroid anti rheumatic agent':ab,ti OR 'nonsteroid anti rheumatic agent':ab,ti) OR ('non steroid anti rheumatic agents':ab,ti OR 'nonsteroid anti rheumatic agents':ab,ti) OR ('non steroidal antiinflammatory agent':ab,ti OR 'nonsteroidal antiinflammatory agent':ab,ti) OR ('non steroidal antiinflammatory agents':ab,ti OR 'nonsteroidal antiinflammatory agents':ab,ti) OR ('non steroidal anti inflammatory agent':ab,ti OR 'nonsteroidal anti inflammatory agent':ab,ti) OR ('non steroidal anti inflammatory agents':ab,ti OR 'nonsteroidal anti inflammatory agents':ab,ti) OR ('non steroidal antiinflammatory drug':ab,ti OR 'nonsteroidal antiinflammatory drug':ab,ti) OR ('non steroidal antiinflammatory drugs':ab,ti OR 'nonsteroidal antiinflammatory drugs':ab,ti) OR ('non steroidal anti inflammatory drug':ab,ti OR 'nonsteroidal anti inflammatory drug':ab,ti) OR ('non steroidal anti inflammatory drugs':ab,ti OR 'nonsteroidal anti inflammatory drugs':ab,ti) OR ('non steroidal antirheumatic agent':ab,ti OR 'nonsteroidal antirheumatic agent':ab,ti) OR ('non steroidal antirheumatic agents':ab,ti OR 'nonsteroidal antirheumatic agents':ab,ti) OR ('non steroidal anti rheumatic agent':ab,ti OR 'nonsteroidal anti rheumatic agent':ab,ti) OR ('non steroidal anti rheumatic agents':ab,ti OR 'nonsteroidal anti rheumatic agents':ab,ti) OR ('anti-inflammatory analgesic':ab,ti OR 'anti-inflammatory analgesics':ab,ti))	8,036
#4	(('perioperative period'/exp) OR ('perioperative nursing'/exp) OR ('perioperative complication'/exp) OR ('preoperative period'/exp) OR (perioperative:ab,ti OR 'peri operative':ab,ti) OR (preoperative:ab,ti OR 'pre operative':ab,ti) OR ('preoperative complication'/exp)) AND (('hydroxymethylglutaryl coenzyme a reductase inhibitor'/exp) OR (statin*:ab,ti OR vastatin:ab,ti) OR ('hmg coa *1 inhibitor':ab,ti OR 'hmg coa *1 inhibitors':ab,ti) OR ('hmg coenzyme a *1 inhibitor':ab,ti OR 'hmg coenzyme a *1 inhibitors':ab,ti) OR ('hydroxymethylglutaryl coa *1 inhibitor':ab,ti OR 'hydroxymethylglutaryl coa *1 inhibitors':ab,ti) OR ('hydroxymethylglutaryl coenzyme a *1 inhibitor':ab,ti OR 'hydroxymethylglutaryl coenzyme a *1 inhibitors':ab,ti))	948
#5	(('perioperative period'/exp) OR ('perioperative nursing'/exp) OR ('perioperative complication'/exp) OR ('preoperative period'/exp) OR (perioperative:ab,ti OR 'peri operative':ab,ti) OR (preoperative:ab,ti OR 'pre operative':ab,ti) OR ('preoperative complication'/exp)) AND (('alternative medicine'/exp) OR ('medicinal plant'/exp) OR ('herbal medicine'/de) OR ('homeopathy'/de) OR ('alternative therapies':ab,ti OR 'alternative therapy':ab,ti) OR ('alternative medicine':ab,ti OR 'alternative medicines':ab,ti) OR ('complementary therapy':ab,ti OR 'complementary therapies':ab,ti) OR ('herbal medicine':ab,ti OR 'herbal medicines':ab,ti OR naturopath*:ab,ti) OR ('medicinal herb':ab,ti OR 'medicinal herbs':ab,ti) OR (homeopathy:ab,ti OR homeotherapy:ab,ti))	915

#	Search	Results
#6	(('perioperative period'/exp) OR ('perioperative nursing'/exp) OR ('perioperative complication'/exp) OR ('preoperative period'/exp) OR (perioperative:ab,ti OR 'peri operative':ab,ti) OR (preoperative:ab,ti OR 'pre operative':ab,ti) OR ('preoperative complication'/exp)) AND (('vitamin'/exp) OR (vitamin*:ab,ti))	3,421
#7	#1 OR #2 OR #3 OR #4 OR #5 OR #6	335,505
#8	'drug withdrawal'/exp	54,280
#9	'treatment withdrawal'/exp	8,363
#10	withdrawal:ab,ti OR withdrawing:ab,ti OR 'drug abstinence':ab,ti	64,464
#11	cessation:ab,ti OR ceasing:ab,ti OR ceased:ab,ti	50,761
#12	suspension:ab,ti OR suspended:ab,ti OR suspending:ab,ti	63,259
#13	discontinuation:ab,ti OR discontinued:ab,ti OR discontinuing:ab,ti	51,389
#14	interruption:ab,ti OR interrupted:ab,ti OR interrupting:ab,ti	34,774
#15	stopped:ab,ti OR stop:ab,ti OR stopping:ab,ti	70,106
#16	#8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15	357,057
#17	#7 AND #16	16,492
#18	'drug substitution'/de	9,321
#19	'substitution therapy'/de	3,072
#20	substitution:ab,ti OR substituting:ab,ti OR substituted:ab,ti	142,754
#21	replacement:ab,ti OR replaced:ab,ti OR replacing:ab,ti	204,297
#22	switch:ab,ti OR switched:ab,ti OR switching:ab,ti	57,547
#23	#18 OR #19 OR #20 OR #21 OR #22	402,347
#24	#7 AND #23	8,281
#25	'time'/exp	416,743
#26	timing:ab,ti	57,737
#27	#25 OR #26	468,526
#28	#7 AND #27	5,663
#29	#17 OR #24 OR #28	3,250

EMBASE.com: Updated search conducted 28 January 2010

No.	Query	Results
#1	'hemostatic agent' OR 'hemostatic agents':ab,ti	218557
#2	'hemostatic agent'/exp	218382
#3	'hemostasis agent' OR 'hemostasis agents':ab,ti	4
#4	'hemostasis agent' OR 'hemostasis agents':ab,ti	4
#5	'anti hemorrhagics' OR 'anti haemorrhagics':ab,ti	0
#6	#1 OR #2 OR #3 OR #4 OR #5	21,8558
#7	'anticoagulant agent'/exp	361,635
#8	'anticoagulant therapy'/de	13,750
#9	'anticoagulation'/de	17,334
#10	anticoagulant* OR 'anti coagulant' OR 'anti coagulants':ab,ti	372,280
#11	'anticoagulating agent'/de OR 'anticoagulating agents':ab,ti	55,824
#12	'anti coagulating agent'/de OR 'anti coagulating agents':ab,ti	55,819
#13	'anticoagulation agent' OR 'anticoagulation agents':ab,ti	55
#14	'anti coagulation agent' OR 'anti coagulation agents':ab,ti	3
#15	'anticoagulation therapy' OR 'anti coagulation therapy':ab,ti	3,113
#16	'anticoagulative agent' OR 'anticoagulative agents':ab,ti	13
#17	'anti coagulative agent' OR 'anti coagulative agents':ab,ti	2
#18	antithrombotic* OR 'anti thrombotic' OR 'anti thrombotics':ab,ti	12,615
#19	'hirudin therapy' OR clopidogrel OR aspirin:ab,ti	50,208
#20	antithrombocytic* OR 'anti thrombocytic' OR 'anti thrombocytics':ab,ti	197,227
#21	'antiplatelet therapy' OR 'anti platelet therapy':ab,ti	3,854
#22	'antiplatelet agent' OR 'antiplatelet agents':ab,ti	3,301
#23	'anti platelet agent' OR 'anti platelet agents':ab,ti	386
#24	'antiplatelet drug' OR 'antiplatelet drugs':ab,ti	1,912
#25	'anti platelet drug' OR 'anti platelet drugs':ab,ti	270
#26	'platelet' NEAR/1 'inhibitor' OR ('platelet' NEAR/1 'inhibitors'):ab,ti	857
#27	'thrombocyte aggregation inhibiting agent':ab,ti	0
#28	'thrombocyte aggregation inhibiting agents':ab,ti	0
#29	'thrombocyte aggregation inhibitor' OR 'thrombocyte aggregation inhibitors':ab,ti	138
#30	'platelet antagonist' OR 'platelet antagonists':ab,ti	86
#31	'platelet antiaggregant' OR 'platelet antiaggregants':ab,ti	255
#32	#7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31	383,536
#33	'nonsteroid antiinflammatory agent'/exp	334,295

No.	Query	Results
#34	nsaid*:ab,ti	17,133
#35	'non steroid antiinflammatory agent' OR 'nonsteroid antiinflammatory agent':ab,ti	38
#36	'non steroid antiinflammatory agents' OR 'nonsteroid antiinflammatory agents':ab,ti	176
#37	'non steroid anti inflammatory agent' OR 'nonsteroid anti inflammatory agent':ab,ti	80
#38	'non steroid anti inflammatory agents' OR 'nonsteroid anti inflammatory agents':ab,ti	226
#39	'non steroid antiinflammatory drug' OR 'nonsteroid antiinflammatory drug':ab,ti	61
#40	'non steroid antiinflammatory drugs' OR 'nonsteroid antiinflammatory drugs':ab,ti	262
#41	'non steroid anti inflammatory drug' OR 'nonsteroid anti inflammatory drug':ab,ti	175
#42	'non steroid anti inflammatory drugs' OR 'nonsteroid anti inflammatory drugs':ab,ti	758
#43	'non steroid antirheumatic agent' OR 'nonsteroid antirheumatic agent':ab,ti	37
#44	'non steroid antirheumatic agents' OR 'nonsteroid antirheumatic agents':ab,ti	69
#45	'non steroid anti rheumatic agent' OR 'nonsteroid anti rheumatic agent':ab,ti	1
#46	'non steroid anti rheumatic agents' OR 'nonsteroid anti rheumatic agents':ab,ti	1
#47	'non steroidal antiinflammatory agent' OR 'nonsteroidal antiinflammatory agent':ab,ti	216
#48	'non steroidal antiinflammatory agents' OR 'nonsteroidal antiinflammatory agents':ab,ti	552
#49	'non steroidal anti inflammatory agent' OR 'nonsteroidal anti inflammatory agent':ab,ti	676
#50	'non steroidal anti inflammatory agents' OR 'nonsteroidal anti inflammatory agents':ab,ti	1,714
#51	'non steroidal antiinflammatory drug' OR 'nonsteroidal antiinflammatory drug':ab,ti	1,080
#52	'non steroidal antiinflammatory drugs' OR 'nonsteroidal antiinflammatory drug':ab,ti	1,722
#53	'non steroidal anti inflammatory drug' OR 'nonsteroidal anti inflammatory drug':ab,ti	4,659
#54	'non steroidal anti inflammatory drugs' OR 'nonsteroidal anti inflammatory drugs':ab,ti	14,452
#55	'non steroidal antirheumatic agent' OR 'nonsteroidal antirheumatic agent':ab,ti	22
#56	'non steroidal antirheumatic agents' OR 'nonsteroidal antirheumatic agents':ab,ti	70
#57	'non steroidal anti rheumatic agent' OR 'nonsteroidal anti rheumatic agent':ab,ti	2
#58	'non steroidal anti rheumatic agents' OR 'nonsteroidal anti rheumatic agents':ab,ti	5
#59	'anti-inflammatory analgesic' OR 'anti-inflammatory analgesics':ab,ti	708
#60	#33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52 OR #53 OR #54 OR #55 OR #56 OR #57 OR #58 OR #59	338,282
#61	'hydroxymethylglutaryl coenzyme a reductase inhibitor'/exp	55,435
#62	statin* OR vastatin:ab,ti	22,495
#63	'hmg coa' NEAR/1 'inhibitor' OR ('hmg coa' NEAR/1 'inhibitors'):ab,ti	108
#64	'hmg coenzyme a' NEAR/1 'inhibitor' OR ('hmg coenzyme a' NEAR/1 'inhibitors'):ab,ti	1
#65	'hydroxymethylglutaryl coa' NEAR/1 'inhibitor' OR ('hydroxymethylglutaryl coa' NEAR/1 'inhibitors'):ab,ti	2
#66	'hydroxymethylglutaryl coenzyme a' NEAR/1 'inhibitor' OR ('hydroxymethylglutaryl coenzyme a' NEAR/1 'inhibitors'):ab,ti	53,862

No.	Query	Results
#67	#61 OR #62 OR #63 OR #64 OR #65 OR #66	62,006
#68	'alternative medicine'/exp	23,941
#69	'medicinal plant'/exp	88,322
#70	'herbal medicine'/de	9,695
#71	'homeopathy'/de	6,671
#72	'alternative therapies' OR 'alternative therapy':ab,ti	6,466
#73	'alternative medicine' OR 'alternative medicines':ab,ti	26,628
#74	'complementary medicine' OR 'complementary medicines':ab,ti	5,231
#75	'complementary therapy' OR 'complementary therapies':ab,ti	1,871
#76	'herbal medicine' OR 'herbal medicines' OR naturopath*:ab,ti	14,048
#77	'medicinal herb' OR 'medicinal herbs':ab,ti	1,834
#78	homeopathy OR homeotherapy:ab,ti	7,091
#79	#68 OR #69 OR #70 OR #71 OR #72 OR #73 OR #74 OR #75 OR #76 OR #77 OR #78	131,284
#80	'vitamin'/exp	362,939
#81	vitamin*:ab,ti	136,373
#82	#80 OR #81	390,813
#83	#6 OR #32 OR #60 OR #67 OR #79 OR #82	1,246,383
#84	'spinal anesthesia'/de	13,664
#85	'spinal anesthesia' OR 'spinal anaesthesia':ab,ti	14,897
#86	'spinal analgesia' OR 'lumbar extradural blockade':ab,ti	609
#87	'lumbar anaesthesia' OR 'lumbar anesthesia':ab,ti	113
#88	'spinal anesthetic' OR 'spinal anesthaetic':ab,ti	224
#89	'spinal cord anesthesia' OR 'spinal cord anaesthesia':ab,ti	7
#90	'spinal block' OR 'subarachnoid block' OR 'intraspinal block':ab,ti	951
#91	'subarachnoid anesthesia' OR 'subarachnoid anaesthesia':ab,ti	302
#92	'subarachnoidal anesthesia' OR 'subarachnoidal anaesthesia':ab,ti	22
#93	'intraspinal anesthesia' OR 'intraspinal anaesthesia':ab,ti	4
#94	#84 OR #85 OR #86 OR #87 OR #88 OR #89 OR #90 OR #91 OR #92 OR #93	15,463
#95	'epidural anesthesia'/exp	23,039
#96	'epidural anesthesia' OR 'epidural anaesthesia':ab,ti	24,480
#97	'epidural anesthetic' OR 'epidural anaesthetic':ab,ti	208
#98	'epidural analgesia' OR 'epidural block' OR 'epidural blockade':ab,ti	7,234
#99	'caudal anesthesia' OR 'caudal anaesthesia':ab,ti	1,196
#100	'caudal block' OR 'caudal blocking' OR 'dural blocking':ab,ti	373
#101	'extradural anesthesia' OR 'extradural anaesthesia':ab,ti	219
#102	'extradural analgesia' OR 'extradural block':ab,ti	402

No.	Query	Results
#103	'peridural anesthesia' OR 'peridural anaesthesia':ab,ti	1,297
#104	'peridural analgesia' OR 'peridural block' OR 'peridural blocking':ab,ti	407
#105	#95 OR #96 OR #97 OR #98 OR #99 OR #100 OR #101 OR #102 OR #103 OR #104	26,536
#106	'endoscopy'/exp	25,1643
#107	endoscopy OR endoscopies OR endoscopic:ab,ti	313,459
#108	gastroscopy OR gastrofibroscopy OR 'stomach endoscopy':ab,ti	15,949
#109	gastroscopic OR fibergastroscopy OR fibrogastroscopy:ab,ti	1,092
#110	cardioendoscopy OR pylorobulboscopy:ab,ti	1
#111	colonoscopy OR coloscopy OR colonoscopic:ab,ti	28,161
#112	sigmoidoscopy OR sigmoideoscopy OR sigmoidoscopic:ab,ti	7,769
#113	proctosigmoidoscopy OR rectoromanoscopy OR rectosigmoidoscopy:ab,ti	516
#114	hysteroscopy OR hysteroscopies OR hysteroscopic:ab,ti	6,214
#115	uteroscopy:ab,ti	9
#116	#106 OR #107 OR #108 OR #109 OR #110 OR #111 OR #112 OR #113 OR #114 OR #115	318,153
#117	'biopsy'/exp	307,188
#118	biopsy OR biopsies OR biopsied:ab,ti	416,814
#119	'bronchus brushing' OR 'tracheobronchial smear':ab,ti	2
#120	'hepatic puncture' OR 'liver puncture':ab,ti	282
#121	'kidney puncture' OR 'renal puncture' OR 'pyelocalycial puncture':ab,ti	191
#122	#117 OR #118 OR #119 OR #120 OR #121	416,966
#123	'central venous catheterization'/de	5,382
#124	(('central venous' OR 'central vein') NEXT/2 catheteri?ation):ab,ti	5,245
#125	#123 OR #124	7,475
#126	'paracentesis'/de	,2616
#127	pericardiocentesis:ab,ti	1,480
#128	paracentesis OR pericardicentesis OR pericardiocentesis:ab,ti	5,244
#129	'pericardial aspiration' OR 'pericardium puncture':ab,ti	49
#130	#126 OR #127 OR #128 OR #129	5,287
#131	'interventional cardiovascular procedure'/exp	51,644
#132	'angiocardiography'/exp	56,196
#133	'epicardial high intensity focused ultrasound cardiac ablation':de	1
#134	'epicardial ablation':de	4
#135	'heart ablation':ab,ti	23
#136	'percutaneous epicardial ablation':de	1
#137	'thoracoscopic microwave epicardial ablation':de	1

No.	Query	Results
#138	'interventional cardiology' OR 'p t c a' OR ptca:ab,ti	12,880
#139	'percutaneous coronary intervention' OR 'percutaneous coronary stent':ab,ti	34,565
#140	(coronary NEXT/2 (angioplasty OR balloon)):ab,ti	13,767
#141	'transluminal coronary artery dilatation':ab,ti	4
#142	'coronary angiography' OR coronarography:ab,ti	21,521
#143	'coronary arteriogram' OR 'coronary arteriography':ab,ti	4,912
#144	(cardiac NEXT/2 ablation):ab,ti	115
#145	#131 OR #132 OR #133 OR #134 OR #135 OR #136 OR #137 OR #138 OR #139 OR #140 OR #141 OR #142 OR #143 OR #144	112,715
#146	'angioplasty'/exp	48,173
#147	angioplasty OR 'endoluminal repair' OR 'endo luminal repair':ab,ti	58,945
#148	#146 OR #147	58,945
#149	'endoluminal stent':de	7
#150	'endoluminal aortic stent grafting':de	1
#151	'endoluminal flow disrupting device':de	1
#152	'endoluminal therapy':de	3
#153	'endoluminal grafting':de	1
#154	'endoluminal stent graft':de	3
#155	'endoluminal repair':de	3
#156	'endoluminal treatment':de	3
#157	#150 OR #151 OR #152 OR #153 OR #154 OR #155 OR #156	15
#158	'stent'/exp	52,609
#159	#157 AND #158	10
#160	'endoluminal stent' OR 'endoluminal stents' OR 'endoluminal stenting':ab,ti	411
#161	'endo luminal stent' OR 'endo luminal stents' OR 'endo luminal stenting':ab,ti	1
#162	#149 OR #159 OR #160 OR #161	418
#163	'lumbar puncture'/de	6,419
#164	'lumbar punction' OR 'thecal puncture' OR rachiocentesis:ab,ti	67
#165	'spinal puncture' OR 'spinal tap':ab,ti	524
#166	#163 OR #164 OR #165	6,905
#167	'thoracocentesis'/de	2,594
#168	thoracentesis OR thoracocentesis:ab,ti	1,578
#169	pleurocantensis OR pleuracentesis OR pleurocentesis:ab,ti	66
#170	'pleura aspiration' OR 'pleural aspiration':ab,ti	81
#171	'pleura punction' OR 'pleura puncture':ab,ti	7
#172	'pleural punction' OR 'pleural puncture':ab,ti	166

No.	Query	Results
#173	#167 OR #168 OR #169 OR #170 OR #171 OR #172	3,510
#174	'regional anesthesia'/exp	25,704
#175	(regional NEXT/2 (anesthesia OR anaesthesia)):ab,ti	6,444
#176	'conduction anesthesia' OR 'conduction anaesthesia':ab,ti	367
#177	'block anesthesia' OR 'block anaesthesia':ab,ti	620
#178	'region anesthesia' OR 'region anaesthesia':ab,ti	4
#179	'anesthesia regionalis' OR 'anaesthesia regionalis':ab,ti	0
#180	regional NEXT/2 analgesia OR 'bier block':ab,ti	760
#181	#174 OR #175 OR #176 OR #177 OR #178 OR #179 OR #180	28,592
#182	'central neural blockade':de	1
#183	'central neural blockade' OR 'central neural block':ab,ti	56
#184	'central nerve blockade' OR 'central nerve block':ab,ti	20
#185	#182 OR #183 OR #184	75
#186	'polypectomy'/de	2,898
#187	polypectomy:ab,ti	3,452
#188	#186 OR #187	4,947
#189	'transjugular intrahepatic portosystemic shunt'/de	331
#190	('transjugular intrahepatic' NEXT/3 (shunt OR shunts OR shunting)):ab,ti	1,979
#191	('transjugular intrahepatic' NEXT/3 (stent OR stents OR stenting)):ab,ti	336
#192	tips OR tipss:ab,ti	17,846
#193	#189 OR #190 OR #191 OR #192	18,633
#194	'angiography'/exp	231,775
#195	angiography OR angioradiology OR arteriography:ab,ti	263,570
#196	'peripheral vasculography' OR 'rheoacroangiography':ab,ti	1
#197	'blood vessel radiography' OR vasography:ab,ti	162
#198	#194 OR #195 OR #196 OR #197	263,691
#199	'retrobulbar anesthesia'/de	787
#200	'retrobulbar anesthesia' OR 'retrobulbar anaesthesia':ab,ti	983
#201	'retrobulbar block' OR 'retrobulbar blockade':ab,ti	228
#202	'retroocular block' OR 'retroocular blockade':ab,ti	0
#203	'retro ocular block' OR 'retro ocular blockade':ab,ti	1
#204	#199 OR #200 OR #201 OR #202 OR #203	1,055
#205	'peribulbar anesthesia'/de	437
#206	'peribulbar anesthesia' OR 'peribulbar anaesthesia':ab,ti	638
#207	'peribulbar block' OR 'peribulbar blockade':ab,ti	173
#208	#205 OR #206 OR #207	696

No.	Query	Results
#209	'intracranial pressure monitoring'/de	530
#210	'intracranial pressure'/de	14,516
#211	'monitoring'/exp	249,249
#212	#210 AND #211	1,780
#213	'intracranial pressure monitoring' OR 'intracranial tension monitoring':ab,ti	1,170
#214	'brain pressure monitoring' OR 'intracerebral pressure monitoring':ab,ti	4
#215	'subarachnoid pressure monitoring':ab,ti	2
#216	#209 OR #212 OR #213 OR #214 OR #215	2,639
#217	'neuroradiology'/exp	58,133
#218	neuroradiology OR neuroradiological:ab,ti	87,219
#219	neuroradiography OR neuroroentgenology:ab,ti	29
#220	#217 OR #218 OR #219	87,231
#221	#94 OR #105 OR #116 OR #122 OR #125 OR #130 OR #145 OR #148 OR #162 OR #166 OR #173 OR #181 OR #185 OR #188 OR #193 OR #198 OR #204 OR #208 OR #216 OR #220	1,136,652
#222	'nonsurgical invasive therapy'/exp	201,895
#223	#221 OR #222	1,229,376
#224	'drug withdrawal'/de	62,136
#225	'treatment withdrawal'/de	,8699
#226	withdrawal OR withdrawing OR 'drug abstinence':ab,ti	139,683
#227	cessation OR ceasing OR ceased:ab,ti	69,103
#228	suspension OR suspended OR suspending:ab,ti	114,880
#229	discontinuation OR discontinued OR discontinuing:ab,ti	55,748
#230	interruption OR interrupted OR interrupting:ab,ti	38,537
#231	stopped OR stop OR stopping:ab,ti	90,052
#232	#224 OR #225 OR #226 OR #227 OR #228 OR #229 OR #230 OR #231	472,066
#233	'drug substitution'/de	11,416
#234	'substitution therapy'/de	3,343
#235	substitution OR substituting OR substituted:ab,ti	290,539
#236	replacement OR replaced OR replacing:ab,ti	346,228
#237	switch OR switched OR switching:ab,ti	65,160
#238	#233 OR #234 OR #235 OR #236 OR #237	658,466
#239	'time'/exp	410,241
#240	timing:ab,ti	62,462
#241	#239 OR #240	466,708
#242	#232 OR #238 OR #241	1,531,253

No.	Query	Results
#243	'adverse outcome'/de	2,302
#244	'outcome assessment'/de	92,748
#245	'morbidity'/exp	120,264
#246	'mortality'/exp	407,859
#247	'comorbidity'/de	68,794
#248	morbidity OR incidence OR prevalence OR occurrence:ab,ti	1,218,630
#249	mortality OR death OR survival:ab,ti	1,382,177
#250	#243 OR #244 OR #245 OR #246 OR #247 OR #248 OR #249	2,400,439
#251	'quality of life'/exp	142,716
#252	qol OR 'quality of life' OR 'quality of wellbeing':ab,ti	173,105
#253	'health related quality' OR hrqol:ab,ti	14,523
#254	qaly* OR 'quality adjusted' OR 'adjusted life':ab,ti	8,643
#255	#251 OR #252 OR #253 OR #254	174,498
#256	'blood component therapy'/exp	18,297
#257	'dose response'/exp	322,005
#258	'drug dose'/exp	206,788
#259	#257 OR #258	500,902
#260	#256 AND #259	1,952
#261	'fresh frozen plasma'/exp/dd_do	30
#262	'recombinant erythropoietin'/exp/dd_do	2,101
#263	'transfusion frequency':ab,ti	48
#264	(frequency NEXT/6 (transfusion OR transfusions)):ab,ti	374
#265	'transfusion rate' OR 'transfusion rates':ab,ti	1,030
#266	((rate OR rates) NEXT/6 transfusion):ab,ti	706
#267	'transfusion requirement' OR 'transfusion requirements':ab,ti	3,566
#268	'transfusion indication' OR 'transfusion indications':ab,ti	50
#269	(indications NEXT/6 (transfusion OR transfusions)):ab,ti	475
#270	(indication NEXT/6 (transfusion OR transfusions)):ab,ti	175
#271	'transfusion interval' OR 'transfusion intervals':ab,ti	46
#272	(need NEXT/4 (transfusion OR transfusions)):ab,ti	2,433
#273	'transfusion need' OR 'transfusion needs':ab,ti	378
#274	(dose NEXT/4 transfusion):ab,ti	68
#275	(dose NEAR/4 (transfused OR transfusions)):ab,ti	136
#276	'transfusion dose' OR 'platelet dose':ab,ti	56
#277	(dose NEXT/4 platelets):ab,ti	93
#278	dose AND transfus*:ti	1,239

No.	Query	Results
#279	#260 OR #261 OR #262 OR #263 OR #264 OR #265 OR #266 OR #267 OR #268 OR #269 OR #270 OR #271 OR #272 OR #273 OR #274 OR #275 OR #276 OR #277 OR #278	12,978
#280	'erythrocyte transfusion'/de	7,776
#281	'erythrocyte transfusion' OR 'erythrocyte transfusions':ab,ti	7,908
#282	(('red blood cell' OR rbc) NEXT/2 transfusion):ab,ti	1,289
#283	(('red blood cell' OR rbc) NEXT/2 transfusions):ab,ti	1,073
#284	('red cell' NEXT/2 (transfusion OR transfusions)):ab,ti	984
#285	'normocyte transfusion' OR 'normocyte transfusions':ab,ti	0
#286	(('red blood cell' OR rbc) NEXT/2 exchange):ab,ti	75
#287	(('red cell' OR 'red cells') NEXT/4 exchange):ab,ti	141
#288	#280 OR #281 OR #282 OR #283 OR #284 OR #285 OR #286 OR #287	9,272
#289	'hemoglobin'/de	70,016
#290	'hemoglobin determination'/de	18,099
#291	'hemoglobin blood level'/de	7,824
#292	'mean corpuscular volume'/de	3,549
#293	'blood haemoglobin' OR 'blood hemoglobin':ab,ti	1,404
#294	((haemoglobin OR hemoglobin) NEXT/2 level):ab,ti	5,438
#295	((haemoglobin OR hemoglobin) NEXT/2 levels):ab,ti	6,809
#296	'hb level' OR 'hb levels':ab,ti	1,884
#297	'haemoglobin determination' OR 'hemoglobin determination':ab,ti	219
#298	'hemoglobin assay' OR 'haemoglobin assay':ab,ti	109
#299	'hemoglobin estimation' OR 'haemoglobin estimation':ab,ti	107
#300	'hb determination' OR 'hb estimation' OR 'hb assay':ab,ti	61
#301	(hemoglobin NEXT/2 (content OR concentration)):ab,ti	6,772
#301	(haemoglobin NEXT/2 (content OR concentration)):ab,ti	2,951
#303	'hb content' OR 'hb concentration':ab,ti	1,260
#304	hemoglobinometry OR haemoglobinometry:ab,ti	183
#305	'plasma haemoglobin' OR 'plasma hemoglobin':ab,ti	683
#306	'serum haemoglobin' OR 'serum hemoglobin':ab,ti	408
#307	'mean corpuscular volume' OR mcv OR mch OR mchc:ab,ti	12,374
#308	'mean corpuscular haemoglobin' OR 'mean corpuscular hemoglobin':ab,ti	1,132
#309	('mean cell' NEXT/2 (haemoglobin OR hemoglobin)):ab,ti	318
#310	'erythrocyte indices' OR 'erythrocyte index' OR 'erythrocyte indexes':ab,ti	200
#311	(red NEXT/2 ('cell indices' OR 'cell index' OR 'cell indexes')):ab,ti	520
#312	'rbc indices' OR 'rbc index' OR 'rbc indexes':ab,ti	97

No.	Query	Results
#313	#289 OR #290 OR #291 OR #292 OR #293 OR #294 OR #295 OR #296 OR #297 OR #298 OR #299 OR #300 OR #301 OR #302 OR #303 OR #304 OR #305 OR #306 OR #307 OR #308 OR #309 OR #310 OR #311 OR #312	10,4087
#314	'reoperation'/de	34,845
#315	'bleeding'/de	100,628
#316	'postoperative hemorrhage'/de	10,306
#317	#315 OR #316	109,974
#318	#314 AND #317	2,333
#319	reoperation* AND (bleeding:ab,ti OR 'blood loss':ab,ti)	3,352
#320	reoperation* AND (hemorrhag*:ab,ti OR haemorrhag*:ab,ti)	1,715
#321	're operation' OR 're operations' AND bleeding:ab,ti	245
#322	're operation' OR 're operations' AND 'blood loss':ab,ti	90
#323	're operation' OR 're operations' AND hemorrhag*:ab,ti	76
#324	're operation' OR 're operations' AND haemorrhag*:ab,ti	59
#325	'repeat surgery' OR 'surgical revision':ab,ti	2,175
#326	#318 OR #319 OR #320 OR #321 OR #322 OR #323 OR #324 OR #325	7,656
#327	'disseminated intravascular clotting'/de	14,764
#328	'consumption coagulopathy' OR 'consumptive coagulopathy':ab,ti	1,310
#329	'defibrination syndrome' OR 'sanarelli shwartzman syndrome':ab,ti	136
#330	'disseminated fibrin thromboembolism':ab,ti	3
#331	'disseminated intravasal thromboembolism':ab,ti	0
#332	'intravasal agglutination' OR ('intravasal' NEAR/1 'clotting'):ab,ti	5
#333	(intravascular NEXT/2 (clotting OR coagulation)):ab,ti	10,458
#334	intravascular NEXT/2 coagulopathy OR (intravenous NEXT/2 coagulation):ab,ti	711
#335	#327 OR #328 OR #329 OR #330 OR #331 OR #332 OR #333 OR #334	18,843
#336	'health economics'/de	29,439
#337	'economic aspect'/de	92,743
#338	'economics'/de	176,777
#339	'finance'/de	8,178
#340	'biomedical technology assessment'/de	10,169
#341	'economic evaluation'/exp	151,167
#342	'health care cost'/exp	145,240
#343	economic* OR pharmacoeconomic*:ab,ti	917,803
#344	cost* OR price* OR pricing:ab,ti	554,298
#345	'burden of illness' OR (value NEXT/2 money):ab,ti	1,626
#346	resource* AND utili*:ab,ti	20,939

No.	Query	Results
#347	'technology assessment' OR 'technology assessments':ab,ti	16,423
#348	'technology appraisal' OR 'technology appraisals':ab,ti	108
#349	#336 OR #337 OR #338 OR #339 OR #340 OR #341 OR #342 OR #343 OR #344 OR #345 OR #346 OR #347 OR #348	1,157,611
#350	'hospitalization'/de	122,438
#351	'child hospitalization'/de	6,981
#352	'length of stay'/de	42,303
#353	hospitaliz* OR hospitalis*:ab,ti	213,768
#354	length NEXT/4 stay OR 'hospital stay':ab,ti	73,357
#355	#350 OR #351 OR #352 OR #353 OR #354	257,371
#356	'intensive care unit'/de	44,849
#357	'intensive care unit' OR icu OR 'intensive care units':ab,ti	94,937
#358	'close attention unit' OR 'close attention units':ab,ti	0
#359	'intensive care department' OR 'intensive care departments':ab,ti	920
#360	'special care unit' OR 'special care units':ab,ti	667
#361	'critical care unit' OR 'critical care units':ab,ti	2,496
#362	#356 OR #357 OR #358 OR #359 OR #360 OR #361	97,606
#363	'hospital admission'/de	68,744
#364	'hospital readmission'/de	4,786
#365	'hospital admission' OR 'hospital admittance':ab,ti	75,175
#366	'patient admission' OR readmission:ab,ti	5,550
#367	rehospitalization OR rehospitalisation:ab,ti	2,078
#668	#363 OR #364 OR #365 OR #366 OR #367	83,102
#369	#250 OR #255 OR #279 OR #288 OR #313 OR #326 OR #335 OR #349 OR #355 OR #362 OR #368	3,751,564
#370	#83 AND #223	98,120
#371	#370 AND #242	14,061
#372	#371 AND #250	4,786
#373	#371 AND #255	372
#374	#371 AND #288	132
#375	#371 AND #313	391
#377	#371 AND #326	64
#378	#371 AND #335	115
#379	#371 AND #349	968
#380	#371 AND #355	672
#381	#371 AND #362	293

No.	Query	Results
#382	#371 AND #368	561
#383	#371 AND #279	176
#384	#372 OR #373 OR #374 OR #375 OR #377 OR #378 OR #379 OR #380 OR #381 OR #382 OR #383	6,447

Cochrane Library Database: search conducted 18 June 2009

No.	Query	Results
#1	MeSH descriptor Preoperative Care explode all trees	4,098
#2	MeSH descriptor Perioperative Care explode all trees	4,254
#3	MeSH descriptor Perioperative Nursing, this term only	51
#4	MeSH descriptor Operating Room Nursing, this term only	20
#5	(preoperative OR "pre operative")	11,093
#6	(perioperative OR "peri operative")	5,196
#7	(#1 OR #2 OR #3 OR #4 OR #5 OR #6)	19,076
#8	MeSH descriptor Hemostatics explode all trees	2,918
#9	"hemostatic agent" OR "hemostatic agents"	78
#10	"hemostasis agent" OR "hemostasis agents"	0
#11	(hemostatics OR Antihemorrhagics OR Antihaemorrhagics)	493
#12	"Anti hemorrhagics" OR "Anti haemorrhagics"	0
#13	(#8 OR #9 OR #10 OR #11 OR #12)	2,970
#14	(#7 AND #13)	382
#15	MeSH descriptor Anticoagulants, this term only	2,593
#16	MeSH descriptor Platelet Aggregation Inhibitors, this term only	1,906
#17	MeSH descriptor Aspirin, this term only	3,659
#18	MeSH descriptor Ticlopidine, this term only with qualifier: AA	375
#19	MeSH descriptor Warfarin, this term only	862
#20	(anticoagulant* OR "anti coagulant" OR "anti coagulants")	4,129
#21	"anticoagulating agent" OR "anticoagulating agents"	1
#22	"anti coagulating agent" OR "anti coagulating agents"	0
#23	"anticoagulation agent" OR "anticoagulation agents"	5
#24	"anti coagulation agent" OR "anti coagulation agents"	0
#25	"anticoagulation therapy" OR "anti coagulation therapy"	188
#26	"anticoagulative agent" OR "anticoagulative agents"	1
#27	"anti coagulative agent" OR "anti coagulative agents"	0
#28	(antithrombotic* OR "anti thrombotic" OR "anti thrombotics")	1,106

No.	Query	Results
#29	"hirudin therapy" OR clopidogrel OR aspirin	7,015
#30	(antithrombocytic* OR "anti thrombocytic" OR "anti thrombocytics")	100
#31	"antiplatelet therapy" OR "anti platelet therapy"	443
#32	"antiplatelet agent" OR "antiplatelet agents"	330
#33	"anti platelet agent" OR "anti platelet agents"	29
#34	"antiplatelet drug" OR "antiplatelet drugs"	211
#35	"anti platelet drug" OR "anti platelet drugs"	21
#36	(platelet NEAR/1 inhibitor*)	172
#37	"thrombocyte aggregation inhibiting agent"	0
#38	"thrombocyte aggregation inhibiting agents"	0
#39	"thrombocyte aggregation inhibitor" OR "thrombocyte aggregation inhibitors"	14
#40	"Platelet Antagonist" OR "Platelet Antagonists"	7
#41	"Platelet Antiaggregant" OR "Platelet Antiaggregants"	33
#42	(#15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41)	12,150
#43	(#7 AND #42)	544
#44	MeSH descriptor Anti-Inflammatory Agents, Non-Steroidal explode all trees	11,833
#45	(NSAID*)	2,165
#46	"non steroid antiinflammatory agent" OR "nonsteroid antiinflammatory agent"	489
#47	"non steroid antiinflammatory agents" OR "nonsteroid antiinflammatory agents"	10
#48	"non steroid anti inflammatory agent" OR "nonsteroid anti inflammatory agent"	13
#49	"non steroid anti inflammatory agents" OR "nonsteroid anti inflammatory agents"	7
#50	"non steroid antiinflammatory drug" OR "nonsteroid antiinflammatory drug"	17
#51	"non steroid antiinflammatory drugs" OR "nonsteroid antiinflammatory drugs"	29
#52	"non steroid anti inflammatory drug" OR "nonsteroid anti inflammatory drug"	37
#53	"non steroid anti inflammatory drugs" OR "nonsteroid anti inflammatory drugs"	52
#54	"Non Steroid AntiRheumatic Agent" OR "NonSteroid AntiRheumatic Agent"	4
#55	"Non Steroid AntiRheumatic Agents" OR "NonSteroid AntiRheumatic Agents"	4
#56	"Non Steroid Anti Rheumatic Agent" OR "NonSteroid Anti Rheumatic Agent"	1
#57	"Non Steroid Anti Rheumatic Agents" OR "NonSteroid Anti Rheumatic Agents"	1
#58	"non steroidal antiinflammatory agent" OR "nonsteroidal antiinflammatory agent"	65
#59	"non steroidal antiinflammatory agents" OR "nonsteroidal antiinflammatory agents"	55
#60	"non steroidal anti inflammatory agent" OR "nonsteroidal anti inflammatory agent"	130
#61	"non steroidal anti inflammatory agents" OR "nonsteroidal anti inflammatory agents"	157
#62	"non steroidal antiinflammatory drug" OR "nonsteroidal antiinflammatory drug"	323

No.	Query	Results
#63	"non steroidal antiinflammatory drugs" OR "nonsteroidal antiinflammatory drug"	358
#64	"non steroidal anti inflammatory drug" OR "nonsteroidal anti inflammatory drug"	785
#65	"non steroidal anti inflammatory drugs" OR "nonsteroidal anti inflammatory drugs"	1,674
#66	"Non Steroidal AntiRheumatic Agent" OR "NonSteroidal AntiRheumatic Agent"	3
#67	"Non Steroidal AntiRheumatic Agents" OR "NonSteroidal AntiRheumatic Agents"	3
#68	"Non Steroidal Anti Rheumatic Agent" OR "NonSteroidal Anti Rheumatic Agent"	1
#69	"Non Steroidal Anti Rheumatic Agents" OR "NonSteroidal Anti Rheumatic Agents"	2
#70	"Anti-Inflammatory Analgesic" OR "Anti-Inflammatory Analgesics"	112
#71	(#44 OR #45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52 OR #53 OR #54 OR #55 OR #56 OR #57 OR #58 OR #59 OR #60 OR #61 OR #62 OR #63 OR #64 OR #65 OR #66 OR #67 OR #68 OR #69 OR #70)	13,818
#72	(#7 AND #71)	743
#73	MeSH descriptor Hydroxymethylglutaryl-CoA Reductase Inhibitors explode all trees	2,548
#74	MeSH descriptor Hydroxymethylglutaryl CoA Reductases explode all trees with qualifier: AI	0
#75	(statin* OR vastatin)	2,320
#76	"HMG CoA" NEAR/1 inhibitor*	4
#77	"hmg coenzyme a" NEAR/1 inhibitor*	0
#78	"hydroxymethylglutaryl coa" NEAR/1 inhibitor*	27
#79	"hydroxymethylglutaryl coenzyme A" NEAR/1 inhibitor*	2
#80	(#73 OR #74 OR #75 OR #76 OR #77 OR #78 OR #79)	3,790
#81	(#7 AND #80)	87
#82	MeSH descriptor Complementary Therapies explode all trees	8,680
#83	MeSH descriptor Herbal Medicine, this term only	19
#84	MeSH descriptor Plants, Medicinal, this term only	802
#85	"alternative therapies" OR "alternative therapy"	701
#86	"alternative medicine" OR "alternative medicines"	519
#87	"complementary medicine" OR "complementary medicines"	779
#88	"complementary therapy" OR "complementary therapies"	710
#89	"herbal medicine" OR "herbal medicines" OR naturopath*	670
#90	"Medicinal Herb" OR "Medicinal Herbs"	118
#91	(homeopathy OR homeotherapy)	348
#92	(#82 OR #83 OR #84 OR #85 OR #86 OR #87 OR #88 OR #89 OR #90 OR #91)	10,987
#93	(#7 AND #92)	286
#94	MeSH descriptor Vitamins explode all trees	8,534
#95	(vitamin*)	8,979
#96	(#94 OR #95)	12,567

No.	Query	Results
#97	(#7 AND #96)	177
#98	(#14 OR #43 OR #72 OR #81 OR #93 OR #97)	1,943
#99	MeSH descriptor Drug Administration Schedule, this term only	15,597
#100	(withdrawal OR withdrawing OR "drug abstinence")	16,174
#101	(cessation OR ceasing OR ceased)	6,727
#102	(suspension OR suspended OR suspending)	2,397
#103	(discontinuation OR discontinued OR discontinuing)	10,966
#104	(interruption OR interrupted OR interrupting)	2,302
#105	(stopped OR stop OR stopping)	6,786
#106	(#99 OR #100 OR #101 OR #102 OR #103 OR #104 OR #105)	52,173
#107	(#98 AND #106)	299
#108	(substitution OR substituting OR substituted)	5,432
#109	(replacement OR replaced OR replacing)	14,621
#110	(switch OR switched OR switching)	3,767
#111	(#108 OR #109 OR #110)	22,557
#112	(#98 AND #111)	272
#113	MeSH descriptor Time Factors, this term only	37,016
#114	(timing)	145,416
#115	(#113 OR #114)	145,416
#116	(#98 AND #115)	912
#117	(#107 OR #112 OR #116)	1,116
#118	MeSH descriptor Morbidity explode all trees	8,475
#119	MeSH descriptor Mortality explode all trees	7,946
#120	(morbidity OR incidence OR prevalence OR occurrence)	62,784
#121	(mortality OR death OR survival)	55,325
#122	(#118 OR #119 OR #120 OR #121)	99,307
#123	(#117 AND #122)	469
#124	MeSH descriptor Quality of Life explode all trees	9,425
#125	MeSH descriptor Quality-Adjusted Life Years explode all trees	2,062
#126	(qol OR "quality of life" OR "quality of wellbeing")	21,521
#127	"health related quality" or hrqol	2,898
#128	(qaly* or "quality adjusted" or "adjusted life")	3,802
#129	(#124 OR #125 OR #126 OR #127 OR #128)	23,436
#130	(#117 AND #129)	104
#131	MeSH descriptor Blood Component Transfusion explode all trees with qualifier: MT	99
#132	(frequency NEAR/5 transfusion*)	84

No.	Query	Results
#133	(rate* NEAR/5 transfusion*)	324
#134	"transfusion requirement" OR "transfusion requirements"	949
#135	(indication* NEAR/5 transfusion*)	45
#136	"transfusion interval" OR "transfusion intervals"	13
#137	(need NEAR/3 transfusion*) OR "transfusion needs"	623
#138	(dose NEAR/3 transfus*)	86
#139	"platelet dose" OR (dose NEAR/3 platelets)	185
#140	(dose and transfus*):ti	72
#141	(#131 OR #132 OR #133 OR #134 OR #135 OR #136 OR #137 OR #138 OR #139 OR #140)	2,061
#142	(#117 AND #141)	129
#143	MeSH descriptor Erythrocyte Transfusion, this term only	346
#144	"erythrocyte transfusion" OR "erythrocyte transfusions"	432
#145	("red blood cell" OR rbc) NEAR/1 transfusion*	142
#146	"red cell" NEAR/1 transfusion*	3
#147	"normocyte transfusion" OR "normocyte transfusions"	0
#148	("red blood cell" OR rbc) NEAR/1 exchange	2
#149	("red cell" OR "red cells") NEAR/3 exchange	3
#150	(#143 OR #144 OR #145 OR #146 OR #147 OR #148 OR #149)	515
#151	(#117 AND #150)	24
#152	MeSH descriptor Hemoglobins, this term only	1,990
#153	MeSH descriptor Hemoglobinometry, this term only	152
#154	MeSH descriptor Erythrocyte Indices, this term only	110
#155	"blood haemoglobin" OR "blood hemoglobin"	241
#156	(haemoglobin OR hemoglobin) NEAR/1 level*	1,228
#157	"hb level" OR "hb levels"	236
#158	"haemoglobin determination" OR "hemoglobin determination"	120
#159	"hemoglobin assay" OR "haemoglobin assay"	4
#160	"hemoglobin estimation" OR "haemoglobin estimation"	5
#161	"hb determination" OR "hb estimation" OR "hb assay"	2
#162	(hemoglobin NEAR/1 (content OR concentration))	904
#163	(haemoglobin NEAR/1 (content OR concentration))	904
#164	"hb content" OR "hb concentration"	110
#165	(hemoglobinometry OR haemoglobinometry)	166
#166	"plasma haemoglobin" OR "plasma hemoglobin"	65
#167	"serum haemoglobin" OR "serum hemoglobin"	47

No.	Query	Results
#168	"mean corpuscular volume" OR mcv OR mch OR mchc	350
#169	"mean corpuscular haemoglobin" OR "mean corpuscular hemoglobin"	41
#170	"Mean Cell" NEAR/1 (Haemoglobin OR Hemoglobin)	2
#171	"erythrocyte indices" OR "Erythrocyte Index" OR "Erythrocyte Indexes"	121
#172	(red NEAR/1 ("cell indices" OR "Cell Index" OR "Cell Indexes"))	14
#173	"rbc indices" OR "RBC Index" OR "RBC Indexes"	2
#174	(#152 OR #153 OR #154 OR #155 OR #156 OR #157 OR #158 OR #159 OR #160 OR #161 OR #162 OR #163 OR #164 OR #165 OR #166 OR #167 OR #168 OR #169 OR #170 OR #171 OR #172 OR #173)	4,252
#175	(#117 AND #174)	66
#176	MeSH descriptor Re-operation, this term only	1,199
#177	MeSH descriptor Hemorrhage, this term only	1,471
#178	MeSH descriptor Postoperative Hemorrhage, this term only	485
#179	(#177 OR #178)	1,950
#180	(#176 AND #179)	45
#181	(re-operation* NEAR/15 (bleeding or "blood loss"))	136
#182	(re-operation* NEAR/15 (hemorrhag* OR haemorrhag*))	69
#183	("re operation" OR "re operations") NEAR/15 bleeding	31
#184	("re operation" OR "re operations") NEAR/15 "blood loss"	15
#185	("re operation" OR "re operations") NEAR/15 hemorrhag*	2
#186	("re operation" OR "re operations") NEAR/15 haemorrhag*	9
#187	"Repeat Surgery" OR "Surgical Revision"	110
#188	(#180 OR #181 OR #182 OR #183 OR #184 OR #185 OR #186 OR #187)	343
#189	(#117 AND #188)	36
#190	MeSH descriptor Disseminated Intravascular Coagulation, this term only	75
#191	"consumption coagulopathy" OR "consumptive coagulopathy"	12
#192	"defibrination syndrome" OR "sanarelli shwartzman syndrome"	1
#193	"disseminated fibrin thromboembolism"	0
#194	"disseminated intravasal thromboembolism"	0
#195	"intravasal agglutination" OR (intravasal NEAR/1 clotting)	0
#196	(intravascular NEAR/1 (clotting OR coagulation OR coagulopathy))	237
#197	(intravenous NEAR/1 coagulation)	1
#198	(#190 OR #191 OR #192 OR #193 OR #194 OR #195 OR #196 OR #197)	246
#199	(#117 AND #198)	6
#200	MeSH descriptor Costs and Cost Analysis explode all trees	26,772
#201	MeSH descriptor Economics, this term only	65

No.	Query	Results
#202	MeSH descriptor Models, Economic explode all trees	1,853
#203	MeSH descriptor Value of Life, this term only	274
#204	MeSH descriptor Utilization Review explode all trees	420
#205	MeSH descriptor Delivery of Health Care, this term only with qualifier: UT	62
#206	(economic* or pharmacoeconomic*)	37,332
#207	(cost* or price* or pricing)	48,938
#208	(resource* near utili*)	1,537
#209	"burden of illness" or (value NEAR/1 money)	87
#210	(#200 OR #201 OR #202 OR #203 OR #204 OR #205 OR #206 OR #207 OR #208 OR #209)	53,740
#211	(#117 AND #210)	200
#212	MeSH descriptor Hospitalization explode all trees	10,690
#213	MeSH descriptor Child, Hospitalized, this term only	82
#214	(hospitaliz* OR hospitalis*)	16,298
#215	(length NEAR/3 stay) OR "hospital stay"	11,735
#216	(#212 OR #213 OR #214 OR #215)	25,607
#217	(#117 AND #216)	199
#218	MeSH descriptor Intensive Care Units explode all trees	1,978
#219	"intensive care unit" OR icu OR "intensive care units"	6,712
#220	"close attention unit" OR "close attention units"	0
#221	"intensive care department" OR "intensive care departments"	56
#222	"special care unit" OR "special care units"	63
#223	"critical care unit" OR "critical care units"	108
#224	(#218 OR #219 OR #220 OR #221 OR #222 OR #223)	7,081
#225	(#117 AND #224)	48
#226	MeSH descriptor Patient Admission, this term only	604
#227	MeSH descriptor Patient Readmission, this term only	593
#228	"hospital admission" OR "hospital admittance"	1,727
#229	"patient admission" OR readmission	2,327
#230	(rehospitalization OR rehospitalisation)	504
#231	(#226 OR #227 OR #228 OR #229 OR #230)	4,163
#232	(#117 AND #231)	33
#233	(#117 AND (#122 OR #129 OR #141 OR #150 OR #174 OR #188 OR #198 OR #210 OR #216 OR #224 OR #231))	665

Cochrane Library Database: updated search conducted 27 January 2010

No.	Query	Results
#1	MeSH descriptor Hemostatics explode all trees	3,050
#2	"hemostatic agent" OR "hemostatic agents"	86
#3	"hemostasis agent" OR "hemostasis agents"	0
#4	hemostatics OR Antihemorrhagics OR Antihaemorrhagics	520
#5	"Anti hemorrhagics" OR "Anti haemorrhagics"	0
#6	#1 OR #2 OR #3 OR #4 OR #5	2,124
#7	MeSH descriptor Anticoagulants, this term only	2,820
#8	MeSH descriptor Platelet Aggregation Inhibitors, this term only	2,128
#9	MeSH descriptor Aspirin, this term only	3,824
#10	MeSH descriptor Ticlopidine, this term only with qualifier: AA	456
#11	MeSH descriptor Warfarin, this term only	918
#12	anticoagulant* OR "anti coagulant" OR "anti coagulants"	4,393
#13	"anticoagulating agent" OR "anticoagulating agents"	1
#14	"anti coagulating agent" OR "anti coagulating agents"	0
#15	"anticoagulation agent" OR "anticoagulation agents"	5
#16	"anti coagulation agent" OR "anti coagulation agents"	0
#17	"anticoagulation therapy" OR "anti coagulation therapy"	209
#18	"anticoagulative agent" OR "anticoagulative agents"	1
#19	"anti coagulative agent" OR "anti coagulative agents"	0
#20	antithrombotic* OR "anti thrombotic" OR "anti thrombotics"	1,160
#21	"hirudin therapy" OR clopidogrel OR aspirin	7,319
#22	antithrombocytic* OR "anti thrombocytic" OR "anti thrombocytics"	104
#23	"antiplatelet therapy" OR "anti platelet therapy"	490
#24	"antiplatelet agent" OR "antiplatelet agents"	348
#25	"anti platelet agent" OR "anti platelet agents"	31
#26	"antiplatelet drug" OR "antiplatelet drugs"	227
#27	"anti platelet drug" OR "anti platelet drugs"	22
#28	platelet NEAR/1 inhibitor*	177
#29	"thrombocyte aggregation inhibiting agent"	0
#30	"thrombocyte aggregation inhibiting agents"	0
#31	"thrombocyte aggregation inhibitor" OR "thrombocyte aggregation inhibitors"	15
#32	"Platelet Antagonist" OR "Platelet Antagonists"	7
#33	"Platelet Antiaggregant" OR "Platelet Antiaggregants"	34
#34	#7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR	1,946

No.	Query	Results
	#29 OR #30 OR #31 OR #32 OR #33	
#35	MeSH descriptor Anti-Inflammatory Agents, Non-Steroidal explode all trees	12,383
#36	NSAID*	2,297
#37	"non steroid antiinflammatory agent" OR "nonsteroid antiinflammatory agent"	507
#38	"non steroid antiinflammatory agents" OR "nonsteroid antiinflammatory agents"	10
#39	"non steroid anti inflammatory agent" OR "nonsteroid anti inflammatory agent"	13
#40	"non steroid anti inflammatory agents" OR "nonsteroid anti inflammatory agents"	7
#41	"non steroid antiinflammatory drug" OR "nonsteroid antiinflammatory drug"	17
#42	"non steroid antiinflammatory drugs" OR "nonsteroid antiinflammatory drugs"	33
#43	"non steroid anti inflammatory drug" OR "nonsteroid anti inflammatory drug"	39
#44	"non steroid anti inflammatory drugs" OR "nonsteroid anti inflammatory drugs"	56
#45	"Non Steroid AntiRheumatic Agent" OR "NonSteroid AntiRheumatic Agent"	4
#46	"Non Steroid AntiRheumatic Agents" OR "NonSteroid AntiRheumatic Agents"	4
#47	"Non Steroid Anti Rheumatic Agent" OR "NonSteroid Anti Rheumatic Agent"	1
#48	"Non Steroid Anti Rheumatic Agents" OR "NonSteroid Anti Rheumatic Agents"	1
#49	"non steroidal antiinflammatory agent" OR "nonsteroidal antiinflammatory agent"	64
#50	"non steroidal antiinflammatory agents" OR "nonsteroidal antiinflammatory agents"	57
#51	"non steroidal anti inflammatory agent" OR "nonsteroidal anti inflammatory agent"	130
#52	"non steroidal anti inflammatory agents" OR "nonsteroidal anti inflammatory agents"	168
#53	"non steroidal antiinflammatory drug" OR "nonsteroidal antiinflammatory drug"	334
#54	"non steroidal antiinflammatory drugs" OR "nonsteroidal antiinflammatory drug"	372
#55	"non steroidal anti inflammatory drug" OR "nonsteroidal anti inflammatory drug"	828
#56	"non steroidal anti inflammatory drugs" OR "nonsteroidal anti inflammatory drugs"	1,800
#57	"Non Steroidal AntiRheumatic Agent" OR "NonSteroidal AntiRheumatic Agent"	3
#58	"Non Steroidal AntiRheumatic Agents" OR "NonSteroidal AntiRheumatic Agents"	3
#59	"Non Steroidal Anti Rheumatic Agent" OR "NonSteroidal Anti Rheumatic Agent"	1
#60	"Non Steroidal Anti Rheumatic Agents" OR "NonSteroidal Anti Rheumatic Agents"	2
#61	"Anti-Inflammatory Analgesic" OR "Anti-Inflammatory Analgesics"	115
#62	#35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52 OR #53 OR #54 OR #55 OR #56 OR #57 OR #58 OR #59 OR #60 OR #61	419
#63	MeSH descriptor Hydroxymethylglutaryl-CoA Reductase Inhibitors, this term only	1,738
#64	MeSH descriptor Hydroxymethylglutaryl CoA Reductases explode all trees with qualifier: AI	0
#65	statin* OR vastatin	2,603
#66	"HMG CoA" NEAR/1 inhibitor*	4
#67	"hmg coenzyme a" NEAR/1 inhibitor*	0
#68	"hydroxymethylglutaryl coa" NEAR/1 inhibitor*	32

No.	Query	Results
#69	"hydroxymethylglutaryl coenzyme A" NEAR/1 inhibitor*	3
#70	#63 OR #64 OR #65 OR #66 OR #67 OR #68 OR #69	83
#71	MeSH descriptor Complementary Therapies explode all trees	9,574
#72	MeSH descriptor Herbal Medicine, this term only	29
#73	MeSH descriptor Plants, Medicinal, this term only	828
#74	"alternative therapies" OR "alternative therapy"	733
#75	"alternative medicine" OR "alternative medicines"	582
#76	"complementary medicine" OR "complementary medicines"	866
#77	"complementary therapy" OR "complementary therapies"	775
#78	"herbal medicine" OR "herbal medicines" OR naturopath*	805
#79	"Medicinal Herb" OR "Medicinal Herbs"	128
#80	homeopathy OR homeotherapy	403
#81	#71 OR #72 OR #73 OR #74 OR #75 OR #76 OR #77 OR #78 OR #79 OR #80	67
#82	MeSH descriptor Vitamins explode all trees	9,063
#83	vitamin*	9,481
#84	#82 OR #83	39
#85	#6 OR #34 OR #62 OR #70 OR #81 OR #84	1,898
#86	MeSH descriptor Anesthesia, Spinal, this term only	1,560
#87	"spinal anesthesia" OR "spinal anaesthesia"	2,192
#88	"spinal analgesia" OR "lumbar extradural blockade"	150
#89	"lumbar anaesthesia" OR "lumbar anesthesia"	9
#90	"spinal anesthetic" OR "spinal anesthaetic"	72
#91	"spinal cord anesthesia" OR "spinal cord anaesthesia"	0
#92	"spinal block" OR "subarachnoid block" OR "intraspinal block"	306
#93	"subarachnoid anesthesia" OR "subarachnoid anaesthesia"	87
#94	"subarachnoidal anesthesia" OR "subarachnoidal anaesthesia"	3
#95	"intraspinal anesthesia" OR "intraspinal anaesthesia"	1
#96	#86 OR #87 OR #88 OR #89 OR #90 OR #91 OR #92 OR #93 OR #94 OR #95	54
#97	#85 AND #96	22
#98	MeSH descriptor Anesthesia, Epidural explode all trees	1,577
#99	"epidural anesthesia" OR "epidural anaesthesia"	2,333
#100	"epidural anesthetic" OR "epidural anaesthetic"	36
#101	"epidural analgesia" OR "epidural block" OR "epidural blockade"	2,377
#102	"caudal anesthesia" OR "caudal anaesthesia"	148
#103	"caudal block" OR "caudal blocking" OR "dural blocking"	169
#104	"extradural anesthesia" OR "extradural anaesthesia"	70

No.	Query	Results
#105	"extradural analgesia" OR "extradural block"	141
#106	"peridural anesthesia" OR "peridural anaesthesia"	61
#107	"peridural analgesia" OR "peridural block" OR "peridural blocking"	42
#108	#98 OR #99 OR #100 OR #101 OR #102 OR #103 OR #104 OR #105 OR #106 OR #107	42
#109	#85 AND #108	13
#110	MeSH descriptor Endoscopy explode all trees	10,758
#111	endoscopy OR endoscopies OR endoscopic	9,926
#112	gastroscopy OR gastrofibroscopy OR "stomach endoscopy"	988
#113	Gastroscopic OR fibergastroscopy OR fibrogastroscopy	77
#114	cardioendoscopy OR pylorobulboscopy	0
#115	colonoscopy OR coloscopy OR Colonoscopic	1,438
#116	sigmoidoscopy OR sigmoideoscopy OR Sigmoidoscopic	582
#117	proctosigmoidoscopy OR rectoromanoscopy OR rectosigmoidoscopy	29
#118	hysteroscopy OR hysteroscopies OR hysteroscopic	467
#119	Uteroscopy	1
#120	#110 OR #111 OR #112 OR #113 OR #114 OR #115 OR #116 OR #117 OR #118 OR #119	28
#121	#85 AND #120	10
#122	MeSH descriptor Biopsy explode all trees	3,407
#123	biopsy OR biopsies OR biopsied	9,853
#124	"bronchus brushing" OR "tracheobronchial smear"	0
#125	"hepatic puncture" OR "liver puncture"	1
#126	"kidney puncture" OR "renal puncture" OR "pyelocalycial puncture"	3
#127	#122 OR #123 OR #124 OR #125 OR #126	14
#128	#85 AND #127	10
#129	MeSH descriptor Catheterization, Central Venous, this term only	623
#130	("central venous" OR "central vein") NEAR/1 catheteri?ation	647
#131	#129 OR #130	11
#132	#85 AND #131	10
#133	MeSH descriptor Paracentesis explode all trees	207
#134	pericardiocentesis	16
#135	paracentesis OR pericardicentesis OR pericardiocentesis	265
#136	"pericardial aspiration" OR "pericardium puncture"	0
#137	#133 OR #134 OR #135 OR #136	11
#138	#85 AND #137	9
#139	MeSH descriptor Coronary Angiography, this term only	2,580

No.	Query	Results
#140	MeSH descriptor Angioplasty, Transluminal, Percutaneous Coronary, this term only	2,914
#141	"interventional cardiology" OR "p t c a" OR ptca	1,275
#142	|"percutaneous coronary intervention" OR "percutaneous coronary stent"	1,478
#143	coronary NEAR/1 (angioplasty OR balloon)	1,784
#144	"transluminal coronary artery dilatation"	0
#145	"coronary angiography" OR coronarography	3,323
#146	"coronary arteriogram" OR "coronary arteriography"	237
#147	cardiac NEAR/1 ablation	4
#148	#139 OR #140 OR #141 OR #142 OR #143 OR #144 OR #145 OR #146 OR #147	17
#149	#85 AND #148	4
#150	MeSH descriptor Angioplasty explode all trees	3,600
#151	angioplasty OR "Endoluminal Repair" OR "Endo luminal Repair"	4,961
#152	#150 OR #151	5
#153	#85 AND #152	3
#154	"endoluminal stent" OR "endoluminal stents" OR "endoluminal stenting"	12
#155	"endo luminal stent" OR "endo luminal stents" OR "endo luminal stenting"	0
#156	#154 OR #155	4
#157	#85 AND #156	3
#158	MeSH descriptor Spinal Puncture, this term only	216
#159	"lumbar punction" OR "thecal puncture" OR rachiocentesis	3
#160	"spinal puncture" OR "spinal tap"	272
#161	#158 OR #159 OR #160	3
#162	#85 AND #161	3
#163	thoracentesis OR thoracocentesis	49
#164	pleurocantensis OR pleuracentesis OR pleurocentesis	3
#165	"pleura aspiration" OR "pleural aspiration"	3
#166	"pleura punction" OR "pleura puncture"	0
#167	"pleural punction" OR "pleural puncture"	4
#168	#164 OR #164 OR #165 OR #166 OR #167	5
#169	#85 AND #168	2
#170	MeSH descriptor Anesthesia, Conduction explode all trees	6,156
#171	regional NEAR/1 (anesthesia OR anaesthesia)	1,613
#172	"conduction anesthesia" OR "conduction anaesthesia"	130
#173	"block anesthesia" OR "block anaesthesia"	86
#174	"region anesthesia" OR "region anaesthesia"	1
#175	"anesthesia regionalis" OR "anaesthesia regionalis"	0

No.	Query	Results
#176	(regional NEAR/1 analgesia) OR "Bier block"	136
#177	#170 OR #171 OR #172 OR #173 OR #174 OR #175 OR #176	12
#178	#85 AND #177	0
#179	"central neural blockade" OR "central neural block"	4
#180	"central nerve blockade" OR "central nerve block"	1
#181	#179 OR #180	3
#182	#85 AND #181	0
#183	MeSH descriptor Polyps explode all trees	460
#184	polypectomy	181
#185	#183 OR #184	1
#186	#85 AND #185	0
#187	MeSH descriptor Portasystemic Shunt, Transjugular Intrahepatic, this term only	87
#188	"transjugular intrahepatic" NEAR/2 (shunt OR shunts OR shunting)	97
#189	"transjugular intrahepatic" NEAR/2 (stent OR stents OR stenting)	2
#190	TIPS OR TIPSS	1,892
#191	#187 OR #188 OR #189 OR #190	1
#192	#85 AND #191	0
#193	MeSH descriptor Angiography explode all trees	4,754
#194	angiography OR angioradiology OR Arteriography	6,701
#195	"peripheral vasculography" OR"rheoacroangiography"	0
#196	"blood vessel radiography" OR vasography	2
#197	#193 OR #194 OR #195 OR #196	1
#198	#85 AND #197	0
#199	"retrobulbar anesthesia" OR "retrobulbar anaesthesia"	158
#200	"retrobulbar block" OR "retrobulbar blockade"	99
#201	"retroocular block" OR "retroocular blockade"	0
#202	"retro ocular block" OR "retro ocular blockade"	0
#203	#199 OR #200 OR #201 OR #202	12
#204	#85 AND #203	0
#205	"peribulbar anesthesia" OR "peribulbar anaesthesia"	155
#206	"peribulbar block" OR "peribulbar blockade"	89
#207	#205 OR #206	5
#208	#85 AND #207	0
#209	MeSH descriptor Intracranial Pressure, this term only	239
#210	MeSH descriptor Monitoring, Physiologic explode all trees	6,946
#211	#209 AND #210	0

No.	Query	Results
#212	"intracranial pressure monitoring" OR "intracranial tension monitoring"	25
#213	"brain pressure monitoring" OR "intracerebral pressure monitoring"	0
#214	"subarachnoid pressure monitoring"	0
#215	#211 OR #212 OR #213 OR #214	3
#216	#85 AND #215	0
#217	MeSH descriptor Neuroradiography explode all trees	652
#218	neuroradiology OR neuroradiological	386
#219	neuroradiography OR neuroroentgenology	10
#220	#217 OR #218 OR #219	3
#221	#85 AND #220	0
#222	#97 OR #109 OR #121 OR #128 OR #132 OR #138 OR #149 OR #153 OR #157 OR #162 OR #169 OR #178 OR #182 OR #186 OR #192 OR #198 OR #204 OR #208 OR #216 OR #221	42

PreMedline: search conducted 18 June 2009

No.	Query	Results
#35	Search #3 and #32	2
#34	Search #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33	137954
#33	Search "Platelet Antiaggregant"[tw] OR "Platelet Antiaggregants"[tw]	185
#32	Search "Platelet Antagonist"[tw] OR "Platelet Antagonists"[tw]	66
#31	Search "thrombocyte aggregation inhibitor"[tw] OR "thrombocyte aggregation inhibitors"[tw]	46
#30	Search "thrombocyte aggregation inhibiting agents"[tw]	0
#29	Search "thrombocyte aggregation inhibiting agent"[tw]	0
#28	Search platelet[tw] AND inhibitor*[tw]	43420
#27	Search "anti platelet drug"[tw] OR "anti platelet drugs"[tw]	191
#26	Search "antiplatelet drug"[tw] OR "antiplatelet drugs"[tw]	1397
#25	Search "anti platelet agent"[tw] OR "anti platelet agents"[tw]	274
#24	Search "antiplatelet agent"[tw] OR "antiplatelet agents"[tw]	2537
#23	Search "antiplatelet therapy"[tw] OR "anti platelet therapy"[tw]	2837
#22	Search antithrombocytic*[tw] OR "anti thrombocytic"[tw] OR "anti thrombocytics"[tw]	45
#19	Search "hirudin therapy"[tw] OR clopidogrel[tw] OR aspirin[tw]	45844
#18	Search antithrombotic*[tw] OR "anti thrombotic"[tw] OR "anti thrombotics"[tw]	9768
#17	Search "anti coagulative agent"[tw] OR "anti coagulative agents"[tw]	0
#16	Search "anticoagulative agent"[tw] OR "anticoagulative agents"[tw]	8

No.	Query	Results
#15	Search "anticoagulation therapy"[tw] OR "anti coagulation therapy"[tw]	2443
#14	Search "anti coagulation agent"[tw] OR "anti coagulation agents"[tw]	0
#13	Search "anticoagulation agent"[tw] OR "anticoagulation agents"[tw]	37
#12	Search "anti coagulating agent"[tw] OR "anti coagulating agents"[tw]	0
#11	Search "anticoagulating agent"[tw] OR "anticoagulating agents"[tw]	9
#10	Search anticoagulant*[tw] OR "anti coagulant"[tw] OR "anti coagulants"[tw]	58917
#9	Search #3 AND #8	379
#8	Search #4 OR #5 OR #6 OR #7	5344
#7	Search "Anti hemorrhagics"[tw] OR "Anti haemorrhagics"[tw]	0
#6	Search hemostatics[tw] OR Antihemorrhagics[tw] OR Antihaemorrhagics[tw]	4951
#5	Search "hemostasis agent"[tw] OR "hemostasis agents"[tw]	3
#4	Search "hemostatic agent"[tw] OR "hemostatic agents"[tw]	766
#3	Search #1 OR #2	182870
#2	Search perioperative[tw] OR "peri operative"[tw]	42999
#1	Search preoperative[tw] OR "pre operative"[tw]	149828

CINAHL: search conducted 16 June 2009

No.	Query	Results
S117	S107 or S112 or S116	178
S116	S98 and S115	77
S115	S113 or S114	45698
S114	TI timing or AB timing	5198
S113	(MH "Time+")	41727
S112	S98 and S111	48
S111	S108 or S109 or S110	16146
S110	TI (switch OR switched OR switching) or AB (switch OR switched OR switching)	2728
S109	TI (replacement OR replaced OR replacing) or AB (replacement OR replaced OR replacing)	11884
S108	TI (substitution OR substituting OR substituted) or AB (substitution OR substituting OR substituted)	1747
S107	S98 and S106	71
S106	S99 or S100 or S101 or S102 or S103 or S104 or S105	25186
S105	TI (stopped OR stop OR stopping) or AB (stopped OR stop OR stopping)	6828
S104	TI (interruption OR interrupted OR interrupting) or AB (interruption OR interrupted OR interrupting)	1699

No.	Query	Results
S103	TI (discontinuation OR discontinued OR discontinuing) or AB (discontinuation OR discontinued OR discontinuing)	3781
S102	TI (suspension OR suspended OR suspending) or AB (suspension OR suspended OR suspending)	1427
S101	TI (cessation OR ceasing OR ceased) or AB (cessation OR ceasing OR ceased)	5985
S100	TI (withdrawal OR withdrawing OR "drug abstinence") or AB (withdrawal OR withdrawing OR "drug abstinence")	4090
S99	(MH "Drug Administration Schedule")	3139
S98	S14 or S43 or S72 or S80 or S93 or S97	1227
S97	S7 and S96	86
S96	S94 or S95	16453
S95	TI vitamin* or AB vitamin*	8347
S94	(MH "Vitamins+")	13963
S93	S7 and S92	464
S92	S81 or S82 or S83 or S84 or S85 or S86 or S87 or S88 or S89 or S90 or S91	80005
S91	TI (homeopathy OR homeotherapy) or AB (homeopathy OR homeotherapy)	968
S90	TI ("Medicinal Herb" OR "Medicinal Herbs") or AB ("Medicinal Herb" OR "Medicinal Herbs")	175
S89	TI ("herbal medicine" OR "herbal medicines" OR naturopath*) or AB ("herbal medicine" OR "herbal medicines" OR naturopath*)	1177
S88	TI ("complementary therapy" OR "complementary therapies") or AB ("complementary therapy" OR "complementary therapies")	1507
S87	TI ("complementary medicine" OR "complementary medicines") or AB ("complementary medicine" OR "complementary medicines")	816
S86	TI ("alternative medicine" OR "alternative medicines") or AB ("alternative medicine" OR "alternative medicines")	2555
S85	TI ("alternative therapies" OR "alternative therapy") or AB ("alternative therapies" OR "alternative therapy")	1274
S84	(MH "Plants, Medicinal+")	17783
S83	(MH "Drugs, Chinese Herbal")	660
S82	(MH "Medicine, Herbal+")	4307
S81	(MH "Alternative Therapies+")	64606
S80	S7 and S79	69
S79	S73 or S74 or S75 or S76 or S77 or S78	5622
S78	TI "hydroxymethylglutaryl coenzyme A" N1 inhibitor* or AB "hydroxymethylglutaryl coenzyme A" N1 inhibitor*	30
S77	TI "hydroxymethylglutaryl coa" N1 inhibitor* or AB "hydroxymethylglutaryl coa" N1 inhibitor*	3
S76	TI "hmg coenzyme a" N1 inhibitor* or AB "hmg coenzyme a" N1 inhibitor*	2
S75	TI "HMG CoA" N1 inhibitor* or AB "HMG CoA" N1 inhibitor*	235

No.	Query	Results
S74	TI (statin* OR vastatin) or AB (statin* OR vastatin)	3009
S73	(MH "Statins+")	4393
S72	S7 and S71	280
S71	S44 or S45 or S46 or S47 or S48 or S49 or S50 or S51 or S52 or S53 or S54 or S55 or S56 or S57 or S58 or S59 or S60 or S61 or S62 or S63 or S64 or S65 or S66 or S67 or S68 or S69 or S70	11361
S70	TI ("Anti-Inflammatory Analgesic" OR "Anti-Inflammatory Analgesics") or AB ("Anti-Inflammatory Analgesic" OR "Anti-Inflammatory Analgesics")	21
S69	TI ("Non Steroidal Anti Rheumatic Agents" OR "NonSteroidal Anti Rheumatic Agents") or AB ("Non Steroidal Anti Rheumatic Agents" OR "NonSteroidal Anti Rheumatic Agents")	0
S68	TI ("Non Steroidal Anti Rheumatic Agent" OR "NonSteroidal Anti Rheumatic Agent") or AB ("Non Steroidal Anti Rheumatic Agent" OR "NonSteroidal Anti Rheumatic Agent")	0
S67	TI ("Non Steroidal AntiRheumatic Agents" OR "NonSteroidal AntiRheumatic Agents") or AB ("Non Steroidal AntiRheumatic Agents" OR "NonSteroidal AntiRheumatic Agents")	0
S66	TI ("Non Steroidal AntiRheumatic Agent" OR "NonSteroidal AntiRheumatic Agent") or AB ("Non Steroidal AntiRheumatic Agent" OR "NonSteroidal AntiRheumatic Agent")	0
S65	TI ("non steroidal anti inflammatory drugs" OR "nonsteroidal anti inflammatory drugs") or AB ("non steroidal anti inflammatory drugs" OR "nonsteroidal anti inflammatory drugs")	1145
S64	TI ("non steroidal anti inflammatory drug" OR "nonsteroidal anti inflammatory drug") or AB ("non steroidal anti inflammatory drug" OR "nonsteroidal anti inflammatory drug")	243
S63	TI ("non steroidal antiinflammatory drugs" OR "nonsteroidal antiinflammatory drug") or AB ("non steroidal antiinflammatory drugs" OR "nonsteroidal antiinflammatory drug")	99
S62	TI ("non steroidal antiinflammatory drug" OR "nonsteroidal antiinflammatory drug") or AB ("non steroidal antiinflammatory drug" OR "nonsteroidal antiinflammatory drug")	90
S61	TI ("non steroidal anti inflammatory agents" OR "nonsteroidal anti inflammatory agents") or AB ("non steroidal anti inflammatory agents" OR "nonsteroidal anti inflammatory agents")	71
S60	TI ("non steroidal anti inflammatory agent" OR "nonsteroidal anti inflammatory agent") or AB ("non steroidal anti inflammatory agent" OR "nonsteroidal anti inflammatory agent")	8
S59	TI ("non steroidal antiinflammatory agents" OR "nonsteroidal antiinflammatory agents") or AB ("non steroidal antiinflammatory agents" OR "nonsteroidal antiinflammatory agents")	22
S58	TI ("non steroidal antiinflammatory agent" OR "nonsteroidal antiinflammatory agent") or AB ("non steroidal antiinflammatory agent" OR "nonsteroidal antiinflammatory agent")	4
S57	TI ("Non Steroid Anti Rheumatic Agents" OR "NonSteroid Anti Rheumatic Agents") or AB ("Non Steroid Anti Rheumatic Agents" OR "NonSteroid Anti Rheumatic Agents")	0
S56	TI ("Non Steroid Anti Rheumatic Agent" OR "NonSteroid Anti Rheumatic Agent") or AB ("Non Steroid Anti Rheumatic Agent" OR "NonSteroid Anti Rheumatic Agent")	0
S55	TI ("Non Steroid AntiRheumatic Agents" OR "NonSteroid AntiRheumatic Agents") or AB ("Non Steroid AntiRheumatic Agents" OR "NonSteroid AntiRheumatic Agents")	0
S54	TI ("Non Steroid AntiRheumatic Agent" OR "NonSteroid AntiRheumatic Agent") or AB ("Non Steroid AntiRheumatic Agent" OR "NonSteroid AntiRheumatic Agent")	0
S53	TI ("non steroid anti inflammatory drugs" OR "nonsteroid anti inflammatory drugs") or AB ("non steroid anti inflammatory drugs" OR "nonsteroid anti inflammatory drugs")	12

No.	Query	Results
S52	TI ("non steroid anti inflammatory drug" OR "nonsteroid anti inflammatory drug") or AB ("non steroid anti inflammatory drug" OR "nonsteroid anti inflammatory drug")	0
S51	TI ("non steroid antiinflammatory drugs" OR "nonsteroid antiinflammatory drugs") or AB ("non steroid antiinflammatory drugs" OR "nonsteroid antiinflammatory drugs")	2
S50	TI ("non steroid antiinflammatory drug" OR "nonsteroid antiinflammatory drug") or TI ("non steroid antiinflammatory drug" OR "nonsteroid antiinflammatory drug")	0
S49	TI ("non steroid anti inflammatory agents" OR "nonsteroid anti inflammatory agents") or AB ("non steroid anti inflammatory agents" OR "nonsteroid anti inflammatory agents")	0
S48	TI ("non steroid anti inflammatory agent" OR "nonsteroid anti inflammatory agent") or AB ("non steroid anti inflammatory agent" OR "nonsteroid anti inflammatory agent")	0
S47	TI ("non steroid antiinflammatory agents" OR "nonsteroid antiinflammatory agents") or AB ("non steroid antiinflammatory agents" OR "nonsteroid antiinflammatory agents")	0
S46	TI ("non steroid antiinflammatory agent" OR "nonsteroid antiinflammatory agent") or AB ("non steroid antiinflammatory agent" OR "nonsteroid antiinflammatory agent")	1
S45	TI NSAID* or AB NSAID*	1787
S44	(MH "Antiinflammatory Agents, Non-Steroidal+")	10591
S43	S7 and S42	400
S42	S15 or S16 or S17 or S18 or S19 or S20 or S21 or S22 or S23 or S24 or S25 or S26 or S27 or S28 or S29 or S30 or S31 or S32 or S33 or S34 or S35 or S36 or S37 or S38 or S39 or S40 or S41	14274
S41	TI ("Platelet Antiaggregant" OR "Platelet Antiaggregants") or AB ("Platelet Antiaggregant" OR "Platelet Antiaggregants")	4
S40	TI ("Platelet Antagonist" OR "Platelet Antagonists") or AB ("Platelet Antagonist" OR "Platelet Antagonists")	2
S39	TI ("thrombocyte aggregation inhibitor" OR "thrombocyte aggregation inhibitors") or AB ("thrombocyte aggregation inhibitor" OR "thrombocyte aggregation inhibitors")	1
S38	TI "thrombocyte aggregation inhibiting agents" or AB "thrombocyte aggregation inhibiting agents"	0
S37	TI "thrombocyte aggregation inhibiting agent" or AB "thrombocyte aggregation inhibiting agent"	0
S36	TI platelet N1 inhibitor* or AB platelet N1 inhibitor*	79
S35	TI ("anti platelet drug" OR "anti platelet drugs") or AB ("anti platelet drug" OR "anti platelet drugs")	6
S34	TI ("antiplatelet drug" OR "antiplatelet drugs") or AB ("antiplatelet drug" OR "antiplatelet drugs")	116
S33	TI ("anti platelet agent" OR "anti platelet agents") or AB ("anti platelet agent" OR "anti platelet agents")	9
S32	TI ("antiplatelet agent" OR "antiplatelet agents") or AB ("antiplatelet agent" OR "antiplatelet agents")	282
S31	TI ("antiplatelet therapy" OR "anti platelet therapy") or AB ("antiplatelet therapy" OR "anti platelet therapy")	392

No.	Query	Results
S30	TI (antithrombocytic* OR "anti thrombocytic" OR "anti thrombocytics") or AB (antithrombocytic* OR "anti thrombocytic" OR "anti thrombocytics")	1
S29	TI ("hirudin therapy" OR clopidogrel OR aspirin) or AB ("hirudin therapy" OR clopidogrel OR aspirin)	3474
S28	TI (antithrombotic* OR "anti thrombotic" OR "anti thrombotics") or AB (antithrombotic* OR "anti thrombotic" OR "anti thrombotics")	708
S27	TI ("anti coagulative agent" OR "anti coagulative agents") or AB ("anti coagulative agent" OR "anti coagulative agents")	0
S26	TI ("anticoagulative agent" OR "anticoagulative agents") or AB ("anticoagulative agent" OR "anticoagulative agents")	0
S25	TI ("anticoagulation therapy" OR "anti coagulation therapy") or AB ("anticoagulation therapy" OR "anti coagulation therapy")	297
S24	TI ("anti coagulation agent" OR "anti coagulation agents") or AB ("anti coagulation agent" OR "anti coagulation agents")	0
S23	TI ("anticoagulation agent" OR "anticoagulation agents") or AB ("anticoagulation agent" OR "anticoagulation agents")	4
S22	TI ("anti coagulating agent" OR "anti coagulating agents") or AB ("anti coagulating agent" OR "anti coagulating agents")	0
S21	TI ("anticoagulating agent" OR "anticoagulating agents") or AB ("anticoagulating agent" OR "anticoagulating agents")	0
S20	TI (anticoagulant* OR "anti coagulant" OR "anti coagulants") or AB (anticoagulant* OR "anti coagulant" OR "anti coagulants")	1693
S19	(MH "Warfarin")	2195
S18	(MH "Clopidogrel Bisulfate")	692
S17	(MH "Aspirin")	3797
S16	(MH "Platelet Aggregation Inhibitors+")	5902
S15	(MH "Anticoagulants+")	7940
S14	S7 and S13	80
S13	S8 or S9 or S10 or S11 or S12	1231
S12	TI ("Anti hemorrhagics" OR "Anti haemorrhagics") or AB ("Anti hemorrhagics" OR "Anti haemorrhagics")	0
S11	TI (hemostatics OR Antihemorrhagics OR Antihaemorrhagics) or AB (hemostatics OR Antihemorrhagics OR Antihaemorrhagics)	1
S10	TI ("hemostasis agent" OR "hemostasis agents") or AB ("hemostasis agent" OR "hemostasis agents")	0
S9	TI ("hemostatic agent" OR "hemostatic agents") or AB ("hemostatic agent" OR "hemostatic agents")	80
S8	(MH "Hemostatics+")	1191
S7	S1 or S2 or S3 or S4 or S5 or S6	24528
S6	TI (preoperative OR "pre operative") or AB (preoperative OR "pre operative")	7246

No.	Query	Results
S5	TI (perioperative OR "peri operative") or AB (perioperative OR "peri operative")	5346
S4	(MH "Perioperative Nursing")	8853
S3	(MH "Perioperative Care")	2631
S2	(MH "Preoperative Period+")	725
S1	(MH "Preoperative Care+")	6945

* The search was conducted using EBSCOhost on 16 June 2009

CINAHL: updated search conducted 21 January 2010

No.	Query	Results
S247	S237 or S242 or S246	389 ^
S246	S228 and S245	210
S245	S243 or S244	49,383
S244	TI timing or AB timing	5,602
S243	(MH "Time+")	45,118
S242	S228 and S241	52
S241	S238 or S239 or S240	17,257
S240	TI (switch OR switched OR switching) or AB (switch OR switched OR switching)	2,937
S239	TI (replacement OR replaced OR replacing) or AB (replacement OR replaced OR replacing)	12,679
S238	TI (substitution OR substituting OR substituted) or AB (substitution OR substituting OR substituted)	1,872
S237	S228 and S236	165
S236	S229 or S230 or S231 or S232 or S233 or S234 or S235	26,902
S235	TI (stopped OR stop OR stopping) or AB (stopped OR stop OR stopping)	7,226
S234	TI (interruption OR interrupted OR interrupting) or AB (interruption OR interrupted OR interrupting)	1,816
S233	TI (discontinuation OR discontinued OR discontinuing) or AB (discontinuation OR discontinued OR discontinuing)	4,055
S232	TI (suspension OR suspended OR suspending) or AB (suspension OR suspended OR suspending)	1,513
S231	TI (cessation OR ceasing OR ceased) or AB (cessation OR ceasing OR ceased)	6,393
S230	TI (withdrawal OR withdrawing OR "drug abstinence") or AB (withdrawal OR withdrawing OR "drug abstinence")	4,348
S229	(MH "Drug Administration Schedule")	3,419
S228	S97 OR S109 OR S121 OR S128 OR S133 OR S139 OR S151 OR S155 OR S159 OR S164 OR S171 OR S182 OR S186 OR S190 OR S200 OR S206 OR S212 OR S216 OR S222 OR S227	3,189

No.	Query	Results
S227	S85 AND S226	73
S226	S223 OR S224 OR S225	1,206
S225	TI (neuroradiography OR neuroroentgenology) or AB (neuroradiography OR neuroroentgenology)	0
S224	TI (neuroradiology OR neuroradiological) or AB (neuroradiology OR neuroradiological)	150
S223	(MH "Neuroradiography+")	1,084
S222	S85 AND S221	3
S221	S217 OR S218 OR S219 OR S220	193
S220	TI "subarachnoid pressure monitoring" OR AB "subarachnoid pressure monitoring"	0
S219	TI ("brain pressure monitoring" OR "intracerebral pressure monitoring") or AB ("brain pressure monitoring" OR "intracerebral pressure monitoring")	0
S218	TI ("intracranial pressure monitoring" OR "intracranial tension monitoring") or AB ("intracranial pressure monitoring" OR "intracranial tension monitoring")	85
S217	(MH "Monitoring, Intracranial Pressure")	134
S216	S85 AND S215	0
S215	S213 OR S214	17
S214	TI ("peribulbar block" OR "peribulbar blockade") or AB ("peribulbar block" OR "peribulbar blockade")	8
S213	TI ("peribulbar anesthesia" OR "peribulbar anaesthesia") or AB ("peribulbar anesthesia" OR "peribulbar anaesthesia")	11
S212	S85 AND S211	1
S211	S207 OR S208 OR S209 OR S210	26
S210	TI ("retro ocular block" OR "retro ocular blockade") or AB ("retro ocular block" OR "retro ocular blockade")	0
S209	TI ("retroocular block" OR "retroocular blockade") or AB ("retroocular block" OR "retroocular blockade")	0
S208	TI ("retrobulbar block" OR "retrobulbar blockade") or AB ("retrobulbar block" OR "retrobulbar blockade")	19
S207	TI ("retrobulbar anesthesia" OR "retrobulbar anaesthesia") or AB ("retrobulbar anesthesia" OR "retrobulbar anaesthesia")	10
S206	S85 AND S205	786
S205	S201 OR S202 OR S203 OR S204	8,531
S204	TI ("blood vessel radiography" OR vasography) or AB ("blood vessel radiography" OR vasography)	0
S203	TI ("peripheral vasculography" OR"rheoacroangiography") or AB ("peripheral vasculography" OR"rheoacroangiography")	0
S202	TI (angiography OR angioradiology OR Arteriography) or AB (angiography OR angioradiology OR Arteriography)	3,337
S201	(MH "Angiography+")	7,207

No.	Query	Results
S200	S85 AND S199	313
S199	S191 OR S192 OR S193 OR S194 OR S195 OR S196 OR S197 OR S198	7,327
S198	TI (TIPS OR TIPSS) or AB (TIPS OR TIPSS)	7,247
S197	TI "transjugular intrahepatic" N2 stenting OR AB "transjugular intrahepatic" N2 stenting	0
S196	TI "transjugular intrahepatic" N2 stents OR AB "transjugular intrahepatic" N2 stents	1
S195	TI "transjugular intrahepatic" N2 stent OR AB "transjugular intrahepatic" N2 stent	11
S194	TI "transjugular intrahepatic" N2 shunting OR AB "transjugular intrahepatic" N2 shunting	5
S193	TI "transjugular intrahepatic" N2 shunts OR AB "transjugular intrahepatic" N2 shunts	11
S192	TI "transjugular intrahepatic" N2 shunt OR AB "transjugular intrahepatic" N2 shunt	55
S191	(MH "Portasystemic Shunt, Surgical")	86
S190	S85 AND S189	21
S189	S187 OR S188	352
S188	TI polypectomy OR AB polypectomy	118
S187	(MH "Polyps+/SU")	288
S186	S85 AND S185	0
S185	S183 OR S184	2
S184	TI ("central nerve blockade" OR "central nerve block") OR AB ("central nerve blockade" OR "central nerve block")	1
S183	TI ("central neural blockade" OR "central neural block") or AB ("central neural blockade" OR "central neural block")	1
S182	S85 AND S181	376
S181	S172 OR S173 OR S174 OR S175 OR S176 OR S177 OR S178 OR S179 OR S180	3,870
S180	TI "Bier block" OR AB "Bier block"	11
S179	TI regional N1 analgesia OR AB regional N1 analgesia	45
S178	TI ("anesthesia regionalis" OR "anaesthesia regionalis") OR AB ("anesthesia regionalis" OR "anaesthesia regionalis")	0
S177	TI ("region anesthesia" OR "region anaesthesia") OR AB ("region anesthesia" OR "region anaesthesia")	0
S176	TI ("block anesthesia" OR "block anaesthesia") or AB ("block anesthesia" OR "block anaesthesia")	25
S175	TI ("conduction anesthesia" OR "conduction anaesthesia") OR AB ("conduction anesthesia" OR "conduction anaesthesia")	5
S174	TI regional N1 anaesthesia OR AB regional N1 anaesthesia	97
S173	TI regional N1 anesthesia OR AB regional N1 anesthesia	452
S172	(MH "Anesthesia, Conduction+")	3,702
S171	S85 AND S170	4
S170	S165 OR S166 OR S167 OR S168 OR S169	139

No.	Query	Results
S169	TI ("pleural punction" OR "pleural puncture") or AB ("pleural punction" OR "pleural puncture")	3
S168	TI ("pleura punction" OR "pleura puncture") or AB ("pleura punction" OR "pleura puncture")	0
S167	TI ("pleura aspiration" OR "pleural aspiration") or AB ("pleura aspiration" OR "pleural aspiration")	2
S166	TI (pleurocantensis OR pleuracentesis OR pleurocentesis) or AB (pleurocantensis OR pleuracentesis OR pleurocentesis)	2
S165	TI (thoracentesis OR thoracocentesis) or AB (thoracentesis OR thoracocentesis)	134
S164	S85 AND S163	32
S163	S160 OR S161 OR S162	582
S162	TI ("spinal puncture" OR "spinal tap") or AB ("spinal puncture" OR "spinal tap")	16
S161	TI ("lumbar punction" OR "thecal puncture" OR rachiocentesis) or AB ("lumbar punction" OR "thecal puncture" OR rachiocentesis)	1
S160	(MH "Spinal Puncture")	573
S159	S85 AND S158	0
S158	S156 OR S157	18
S157	TI ("endo luminal stent" OR "endo luminal stents" OR "endo luminal stenting") OR AB ("endo luminal stent" OR "endo luminal stents" OR "endo luminal stenting")	0
S156	TI ("endoluminal stent" OR "endoluminal stents" OR "endoluminal stenting") OR AB ("endoluminal stent" OR "endoluminal stents" OR "endoluminal stenting")	18
S155	S85 AND S154	1,301
S154	S152 OR S153	6,052
S153	TI (angioplasty OR "Endoluminal Repair" OR "Endo luminal Repair") or AB (angioplasty OR "Endoluminal Repair" OR "Endo luminal Repair")	2,045
S152	(MH "Angioplasty+")	5,528
S151	S85 AND S150	1,437
S150	S140 OR S141 OR S142 OR S143 OR S144 OR S145 OR S146 OR S147 OR S148 OR S149	7,767
S149	TI cardiac N1 ablation OR AB cardiac N1 ablation	43
S148	TI ("coronary arteriogram" OR "coronary arteriography") or AB ("coronary arteriogram" OR "coronary arteriography")	58
S147	TI ("coronary angiography" OR coronarography) or AB ("coronary angiography" OR coronarography)	996
S146	TI "transluminal coronary artery dilatation" or AB "transluminal coronary artery dilatation"	0
S145	TI coronary N1 balloon OR AB coronary N1 balloon	28
S144	TI coronary N1 angioplasty OR AB coronary N1 angioplasty	727
S143	TI ("percutaneous coronary intervention" OR "percutaneous coronary stent") or AB ("percutaneous coronary intervention" OR "percutaneous coronary stent")	1,578

No.	Query	Results
S142	TI ("interventional cardiology" OR "p t c a" OR ptca) or AB ("interventional cardiology" OR "p t c a" OR ptca)	419
S141	(MH "Angioplasty, Transluminal, Percutaneous Coronary")	4,117
S140	(MH "Coronary Angiography")	3,051
S139	S85 AND S138	18
S138	S134 OR S135 OR S136 OR S137	432
S137	TI ("pericardial aspiration" OR "pericardium puncture") or AB ("pericardial aspiration" OR "pericardium puncture")	0
S136	TI (paracentesis OR pericardicentesis OR pericardiocentesis) or AB (paracentesis OR pericardicentesis OR pericardiocentesis)	145
S135	TI pericardiocentesis or AB pericardiocentesis	74
S134	(MH "Paracentesis+")	348
S133	S85 AND S132	90
S132	S129 OR S130 OR S131	1,449
S131	TI "central vein" N1 catheteri?ation or AB "central vein" N1 catheteri?ation	2
S130	TI "central venous" N1 catheteri?ation or AB "central venous" N1 catheteri?ation	86
S129	(MH "Catheterization, Central Venous+")	1,423
S128	S85 AND S127	423
S127	S122 OR S123 OR S124 OR S125 OR S126	12,245
S126	TI ("kidney puncture" OR "renal puncture" OR "pyelocalycial puncture") or AB ("kidney puncture" OR "renal puncture" OR "pyelocalycial puncture")	2
S125	TI ("hepatic puncture" OR "liver puncture") or AB ("hepatic puncture" OR "liver puncture")	0
S124	TI ("bronchus brushing" OR "tracheobronchial smear") or AB ("bronchus brushing" OR "tracheobronchial smear")	0
S123	TI (biopsy OR biopsies OR biopsied) or AB (biopsy OR biopsies OR biopsied)	7,216
S122	(MH "Biopsy+")	8,091
S121	S85 AND S120	671
S120	S110 OR S111 OR S112 OR S113 OR S114 OR S115 OR S116 OR S117 OR S118 OR S119	18,299
S119	TI Uteroscopy or AB Uteroscopy	0
S118	TI (hysteroscopy OR hysteroscopies OR hysteroscopic) or AB (hysteroscopy OR hysteroscopies OR hysteroscopic)	201
S117	TI (proctosigmoidoscopy OR rectoromanoscopy OR rectosigmoidoscopy) or AB (proctosigmoidoscopy OR rectoromanoscopy OR rectosigmoidoscopy)	11
S116	TI (sigmoidoscopy OR sigmoideoscopy OR Sigmoidoscopic) or AB (sigmoidoscopy OR sigmoideoscopy OR Sigmoidoscopic)	349
S115	TI (colonoscopy OR coloscopy OR Colonoscopic) or AB (colonoscopy OR coloscopy OR Colonoscopic)	1,174

No.	Query	Results
S114	TI (cardioendoscopy OR pylorobulboscopy) or AB (cardioendoscopy OR pylorobulboscopy)	0
S113	TI (Gastroscopic OR fibergastroscopy OR fibrogastroscopy) or AB (Gastroscopic OR fibergastroscopy OR fibrogastroscopy)	9
S112	TI (gastroscopy OR gastrofibroscopy OR "stomach endoscopy") or AB (gastroscopy OR gastrofibroscopy OR "stomach endoscopy")	106
S111	TI (endoscopy OR endoscopies OR endoscopic) or AB (endoscopy OR endoscopies OR endoscopic)	6,195
S110	(MH "Endoscopy+")	15,819
S109	S85 AND S108	93
S108	S98 OR S99 OR S100 OR S101 OR S102 OR S103 OR S104 OR S105 OR S106 OR S107	1,349
S107	TI ("peridural analgesia" OR "peridural block" OR "peridural blocking") or AB ("peridural analgesia" OR "peridural block" OR "peridural blocking")	2
S106	TI ("peridural anesthesia" OR "peridural anaesthesia") or AB ("peridural anesthesia" OR "peridural anaesthesia")	4
S105	TI ("extradural analgesia" OR "extradural block") or AB ("extradural analgesia" OR "extradural block")	0
S104	TI ("extradural anesthesia" OR "extradural anaesthesia") or AB ("extradural anesthesia" OR "extradural anaesthesia")	1
S103	TI ("caudal block" OR "caudal blocking" OR "dural blocking") or AB ("caudal block" OR "caudal blocking" OR "dural blocking")	10
S102	TI ("caudal anesthesia" OR "caudal anaesthesia") or AB ("caudal anesthesia" OR "caudal anaesthesia")	6
S101	TI ("epidural analgesia" OR "epidural block" OR "epidural blockade") or AB ("epidural analgesia" OR "epidural block" OR "epidural blockade")	611
S100	TI ("epidural anesthetic" OR "epidural anaesthetic") or AB ("epidural anesthetic" OR "epidural anaesthetic")	19
S99	TI ("epidural anesthesia" OR "epidural anaesthesia") or AB ("epidural anesthesia" OR "epidural anaesthesia")	346
S98	(MH "Anesthesia, Epidural")	696
S97	S85 AND S96	36
S96	S86 OR S87 OR S88 OR S89 OR S90 OR S91 OR S92 OR S93 OR S94 OR S95	618
S95	TI ("intraspinal anesthesia" OR "intraspinal anaesthesia") or AB ("intraspinal anesthesia" OR "intraspinal anaesthesia")	0
S94	TI ("subarachnoidal anesthesia" OR "subarachnoidal anaesthesia") or AB ("subarachnoidal anesthesia" OR "subarachnoidal anaesthesia")	0
S93	TI ("subarachnoid anesthesia" OR "subarachnoid anaesthesia") or AB ("subarachnoid anesthesia" OR "subarachnoid anaesthesia")	5
S92	TI ("spinal block" OR "subarachnoid block" OR "intraspinal block") or AB ("spinal block" OR "subarachnoid block" OR "intraspinal block")	38

No.	Query	Results
S91	TI ("spinal cord anesthesia" OR "spinal cord anaesthesia") or AB ("spinal cord anesthesia" OR "spinal cord anaesthesia")	0
S90	TI ("spinal anesthetic" OR "spinal anesthaetic") or AB ("spinal anesthetic" OR "spinal anesthaetic")	18
S89	TI ("lumbar anaesthesia" OR "lumbar anesthesia") or AB ("lumbar anaesthesia" OR "lumbar anesthesia")	0
S88	TI ("spinal analgesia" OR "lumbar extradural blockade") or AB ("spinal analgesia" OR "lumbar extradural blockade")	33
S87	TI ("spinal anesthesia" OR "spinal anaesthesia") or AB ("spinal anesthesia" OR "spinal anaesthesia")	299
S86	(MH "Anesthesia, Spinal")	481
S85	S6 or S34 or S62 or S69 or S81 or S84	128,170
S84	S82 or S83	17,392
S83	TI vitamin* or AB vitamin*	8,945
S82	(MH "Vitamins+")	14,627
S81	S70 or S71 or S72 or S73 or S74 or S75 or S76 or S77 or S78 or S79 or S80	85,682
S80	TI (homeopathy OR homeotherapy) or AB (homeopathy OR homeotherapy)	1,013
S79	TI ("Medicinal Herb" OR "Medicinal Herbs") or AB ("Medicinal Herb" OR "Medicinal Herbs")	194
S78	TI ("herbal medicine" OR "herbal medicines" OR naturopath*) or AB ("herbal medicine" OR "herbal medicines" OR naturopath*)	1,252
S77	TI ("complementary therapy" OR "complementary therapies") or AB ("complementary therapy" OR "complementary therapies")	1,567
S76	TI ("complementary medicine" OR "complementary medicines") or AB ("complementary medicine" OR "complementary medicines")	851
S75	TI ("alternative medicine" OR "alternative medicines") or AB ("alternative medicine" OR "alternative medicines")	2,695
S74	TI ("alternative therapies" OR "alternative therapy") or AB ("alternative therapies" OR "alternative therapy")	1,327
S73	(MH "Plants, Medicinal+")	19,384
S72	(MH "Drugs, Chinese Herbal")	720
S71	(MH "Medicine, Herbal+")	4,602
S70	(MH "Alternative Therapies+")	68,996
S69	S63 or S64 or S65 or S66 or S67 or S68	5,947
S68	TI "hydroxymethylglutaryl coenzyme A" N1 inhibitor* or AB "hydroxymethylglutaryl coenzyme A" N1 inhibitor*	32
S67	TI "hydroxymethylglutaryl coa" N1 inhibitor* or AB "hydroxymethylglutaryl coa" N1 inhibitor*	4
S66	TI "hmg coenzyme a" N1 inhibitor* or AB "hmg coenzyme a" N1 inhibitor*	2
S65	TI "HMG CoA" N1 inhibitor* or AB "HMG CoA" N1 inhibitor*	241

No.	Query	Results
S64	TI (statin* OR vastatin) or AB (statin* OR vastatin)	3,205
S63	(MH "Statins+")	4,611
S62	S35 or S36 or S37 or S38 or S39 or S40 or S41 or S42 or S43 or S44 or S45 or S46 or S47 or S48 or S49 or S50 or S51 or S52 or S53 or S54 or S55 or S56 or S57 or S58 or S59 or S60 or S61	12,026
S61	TI ("Anti-Inflammatory Analgesic" OR "Anti-Inflammatory Analgesics") or AB ("Anti-Inflammatory Analgesic" OR "Anti-Inflammatory Analgesics")	22
S60	TI ("Non Steroidal Anti Rheumatic Agents" OR "NonSteroidal Anti Rheumatic Agents") or AB ("Non Steroidal Anti Rheumatic Agents" OR "NonSteroidal Anti Rheumatic Agents")	0
S59	TI ("Non Steroidal Anti Rheumatic Agent" OR "NonSteroidal Anti Rheumatic Agent") or AB ("Non Steroidal Anti Rheumatic Agent" OR "NonSteroidal Anti Rheumatic Agent")	0
S58	TI ("Non Steroidal AntiRheumatic Agents" OR "NonSteroidal AntiRheumatic Agents") or AB ("Non Steroidal AntiRheumatic Agents" OR "NonSteroidal AntiRheumatic Agents")	0
S57	TI ("Non Steroidal AntiRheumatic Agent" OR "NonSteroidal AntiRheumatic Agent") or AB ("Non Steroidal AntiRheumatic Agent" OR "NonSteroidal AntiRheumatic Agent")	0
S56	TI ("non steroidal anti inflammatory drugs" OR "nonsteroidal anti inflammatory drugs") or AB ("non steroidal anti inflammatory drugs" OR "nonsteroidal anti inflammatory drugs")	1,200
S55	TI ("non steroidal anti inflammatory drug" OR "nonsteroidal anti inflammatory drug") or AB ("non steroidal anti inflammatory drug" OR "nonsteroidal anti inflammatory drug")	266
S54	TI ("non steroidal antiinflammatory drugs" OR "nonsteroidal antiinflammatory drug") or AB ("non steroidal antiinflammatory drugs" OR "nonsteroidal antiinflammatory drug")	98
S53	TI ("non steroidal antiinflammatory drug" OR "nonsteroidal antiinflammatory drug") or AB ("non steroidal antiinflammatory drug" OR "nonsteroidal antiinflammatory drug")	89
S52	TI ("non steroidal anti inflammatory agents" OR "nonsteroidal anti inflammatory agents") or AB ("non steroidal anti inflammatory agents" OR "nonsteroidal anti inflammatory agents")	73
S51	TI ("non steroidal anti inflammatory agent" OR "nonsteroidal anti inflammatory agent") or AB ("non steroidal anti inflammatory agent" OR "nonsteroidal anti inflammatory agent")	8
S50	TI ("non steroidal antiinflammatory agents" OR "nonsteroidal antiinflammatory agents") or AB ("non steroidal antiinflammatory agents" OR "nonsteroidal antiinflammatory agents")	22
S49	TI ("non steroidal antiinflammatory agent" OR "nonsteroidal antiinflammatory agent") or AB ("non steroidal antiinflammatory agent" OR "nonsteroidal antiinflammatory agent")	4
S48	TI ("Non Steroid Anti Rheumatic Agents" OR "NonSteroid Anti Rheumatic Agents") or AB ("Non Steroid Anti Rheumatic Agents" OR "NonSteroid Anti Rheumatic Agents")	0
S47	TI ("Non Steroid Anti Rheumatic Agent" OR "NonSteroid Anti Rheumatic Agent") or AB ("Non Steroid Anti Rheumatic Agent" OR "NonSteroid Anti Rheumatic Agent")	0
S46	TI ("Non Steroid AntiRheumatic Agents" OR "NonSteroid AntiRheumatic Agents") or AB ("Non Steroid AntiRheumatic Agents" OR "NonSteroid AntiRheumatic Agents")	0
S45	TI ("Non Steroid AntiRheumatic Agent" OR "NonSteroid AntiRheumatic Agent") or AB ("Non Steroid AntiRheumatic Agent" OR "NonSteroid AntiRheumatic Agent")	0
S44	TI ("non steroid anti inflammatory drugs" OR "nonsteroid anti inflammatory drugs") or AB ("non steroid anti inflammatory drugs" OR "nonsteroid anti inflammatory drugs")	14

No.	Query	Results
S43	TI ("non steroid anti inflammatory drug" OR "nonsteroid anti inflammatory drug") or AB ("non steroid anti inflammatory drug" OR "nonsteroid anti inflammatory drug")	2
S42	TI ("non steroid antiinflammatory drugs" OR "nonsteroid antiinflammatory drugs") or AB ("non steroid antiinflammatory drugs" OR "nonsteroid antiinflammatory drugs")	2
S41	TI ("non steroid antiinflammatory drug" OR "nonsteroid antiinflammatory drug") or TI ("non steroid antiinflammatory drug" OR "nonsteroid antiinflammatory drug")	0
S40	TI ("non steroid anti inflammatory agents" OR "nonsteroid anti inflammatory agents") or AB ("non steroid anti inflammatory agents" OR "nonsteroid anti inflammatory agents")	0
S39	TI ("non steroid anti inflammatory agent" OR "nonsteroid anti inflammatory agent") or AB ("non steroid anti inflammatory agent" OR "nonsteroid anti inflammatory agent")	0
S38	TI ("non steroid antiinflammatory agents" OR "nonsteroid antiinflammatory agents") or AB ("non steroid antiinflammatory agents" OR "nonsteroid antiinflammatory agents")	0
S37	TI ("non steroid antiinflammatory agent" OR "nonsteroid antiinflammatory agent") or AB ("non steroid antiinflammatory agent" OR "nonsteroid antiinflammatory agent")	1
S36	TI NSAID* or AB NSAID*	1,880
S35	(MH "Antiinflammatory Agents, Non-Steroidal+")	11,208
S34	S7 or S8 or S9 or S10 or S11 or S12 or S13 or S14 or S15 or S16 or S17 or S18 or S19 or S20 or S21 or S22 or S23 or S24 or S25 or S26 or S27 or S28 or S29 or S30 or S31 or S32 or S33	15,273
S33	TI ("Platelet Antiaggregant" OR "Platelet Antiaggregants") or AB ("Platelet Antiaggregant" OR "Platelet Antiaggregants")	4
S32	TI ("Platelet Antagonist" OR "Platelet Antagonists") or AB ("Platelet Antagonist" OR "Platelet Antagonists")	2
S31	TI ("thrombocyte aggregation inhibitor" OR "thrombocyte aggregation inhibitors") or AB ("thrombocyte aggregation inhibitor" OR "thrombocyte aggregation inhibitors")	1
S30	TI "thrombocyte aggregation inhibiting agents" or AB "thrombocyte aggregation inhibiting agents"	0
S29	TI "thrombocyte aggregation inhibiting agent" or AB "thrombocyte aggregation inhibiting agent"	0
S28	TI platelet N1 inhibitor* or AB platelet N1 inhibitor*	83
S27	TI ("anti platelet drug" OR "anti platelet drugs") or AB ("anti platelet drug" OR "anti platelet drugs")	6
S26	TI ("antiplatelet drug" OR "antiplatelet drugs") or AB ("antiplatelet drug" OR "antiplatelet drugs")	125
S25	TI ("anti platelet agent" OR "anti platelet agents") or AB ("anti platelet agent" OR "anti platelet agents")	9
S24	TI ("antiplatelet agent" OR "antiplatelet agents") or AB ("antiplatelet agent" OR "antiplatelet agents")	309
S23	TI ("antiplatelet therapy" OR "anti platelet therapy") or AB ("antiplatelet therapy" OR "anti platelet therapy")	430
S22	TI (antithrombocytic* OR "anti thrombocytic" OR "anti thrombocytics") or AB (antithrombocytic* OR "anti thrombocytic" OR "anti thrombocytics")	1

No.	Query	Results
S21	TI ("hirudin therapy" OR clopidogrel OR aspirin) or AB ("hirudin therapy" OR clopidogrel OR aspirin)	3,744
S20	TI (antithrombotic* OR "anti thrombotic" OR "anti thrombotics") or AB (antithrombotic* OR "anti thrombotic" OR "anti thrombotics")	768
S19	TI ("anti coagulative agent" OR "anti coagulative agents") or AB ("anti coagulative agent" OR "anti coagulative agents")	0
S18	TI ("anticoagulative agent" OR "anticoagulative agents") or AB ("anticoagulative agent" OR "anticoagulative agents")	0
S17	TI ("anticoagulation therapy" OR "anti coagulation therapy") or AB ("anticoagulation therapy" OR "anti coagulation therapy")	316
S16	TI ("anti coagulation agent" OR "anti coagulation agents") or AB ("anti coagulation agent" OR "anti coagulation agents")	0
S15	TI ("anticoagulation agent" OR "anticoagulation agents") or AB ("anticoagulation agent" OR "anticoagulation agents")	4
S14	TI ("anti coagulating agent" OR "anti coagulating agents") or AB ("anti coagulating agent" OR "anti coagulating agents")	0
S13	TI ("anticoagulating agent" OR "anticoagulating agents") or AB ("anticoagulating agent" OR "anticoagulating agents")	0
S12	TI (anticoagulant* OR "anti coagulant" OR "anti coagulants") or AB (anticoagulant* OR "anti coagulant" OR "anti coagulants")	1,796
S11	(MH "Warfarin")	2,318
S10	(MH "Clopidogrel Bisulfate")	746
S9	(MH "Aspirin")	4,041
S8	(MH "Platelet Aggregation Inhibitors+")	6,369
S7	(MH "Anticoagulants+")	8,530
S6	S1 or S2 or S3 or S4 or S5	1,328
S5	TI ("Anti hemorrhagics" OR "Anti haemorrhagics") or AB ("Anti hemorrhagics" OR "Anti haemorrhagics")	0
S4	TI (hemostatics OR Antihemorrhagics OR Antihaemorrhagics) or AB (hemostatics OR Antihemorrhagics OR Antihaemorrhagics)	2
S3	TI ("hemostasis agent" OR "hemostasis agents") or AB ("hemostasis agent" OR "hemostasis agents")	0
S2	TI ("hemostatic agent" OR "hemostatic agents") or AB ("hemostatic agent" OR "hemostatic agents")	89
S1	(MH "Hemostatics+")	1,284

* The search was conducted using EBSCOhost on 21 January 2010

AMI: search conducted 16 June 2009

No.	Query	Results
#26	((((((TI=(timing) OR AB=(timing)) OR (MH_PHRASE="Time") OR ((MH_PHRASE="Time Factors")))) AND (((TI=(perioperative OR "peri operative") OR AB=(perioperative OR "peri operative")) OR (TI=(preoperative OR "pre operative") OR AB=(preoperative OR "pre operative")) OR ((MH_PHRASE="Perioperative Care")) OR ((MH_PHRASE="Perioperative Nursing")) OR ((MH_PHRASE="Preoperative Care")))))) OR (((((TI=(switch OR switched OR switching) OR AB=(switch OR switched OR switching)) OR (TI=(replacement OR replaced OR replacing) OR AB=(replacement OR replaced OR replacing)) OR (TI=(substitution OR substituting OR substituted) OR AB=(substitution OR substituting OR substituted)))) AND (((TI=(perioperative OR "peri operative") OR AB=(perioperative OR "peri operative")) OR (TI=(preoperative OR "pre operative") OR AB=(preoperative OR "pre operative")) OR ((MH_PHRASE="Perioperative Care")) OR ((MH_PHRASE="Perioperative Nursing")) OR ((MH_PHRASE="Preoperative Care")))))) OR (((((TI=(stopped OR stop OR stopping) OR AB=(stopped OR stop OR stopping)) OR (TI=(interruption OR interrupted OR interrupting) OR AB=(interruption OR interrupted OR interrupting)) OR (TI=(discontinuation OR discontinued OR discontinuing) OR AB=(discontinuation OR discontinued OR discontinuing)) OR (TI=(suspension OR suspended OR suspending) OR AB=(suspension OR suspended OR suspending)) OR (TI=(cessation OR ceasing OR ceased) OR AB=(cessation OR ceasing OR ceased)) OR (TI=(withdrawal OR withdrawing OR "drug abstinence") OR AB=(withdrawal OR withdrawing OR "drug abstinence")) OR ((MH_PHRASE="Drug Administration Schedule")))) AND (((TI=(perioperative OR "peri operative") OR AB=(perioperative OR "peri operative")) OR (TI=(preoperative OR "pre operative") OR AB=(preoperative OR "pre operative")) OR ((MH_PHRASE="Perioperative Care")) OR ((MH_PHRASE="Perioperative Nursing")) OR ((MH_PHRASE="Preoperative Care")))))	381
#25	((((TI=(timing) OR AB=(timing)) OR (MH_PHRASE="Time") OR ((MH_PHRASE="Time Factors")))) AND (((TI=(perioperative OR "peri operative") OR AB=(perioperative OR "peri operative")) OR (TI=(preoperative OR "pre operative") OR AB=(preoperative OR "pre operative")) OR ((MH_PHRASE="Perioperative Care")) OR ((MH_PHRASE="Perioperative Nursing")) OR ((MH_PHRASE="Preoperative Care")))))	326
#24	((TI=(timing) OR AB=(timing)) OR (MH_PHRASE="Time") OR ((MH_PHRASE="Time Factors")))	2927
#23	TI=(timing) OR AB=(timing)	378
#22	MH_PHRASE="Time"	57
#21	(MH_PHRASE="Time Factors")	2541
#20	((((TI=(switch OR switched OR switching) OR AB=(switch OR switched OR switching)) OR (TI=(replacement OR replaced OR replacing) OR AB=(replacement OR replaced OR replacing)) OR (TI=(substitution OR substituting OR substituted) OR AB=(substitution OR substituting OR substituted)))) AND (((TI=(perioperative OR "peri operative") OR AB=(perioperative OR "peri operative")) OR (TI=(preoperative OR "pre operative") OR AB=(preoperative OR "pre operative")) OR ((MH_PHRASE="Perioperative Care")) OR ((MH_PHRASE="Perioperative Nursing")) OR ((MH_PHRASE="Preoperative Care")))))	312
#19	((TI=(switch OR switched OR switching) OR AB=(switch OR switched OR switching)) OR (TI=(replacement OR replaced OR replacing) OR AB=(replacement OR replaced OR replacing)) OR (TI=(substitution OR substituting OR substituted) OR AB=(substitution OR substituting OR substituted)))	1704
#18	TI=(switch OR switched OR switching) OR AB=(switch OR switched OR switching)	221

No.	Query	Results
#17	TI=(replacement OR replaced OR replacing) OR AB=(replacement OR replaced OR replacing)	1286
#16	TI=(substitution OR substituting OR substituted) OR AB=(substitution OR substituting OR substituted)	217
#15	((((TI=(stopped OR stop OR stopping) OR AB=(stopped OR stop OR stopping)) OR (TI=(interruption OR interrupted OR interrupting) OR AB=(interruption OR interrupted OR interrupting)) OR (TI=(discontinuation OR discontinued OR discontinuing) OR AB=(discontinuation OR discontinued OR discontinuing)) OR (TI=(suspension OR suspended OR suspending) OR AB=(suspension OR suspended OR suspending)) OR (TI=(cessation OR ceasing OR ceased) OR AB=(cessation OR ceasing OR ceased)) OR (TI=(withdrawal OR withdrawing OR "drug abstinence") OR AB=(withdrawal OR withdrawing OR "drug abstinence")) OR ((MH_PHRASE="Drug Administration Schedule")))) AND (((TI=(perioperative OR "peri operative") OR AB=(perioperative OR "peri operative")) OR (TI=(preoperative OR "pre operative") OR AB=(preoperative OR "pre operative")) OR ((MH_PHRASE="Perioperative Care")) OR ((MH_PHRASE="Perioperative Nursing")) OR ((MH_PHRASE="Preoperative Care")))))	284
#14	((TI=(stopped OR stop OR stopping) OR AB=(stopped OR stop OR stopping)) OR (TI=(interruption OR interrupted OR interrupting) OR AB=(interruption OR interrupted OR interrupting)) OR (TI=(discontinuation OR discontinued OR discontinuing) OR AB=(discontinuation OR discontinued OR discontinuing)) OR (TI=(suspension OR suspended OR suspending) OR AB=(suspension OR suspended OR suspending)) OR (TI=(cessation OR ceasing OR ceased) OR AB=(cessation OR ceasing OR ceased)) OR (TI=(withdrawal OR withdrawing OR "drug abstinence") OR AB=(withdrawal OR withdrawing OR "drug abstinence")) OR ((MH_PHRASE="Drug Administration Schedule")))	2194
#13	TI=(stopped OR stop OR stopping) OR AB=(stopped OR stop OR stopping)	504
#12	TI=(interruption OR interrupted OR interrupting) OR AB=(interruption OR interrupted OR interrupting)	105
#11	TI=(discontinuation OR discontinued OR discontinuing) OR AB=(discontinuation OR discontinued OR discontinuing)	178
#10	TI=(suspension OR suspended OR suspending) OR AB=(suspension OR suspended OR suspending)	127
#9	TI=(cessation OR ceasing OR ceased) OR AB=(cessation OR ceasing OR ceased)	707
#8	TI=(withdrawal OR withdrawing OR "drug abstinence") OR AB=(withdrawal OR withdrawing OR "drug abstinence")	554
#7	(MH_PHRASE="Drug Administration Schedule")	159
#6	((TI=(perioperative OR "peri operative") OR AB=(perioperative OR "peri operative")) OR (TI=(preoperative OR "pre operative") OR AB=(preoperative OR "pre operative")) OR ((MH_PHRASE="Perioperative Care")) OR ((MH_PHRASE="Perioperative Nursing")) OR ((MH_PHRASE="Preoperative Care")))	1057
#5	TI=(perioperative OR "peri operative") OR AB=(perioperative OR "peri operative")	369
#4	TI=(preoperative OR "pre operative") OR AB=(preoperative OR "pre operative")	621
#3	(MH_PHRASE="Perioperative Care")	37
#2	(MH_PHRASE="Perioperative Nursing")	61
#1	(MH_PHRASE="Preoperative Care")	212

* The search was conducted using Informit online platform on 16 June 2009

A3 Literature searches, Question 3

In patients undergoing surgery, what is the effect of perioperative strategies that minimise blood loss on morbidity, mortality, and blood transfusion?

The body of evidence found by the systematic literature review and associated appendixes for Perioperative Foreground Question 3 are presented in a separate report.

A4 Literature searches, Question 4

In patients undergoing surgery, is anaemia an independent risk factor for adverse outcomes?

EMBASE.com: search conducted 29 April 2009

No.	Query	Results
#1	('perioperative period'/exp) OR ('perioperative nursing'/exp) OR ('perioperative complication'/exp) OR ('preoperative period'/exp) OR ('preoperative complication'/exp) OR ('intraoperative period'/exp) OR (perioperative:ab,ti OR 'peri operative':ab,ti) OR (preoperative:ab,ti OR 'pre operative':ab,ti) OR (intraoperative:ab,ti OR 'intra operative':ab,ti) OR (peroperative:ab,ti OR 'per operative':ab,ti)	332,345
#2	'postoperative period'/exp	211,165
#3	postoperative:ab,ti OR 'post operative':ab,ti	279,491
#4	#1 OR #2 OR #3	642,605
#5	(('injury'/exp) OR (injur*:ab,ti OR trauma*:ab,ti)) OR ((((('blood transfusion'/exp) OR (('bleeding'/exp) AND ('transfusion'/exp))) AND (massive:ab,ti)) OR ('massive transfusion':de) OR ('massive transfusion protocol':de) OR ('massive *3 transfusion':ab,ti OR 'massive *3 transfusions':ab,ti))	1,259,617
#6	('surgery'/exp) OR ('surgical ward'/exp) OR ('surgical patient'/exp) OR (surgical:ab,ti OR surgery:ab,ti OR operation:ab,ti OR resection:ab,ti)	2,717,431
#7	#4 OR #5 OR #6	3,555,674
#8	'anemia'/exp	145,046
#9	anemia:ab,ti OR anaemia:ab,ti	84,969
#10	#8 OR #9	170,074
#11	#7 AND #10	37,319

No.	Query	Results
#12	(('adverse outcome'/exp) OR ('outcome assessment'/exp) OR ('morbidity'/exp) OR ('mortality'/exp) OR (morbidity:ab,ti OR incidence:ab,ti OR prevalence:ab,ti OR occurrence:ab,ti) OR (mortality:ab,ti OR death:ab,ti OR survival:ab,ti)) OR (('quality of life'/exp) OR (qol:ab,ti OR 'quality of life':ab,ti OR 'quality of wellbeing':ab,ti) OR ('health related quality':ab,ti OR hrqol:ab,ti) OR (qaly*:ab,ti OR 'quality adjusted':ab,ti OR 'adjusted life':ab,ti)) OR (('blood transfusion'/exp) OR ('frequency *5 transfusion':ab,ti OR 'frequency *5 transfusions':ab,ti) OR ('transfusion frequency':ab,ti) OR ('transfusion rate':ab,ti OR 'transfusion rates':ab,ti) OR ('rate *5 transfusion':ab,ti OR 'rates *5 transfusion':ab,ti) OR ('transfusion requirement':ab,ti OR 'transfusion requirements':ab,ti) OR ('transfusion indication':ab,ti OR 'transfusion indications':ab,ti) OR ('indications *5 transfusion':ab,ti OR 'indications *5 transfusions':ab,ti) OR ('indication *5 transfusion':ab,ti OR 'indication *5 transfusions':ab,ti)) OR (('health economics'/exp) OR ('economic aspect'/exp) OR ('biomedical technology assessment'/exp) OR ('economic evaluation'/exp) OR ('health care cost'/exp) OR (economic*:ab,ti OR pharmacoeconomic*:ab,ti) OR (cost*:ab,ti OR price*:ab,ti OR pricing:ab,ti) OR ('burden of illness':ab,ti)) OR (('hospitalization'/exp) OR ('length of stay'/exp) OR (hospitaliz*:ab,ti OR hospitalis*:ab,ti) OR ('length *3 stay':ab,ti OR 'hospital stay':ab,ti)) OR (('intensive care unit'/exp) OR ('intensive care unit':ab,ti OR icu:ab,ti OR 'intensive care units':ab,ti) OR ('close attention unit':ab,ti OR 'close attention units':ab,ti) OR ('intensive care department':ab,ti OR 'intensive care departments':ab,ti) OR ('special care unit':ab,ti OR 'special care units':ab,ti) OR ('critical care unit':ab,ti OR 'critical care units':ab,ti)) OR (('hospital admission'/exp) OR ('hospital readmission'/exp) OR ('hospital admission':ab,ti OR 'hospital admittance':ab,ti) OR ('patient admission':ab,ti OR readmission:ab,ti) OR (rehospitalization:ab,ti OR rehospitalisation:ab,ti))	3,114,709
#13	#11 AND #12	17,893

Cochrane Library Database: search conducted 14 May 2009

#	Query	Results
#1	MeSH descriptor **Blood Transfusion** explode all trees	2628
#2	blood NEAR/1 transfusion*	3768
#3	"blood exchange" OR "blood infusion"	42
#4	"blood replacement" OR "blood retransfusion"	73
#5	hemotherapy OR hematherapy OR hematotherapy	55
#6	haemotherapy OR haematherapy OR haematotherapy	5
#7	multitransfusion OR polytransfusion OR retransfusion	66
#8	"transfusion blood" OR "transfusion therapy"	224
#9	"exchange transfusion" OR autotransfusion	390
#10	"replacement transfusion" OR "substitution transfusion"	1
#11	"erythrocyte transfusion" OR "leukocyte transfusion"	452

#	Query	Results
#12	"lymphocyte transfusion" OR "thrombocytic transfusion"	21
#13	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12	1946
#14	MeSH descriptor Perioperative Care explode all trees	4254
#15	MeSH descriptor Preoperative Care explode all trees	4098
#16	MeSH descriptor Postoperative Complications explode all trees	21418
#17	MeSH descriptor Postoperative Period explode all trees	3483
#18	MeSH descriptor Intraoperative Complications explode all trees	2476
#19	MeSH descriptor Intraoperative Period explode all trees	919
#20	perioperative OR "peri operative"	5196
#21	preoperative OR "pre operative"	11093
#22	intraoperative OR "intra operative"	8039
#23	peroperative OR "per operative"	474
#24	postoperative OR "post operative"	40236
#25	#14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24	1196
#26	#13 AND #25	512
#27	MeSH descriptor Wounds and Injuries explode all trees	10953
#28	injur* OR trauma*	20750
#29	#27 OR #28	474
#30	#13 AND #29	386
#31	MeSH descriptor Shock explode all trees	930
#32	shock OR "cardiovascular collapse" OR "circulatory collapse"	3179
#33	#31 OR #32	356
#34	#13 AND #33	286
#35	MeSH descriptor Blood Transfusion explode all trees	2628
#36	massive	599
#37	#35 AND #36	260

#	Query	Results
#38	massive NEAR/3 transfusion*	20
#39	"massive infusion" OR "massively transfused"	3
#40	massive NEAR/1 (bleeding OR haemorrhage OR hemorrhage)	47
#41	#37 OR #38 OR #39 OR #40	274
#42	#13 AND #41	194
#43	MeSH descriptor Thoracic Surgical Procedures explode all trees	10297
#44	MeSH descriptor Thoracic Surgery explode all trees	130
#45	MeSH descriptor Cardiovascular Surgical Procedures explode all trees	10930
#46	"cardiothoracic surgery" OR (chest NEAR/1 surgery)	675
#47	cardiothoracic NEAR/1 patient*	4
#48	"thoracic operation" OR "thoracic surgery" OR thoracoplasty	2131
#49	thoracic NEAR/1 procedure*	16
#50	#43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49	209
#51	#13 AND #50	117
#52	MeSH descriptor Surgical Procedures, Operative explode all trees	68578
#53	MeSH descriptor General Surgery explode all trees	167
#54	MeSH descriptor Surgery Department, Hospital explode all trees	68
#55	surgical OR surgery OR operation OR resection	91783
#56	#52 OR #53 OR #54 OR #55	118
#57	#13 AND #56	82
#58	MeSH descriptor Orthopedic Procedures explode all trees	5335
#59	MeSH descriptor Orthopedics explode all trees	272
#60	"orthopedic surgery" OR "orthopaedic surgery"	2339
#61	"bone surgery" OR orthopaedics or orthopedics	7975
#62	(orthopedic OR orthopaedic) NEAR/1 patient*	223
#63	"orthopedic operation" OR "orthopaedic operation"	6

#	Query	Results
#64	(orthopedic OR orthopaedic) NEAR/1 procedure*	638
#65	#58 OR #59 OR #60 OR #61 OR #62 OR #63 OR #64	98
#66	#13 AND #65	57
#67	#26 OR #30 OR #34 OR #42 OR #51 OR #57 OR #66	619
#68	MeSH descriptor Morbidity explode all trees	8475
#69	MeSH descriptor Mortality explode all trees	7946
#70	morbidity OR incidence OR prevalence OR occurrence	62784
#71	mortality OR death OR survival	55325
#72	#68 OR #69 OR #70 OR #71	61
#73	#67 AND #72	48
#74	MeSH descriptor Quality of Life explode all trees	9425
#75	MeSH descriptor Quality-Adjusted Life Years explode all trees	2062
#76	qol OR "quality of life" OR "quality of wellbeing"	21521
#77	"health related quality" or hrqol	2898
#78	qaly* or "quality adjusted" or "adjusted life"	3802
#79	#74 OR #75 OR #76 OR #77 OR #78	55
#80	#67 AND #79	39
#81	MeSH descriptor Blood Component Transfusion explode all trees	640
#82	frequency NEAR/5 transfusion*	84
#83	rate* NEAR/5 transfusion*	324
#84	"transfusion requirement" OR "transfusion requirements"	949
#85	indication* NEAR/5 transfusion*	45
#86	"transfusion interval" OR "transfusion intervals"	13
#87	(need NEAR/3 transfusion*) OR "transfusion needs"	623
#88	dose NEAR/3 transfus*	86
#89	"platelet dose" OR (dose NEAR/3 platelets)	185

#	Query	Results
#90	(dose and transfus*):ti	72
#91	#81 OR #82 OR #83 OR #84 OR #85 OR #86 OR #87 OR #88 OR #89 OR #90	54
#92	#67 AND #91	25
#93	MeSH descriptor Costs and Cost Analysis explode all trees	26772
#94	MeSH descriptor Economics explode all trees	28552
#95	MeSH descriptor Models, Economic explode all trees	1853
#96	MeSH descriptor Value of Life explode all trees	274
#97	MeSH descriptor Utilization Review explode all trees	420
#98	MeSH descriptor Delivery of Health Care explode all trees with qualifier: UT	762
#99	economic* or pharmacoeconomic*	37332
#100	cost* or price* or pricing	48938
#101	resource* near utili*	1537
#102	"burden of illness" or (value NEAR/1 money)	87
#103	#93 or #94 or #95 or #96 or #97 or #98 or #99 OR #100 or #101 OR #102	50
#104	#67 and #103	15
#105	MeSH descriptor Hospitalization explode all trees	10690
#106	MeSH descriptor Child, Hospitalized explode all trees	82
#107	hospitaliz* OR hospitalis*	16298
#108	(length NEAR/3 stay) OR "hospital stay"	11735
#109	#105 OR #106 OR #107 OR #108	19
#110	#67 AND #109	13
#111	MeSH descriptor Intensive Care Units explode all trees	1978
#112	"intensive care unit" OR icu OR "intensive care units"	6712
#113	"close attention unit" OR "close attention units"	0
#114	"intensive care department" OR "intensive care departments"	56
#115	"special care unit" OR "special care units"	63

#	Query	Results
#116	"critical care unit" OR "critical care units"	108
#117	#111 OR #112 OR #113 OR #114 OR #115 OR #116	23
#118	#67 AND #117	11
#119	MeSH descriptor Patient Admission explode all trees	604
#120	MeSH descriptor Patient Readmission explode all trees	593
#121	"hospital admission" OR "hospital admittance"	1727
#122	"patient admission" OR readmission	2327
#123	rehospitalization OR rehospitalisation	504
#124	#119 OR #120 OR #121 OR #122 OR #123	23
#125	#67 AND #124	9
#126	#73 OR #80 OR #92 OR #104 OR #110 OR #118 OR #125	56

PreMedline: search conducted 14 May 2009

No.	Query	Results
#56	Select 29 document(s)	29
#55	Search #53 AND #54	29
#54	Search anemia[tw] OR anaemia[tw]	125758
#53	Search #50 OR #51 OR #52	449
#52	Search #49 AND pubmednotmedline[sb]	62
#51	Search #49 AND in process[sb]	246
#50	Search #49 NOT (medline[SB] OR oldmedline[sb])	449
#49	Search #20 OR #22 OR #24 OR #31 OR #37 OR #39 OR #48	24198
#48	Search #13 AND #47	736
#47	Search #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46	42676
#46	Search orthopedic[tw] AND procedure*[tw]	11036
#45	Search orthopaedic[tw] AND procedure*[tw]	3340
#44	Search "orthopedic operation"[tw] OR "orthopaedic operation"[tw]	73
#43	Search orthopaedic[tw] AND patient*[tw]	8073

No.	Query	Results
#42	Search orthopedic[tw] AND patient*[tw]	15050
#41	Search "bone surgery"[tw] OR orthopaedics[tw] or orthopedics[tw]	17574
#40	Search "orthopedic surgery"[tw] OR "orthopaedic surgery"[tw]	5983
#39	Search #13 AND #38	17297
#38	Search surgical[tw] OR surgery[tw] OR operation[tw] OR resection[tw]	1871038
#37	Search #13 AND #36	775
#36	Search #32 OR #33 OR #34 OR #35	53886
#35	Search thoracic[tw] AND procedure*[tw]	19053
#34	Search "thoracic operation"[tw] OR "thoracic surgery"[tw] OR thoracoplasty[tw]	16674
#33	Search cardiothoracic[tw] AND patient*[tw]	2265
#32	Search "cardiothoracic surgery"[tw] OR (chest[tw] AND surgery[tw])	24296
#31	Search #13 AND #30	1749
#30	Search #25 OR #26 OR #27 OR #28 OR #29	11274
#29	Search massive[tw] AND haemorrhage[tw]	1180
#28	Search massive[tw] AND hemorrhage[tw]	7688
#27	Search massive[tw] AND bleeding[tw]	4937
#26	Search "massive infusion"[tw] OR "massively transfused"[tw]	100
#25	Search massive[tw] AND transfusion*[tw]	2296
#24	Search #13 AND #23	3087
#23	Search shock[tw] OR "cardiovascular collapse"[tw] OR "circulatory collapse"[tw]	134407
#22	Search #13 AND #21	4592
#21	Search injur*[tw] OR trauma*[tw]	716019
#20	Search #13 AND #19	11631
#19	Search #14 OR #15 OR #16 OR #17 OR #18	609868
#18	Search postoperative[tw] OR "post operative"[tw]	466722
#17	Search peroperative[tw] OR "per operative"[tw]	3704
#16	Search intraoperative[tw] OR "intra operative"[tw]	87796
#15	Search preoperative[tw] OR "pre operative"[tw]	148907
#14	Search perioperative[tw] OR "peri operative"[tw]	42587
#13	Search #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12	76495

No.	Query	Results
#12	Search "lymphocyte transfusion"[tw] OR "thrombocytic transfusion"	2968
#11	Search "erythrocyte transfusion"[tw] OR "leukocyte transfusion"[tw]	5436
#10	Search "replacement transfusion"[tw] OR "substitution transfusion"[tw]	46
#9	Search "exchange transfusion"[tw] OR autotransfusion[tw]	6690
#8	Search "transfusion blood"[tw] OR "transfusion therapy"[tw]	1477
#7	Search multitransfusion[tw] OR polytransfusion[tw] OR retransfusion[tw]	476
#6	Search haemotherapy[tw] OR haematherapy[tw] OR haematotherapy[tw]	67
#5	Search hemotherapy[tw] OR hematherapy[tw] OR hematotherapy[tw]	511
#4	Search "blood replacement"[tw] OR "blood retransfusion"[tw]	569
#3	Search "blood exchange"[tw] OR "blood infusion"[tw]	482
#2	Search "blood cell transfusion"[tw] OR "blood cell transfusions"[tw]	1114
#1	Search "blood transfusion"[tw] OR "blood transfusions"[tw]	64790

CINAHL: search conducted 14 May 2009

No.	Query	Results
S138	S134 and S137	109
S137	S135 or S136	7549
S136	TI (anaemia OR anemia) or AB (anaemia OR anemia)	3956
S135	(MH "Anemia+")	6210
S134	S78 or S84 or S98 or S110 or S117 or S126 or S133	1021
S133	s72 and s132	20
S132	S127 or S128 or S129 or S130 OR S131	7164
S131	TI (rehospitalization OR rehospitalisation) or AB (rehospitalization OR rehospitalisation)	437
S130	TI ("patient admission" OR readmission) or AB ("patient admission" OR readmission)	1114
S129	TI ("hospital admission" OR "hospital admittance") or AB ("hospital admission" OR "hospital admittance")	1894
S128	(MH "Patient Admission")	4242
S127	(MH "Patient Admission")	4242
S126	s72 and s125	215

No.	Query	Results
S125	S118 or S119 or S120 or S122 or S123 OR S124	32219
S124	TI ("critical care unit" OR "critical care units") or AB ("critical care unit" OR "critical care units")	856
S123	TI ("special care unit" OR "special care units") or AB ("special care unit" OR "special care units")	262
S122	TI ("intensive care department" OR "intensive care departments") or AB ("intensive care department" OR "intensive care departments")	33
S121	TI ("close attention unit" OR "close attention units") or AB ("close attention unit" OR "close attention units")	0
S120	TI ("intensive care unit" OR icu OR "intensive care units") or AB ("intensive care unit" OR icu OR "intensive care units")	13463
S119	(MH "Critical Care Nursing+")	15220
S118	(MH "Intensive Care Units+")	14257
S117	S72 AND S116	257
S116	S111 OR S112 OR S113 OR S114 OR S115	41459
S115	TI ("hospital stay") or AB ("hospital stay")	3269
S114	TI (length N3 stay) or AB (length N3 stay)	5750
S113	TI (hospitaliz* OR hospitalis*) or AB (hospitaliz* OR hospitalis*)	17920
S112	(MH "Child, Hospitalized")	2159
S111	(MH "Hospitalization+")	20460
S110	s72 and s109	186
S109	S99 or S100 or S101 or S102 or S103 OR S104 OR S105 OR S106 OR S107 OR S108	80863
S108	TI (value N1 money) or AB (value N1 money)	212
S107	TI ("burden of illness") or AB ("burden of illness")	172
S106	TI (resource* and utili*) or AB (resource* and utili*)	3116
S105	TI (cost* or price* or pricing) or AB (cost* or price* or pricing)	45423
S104	TI (economic* or pharmacoeconomic*) or AB (economic* or pharmacoeconomic*)	16024
S103	(MH "Health Care Delivery/UT")	63
S102	(MH "Utilization Review+")	3370
S101	(MH "Economic Value of Life")	231

No.	Query	Results
S100	(MH "Economics")	2328
S99	(MH "Costs and Cost Analysis+")	32259
S98	s72 and s97	397
S97	S85 or S86 or S87 or S88 or S89 or S90 or S91 or S92 OR S93 OR S94 OR S95 OR S96	799
S96	TI (dose and transfus*)	7
S95	TI (dose N3 platelets) or AB (dose N3 platelets)	2
S94	TI ("platelet dose") or AB ("platelet dose")	3
S93	TI (dose N3 transfus*) or AB (dose N3 transfus*)	14
S92	TI ("transfusion needs") or AB ("transfusion needs")	25
S91	TI (need N3 transfusion*) or AB (need N3 transfusion*)	234
S90	TI ("transfusion interval" OR "transfusion intervals") or AB ("transfusion interval" OR "transfusion intervals")	4
S89	TI (indication* N5 transfusion*) or AB (indication* N5 transfusion*)	34
S88	TI ("transfusion requirement" OR "transfusion requirements") or AB ("transfusion requirement" OR "transfusion requirements")	254
S87	TI (rate* N5 transfusion*) or AB (rate* N5 transfusion*)	168
S86	TI (frequency N5 transfusion*) or AB (frequency N5 transfusion*)	19
S85	(MH "Blood Component Transfusion+/MT")	137
S84	s72 and s83	24
S83	S79 or S80 or S81 or S82	36753
S82	TI (qaly* or "quality adjusted" or "adjusted life") or AB (qaly* or "quality adjusted" or "adjusted life")	811
S81	TI ("health related quality" or hrqol) or AB ("health related quality" or hrqol)	3359
S80	TI (qol OR "quality of life" OR "quality of wellbeing") or AB (qol OR "quality of life" OR "quality of wellbeing")	23338
S79	(MH "Quality of Life+")	26373
S78	s72 and s77	706
S77	S73 or S74 or S75 or S76	149826
S76	TI (mortality OR death OR survival) or AB (mortality OR death OR survival)	71084

No.	Query	Results
S75	TI (morbidity OR incidence OR prevalence OR occurrence) or AB (morbidity OR incidence OR prevalence OR occurrence)	77393
S74	(MH "Mortality+")	18436
S73	(MH "Morbidity+")	27551
S72	S27 OR S33 OR S37 OR S45 OR S54 OR S59 OR S71	2455
S71	s13 and s70	274
S70	S60 or S61 or S62 or S63 or S64 or S65 or S66 OR S67 OR S68 OR S69	25842
S69	TI (orthopaedic N1 procedure*) or AB (orthopeadic N1 procedure*)	14
S68	TI (orthopedic N1 procedure*) or AB (orthopedic N1 procedure*)	115
S67	TI ("orthopedic operation" OR "orthopaedic operation") or AB ("orthopedic operation" OR "orthopaedic operation")	6
S66	TI (orthopaedic N1 patient*) or AB (orthopaedic N1 patient*)	355
S65	TI (orthopedic N1 patient*) or AB (orthopedic N1 patient*)	245
S64	TI ("bone surgery" OR orthopaedics or orthopedics) or AB ("bone surgery" OR orthopaedics or orthopedics)	911
S63	TI ("orthopedic surgery" OR "orthopaedic surgery") or AB ("orthopedic surgery" OR "orthopaedic surgery")	790
S62	(MH "Orthopedic Nursing")	1422
S61	(MH "Orthopedics")	3289
S60	(MH "Orthopedic Surgery+")	21259
S59	s13 and s58	1834
S58	S55 or S56 OR S57	170781
S57	TI (surgical OR surgery OR operation OR resection) or AB (surgical OR surgery OR operation OR resection)	69889
S56	(MH "Medical-Surgical Nursing")	2427
S55	(MH "Surgery, Operative+")	136639
S54	s13 and s53	325
S53	S46 or S47 or S48 or S49 or S50 or S51 OR S52	23228
S52	TI (thoracic N1 procedure*) or AB (thoracic N1 procedure*)	32

No.	Query	Results
S51	TI ("thoracic operation" OR "thoracic surgery" OR thoracoplasty) or AB ("thoracic operation" OR "thoracic surgery" OR thoracoplasty)	253
S50	TI (cardiothoracic N1 patient*) or AB (cardiothoracic N1 patient*)	56
S49	TI ("cardiothoracic surgery" OR (chest N1 surgery)) or AB ("cardiothoracic surgery" OR (chest N1 surgery))	166
S48	(MH "Cardiovascular Nursing+")	2655
S47	(MH "Surgery, Cardiovascular+")	16879
S46	(MH "Thoracic Surgery+")	16901
S45	s13 and s44	398
S44	S40 or S41 or S42 OR S43	5209
S43	TI (massive N1 (bleeding OR haemorrhage OR hemorrhage)) or AB (massive N1 (bleeding OR haemorrhage OR hemorrhage))	5042
S42	TI ("massive infusion" OR "massively transfused") or AB ("massive infusion" OR "massively transfused")	10
S41	TI (massive N3 transfusion*) or AB (massive N3 transfusion*)	87
S40	S37 and S38	124
S39	TI (massive) or AB (massive)	1888
S38	(MH "Blood Transfusion")	3427
S37	s13 and s36	215
S36	S34 or S35	6687
S35	TI (shock OR "cardiovascular collapse" OR "circulatory collapse") or AB (shock OR "cardiovascular collapse" OR "circulatory collapse")	5193
S34	(MH "Shock+")	3242
S33	S13 and S32	711
S32	S28 OR S29 or S30 OR S31	121361
S31	TI (injur* OR trauma*) or AB (injur* OR trauma*)	67640
S30	(MH "Trauma Nursing")	526
S29	(MH "Trauma+")	5857
S28	(MH "Wounds and Injuries+")	90837
S27	S13 AND S26	939

No.	Query	Results
S26	S14 OR S15 or S16 or S17 or S18 or S19 or S20 or S21 or S22 or S23 or S24 or S25	54117
S25	TI (postoperative OR "post operative") or AB (postoperative OR "post operative")	14379
S24	TI (peroperative OR "per operative") or AB (peroperative OR "per operative")	51
S23	TI (intraoperative OR "intra operative") or AB (intraoperative OR "intra operative")	2954
S22	TI (preoperative OR "pre operative") or AB (preoperative OR "pre operative")	7186
S21	TI (perioperative OR "peri operative") or AB (perioperative OR "peri operative")	5307
S20	(MH "Postoperative Period")	1898
S19	(MH "Postoperative Complications+")	21107
S18	(MH "Intraoperative Period")	364
S17	(MH "Intraoperative Complications+")	1795
S16	(MH "Preoperative Period+")	719
S15	(MH "Perioperative Nursing")	8787
S14	(MH "Perioperative Care+")	16023
S13	S1 or S2 or S3 or S4 or S5 or S7 or S8 or S9 or S11 or S12	5828
S12	TI ("lymphocyte transfusion" OR "thrombocytic transfusion") or AB ("lymphocyte transfusion" OR "thrombocytic transfusion")	1
S11	TI ("erythrocyte transfusion" OR "leukocyte transfusion") or AB ("erythrocyte transfusion" OR "leukocyte transfusion")	11
S10	TI ("replacement transfusion" OR "substitution transfusion") or AB ("replacement transfusion" OR "substitution transfusion")	0
S9	TI ("exchange transfusion" OR autotransfusion) or AB ("exchange transfusion" OR autotransfusion)	216
S8	TI ("transfusion blood" OR "transfusion therapy") or AB ("transfusion blood" OR "transfusion therapy")	142
S7	TI (multitransfusion OR polytransfusion OR retransfusion) OR AB (multitransfusion OR polytransfusion OR retransfusion)	23
S6	TI (haemotherapy OR haematherapy OR haematotherapy) or AB (haemotherapy OR haematherapy OR haematotherapy)	0
S5	TI (hemotherapy OR hematherapy OR hematotherapy) or AB (hemotherapy OR hematherapy OR hematotherapy)	14
S4	TI ("blood replacement" OR "blood retransfusion") or AB ("blood replacement" OR "blood retransfusion")	18

No.	Query	Results
S3	TI ("blood exchange" OR "blood infusion") or AB ("blood exchange" OR "blood infusion")	16
S2	TI (blood N1 transfusion*) or AB (blood N1 transfusion*)	1886
S1	(MH "Blood Transfusion+")	5001

* The search was conducted using EBSCOhost on 14 May 2009

AMI: search conducted 26 June 2009

No.	Query	Results
#80	#39 OR #43 OR #47 OR #55 OR #64 OR #69 OR #79	251[a]
#79	((((TI=((orthopedic OR orthopaedic) %1 procedure*)) OR (TI=("orthopedic operation" OR "orthopaedic operation") OR AB=("orthopedic operation" OR "orthopaedic operation")) OR (TI=((orthopedic OR orthopaedic) %1 patient*) OR AB=((orthopedic OR orthopaedic) %1 patient*)) OR (TI=("bone surgery" OR orthopaedics or orthopedics) OR AB=("bone surgery" OR orthopaedics or orthopedics)) OR (TI=("orthopedic surgery" OR "orthopaedic surgery") OR AB=("orthopedic surgery" OR "orthopaedic surgery")) OR ((MH_PHRASE="Orthopedic Nursing")) OR (MH_PHRASE="Orthopedics") OR ((MH_PHRASE="Orthopedic Procedures")))) AND (((TI=(anaemia OR anemia) OR AB=(anaemia OR anemia)) OR ((MH_PHRASE="Anemia, Hypochromic")) OR ((MH_PHRASE="Anemia, Hemolytic, Autoimmune")) OR ((MH_PHRASE="Anemia, Sickle Cell")) OR ((MH_PHRASE="Anemia, Hemolytic, Congenital Nonspherocytic")) OR ((MH_PHRASE="Anemia, Pernicious")) OR ((MH_PHRASE="Anemia, Diamond-Blackfan")) OR ((MH_PHRASE="Anemia, Dyserythropoietic, Congenital")) OR ((MH_PHRASE="Anemia, Macrocytic")) OR ((MH_PHRASE="Anemia, Refractory")) OR ((MH_PHRASE="Anemia, Megaloblastic")) OR ((MH_PHRASE="Anemia, Hypoplastic, Congenital")) OR ((MH_PHRASE="Anemia, Sideroblastic")) OR ((MH_PHRASE="Anemia, Neonatal")) OR ((MH_PHRASE="Anemia, Iron-Deficiency")) OR ((MH_PHRASE="Anemia, Myelophthisic")) OR ((MH_PHRASE="Anemia, Aplastic")) OR ((MH_PHRASE="Anemia, Hemolytic, Congenital")) OR ((MH_PHRASE="Anemia, Hemolytic")) OR (MH_PHRASE="Anemia"))))	30
#78	((TI=((orthopedic OR orthopaedic) %1 procedure*)) OR (TI=("orthopedic operation" OR "orthopaedic operation") OR AB=("orthopedic operation" OR "orthopaedic operation")) OR (TI=((orthopedic OR orthopaedic) %1 patient*) OR AB=((orthopedic OR orthopaedic) %1 patient*)) OR (TI=("bone surgery" OR orthopaedics or orthopedics) OR AB=("bone surgery" OR orthopaedics or orthopedics)) OR (TI=("orthopedic surgery" OR "orthopaedic surgery") OR AB=("orthopedic surgery" OR "orthopaedic surgery")) OR ((MH_PHRASE="Orthopedic Nursing")) OR (MH_PHRASE="Orthopedics") OR ((MH_PHRASE="Orthopedic Procedures")))	140
#77	TI=((orthopedic OR orthopaedic) %1 procedure*)	2
#76	TI=("orthopedic operation" OR "orthopaedic operation") OR AB=("orthopedic operation" OR "orthopaedic operation")	1
#75	TI=((orthopedic OR orthopaedic) %1 patient*) OR AB=((orthopedic OR orthopaedic) %1 patient*)	12
#74	TI=("bone surgery" OR orthopaedics or orthopedics) OR AB=("bone surgery" OR orthopaedics or orthopedics)	29

No.	Query	Results
#73	TI=("orthopedic surgery" OR "orthopaedic surgery") OR AB=("orthopedic surgery" OR "orthopaedic surgery")	43
#72	(MH_PHRASE="Orthopedic Nursing")	3
#71	MH_PHRASE="Orthopedics"	47
#70	(MH_PHRASE="Orthopedic Procedures")	30
#69	((((TI=(surgical OR surgery OR operation OR resection) OR AB=(surgical OR surgery OR operation OR resection)) OR (MH_PHRASE="Surgery") OR ((MH_PHRASE="Surgical Procedures, Operative")))) AND (((TI=(anaemia OR anemia) OR AB=(anaemia OR anemia)) OR ((MH_PHRASE="Anemia, Hypochromic")) OR ((MH_PHRASE="Anemia, Hemolytic, Autoimmune")) OR ((MH_PHRASE="Anemia, Sickle Cell")) OR ((MH_PHRASE="Anemia, Hemolytic, Congenital Nonspherocytic")) OR ((MH_PHRASE="Anemia, Pernicious")) OR ((MH_PHRASE="Anemia, Diamond-Blackfan")) OR ((MH_PHRASE="Anemia, Dyserythropoietic, Congenital")) OR ((MH_PHRASE="Anemia, Macrocytic")) OR ((MH_PHRASE="Anemia, Refractory")) OR ((MH_PHRASE="Anemia, Megaloblastic")) OR ((MH_PHRASE="Anemia, Hypoplastic, Congenital")) OR ((MH_PHRASE="Anemia, Sideroblastic")) OR ((MH_PHRASE="Anemia, Neonatal")) OR ((MH_PHRASE="Anemia, Iron-Deficiency")) OR ((MH_PHRASE="Anemia, Myelophthisic")) OR ((MH_PHRASE="Anemia, Aplastic")) OR ((MH_PHRASE="Anemia, Hemolytic, Congenital")) OR ((MH_PHRASE="Anemia, Hemolytic")) OR (MH_PHRASE="Anemia"))))	49
#68	((TI=(surgical OR surgery OR operation OR resection) OR AB=(surgical OR surgery OR operation OR resection)) OR (MH_PHRASE="Surgery") OR ((MH_PHRASE="Surgical Procedures, Operative")))	6962
#67	TI=(surgical OR surgery OR operation OR resection) OR AB=(surgical OR surgery OR operation OR resection)	6890
#66	MH_PHRASE="Surgery"	119
#65	(MH_PHRASE="Surgical Procedures, Operative")	63
#64	((((TI=(thoracic %1 procedure*) OR AB=(thoracic %1 procedure*)) OR (TI=("thoracic operation" OR "thoracic surgery" OR thoracoplasty) OR AB=("thoracic operation" OR "thoracic surgery" OR thoracoplasty)) OR (TI=(cardiothoracic %1 patient*) OR AB=(cardiothoracic %1 patient*)) OR (TI=("cardiothoracic surgery" OR (chest %1 surgery)) OR AB=("cardiothoracic surgery" OR (chest %1 surgery))) OR ((MH_PHRASE="Cardiovascular Surgical Procedures")) OR ((MH_PHRASE="Thoracic Surgery")) OR ((MH_PHRASE="Thoracic Surgical Procedures")))) AND (((TI=(anaemia OR anemia) OR AB=(anaemia OR anemia)) OR ((MH_PHRASE="Anemia, Hypochromic")) OR ((MH_PHRASE="Anemia, Hemolytic, Autoimmune")) OR ((MH_PHRASE="Anemia, Sickle Cell")) OR ((MH_PHRASE="Anemia, Hemolytic, Congenital Nonspherocytic")) OR ((MH_PHRASE="Anemia, Pernicious")) OR ((MH_PHRASE="Anemia, Diamond-Blackfan")) OR ((MH_PHRASE="Anemia, Dyserythropoietic, Congenital")) OR ((MH_PHRASE="Anemia, Macrocytic")) OR ((MH_PHRASE="Anemia, Refractory")) OR ((MH_PHRASE="Anemia, Megaloblastic")) OR ((MH_PHRASE="Anemia, Hypoplastic, Congenital")) OR ((MH_PHRASE="Anemia, Sideroblastic")) OR ((MH_PHRASE="Anemia, Neonatal")) OR ((MH_PHRASE="Anemia, Iron-Deficiency")) OR ((MH_PHRASE="Anemia, Myelophthisic")) OR ((MH_PHRASE="Anemia, Aplastic")) OR ((MH_PHRASE="Anemia, Hemolytic, Congenital")) OR ((MH_PHRASE="Anemia, Hemolytic")) OR (MH_PHRASE="Anemia"))))	29

No.	Query	Results
#63	((TI=(thoracic %1 procedure*) OR AB=(thoracic %1 procedure*)) OR (TI=("thoracic operation" OR "thoracic surgery" OR thoracoplasty) OR AB=("thoracic operation" OR "thoracic surgery" OR thoracoplasty)) OR (TI=(cardiothoracic %1 patient*) OR AB=(cardiothoracic %1 patient*)) OR (TI=("cardiothoracic surgery" OR (chest %1 surgery)) OR AB=("cardiothoracic surgery" OR (chest %1 surgery))) OR ((MH_PHRASE="Cardiovascular Surgical Procedures")) OR ((MH_PHRASE="Thoracic Surgery")) OR ((MH_PHRASE="Thoracic Surgical Procedures")))	86
#62	TI=(thoracic %1 procedure*) OR AB=(thoracic %1 procedure*)	2
#61	TI=("thoracic operation" OR "thoracic surgery" OR thoracoplasty) OR AB=("thoracic operation" OR "thoracic surgery" OR thoracoplasty)	27
#60	TI=(cardiothoracic %1 patient*) OR AB=(cardiothoracic %1 patient*)	2
#59	TI=("cardiothoracic surgery" OR (chest %1 surgery)) OR AB=("cardiothoracic surgery" OR (chest %1 surgery))	37
#58	(MH_PHRASE="Cardiovascular Surgical Procedures")	7
#57	(MH_PHRASE="Thoracic Surgery")	19
#56	(MH_PHRASE="Thoracic Surgical Procedures")	6
#55	((((TI=(massive %1 (bleeding OR haemorrhage OR hemorrhage)) OR AB=(massive %1 (bleeding OR haemorrhage OR hemorrhage))) OR (TI=("massive infusion" OR "massively transfused") OR AB=("massive infusion" OR "massively transfused")) OR (TI=(massive %3 transfusion*) OR AB=(massive %3 transfusion*)) OR (((TI=(massive) OR AB=(massive)) AND ((MH_PHRASE="Blood Transfusion")))))) AND (((TI=(anaemia OR anemia) OR AB=(anaemia OR anemia)) OR ((MH_PHRASE="Anemia, Hypochromic")) OR ((MH_PHRASE="Anemia, Hemolytic, Autoimmune")) OR ((MH_PHRASE="Anemia, Sickle Cell")) OR ((MH_PHRASE="Anemia, Hemolytic, Congenital Nonspherocytic")) OR ((MH_PHRASE="Anemia, Pernicious")) OR ((MH_PHRASE="Anemia, Diamond-Blackfan")) OR ((MH_PHRASE="Anemia, Dyserythropoietic, Congenital")) OR ((MH_PHRASE="Anemia, Macrocytic")) OR ((MH_PHRASE="Anemia, Refractory")) OR ((MH_PHRASE="Anemia, Megaloblastic")) OR ((MH_PHRASE="Anemia, Hypoplastic, Congenital")) OR ((MH_PHRASE="Anemia, Sideroblastic")) OR ((MH_PHRASE="Anemia, Neonatal")) OR ((MH_PHRASE="Anemia, Iron-Deficiency")) OR ((MH_PHRASE="Anemia, Myelophthisic")) OR ((MH_PHRASE="Anemia, Aplastic")) OR ((MH_PHRASE="Anemia, Hemolytic, Congenital")) OR ((MH_PHRASE="Anemia, Hemolytic")) OR (MH_PHRASE="Anemia"))))	32
#54	((TI=(massive %1 (bleeding OR haemorrhage OR hemorrhage)) OR AB=(massive %1 (bleeding OR haemorrhage OR hemorrhage))) OR (TI=("massive infusion" OR "massively transfused") OR AB=("massive infusion" OR "massively transfused")) OR (TI=(massive %3 transfusion*) OR AB=(massive %3 transfusion*)) OR (((TI=(massive) OR AB=(massive)) AND ((MH_PHRASE="Blood Transfusion")))))	21
#53	TI=(massive %1 (bleeding OR haemorrhage OR hemorrhage)) OR AB=(massive %1 (bleeding OR haemorrhage OR hemorrhage))	11
#52	TI=("massive infusion" OR "massively transfused") OR AB=("massive infusion" OR "massively transfused")	1
#51	TI=(massive %3 transfusion*) OR AB=(massive %3 transfusion*)	9
#50	((TI=(massive) OR AB=(massive)) AND ((MH_PHRASE="Blood Transfusion")))	4
#49	TI=(massive) OR AB=(massive)	237

No.	Query	Results
#48	(MH_PHRASE="Blood Transfusion")	179
#47	((((TI=(shock OR "cardiovascular collapse" OR "circulatory collapse") OR AB=(shock OR "cardiovascular collapse" OR "circulatory collapse")) OR (MH_PHRASE="Shock"))) AND (((TI=(anaemia OR anemia) OR AB=(anaemia OR anemia)) OR ((MH_PHRASE="Anemia, Hypochromic")) OR ((MH_PHRASE="Anemia, Hemolytic, Autoimmune")) OR ((MH_PHRASE="Anemia, Sickle Cell")) OR ((MH_PHRASE="Anemia, Hemolytic, Congenital Nonspherocytic")) OR ((MH_PHRASE="Anemia, Pernicious")) OR ((MH_PHRASE="Anemia, Diamond-Blackfan")) OR ((MH_PHRASE="Anemia, Dyserythropoietic, Congenital")) OR ((MH_PHRASE="Anemia, Macrocytic")) OR ((MH_PHRASE="Anemia, Refractory")) OR ((MH_PHRASE="Anemia, Megaloblastic")) OR ((MH_PHRASE="Anemia, Hypoplastic, Congenital")) OR ((MH_PHRASE="Anemia, Sideroblastic")) OR ((MH_PHRASE="Anemia, Neonatal")) OR ((MH_PHRASE="Anemia, Iron-Deficiency")) OR ((MH_PHRASE="Anemia, Myelophthisic")) OR ((MH_PHRASE="Anemia, Aplastic")) OR ((MH_PHRASE="Anemia, Hemolytic, Congenital")) OR ((MH_PHRASE="Anemia, Hemolytic")) OR (MH_PHRASE="Anemia"))))	30
#46	((TI=(shock OR "cardiovascular collapse" OR "circulatory collapse") OR AB=(shock OR "cardiovascular collapse" OR "circulatory collapse")) OR (MH_PHRASE="Shock"))	465
#45	TI=(shock OR "cardiovascular collapse" OR "circulatory collapse") OR AB=(shock OR "cardiovascular collapse" OR "circulatory collapse")	461
#44	MH_PHRASE="Shock"	6
#43	((((TI=(injur* OR trauma*) OR AB=(injur* OR trauma*)) OR ((MH_PHRASE="Wounds and Injuries")))) AND (((TI=(anaemia OR anemia) OR AB=(anaemia OR anemia)) OR ((MH_PHRASE="Anemia, Hypochromic")) OR ((MH_PHRASE="Anemia, Hemolytic, Autoimmune")) OR ((MH_PHRASE="Anemia, Sickle Cell")) OR ((MH_PHRASE="Anemia, Hemolytic, Congenital Nonspherocytic")) OR ((MH_PHRASE="Anemia, Pernicious")) OR ((MH_PHRASE="Anemia, Diamond-Blackfan")) OR ((MH_PHRASE="Anemia, Dyserythropoietic, Congenital")) OR ((MH_PHRASE="Anemia, Macrocytic")) OR ((MH_PHRASE="Anemia, Refractory")) OR ((MH_PHRASE="Anemia, Megaloblastic")) OR ((MH_PHRASE="Anemia, Hypoplastic, Congenital")) OR ((MH_PHRASE="Anemia, Sideroblastic")) OR ((MH_PHRASE="Anemia, Neonatal")) OR ((MH_PHRASE="Anemia, Iron-Deficiency")) OR ((MH_PHRASE="Anemia, Myelophthisic")) OR ((MH_PHRASE="Anemia, Aplastic")) OR ((MH_PHRASE="Anemia, Hemolytic, Congenital")) OR ((MH_PHRASE="Anemia, Hemolytic")) OR (MH_PHRASE="Anemia"))))	41
#42	((TI=(injur* OR trauma*) OR AB=(injur* OR trauma*)) OR ((MH_PHRASE="Wounds and Injuries")))	5555
#41	TI=(injur* OR trauma*) OR AB=(injur* OR trauma*)	5507
#40	(MH_PHRASE="Wounds and Injuries")	106

No.	Query	Results
#39	((((TI=(postoperative OR "post operative") OR AB=(postoperative OR "post operative")) OR (TI=(peroperative OR "per operative") OR AB=(peroperative OR "per operative")) OR (TI=(intraoperative OR "intra operative") OR AB=(intraoperative OR "intra operative")) OR (TI=(preoperative OR "pre operative") OR AB=(preoperative OR "pre operative")) OR (TI=(perioperative OR "peri operative") OR AB=(perioperative OR "peri operative")) OR ((MH_PHRASE="Intraoperative Care")) OR ((MH_PHRASE="Intraoperative Complications")) OR ((MH_PHRASE="Intraoperative Period")) OR ((MH_PHRASE="Postoperative Hemorrhage")) OR ((MH_PHRASE="Postoperative Complications")) OR ((MH_PHRASE="Postoperative Care")) OR ((MH_PHRASE="Postoperative Period")) OR ((MH_PHRASE="Preoperative Care")) OR ((MH_PHRASE="Perioperative Nursing")) OR ((MH_PHRASE="Perioperative Care")))) AND (((TI=(anaemia OR anemia) OR AB=(anaemia OR anemia)) OR ((MH_PHRASE="Anemia, Hypochromic")) OR ((MH_PHRASE="Anemia, Hemolytic, Autoimmune")) OR ((MH_PHRASE="Anemia, Sickle Cell")) OR ((MH_PHRASE="Anemia, Hemolytic, Congenital Nonspherocytic")) OR ((MH_PHRASE="Anemia, Pernicious")) OR ((MH_PHRASE="Anemia, Diamond-Blackfan")) OR ((MH_PHRASE="Anemia, Dyserythropoietic, Congenital")) OR ((MH_PHRASE="Anemia, Macrocytic")) OR ((MH_PHRASE="Anemia, Refractory")) OR ((MH_PHRASE="Anemia, Megaloblastic")) OR ((MH_PHRASE="Anemia, Hypoplastic, Congenital")) OR ((MH_PHRASE="Anemia, Sideroblastic")) OR ((MH_PHRASE="Anemia, Neonatal")) OR ((MH_PHRASE="Anemia, Iron-Deficiency")) OR ((MH_PHRASE="Anemia, Myelophthisic")) OR ((MH_PHRASE="Anemia, Aplastic")) OR ((MH_PHRASE="Anemia, Hemolytic, Congenital")) OR ((MH_PHRASE="Anemia, Hemolytic")) OR (MH_PHRASE="Anemia"))))	40
#38	((TI=(postoperative OR "post operative") OR AB=(postoperative OR "post operative")) OR (TI=(peroperative OR "per operative") OR AB=(peroperative OR "per operative")) OR (TI=(intraoperative OR "intra operative") OR AB=(intraoperative OR "intra operative")) OR (TI=(preoperative OR "pre operative") OR AB=(preoperative OR "pre operative")) OR (TI=(perioperative OR "peri operative") OR AB=(perioperative OR "peri operative")) OR ((MH_PHRASE="Intraoperative Care")) OR ((MH_PHRASE="Intraoperative Complications")) OR ((MH_PHRASE="Intraoperative Period")) OR ((MH_PHRASE="Postoperative Hemorrhage")) OR ((MH_PHRASE="Postoperative Complications")) OR ((MH_PHRASE="Postoperative Care")) OR ((MH_PHRASE="Postoperative Period")) OR ((MH_PHRASE="Preoperative Care")) OR ((MH_PHRASE="Perioperative Nursing")) OR ((MH_PHRASE="Perioperative Care")))	2443
#37	TI=(postoperative OR "post operative") OR AB=(postoperative OR "post operative")	1111
#36	TI=(peroperative OR "per operative") OR AB=(peroperative OR "per operative")	7
#35	TI=(intraoperative OR "intra operative") OR AB=(intraoperative OR "intra operative")	251
#34	TI=(preoperative OR "pre operative") OR AB=(preoperative OR "pre operative")	622
#33	TI=(perioperative OR "peri operative") OR AB=(perioperative OR "peri operative")	369
#32	(MH_PHRASE="Intraoperative Care")	74
#31	(MH_PHRASE="Intraoperative Complications")	99
#30	(MH_PHRASE="Intraoperative Period")	77
#29	(MH_PHRASE="Postoperative Hemorrhage")	5
#28	(MH_PHRASE="Postoperative Complications")	378
#27	(MH_PHRASE="Postoperative Care")	197

No.	Query	Results
#26	(MH_PHRASE="Postoperative Period")	146
#25	(MH_PHRASE="Preoperative Care")	212
#24	(MH_PHRASE="Perioperative Nursing")	61
#22	(MH_PHRASE="Perioperative Care")	37
#21	((TI=(anaemia OR anemia) OR AB=(anaemia OR anemia)) OR ((MH_PHRASE="Anemia, Hypochromic")) OR ((MH_PHRASE="Anemia, Hemolytic, Autoimmune")) OR ((MH_PHRASE="Anemia, Sickle Cell")) OR ((MH_PHRASE="Anemia, Hemolytic, Congenital Nonspherocytic")) OR ((MH_PHRASE="Anemia, Pernicious")) OR ((MH_PHRASE="Anemia, Diamond-Blackfan")) OR ((MH_PHRASE="Anemia, Dyserythropoietic, Congenital")) OR ((MH_PHRASE="Anemia, Macrocytic")) OR ((MH_PHRASE="Anemia, Refractory")) OR ((MH_PHRASE="Anemia, Megaloblastic")) OR ((MH_PHRASE="Anemia, Hypoplastic, Congenital")) OR ((MH_PHRASE="Anemia, Sideroblastic")) OR ((MH_PHRASE="Anemia, Neonatal")) OR ((MH_PHRASE="Anemia, Iron-Deficiency")) OR ((MH_PHRASE="Anemia, Myelophthisic")) OR ((MH_PHRASE="Anemia, Aplastic")) OR ((MH_PHRASE="Anemia, Hemolytic, Congenital")) OR ((MH_PHRASE="Anemia, Hemolytic")) OR (MH_PHRASE="Anemia"))	409
#20	TI=(anaemia OR anemia) OR AB=(anaemia OR anemia)	397
#19	(MH_PHRASE="Anemia, Hypochromic")	6
#18	(MH_PHRASE="Anemia, Hemolytic, Autoimmune")	0
#17	(MH_PHRASE="Anemia, Sickle Cell")	3
#16	(MH_PHRASE="Anemia, Hemolytic, Congenital Nonspherocytic")	1
#15	(MH_PHRASE="Anemia, Pernicious")	2
#14	(MH_PHRASE="Anemia, Diamond-Blackfan")	0
#13	(MH_PHRASE="Anemia, Dyserythropoietic, Congenital")	0
#12	(MH_PHRASE="Anemia, Macrocytic")	2
#11	(MH_PHRASE="Anemia, Refractory")	0
#10	(MH_PHRASE="Anemia, Megaloblastic")	2
#9	(MH_PHRASE="Anemia, Hypoplastic, Congenital")	0
#8	(MH_PHRASE="Anemia, Sideroblastic")	0
#7	(MH_PHRASE="Anemia, Neonatal")	1
#6	(MH_PHRASE="Anemia, Iron-Deficiency")	7
#5	(MH_PHRASE="Anemia, Myelophthisic")	0
#4	(MH_PHRASE="Anemia, Aplastic")	4
#3	(MH_PHRASE="Anemia, Hemolytic, Congenital")	2
#2	(MH_PHRASE="Anemia, Hemolytic")	3
#1	MH_PHRASE="Anemia"	7

* The search was conducted using Informit online platform on 26 June 2009

[a]The records from each of these search statements were exported separately owing to technical difficulties experienced with Informit when processing this search statement. Consequently, there were duplicated records in this number. After exclusion of duplicates 66 unique records from AMI were identified

A5 Literature searches, Question 5

In patients undergoing surgery, what is the effect of red blood cell (RBC) transfusion on patient outcomes?

EMBASE.com: search conducted 13 May 2009

Red blood cell transfusion

No.	Query	Results
#1	'erythrocyte transfusion'/exp	7,121
#2	'erythrocyte transfusion':ab,ti OR 'erythrocyte transfusions':ab,ti	293
#3	'red blood cell *1 transfusion':ab,ti OR 'rbc *1 transfusion':ab,ti	1,089
#4	'red blood cell *1 transfusions':ab,ti OR 'rbc *1 transfusions':ab,ti	928
#5	'red cell *1 transfusion':ab,ti OR 'normocyte transfusion':ab,ti	523
#6	'red cell *1 transfusions':ab,ti OR 'normocyte transfusions':ab,ti	384
#7	'red blood cell *1 exchange':ab,ti OR 'rbc *1 exchange':ab,ti	68
#8	'red cell *3 exchange':ab,ti OR 'red cells *3 exchange':ab,ti	108
#9	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8	8,382

Restrictive transfusion trigger

No.	Query	Results
#1	'restrictive transfusion trigger':de	1
#2	restrictive:ti AND transfus*:ti	37
#3	'restrictive *3 transfusion':ab,ti OR 'low *3 transfusion':ab,ti	321
#4	'restrictive *3 transfusions':ab,ti OR 'low *3 transfusions':ab,ti	35
#5	#1 OR #2 OR #3 OR #4	357

Liberal transfusion

No.	Query	Results
#1	liberal:ti AND transfus*:ti	16
#2	'liberal *3 transfusion':ti,ab OR 'high *3 transfusion':ti,ab	315
#3	'liberal *3 transfusions':ab,ti OR 'high *3 transfusions':ab,ti	46
#4	#1 OR #2 OR #3	362

Transfusion threshold

No.	Query	Results
#1	'transfusion threshold':ab,ti OR 'transfusion thresholds':ab,ti	143
#2	'transfusion trigger':ab,ti OR 'trigger *1 transfusion':ab,ti	208
#3	'transfusion triggers':ab,ti OR 'triggers *1 transfusion':ab,ti	116
#4	'transfusion strategy':ab,ti OR 'transfusion strategies':ab,ti	179
#5	'transfusion policy':ab,ti OR 'transfusion policies':ab,ti	204
#6	'transfusion practice':ab,ti OR 'transfusion practices':ab,ti	915
#7	'transfusion protocol':ti,ab OR 'transfusion protocols':ti,ab	168
#8	'transfusion *1 guideline':ab,ti OR 'transfusion *1 guidelines':ab,ti	166
#9	'hemoglobin threshold':ti,ab OR 'hemoglobin trigger':ti,ab	27
#10	'haemoglobin threshold':ab,ti OR 'haemoglobin trigger':ab,ti	13
#11	'hb threshold':ab,ti OR 'hb trigger':ab,ti	12
#12	'hemoglobin thresholds':ab,ti OR 'hemoglobin triggers':ab,ti	19
#13	'haemoglobin thresholds':ab,ti OR 'haemoglobin triggers':ab,ti	7
#14	'hb thresholds':ab,ti OR 'hb triggers':ab,ti	1
#15	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14	1,839

Haemoglobin

No.	Query	Results
#1	'hemoglobin'/de	63,298
#2	'hemoglobin determination'/de	17,180
#3	'hemoglobin blood level'/de	5,457
#4	'mean corpuscular volume'/de	3,287
#5	'blood haemoglobin':ab,ti OR 'blood hemoglobin':ab,ti	1,154
#6	'haemoglobin *1 level':ab,ti OR 'hemoglobin *1 level':ab,ti	4,664
#7	'haemoglobin *1 levels':ab,ti OR 'hemoglobin *1 levels':ab,ti	5,800
#8	'hb level':ab,ti OR 'hb levels':ab,ti	1,621
#9	'haemoglobin determination':ab,ti OR 'hemoglobin determination':ab,ti	178
#10	'hemoglobin assay':ab,ti OR 'haemoglobin assay':ab,ti	92
#11	'hemoglobin estimation':ab,ti OR 'haemoglobin estimation':ab,ti	100
#12	'hb determination':ab,ti OR 'hb estimation':ab,ti OR 'hb assay':ab,ti	47
#13	'hemoglobin *1 content':ab,ti OR 'hemoglobin *1 concentration':ab,ti	5,608
#14	'haemoglobin *1 content':ti,ab OR 'haemoglobin *1 concentration':ti,ab	2,489
#15	'hb content':ab,ti OR 'hb concentration':ab,ti	1,076
#16	hemoglobinometry:ab,ti OR haemoglobinometry:ab,ti	114
#17	'plasma haemoglobin':ab,ti OR 'plasma hemoglobin':ab,ti	588
#18	'serum haemoglobin':ab,ti OR 'serum hemoglobin':ab,ti	354
#19	'mean corpuscular volume':ab,ti OR mcv:ab,ti OR mch:ab,ti OR mchc:ab,ti	6,617
#20	'mean corpuscular haemoglobin':ab,ti OR 'mean corpuscular hemoglobin':ab,ti	957
#21	'mean cell *1 haemoglobin':ab,ti OR 'mean cell *1 hemoglobin':ab,ti	285
#22	'erythrocyte indices':ti,ab OR 'erythrocyte index':ti,ab OR 'erythrocyte indexes':ti,ab	167
#23	'red *1 cell indices':ab,ti OR 'red *1 cell index':ab,ti OR 'red *1 cell indexes':ab,ti	436
#24	'rbc indices':ab,ti OR 'rbc index':ab,ti OR 'rbc indexes':ab,ti	75
#25	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #20 OR #21 OR #22 OR #23 OR #24	86,709

Re-operation

No.	Query	Results
#1	're-operation'/de	33,578
#2	'bleeding'/de	91,781
#3	'postoperative hemorrhage'/de	9,331
#4	#2 OR #3	100,287
#5	#1 OR #3	42,145
#6	re-operation*:ti AND (bleeding:ti OR 'blood loss':ti)	14
#7	re-operation*:ti AND (hemorrhag*:ti OR haemorrhag*:ti)	7
#8	('re operation':ti OR 're operations':ti) AND bleeding:ti	3
#9	('re operation':ti OR 're operations':ti) AND 'blood loss':ti	0
#10	('re operation':ti OR 're operations':ti) AND hemorrhag*:ti	1
#11	('re operation':ti OR 're operations':ti) AND haemorrhag*:ti	0
#12	re-operation*:ab AND (bleeding:ab OR 'blood loss':ab)	1,926
#13	re-operation*:ab AND (hemorrhag*:ab OR haemorrhag*:ab)	945
#14	('re operation':ab OR 're operations':ab) AND bleeding:ab	229
#15	('re operation':ab OR 're operations':ab) AND 'blood loss':ab	84
#16	('re operation':ab OR 're operations':ab) AND hemorrhag*:ab	67
#17	('re operation':ab OR 're operations':ab) AND haemorrhag*:ab	58
#18	'repeat surgery':ab,ti OR 'surgical revision':ab,ti	2,033
#19	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18	134,493

Hospital discharge

No.	Query	Results
#1	'hospital discharge'/de	29,496
#2	'patient transport'/de	13,541
#3	'hospital discharge':ab,ti OR 'patient discharge':ab,ti	12,048
#4	'discharge planning':ab,ti OR 'discharge plan':ab,ti	1,861
#5	'intrahospital transfer':ab,ti OR 'patient transfer':ab,ti	399
#6	'patient dumping':ab,ti OR 'discharge home':ab,ti	662
#7	'patients discharged':ab,ti OR 'patient discharged':ab,ti	3,152
#8	'patient discharges':ab,ti OR 'discharge management':ab,ti	180
#9	'discharged patient':ab,ti OR 'discharged patients':ab,ti	864
#10	'discharge program':ab,ti OR 'home discharge':ab,ti	250
#11	'early discharge':ab,ti OR 'admission discharge':ab,ti	1,989
#12	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11	55,207

Disseminated intravascular clotting

No.	Query	Results
#1	'disseminated intravascular clotting'/de	14,564
#2	'consumption coagulopathy':ab,ti OR 'consumptive coagulopathy':ab,ti	1,259
#3	'defibrination syndrome':ab,ti OR 'sanarelli shwartzman syndrome':ab,ti	120
#4	'disseminated fibrin thromboembolism':ab,ti	3
#5	'disseminated intravasal thromboembolism':ab,ti	0
#6	'intravasal agglutination':ab,ti OR 'intravasal *1 clotting':ab,ti	5
#7	'intravascular *1 clotting':ab,ti OR 'intravascular *1 coagulation':ab,ti	10,134
#8	'intravascular *1 coagulopathy':ti,ab OR 'intravenous *1 coagulation':ti,ab	669
#9	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8	18,446

Complete EMBASE Search

No.	Query	Results
#1	('erythrocyte transfusion'/exp) OR ('erythrocyte transfusion':ab,ti OR 'erythrocyte transfusions':ab,ti) OR ('red blood cell *1 transfusion':ab,ti OR 'rbc *1 transfusion':ab,ti) OR ('red blood cell *1 transfusions':ab,ti OR 'rbc *1 transfusions':ab,ti) OR ('red cell *1 transfusion':ab,ti OR 'normocyte transfusion':ab,ti) OR ('red cell *1 transfusions':ab,ti OR 'normocyte transfusions':ab,ti) OR ('red blood cell *1 exchange':ab,ti OR 'rbc *1 exchange':ab,ti) OR ('red cell *3 exchange':ab,ti OR 'red cells *3 exchange':ab,ti)	8,382
#2	('restrictive transfusion trigger':de) OR (restrictive:ti AND transfus*:ti) OR ('restrictive *3 transfusion':ab,ti OR 'low *3 transfusion':ab,ti) OR ('restrictive *3 transfusions':ab,ti OR 'low *3 transfusions':ab,ti)	357
#3	(liberal:ti AND transfus*:ti) OR ('liberal *3 transfusion':ti,ab OR 'high *3 transfusion':ti,ab) OR ('liberal *3 transfusions':ab,ti OR 'high *3 transfusions':ab,ti)	362
#4	('transfusion threshold':ab,ti OR 'transfusion thresholds':ab,ti) OR ('transfusion trigger':ab,ti OR 'trigger *1 transfusion':ab,ti) OR ('transfusion triggers':ab,ti OR 'triggers *1 transfusion':ab,ti) OR ('transfusion strategy':ab,ti OR 'transfusion strategies':ab,ti) OR ('transfusion policy':ab,ti OR 'transfusion policies':ab,ti) OR ('transfusion practice':ab,ti OR 'transfusion practices':ab,ti) OR ('transfusion protocol':ti,ab OR 'transfusion protocols':ti,ab) OR ('transfusion *1 guideline':ab,ti OR 'transfusion *1 guidelines':ab,ti) OR ('hemoglobin threshold':ti,ab OR 'hemoglobin trigger':ti,ab) OR ('haemoglobin threshold':ab,ti OR 'haemoglobin trigger':ab,ti) OR ('hb threshold':ab,ti OR 'hb trigger':ab,ti) OR ('hemoglobin thresholds':ab,ti OR 'hemoglobin triggers':ab,ti) OR ('haemoglobin thresholds':ab,ti OR 'haemoglobin triggers':ab,ti) OR ('hb thresholds':ab,ti OR 'hb triggers':ab,ti)	1,839
#5	#1 OR #2 OR #3 OR #4	10,133
#6	('perioperative period'/exp) OR ('perioperative nursing'/exp) OR ('perioperative complication'/exp) OR ('preoperative period'/exp) OR ('preoperative complication'/exp) OR ('intraoperative period'/exp) OR (perioperative:ab,ti OR 'peri operative':ab,ti) OR (preoperative:ab,ti OR 'pre operative':ab,ti) OR (intraoperative:ab,ti OR 'intra operative':ab,ti) OR (peroperative:ab,ti OR 'per operative':ab,ti)	333,328
#7	'postoperative period'/exp	211,781
#8	'postoperative complication'/exp	353,284
#9	postoperative:ab,ti OR 'post operative':ab,ti	280,258
#10	#6 OR #7 OR #8 OR #9	863,981
#11	('injury'/exp) OR (injur*:ab,ti OR trauma*:ab,ti)	1,260,839
#12	('shock'/exp) OR (shock:ab,ti OR 'cardiovascular collapse':ab,ti OR 'circulatory collapse':ab,ti)	135,313
#13	((('blood transfusion'/exp) OR (('bleeding'/exp) AND ('transfusion'/exp))) AND (massive:ab,ti)) OR ('massive transfusion':ab,ti) OR ('massive blood transfusion':ab,ti) OR ('massive transfusion protocol':ab,ti) OR ('massive *3 transfusion':ab,ti OR 'massive *3 transfusions':ab,ti) OR ('massive infusion':ab,ti OR 'massively transfused':ab,ti) OR ('massive *1 bleeding':ab,ti) OR ('massive *1 haemorrhage':ab,ti OR 'massive *1 hemorrhage':ab,ti)	8,395

No.	Query	Results
#14	('thorax surgery'/exp) OR ('heart surgery'/exp) OR ('cardiothoracic surgery':ab,ti OR 'chest *1 surgery':ab,ti) OR ('cardiothoracic *1 patient':ab,ti OR 'cardiothoracic *1 patients':ab,ti) OR ('thoracic operation':ab,ti OR 'thoracic surgery':ab,ti OR thoracoplasty:ab,ti) OR ('thoracic *1 procedure':ab,ti OR 'thoracic *1 procedures':ab,ti)	284,912
#15	('surgery'/exp) OR ('surgical ward'/exp) OR ('surgical patient'/exp) OR (surgical:ab,ti OR surgery:ab,ti OR operation:ab,ti OR resection:ab,ti)	2,723,714
#16	('orthopedic surgery'/exp) OR ('orthopedic surgery':ab,ti OR 'orthopaedic surgery':ab,ti) OR ('bone surgery':ab,ti OR orthopaedics:ab,ti OR orthopedics:ab,ti) OR ('orthopedic *1 patient':ab,ti OR 'orthopedic *1 patients':ab,ti) OR ('orthopaedic *1 patient':ab,ti OR 'orthopaedic *1 patients':ab,ti) OR ('orthopedic operation':ab,ti OR 'orthopedic *1 procedures':ab,ti) OR ('orthopaedic operation':ab,ti OR 'orthopaedic *1 procedures':ab,ti) OR ('orthopedic *1 procedure':ab,ti OR 'orthopaedic *1 procedure':ab,ti)	257,834
#17	#10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16	3,678,764
#18	#5 AND #17	5,209
#19	('adverse outcome'/exp) OR ('outcome assessment'/exp) OR ('morbidity'/exp) OR ('mortality'/exp) OR (morbidity:ab,ti OR incidence:ab,ti OR prevalence:ab,ti OR occurrence:ab,ti) OR (mortality:ab,ti OR death:ab,ti OR survival:ab,ti)	1,921,554
#20	('quality of life'/exp) OR (qol:ab,ti OR 'quality of life':ab,ti OR 'quality of wellbeing':ab,ti) OR ('health related quality':ab,ti OR hrqol:ab,ti) OR (qaly*:ab,ti OR 'quality adjusted':ab,ti OR 'adjusted life':ab,ti)	159,310
#21	(('blood component therapy'/exp) AND (('dose response'/exp) OR ('drug dose'/exp))) OR ('fresh frozen plasma'/exp/dd_do) OR ('recombinant erythropoietin'/exp/dd_do) OR ('transfusion frequency':ab,ti) OR ('frequency *5 transfusion':ab,ti OR 'frequency *5 transfusions':ab,ti) OR ('transfusion rate':ab,ti OR 'transfusion rates':ab,ti) OR ('rate *5 transfusion':ab,ti OR 'rates *5 transfusion':ab,ti) OR ('transfusion requirement':ab,ti OR 'transfusion requirements':ab,ti) OR ('transfusion indication':ab,ti OR 'transfusion indications':ab,ti) OR ('indications *5 transfusion':ab,ti OR 'indications *5 transfusions':ab,ti) OR ('indication *5 transfusion':ab,ti OR 'indication *5 transfusions':ab,ti) OR ('transfusion interval':ab,ti OR 'transfusion intervals':ab,ti) OR ('need *3 transfusion':ab,ti OR 'need *3 transfusions':ab,ti) OR ('transfusion need':ab,ti OR 'transfusion needs':ab,ti) OR ('dose *3 transfusion':ab,ti OR 'dose *3 transfusions':ab,ti) OR ('dose *3 transfused':ab,ti OR 'transfusions *3 dose':ab,ti) OR ('transfusion dose':ab,ti OR 'transfused *3 dose':ab,ti) OR ('platelet dose':ab,ti OR 'dose *3 platelets':ab,ti) OR (dose:ab,ti AND transfus*:ab,ti)	17,357

No.	Query	Results
#22	('hemoglobin'/de) OR ('hemoglobin determination'/de) OR ('hemoglobin blood level'/de) OR ('mean corpuscular volume'/de) OR ('blood haemoglobin':ab,ti OR 'blood hemoglobin':ab,ti) OR ('haemoglobin *1 level':ab,ti OR 'hemoglobin *1 level':ab,ti) OR ('haemoglobin *1 levels':ab,ti OR 'hemoglobin *1 levels':ab,ti) OR ('hb level':ab,ti OR 'hb levels':ab,ti) OR ('haemoglobin determination':ab,ti OR 'hemoglobin determination':ab,ti) OR ('hemoglobin assay':ab,ti OR 'haemoglobin assay':ab,ti) OR ('hemoglobin estimation':ab,ti OR 'haemoglobin estimation':ab,ti) OR ('hb determination':ab,ti OR 'hb estimation':ab,ti OR 'hb assay':ab,ti) OR ('hemoglobin *1 content':ab,ti OR 'hemoglobin *1 concentration':ab,ti) OR ('haemoglobin *1 content':ti,ab OR 'haemoglobin *1 concentration':ti,ab) OR ('hb content':ab,ti OR 'hb concentration':ab,ti) OR (hemoglobinometry:ab,ti OR haemoglobinometry:ab,ti) OR ('plasma haemoglobin':ab,ti OR 'plasma hemoglobin':ab,ti) OR ('serum haemoglobin':ab,ti OR 'serum hemoglobin':ab,ti) OR ('mean corpuscular haemoglobin':ab,ti OR 'mean corpuscular hemoglobin':ab,ti) OR ('mean cell *1 haemoglobin':ab,ti OR 'mean cell *1 hemoglobin':ab,ti) OR ('erythrocyte indices':ti,ab OR 'erythrocyte index':ti,ab OR 'erythrocyte indexes':ti,ab) OR ('red *1 cell indices':ab,ti OR 'red *1 cell index':ab,ti OR 'red *1 cell indexes':ab,ti) OR ('rbc indices':ab,ti OR 'rbc index':ab,ti OR 'rbc indexes':ab,ti)	86,709
#23	('health economics'/exp) OR ('economic aspect'/exp) OR ('economics'/exp) OR ('finance'/exp) OR ('biomedical technology assessment'/exp) OR ('economic evaluation'/exp) OR ('health care cost'/exp) OR (economic*:ab,ti OR pharmacoeconomic*:ab,ti) OR (cost*:ab,ti OR price*:ab,ti OR pricing:ab,ti) OR ('burden of illness':ab,ti OR 'value *1 money':ab,ti) OR (resource*:ab,ti AND utili*:ab,ti) OR (resource*:ab,ti AND utili*:ab,ti) OR ('technology assessment':ab,ti OR 'technology assessments':ab,ti) OR ('technology appraisal':ab,ti OR 'technology appraisals':ab,ti)	994,511
#24	('hospitalization'/exp) OR ('length of stay'/exp) OR (hospitaliz*:ab,ti OR hospitalis*:ab,ti) OR ('length *3 stay':ab,ti OR 'hospital stay':ab,ti)	244,094
#25	('intensive care unit'/exp) OR ('intensive care unit':ab,ti OR icu:ab,ti OR 'intensive care units':ab,ti) OR ('close attention unit':ab,ti OR 'close attention units':ab,ti) OR ('intensive care department':ab,ti OR 'intensive care departments':ab,ti) OR ('special care unit':ab,ti OR 'special care units':ab,ti) OR ('critical care unit':ab,ti OR 'critical care units':ab,ti)	76,464
#26	('re-operation'/de) OR ('bleeding'/de) OR ('postoperative hemorrhage'/de) OR (('bleeding'/de) OR ('postoperative hemorrhage'/de)) OR (('re-operation'/de) OR ('postoperative hemorrhage'/de)) OR (re-operation*:ti AND (bleeding:ti OR 'blood loss':ti)) OR (re-operation*:ti AND (hemorrhag*:ti OR haemorrhag*:ti)) OR (('re operation':ti OR 're operations':ti) AND bleeding:ti) OR (('re operation':ti OR 're operations':ti) AND 'blood loss':ti) OR (('re operation':ti OR 're operations':ti) AND hemorrhag*:ti) OR (('re operation':ti OR 're operations':ti) AND haemorrhag*:ti) OR (re-operation*:ab AND (bleeding:ab OR 'blood loss':ab)) OR (re-operation*:ab AND (hemorrhag*:ab OR haemorrhag*:ab)) OR (('re operation':ab OR 're operations':ab) AND bleeding:ab) OR (('re operation':ab OR 're operations':ab) AND 'blood loss':ab) OR (('re operation':ab OR 're operations':ab) AND hemorrhag*:ab) OR (('re operation':ab OR 're operations':ab) AND haemorrhag*:ab) OR ('repeat surgery':ab,ti OR 'surgical revision':ab,ti)	134,493
#27	('hospital admission'/exp) OR ('hospital readmission'/exp) OR ('hospital admission':ab,ti OR 'hospital admittance':ab,ti) OR ('patient admission':ab,ti OR readmission:ab,ti) OR (rehospitalization:ab,ti OR rehospitalisation:ab,ti)	77,348

No.	Query	Results
#28	('hospital discharge'/de) OR ('patient transport'/de) OR ('hospital discharge':ab,ti OR 'patient discharge':ab,ti) OR ('discharge planning':ab,ti OR 'discharge plan':ab,ti) OR ('intrahospital transfer':ab,ti OR 'patient transfer':ab,ti) OR ('patient dumping':ab,ti OR 'discharge home':ab,ti) OR ('patients discharged':ab,ti OR 'patient discharged':ab,ti) OR ('patient discharges':ab,ti OR 'discharge management':ab,ti) OR ('discharged patient':ab,ti OR 'discharged patients':ab,ti) OR ('discharge program':ab,ti OR 'home discharge':ab,ti) OR ('early discharge':ab,ti OR 'admission discharge':ab,ti)	55,207
#29	('disseminated intravascular clotting'/de) OR ('consumption coagulopathy':ab,ti OR 'consumptive coagulopathy':ab,ti) OR ('defibrination syndrome':ab,ti OR 'sanarelli shwartzman syndrome':ab,ti) OR ('disseminated fibrin thromboembolism':ab,ti) OR ('disseminated intravasal thromboembolism':ab,ti) OR ('intravasal agglutination':ab,ti OR 'intravasal *1 clotting':ab,ti) OR ('intravascular *1 clotting':ab,ti OR 'intravascular *1 coagulation':ab,ti) OR ('intravascular *1 coagulopathy':ti,ab OR 'intravenous *1 coagulation':ti,ab)	18,446
#30	#19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29	3,242,933
#31	#18 AND #30	3,889

Cochrane Library Database: search conducted 13 May 2009

No.	Query	Results
#1	MeSH descriptor Erythrocyte Transfusion explode all trees	346
#2	"erythrocyte transfusion" OR "erythrocyte transfusions"	432
#3	("red blood cell" OR rbc) NEAR/1 transfusion*	142
#4	"red cell" NEAR/1 transfusion*	3
#5	"normocyte transfusion" OR "normocyte transfusions"	0
#6	("red blood cell" OR rbc) NEAR/1 exchange	2
#7	("red cell" OR "red cells") NEAR/3 exchange	3
#8	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7	1916
#9	(restrictive AND transfus*):ti	13
#10	(restrictive OR low) NEAR/3 transfusion*	201
#11	#9 OR #10	1473
#12	(liberal AND transfus*):ti	6
#13	(liberal OR high) NEAR/3 transfusion*	151
#14	#12 OR #13	1257
#15	"transfusion threshold" OR "transfusion thresholds"	32
#16	transfusion NEAR/1 trigger*	49
#17	"transfusion strategy" OR "transfusion strategies"	24
#18	"transfusion policy" OR "transfusion policies"	20
#19	"transfusion practice" OR "transfusion practices"	48
#20	"transfusion protocol" OR "transfusion protocols"	43
#21	transfusion NEAR/1 guideline*	29
#22	"hemoglobin threshold" OR "hemoglobin trigger"	4
#23	"haemoglobin threshold" OR "haemoglobin trigger"	5
#24	"hb threshold" OR "hb trigger"	8
#25	"hemoglobin thresholds" OR "hemoglobin triggers"	4
#26	"haemoglobin thresholds" OR "haemoglobin triggers"	1
#27	"hb thresholds" OR "hb triggers"	2
#28	#15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27	1137

No.	Query	Results
#29	#8 OR #11 OR #14 OR #28	1541
#30	MeSH descriptor Perioperative Care explode all trees	4254
#31	MeSH descriptor Preoperative Care explode all trees	4098
#32	MeSH descriptor Postoperative Complications explode all trees	21418
#33	Postoperative Period	10851
#34	MeSH descriptor Intraoperative Complications explode all trees	2476
#35	MeSH descriptor Intraoperative Period explode all trees	919
#36	(perioperative OR "peri operative")	5196
#37	preoperative OR "pre operative"	11093
#38	intraoperative OR "intra operative"	8039
#39	peroperative OR "per operative"	474
#40	postoperative OR "post operative"	40236
#41	#30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40	494
#42	#29 AND #41	194
#43	MeSH descriptor Wounds and Injuries explode all trees	10953
#44	(injur* OR trauma*)	20750
#45	#43 OR #44	189
#46	#29 AND #45	158
#47	MeSH descriptor Shock explode all trees	930
#48	(shock OR "cardiovascular collapse" OR "circulatory collapse")	3179
#49	#47 OR #48	149
#50	#29 AND #49	125
#51	MeSH descriptor Blood Transfusion explode all trees	2628
#52	massive	599
#53	#51 AND #52	107
#54	massive NEAR/3 transfusion*	20
#55	"massive infusion" OR "massively transfused"	3
#56	massive NEAR/1 (bleeding OR haemorrhage OR hemorrhage)	47
#57	#53 OR #54 OR #55 OR #56	106
#58	#29 AND #57	77

No.	Query	Results
#59	MeSH descriptor Thoracic Surgical Procedures explode all trees	10297
#60	MeSH descriptor Thoracic Surgery explode all trees	130
#61	MeSH descriptor Cardiovascular Surgical Procedures explode all trees	10930
#62	"cardiothoracic surgery" OR (chest NEAR/1 surgery)	675
#63	cardiothoracic NEAR/1 patient*	4
#64	"thoracic operation" OR "thoracic surgery" OR thoracoplasty	2131
#65	thoracic NEAR/1 procedure*	16
#66	#59 OR #60 OR #61 OR #62 OR #63 OR #64 OR #65	93
#67	#29 AND #66	57
#68	MeSH descriptor Surgical Procedures, Operative explode all trees	68578
#69	MeSH descriptor General Surgery explode all trees	167
#70	MeSH descriptor Surgery Department, Hospital explode all trees	68
#71	surgical OR surgery OR operation OR resection	91783
#72	#68 OR #69 OR #70 OR #71	61
#73	#29 AND #72	49
#74	MeSH descriptor Orthopedic Procedures explode all trees	5335
#75	MeSH descriptor Orthopedics explode all trees	272
#76	"orthopedic surgery" OR "orthopaedic surgery"	2339
#77	"bone surgery" OR orthopaedics or orthopedics	7975
#78	(orthopedic OR orthopaedic) NEAR/1 patient*	223
#79	"orthopedic operation" OR "orthopaedic operation"	6
#80	(orthopedic OR orthopaedic) NEAR/1 procedure*	638
#81	#74 OR #75 OR #76 OR #77 OR #78 OR #79 OR #80	59
#82	#29 AND #81	37
#83	#42 OR #46 OR #50 OR #58 OR #67 OR #73 OR #82	244
#84	MeSH descriptor Morbidity explode all trees	8475
#85	MeSH descriptor Mortality explode all trees	7946
#86	morbidity OR incidence OR prevalence OR occurrence	62784
#87	mortality OR death OR survival	55325
#88	#84 OR #85 OR #86 OR #87	45

No.	Query	Results
#89	#83 AND #88	28
#90	MeSH descriptor Quality of Life explode all trees	9425
#91	MeSH descriptor Quality-Adjusted Life Years explode all trees	2062
#92	qol OR "quality of life" OR "quality of wellbeing"	21521
#93	"health related quality" or hrqol	2898
#94	qaly* or "quality adjusted" or "adjusted life"	3802
#95	#90 OR #91 OR #92 OR #93 OR #94	38
#96	#83 AND #95	21
#97	MeSH descriptor Blood Component Transfusion explode all trees with qualifier: MT	99
#98	frequency NEAR/5 transfusion*	84
#99	rate* NEAR/5 transfusion*	324
#100	"transfusion requirement" OR "transfusion requirements"	949
#101	indication* NEAR/5 transfusion*	45
#102	"transfusion interval" OR "transfusion intervals"	13
#103	(need NEAR/3 transfusion*) OR "transfusion needs"	623
#104	dose NEAR/3 transfus*	86
#105	"platelet dose" OR (dose NEAR/3 platelets)	185
#106	(dose and transfus*):ti	72
#107	#97 OR #98 OR #99 OR #100 OR #101 OR #102 OR #103 OR #104 OR #105 OR #106	45
#108	#83 AND #107	13
#109	MeSH descriptor Hemoglobins explode all trees	4487
#110	MeSH descriptor Hemoglobinometry explode all trees	152
#111	MeSH descriptor Erythrocyte Indices explode all trees	110
#112	"blood haemoglobin" OR "blood hemoglobin"	241
#113	(haemoglobin OR hemoglobin) NEAR/1 level*	1228
#114	"hb level" OR "hb levels"	236
#115	"haemoglobin determination" OR "hemoglobin determination"	120
#116	"hemoglobin assay" OR "haemoglobin assay"	4
#117	"hemoglobin estimation" OR "haemoglobin estimation"	5
#118	"hb determination" OR "hb estimation" OR "hb assay"	2

No.	Query	Results
#119	hemoglobin NEAR/1 (content OR concentration)	904
#120	haemoglobin NEAR/1 (content OR concentration)	904
#121	"hb content" OR "hb concentration"	110
#122	hemoglobinometry OR haemoglobinometry	166
#123	"plasma haemoglobin" OR "plasma hemoglobin"	65
#124	"serum haemoglobin" OR "serum hemoglobin"	47
#125	"mean corpuscular volume" OR mcv OR mch OR mchc	350
#126	"mean corpuscular haemoglobin" OR "mean corpuscular hemoglobin"	41
#127	"Mean Cell" NEAR/1 (Haemoglobin OR Hemoglobin)	2
#128	"erythrocyte indices" OR "Erythrocyte Index" OR "Erythrocyte Indexes"	121
#129	red NEAR/1 ("cell indices" OR "Cell Index" OR "Cell Indexes")	14
#130	"rbc indices" OR "RBC Index" OR "RBC Indexes"	2
#131	#109 OR #110 OR #111 OR #112 OR #113 OR #114 OR #115 OR #116 OR #117 OR #118 OR #119 OR #120 OR #121 OR #122 OR #123 OR #124 OR #125 OR #126 OR #127 OR #128 OR #129 OR #130	49
#132	#83 AND #131	9
#133	MeSH descriptor Costs and Cost Analysis explode all trees	26772
#134	MeSH descriptor Economics explode all trees	28552
#135	MeSH descriptor Models, Economic explode all trees	1853
#136	MeSH descriptor Value of Life explode all trees	274
#137	MeSH descriptor Utilization Review explode all trees	420
#138	MeSH descriptor Delivery of Health Care explode all trees with qualifier: UT	762
#139	economic* or pharmacoeconomic*	37332
#140	cost* or price* or pricing	48938
#141	resource* near utili*	1537
#142	"burden of illness" or (value NEAR/1 money)	87
#143	#133 or #134 or #135 or #136 or #137 or #138 or #139 or #140 or #141 OR #142	15
#144	#83 and #143	7
#145	MeSH descriptor Hospitalization explode all trees	10690
#146	MeSH descriptor Child, Hospitalized explode all trees	82
#147	hospitaliz* OR hospitalis*	16298

No.	Query	Results
#148	(length NEAR/3 stay) OR "hospital stay"	11735
#149	#145 OR #146 OR #147 OR #148	8
#150	#83 AND #149	1
#151	MeSH descriptor Intensive Care Units explode all trees	1978
#152	"intensive care unit" OR icu OR "intensive care units"	6712
#153	"close attention unit" OR "close attention units"	0
#154	"intensive care department" OR "intensive care departments"	56
#155	"special care unit" OR "special care units"	63
#156	"critical care unit" OR "critical care units"	108
#157	#151 OR #152 OR #153 OR #154 OR #155 OR #156	3
#158	#83 AND #157	1
#159	MeSH descriptor Re-operation explode all trees	1199
#160	MeSH descriptor Hemorrhage explode all trees	7284
#161	MeSH descriptor Postoperative Hemorrhage explode all trees	485
#162	MeSH descriptor Blood Loss, Surgical explode all trees	1399
#163	#160 OR #161 OR #162	2
#164	#159 AND #163	1
#165	re-operation* NEAR/15 (bleeding or "blood loss")	136
#166	re-operation* NEAR/15 (hemorrhag* OR haemorrhag*)	69
#167	("re operation" OR "re operations") NEAR/15 bleeding	31
#168	("re operation" OR "re operations") NEAR/15 "blood loss"	15
#169	("re operation" OR "re operations") NEAR/15 hemorrhag*	2
#170	("re operation" OR "re operations") NEAR/15 haemorrhag*	9
#171	"Repeat Surgery" OR "Surgical Revision"	110
#172	#164 OR #165 OR #166 OR #167 OR #168 OR #169 OR #170 OR #171	6
#173	#83 AND #172	0
#174	MeSH descriptor Patient Admission explode all trees	604
#175	MeSH descriptor Patient Readmission explode all trees	593
#176	"hospital admission" OR "hospital admittance"	1727
#177	"patient admission" OR readmission	2327

No.	Query	Results
#178	rehospitalization OR rehospitalisation	504
#179	#174 OR #175 OR #176 OR #177 OR #178	6
#180	#83 AND #179	0
#181	MeSH descriptor Patient Discharge explode all trees	822
#182	MeSH descriptor Patient Transfer explode all trees	105
#183	"hospital discharge" OR "patient discharge"	2727
#184	"discharge planning" OR "discharge plan"	312
#185	"intrahospital transfer" OR "patient transfer"	133
#186	"Patient Dumping" OR "discharge home"	181
#187	"patients discharged" OR "patient discharged"	341
#188	"patient discharges" OR "discharge management"	12
#189	"discharged patient" OR "discharged patients"	73
#190	"discharge program" OR "home discharge"	78
#191	"early discharge" OR "admission discharge"	353
#192	#181 OR #182 OR #183 OR #184 OR #185 OR #186 OR #187 OR #188 OR #189 OR #190 OR #191	7
#193	#83 AND #192	0
#194	MeSH descriptor Disseminated Intravascular Coagulation explode all trees	75
#195	"consumption coagulopathy" OR "consumptive coagulopathy"	12
#196	"defibrination syndrome" OR "sanarelli shwartzman syndrome"	1
#197	"disseminated fibrin thromboembolism"	0
#198	"disseminated intravasal thromboembolism"	0
#199	"intravasal agglutination" OR (intravasal NEAR/1 clotting)	0
#200	intravascular NEAR/1 (clotting OR coagulation OR coagulopathy)	237
#201	intravenous NEAR/1 coagulation	1
#202	#194 OR #195 OR #196 OR #197 OR #198 OR #199 OR #200 OR #201	7
#203	#83 AND #202	0
#204	#89 OR #96 OR #108 OR #132 OR #144 OR #150 OR #158 OR #173 OR #180 OR #193 OR #203	45
#205	#89 OR #96 OR #108 OR #132 OR #144 OR #150 OR #158 OR #173 OR #180 OR #193 OR #203	45

PreMedline: search conducted 18 May 2009

No.	Query	Results
#69	Search #66 OR #67 OR #68	314
#68	Search #65 AND pubmednotmedline[sb]	36
#67	Search #65 AND in process[sb]	176
#66	Search #65 NOT (medline[SB] OR oldmedline[sb])	314
#65	Search #36 OR #38 OR #40 OR #47 OR #53 OR #55 OR #64	8,906
#64	Search #29 AND #63	331
#63	Search #56 OR #57 OR #58 OR #59 OR #60 OR #61 OR #62	42779
#62	Search orthopedic[tw] AND procedure*[tw]	11073
#61	Search orthopaedic[tw] AND procedure*[tw]	3355
#60	Search "orthopedic operation"[tw] OR "orthopaedic operation"[tw]	74
#59	Search orthopaedic[tw] AND patient*[tw]	8103
#58	Search orthopedic[tw] AND patient*[tw]	15087
#57	Search "bone surgery"[tw] OR orthopaedics[tw] or orthopedics[tw]	17595
#56	Search "orthopedic surgery"[tw] OR "orthopaedic surgery"[tw]	5995
#55	Search #29 AND #54	6746
#54	Search surgical[tw] OR surgery[tw] OR operation[tw] OR resection[tw]	1874663
#53	Search #29 AND #52	353
#52	Search #48 OR #49 OR #50 OR #51	54029
#51	Search thoracic[tw] AND procedure*[tw]	19117
#50	Search "thoracic operation"[tw] OR "thoracic surgery"[tw] OR thoracoplasty[tw]	16701
#49	Search cardiothoracic[tw] AND patient*[tw]	2273
#48	Search "cardiothoracic surgery"[tw] OR (chest[tw] AND surgery[tw])	24366
#47	Search #29 AND #46	713
#46	Search #41 OR #42 OR #43 OR #44 OR #45	11296
#45	Search massive[tw] AND haemorrhage[tw]	1180
#44	Search massive[tw] AND hemorrhage[tw]	7704
#43	Search massive[tw] AND bleeding[tw]	4946
#42	Search "massive infusion"[tw] OR "massively transfused"[tw]	101
#41	Search massive[tw] AND transfusion*[tw]	2305

No.	Query	Results
#40	Search #29 AND #39	781
#39	Search shock[tw] OR "cardiovascular collapse"[tw] OR "circulatory collapse"[tw]	134680
#38	Search #29 AND #37	1690
#37	Search injur*[tw] OR trauma*[tw]	717377
#36	Search #29 AND #35	4687
#35	Search #30 OR #31 OR #32 OR #33 OR #34	611091
#34	Search postoperative[tw] OR "post operative"[tw]	467606
#33	Search peroperative[tw] OR "per operative"[tw]	3707
#32	Search intraoperative[tw] OR "intra operative"[tw]	88027
#31	Search preoperative[tw] OR "pre operative"[tw]	149265
#30	Search perioperative[tw] OR "peri operative"[tw]	42750
#29	Search #7 OR #10 OR #13 OR #28	27075
#28	Search #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27	3374
#27	Search "hb thresholds"[tw] OR "hb triggers"[tw]	0
#26	Search "haemoglobin thresholds"[tw] OR "haemoglobin triggers"[tw]	7
#25	Search "hemoglobin thresholds"[tw] OR "hemoglobin triggers"[tw]	14
#24	Search "hb threshold"[tw] OR "hb trigger"[tw]	11
#23	Search "haemoglobin threshold"[tw] OR "haemoglobin trigger"[tw]	8
#22	Search "hemoglobin threshold"[tw] OR "hemoglobin trigger"[tw]	23
#21	Search transfusion[tw] AND guideline*[tw]	1792
#20	Search "transfusion protocol"[tw] OR "transfusion protocols"[tw]	158
#19	Search "transfusion practice"[tw] OR "transfusion practices"[tw]	819
#18	Search "transfusion policy"[tw] OR "transfusion policies"[tw]	171
#17	Search "transfusion strategy"[tw] OR "transfusion strategies"[tw]	153
#16	Search "transfusion trigger"[tw] OR "transfusion triggers"[tw]	252
#15	Search trigger*[tw] AND transfusion[tw])	625
#14	Search "transfusion threshold"[tw] OR "transfusion thresholds"[tw]	131
#13	Search #11 OR #12	10474
#12	Search (liberal[tw} OR high[tw]) AND transfusion*[tw]	10474
#11	Search liberal[title] AND transfus*[title]	9

No.	Query	Results
#10	Search #8 OR #9	7564
#9	Search (restrictive[tw] OR low[tw]) AND transfusion*[tw]	7564
#8	Search restrictive[title] AND transfus*[title]	28
#7	Search #1 OR #2 OR #3 OR #4 OR #5 OR #6	11557
#6	Search ("red cell"[tw] OR "red cells"[tw]) AND exchange[tw]	1734
#5	Search ("red blood cell[tw] OR rbc[tw]) AND exchange	1021
#4	Search "normocyte transfusion"[tw] OR "normocyte transfusions"[tw]	0
#3	Search "red cell"[tw] AND transfusion*[tw]	3236
#2	Search ("red blood cell"[tw] OR rbc[tw]) AND transfusion*[tw]	3870
#1	Search "erythrocyte transfusion"[tw] OR "erythrocyte transfusions"[tw]	4583

CINAHL: search conducted 28 May 2009

No.	Query	Results
S232	s99 OR s105 OR s119 OR s149 OR s161 OR s168 OR s177 OR s198 OR s205 OR s218 OR s231	666^
S231	s93 AND s230	10
S230	s219 OR s220 OR s221 OR s226 OR S227 OR S228	634
S229	TI (intravenous N1 coagulation) OR AB (intravenous N1 coagulation)	0
S228	TI (intravascular N1 coagulopathy) OR AB (intravascular N1 coagulopathy)	36
S227	TI (intravascular N1 coagulation) OR AB (intravascular N1 coagulation)	261
S226	TI (intravascular N1 clotting) OR AB (intravascular N1 clotting)	1
S225	TI (intravasal N1 clotting) OR AB (intravasal N1 clotting)	0
S224	TI ("intravasal agglutination") OR AB ("intravasal agglutination")	0
S223	TI ("disseminated intravasal thromboembolism") OR AB ("disseminated intravasal thromboembolism")	0
S222	TI ("disseminated fibrin thromboembolism") OR AB ("disseminated fibrin thromboembolism")	0
S221	TI ("defibrination syndrome" OR "sanarelli shwartzman syndrome") OR AB ("defibrination syndrome" OR "sanarelli shwartzman syndrome")	1
S220	TI ("consumption coagulopathy" OR "consumptive coagulopathy") OR AB ("consumption coagulopathy" OR "consumptive coagulopathy")	18
S219	(MH "Disseminated Intravascular Coagulation")	492

No.	Query	Results
S218	s93 AND s217	9
S217	s206 OR s207 OR s208 OR s209 OR s210 OR s211 OR s212 OR s213 OR s214 OR s215 OR s216	13207
S216	TI ("early discharge" OR "admission discharge") OR AB ("early discharge" OR "admission discharge")	601
S215	TI ("discharge program" OR "home discharge") OR AB ("discharge program" OR "home discharge")	103
S214	TI ("discharged patient" OR "discharged patients") OR AB ("discharged patient" OR "discharged patients")	184
S213	TI ("patient discharges" OR "discharge management") OR AB ("patient discharges" OR "discharge management")	57
S212	TI ("patients discharged" OR "patient discharged") OR AB ("patients discharged" OR "patient discharged")	601
S211	TI ("Patient Dumping" OR "discharge home") OR AB ("Patient Dumping" OR "discharge home")	248
S210	TI ("intrahospital transfer" OR "patient transfer") OR AB ("intrahospital transfer" OR "patient transfer")	131
S209	TI ("discharge planning" OR "discharge plan") OR AB ("discharge planning" OR "discharge plan")	1274
S208	TI ("hospital discharge" OR "patient discharge") OR AB ("hospital discharge" OR "patient discharge")	2740
S207	(MH "Patient Dumping")	26
S206	(MH "Patient Discharge+")	9942
S205	s93 and s204	2
S204	S199 or S200 or S201 or S202 OR S203	8269
S203	TI (rehospitalization OR rehospitalisation) or AB (rehospitalization OR rehospitalisation)	437
S202	TI ("patient admission" OR readmission) or AB ("patient admission" OR readmission)	1117
S201	TI ("hospital admission" OR "hospital admittance") or AB ("hospital admission" OR "hospital admittance")	1910
S200	(MH "Readmission")	1892
S199	(MH "Patient Admission")	4267
S198	s93 AND s197	11
S197	s183 OR s184 OR s185 OR s186 OR s187 OR s188 OR S190 OR S192 OR S194 OR S196	211
S196	TI ("Repeat Surgery" OR "Surgical Revision") OR AB ("Repeat Surgery" OR "Surgical	92

No.	Query	Results
	Revision")	
S195	TI ("re operations" N15 haemorrhag*) OR AB ("re operations" N15 haemorrhag*)	0
S194	TI ("re operation" N15 haemorrhag*) OR AB ("re operation" N15 haemorrhag*)	1
S193	TI ("re operations" N15 hemorrhag*) OR AB ("re operations" N15 hemorrhag*)	0
S192	TI ("re operation" N15 hemorrhag*) OR AB ("re operation" N15 hemorrhag*)	1
S191	TI ("re operations" N15 "blood loss") OR AB ("re operations" N15 "blood loss")	0
S190	TI ("re operation" N15 "blood loss") OR AB ("re operation" N15 "blood loss")	4
S189	TI ("re operations" N15 bleeding) OR AB ("re operations" N15 bleeding)	0
S188	TI ("re operation" N15 bleeding) OR AB ("re operation" N15 bleeding)	5
S187	TI (re-operation* N15 haemorrhag*) OR AB (re-operation* N15 haemorrhag*)	2
S186	TI (re-operation* N15 hemorrhag) OR AB (re-operation* N15 hemorrhag*)	9
S185	TI (re-operation* N15 "blood loss") OR AB (re-operation* N15 "blood loss")	5
S184	TI (re-operation* N15 bleeding) OR AB (re-operation* N15 bleeding)	40
S183	s178 AND s182	62
S182	s179 OR s180 OR s181	4094
S181	(MH "Blood Loss, Surgical")	612
S180	(MH "postoperative hemorrhage")	493
S179	(MH "hemorrhage")	3082
S178	(MH "Repeat Procedures+")	3100
S177	s93 and s176	87
S176	S169 or S170 or S171 or S173 OR S174 OR S175	32514
S175	TI ("critical care unit" OR "critical care units") or AB ("critical care unit" OR "critical care units")	862
S174	TI ("special care unit" OR "special care units") or AB ("special care unit" OR "special care units")	263
S173	TI ("intensive care department" OR "intensive care departments") or AB ("intensive care department" OR "intensive care departments")	33
S172	TI ("close attention unit" OR "close attention units") or AB ("close attention unit" OR "close attention units")	0
S171	TI ("intensive care unit" OR icu OR "intensive care units") or AB ("intensive care unit" OR icu OR "intensive care units")	13551

No.	Query	Results
S170	(MH "Critical Care Nursing+")	15379
S169	(MH "Intensive Care Units+")	14523
S168	S93 AND S167	68
S167	S162 OR S163 OR S164 OR S165 OR S166	41714
S166	TI ("hospital stay") or AB ("hospital stay")	3282
S165	TI (length N3 stay) or AB (length N3 stay)	5786
S164	TI (hospitaliz* OR hospitalis*) or AB (hospitaliz* OR hospitalis*)	18023
S163	(MH "Child, Hospitalized")	2168
S162	(MH "Hospitalization+")	20615
S161	s93 and s160	42
S160	S150 or S151 or S152 or S153 OR S154 OR S155 OR S156 OR S157 OR S158 OR S159	81392
S159	TI (value N1 money) or AB (value N1 money)	212
S158	TI ("burden of illness") or AB ("burden of illness")	174
S157	TI (resource* and utili*) or AB (resource* and utili*)	3133
S156	TI (cost* or price* or pricing) or AB (cost* or price* or pricing)	45635
S155	TI (economic* or pharmacoeconomic*) or AB (economic* or pharmacoeconomic*)	16140
S154	(MH "Health Care Delivery/UT")	63
S153	(MH "Utilization Review+")	3381
S152	(MH "Economic Value of Life")	236
S151	(MH "Economics")	2401
S150	(MH "Costs and Cost Analysis+")	32489
S149	S93 AND S148	72
S148	S120 OR S121 OR S122 OR S123 OR S124 OR S125 OR S126 OR S127 OR S128 OR S129 OR S130 OR S131 OR S132 OR S133 OR S134 OR S135 OR S136 OR S137 OR S138 OR S139 OR S140 OR S141 OR S142 OR S143 OR S144 OR S146 OR S147	3631
S147	TI ("rbc indices" OR "RBC Index" OR "RBC Indexes") OR AB ("rbc indices" OR "RBC Index" OR "RBC Indexes")	8
S146	TI (red N1 "Cell Indexes") OR AB (red N1 "Cell Indexes")	6
S145	TI (red N1 "Cell Index") OR AB (red N1 "Cell Index")	0

No.	Query	Results
S144	TI (red N1 "cell indices") OR AB (red N1 "cell indices")	24
S143	TI ("erythrocyte indices" OR "Erythrocyte Index" OR "Erythrocyte Indexes") OR AB ("erythrocyte indices" OR "Erythrocyte Index" OR "Erythrocyte Indexes")	8
S142	TI ("Mean Cell" N1 Haemoglobin) OR AB ("Mean Cell" N1 Haemoglobin)	3
S141	TI ("Mean Cell" N1 Hemoglobin) OR AB ("Mean Cell" N1 Hemoglobin)	10
S140	TI ("mean corpuscular haemoglobin" OR "mean corpuscular hemoglobin") OR AB ("mean corpuscular haemoglobin" OR "mean corpuscular hemoglobin")	30
S139	TI ("mean corpuscular volume" OR mcv OR mch OR mchc) OR AB ("mean corpuscular volume" OR mcv OR mch OR mchc)	356
S138	TI ("serum haemoglobin" OR "serum hemoglobin") OR AB ("serum haemoglobin" OR "serum hemoglobin")	14
S137	TI ("plasma haemoglobin" OR "plasma hemoglobin") OR AB ("plasma haemoglobin" OR "plasma hemoglobin")	30
S136	TI (hemoglobinometry OR haemoglobinometry) OR AB (hemoglobinometry OR haemoglobinometry)	2
S135	TI ("hb content" OR "hb concentration") OR AB ("hb content" OR "hb concentration")	50
S134	TI (haemoglobin N1 concentration) OR AB (haemoglobin N1 concentration)	70
S133	TI (haemoglobin N1 content) OR AB (haemoglobin N1 content)	4
S132	TI (hemoglobin N1 concentration) OR AB (hemoglobin N1 concentration)	273
S131	TI (hemoglobin N1 content) OR AB (hemoglobin N1 content)	26
S130	TI ("hb determination" OR "hb estimation" OR "hb assay") OR AB ("hb determination" OR "hb estimation" OR "hb assay")	3
S129	TI ("hemoglobin estimation" OR "haemoglobin estimation") OR AB ("hemoglobin estimation" OR "haemoglobin estimation")	3
S128	TI ("hemoglobin assay" OR "haemoglobin assay") OR AB ("hemoglobin assay" OR "haemoglobin assay")	6
S127	TI ("haemoglobin determination" OR "hemoglobin determination") OR AB ("haemoglobin determination" OR "hemoglobin determination")	7
S126	TI ("hb level" OR "hb levels") OR AB ("hb level" OR "hb levels")	171
S125	TI (haemoglobin N1 level*) OR AB (haemoglobin N1 level*)	150
S124	TI (hemoglobin N1 level*) OR AB (hemoglobin N1 level*)	670
S123	TI ("blood haemoglobin" OR "blood hemoglobin") OR AB ("blood haemoglobin" OR "blood hemoglobin")	45

No.	Query	Results
S122	(MH "Erythrocyte Indices")	97
S121	(MH "Hemoglobinometry")	21
S120	(MH "Hemoglobins")	2501
S119	s93 and s118	139
S118	S106 or S107 or S108 OR S109 OR S110 OR S111 OR S112 or S113 or S114 or S115 or S116 or S117	807
S117	TI (dose and transfus*)	7
S116	TI (dose N3 platelets) or AB (dose N3 platelets)	2
S115	TI ("platelet dose") or AB ("platelet dose")	3
S114	TI (dose N3 transfus*) or AB (dose N3 transfus*)	14
S113	TI ("transfusion needs") or AB ("transfusion needs")	25
S112	TI (need N3 transfusion*) or AB (need N3 transfusion*)	234
S111	TI ("transfusion interval" OR "transfusion intervals") or AB ("transfusion interval" OR "transfusion intervals")	4
S110	TI (indication* N5 transfusion*) or AB (indication* N5 transfusion*)	34
S109	TI ("transfusion requirement" OR "transfusion requirements") or AB ("transfusion requirement" OR "transfusion requirements")	254
S108	TI (rate* N5 transfusion*) or AB (rate* N5 transfusion*)	170
S107	TI (frequency N5 transfusion*) or AB (frequency N5 transfusion*)	21
S106	(MH "Blood Component Transfusion+/MT")	141
S105	s93 and s104	7
S104	S100 or S101 or S102 or S103	36997
S103	TI (qaly* or "quality adjusted" or "adjusted life") or AB (qaly* or "quality adjusted" or "adjusted life")	824
S102	TI ("health related quality" or hrqol) or AB ("health related quality" or hrqol)	3387
S101	TI (qol OR "quality of life" OR "quality of wellbeing") or AB (qol OR "quality of life" OR "quality of wellbeing")	23497
S100	(MH "Quality of Life+")	26550
S99	s93 and s98	219
S98	S94 or S95 or S96 or S97	150803

No.	Query	Results
S97	TI (mortality OR death OR survival) or AB (mortality OR death OR survival)	71523
S96	TI (morbidity OR incidence OR prevalence OR occurrence) or AB (morbidity OR incidence OR prevalence OR occurrence)	77942
S95	(MH "Mortality+")	18554
S94	(MH "Morbidity+")	27736
S93	S48 OR S54 OR S58 OR S66 OR S75 OR S80 OR S92	554
S92	s34 and s91	45
S91	S81 or S82 OR S83 OR S84 OR S85 or S86 or S87 or S88 or S89 or S90	26008
S90	TI (orthopaedic N1 procedure*) or AB (orthopeadic N1 procedure*)	14
S89	TI (orthopedic N1 procedure*) or AB (orthopedic N1 procedure*)	115
S88	TI ("orthopedic operation" OR "orthopaedic operation") or AB ("orthopedic operation" OR "orthopaedic operation")	6
S87	TI (orthopaedic N1 patient*) or AB (orthopaedic N1 patient*)	357
S86	TI (orthopedic N1 patient*) or AB (orthopedic N1 patient*)	245
S85	TI ("bone surgery" OR orthopaedics or orthopedics) or AB ("bone surgery" OR orthopaedics or orthopedics)	917
S84	TI ("orthopedic surgery" OR "orthopaedic surgery") or AB ("orthopedic surgery" OR "orthopaedic surgery")	801
S83	(MH "Orthopedic Nursing")	1422
S82	(MH "Orthopedics")	3339
S81	(MH "Orthopedic Surgery+")	21376
S80	s34 and s79	360
S79	S76 or S77 or S78	171915
S78	TI (surgical OR surgery OR operation OR resection) or AB (surgical OR surgery OR operation OR resection)	70282
S77	(MH "Medical-Surgical Nursing")	2436
S76	(MH "Surgery, Operative+")	137624
S75	s34 and s74	87
S74	S67 or S68 or S69 or S70 or S71 or S72 OR S73	23356
S73	TI (thoracic N1 procedure*) or AB (thoracic N1 procedure*)	32

No.	Query	Results
S72	TI ("thoracic operation" OR "thoracic surgery" OR thoracoplasty) or AB ("thoracic operation" OR "thoracic surgery" OR thoracoplasty)	253
S71	TI (cardiothoracic N1 patient*) or AB (cardiothoracic N1 patient*)	57
S70	TI ("cardiothoracic surgery" OR (chest N1 surgery)) or AB ("cardiothoracic surgery" OR (chest N1 surgery)	167
S69	(MH "Cardiovascular Nursing+")	2667
S68	(MH "Surgery, Cardiovascular+")	16971
S67	(MH "Thoracic Surgery+")	17001
S66	s34 and s65	96
S65	S61 or S62 or S63 OR S64	5151
S64	TI (massive N1 (bleeding OR haemorrhage OR hemorrhage)) or AB (massive N1 (bleeding OR haemorrhage OR hemorrhage))	5072
S63	TI ("massive infusion" OR "massively transfused") or AB ("massive infusion" OR "massively transfused")	10
S62	TI (massive N3 transfusion*) or AB (massive N3 transfusion*)	87
S61	S59 and S60	74
S60	TI (massive) or AB (massive)	1894
S59	(MH "Blood Transfusion")	3449
S58	s34 and s57	57
S57	S55 or S56	6716
S56	TI (shock OR "cardiovascular collapse" OR "circulatory collapse") or AB (shock OR "cardiovascular collapse" OR "circulatory collapse")	5211
S55	(MH "Shock+")	3283
S54	S34 and S53	202
S53	S49 OR S50 or S51 OR S52	121873
S52	TI (injur* OR trauma*) or AB (injur* OR trauma*)	67919
S51	(MH "Trauma Nursing")	531
S50	(MH "Trauma+")	5896
S49	(MH "Wounds and Injuries+")	91270
S48	S34 AND S47	210

No.	Query	Results
S47	S35 or S36 or S37 or S38 or S39 or S40 or S41 or S42 OR S43 or S44 or S45 or S46	54455
S46	TI (postoperative OR "post operative") or AB (postoperative OR "post operative")	14432
S45	TI (peroperative OR "per operative") or AB (peroperative OR "per operative")	51
S44	TI (intraoperative OR "intra operative") or AB (intraoperative OR "intra operative")	2969
S43	TI (preoperative OR "pre operative") or AB (preoperative OR "pre operative")	7216
S42	TI (perioperative OR "peri operative") or AB (perioperative OR "peri operative")	5331
S41	(MH "Postoperative Period")	1907
S40	(MH "Postoperative Complications+")	21289
S39	(MH "Intraoperative Period")	366
S38	(MH "Intraoperative Complications+")	1808
S37	(MH "Preoperative Period+")	721
S36	(MH "Perioperative Nursing")	8844
S35	(MH "Perioperative Care+")	16111
S34	s11 OR s15 OR s19 OR s33	1245
S33	s20 OR s21 OR s22 OR s23 OR s24 OR s25 OR s26 OR s27 OR s28 OR s29 OR s30 OR s31	285
S32	TI ("hb thresholds" OR "hb triggers") OR AB ("hb thresholds" OR "hb triggers")	0
S31	TI ("haemoglobin thresholds" OR "haemoglobin triggers") OR AB ("haemoglobin thresholds" OR "haemoglobin triggers")	1
S30	TI ("hemoglobin thresholds" OR "hemoglobin triggers") OR AB ("hemoglobin thresholds" OR "hemoglobin triggers")	3
S29	TI ("hb threshold" OR "hb trigger") OR AB ("hb threshold" OR "hb trigger")	2
S28	TI ("haemoglobin threshold" OR "haemoglobin trigger") OR AB ("haemoglobin threshold" OR "haemoglobin trigger")	1
S27	TI ("hemoglobin threshold" OR "hemoglobin trigger") OR AB ("hemoglobin threshold" OR "hemoglobin trigger")	8
S26	TI (transfusion N1 guideline*) OR AB (transfusion N1 guideline*)	46
S25	TI ("transfusion protocol" OR "transfusion protocols") OR AB ("transfusion protocol" OR "transfusion protocols")	25
S24	TI ("transfusion practice" OR "transfusion practices") OR AB ("transfusion practice" OR "transfusion practices")	126
S23	TI ("transfusion policy" OR "transfusion policies") OR AB ("transfusion policy" OR "transfusion	18

No.	Query	Results
	policies")	
S22	TI ("transfusion strategy" OR "transfusion strategies") OR AB ("transfusion strategy" OR "transfusion strategies")	34
S21	TI (transfusion N1 trigger*) OR AB (transfusion N1 trigger*)	42
S20	TI ("transfusion threshold" OR "transfusion thresholds") OR AB ("transfusion threshold" OR "transfusion thresholds")	38
S19	s16 OR s17 OR S18	63
S18	TI (high N3 transfusion*) OR AB (high N3 transfusion*)	43
S17	TI (liberal N3 transfusion*) OR AB (liberal N3 transfusion*)	20
S16	TI (liberal AND transfus*)	8
S15	s12 OR s13 OR s14	79
S14	TI (low N3 transfusion*) OR AB (low N3 transfusion*)	43
S13	TI (restrictive N3 transfusion*) OR AB (restrictive N3 transfusion*)	34
S12	TI (restrictive AND transfus*)	17
S11	s1 OR s2 OR s3 OR s4 OR s5 OR s7 OR s8 OR s9	1021
S10	TI ("red cells" N3 exchange) OR AB ("red cells" N3 exchange)	0
S9	TI ("red cell" N3 exchange) OR AB ("red cell" N3 exchange)	5
S8	TI (rbc N1 exchange) OR AB (rbc N1 exchange)	3
S7	TI ("red blood cell" N1 exchange) OR AB ("red blood cell" N1 exchange)	5
S6	TI ("normocyte transfusion" OR "normocyte transfusions") OR AB ("normocyte transfusion" OR "normocyte transfusions")	0
S5	TI ("red cell" N1 transfusion*) OR AB ("red cell" N1 transfusion*)	64
S4	TI (rbc N1 transfusion*) OR AB (rbc N1 transfusion*)	121
S3	TI ("red blood cell" N1 transfusion*) OR AB ("red blood cell" N1 transfusion*)	213
S2	TI ("erythrocyte transfusion" OR "erythrocyte transfusions") OR AB ("erythrocyte transfusion" OR "erythrocyte transfusions")	16
S1	(MH "Blood Component Transfusion")	829

* The search was conducted using EBSCOhost on 28 May 2009
^ The records from each of these search statements were exported separately owing to technical difficulties experienced with EBSCOhost when processing this search statement – as a consequence there may be duplicated records in this number.

AMI: search conducted 11 June 2009

No.	Query	Results
#14	((SUBJECT=(blood transfusion)) OR (TI=("lymphocyte transfusion" OR "thrombocytic transfusion") OR AB=("lymphocyte transfusion" OR "thrombocytic transfusion")) OR (TI=("erythrocyte transfusion" OR "leukocyte transfusion") OR AB=("erythrocyte transfusion" OR "leukocyte transfusion")) OR (TI=("replacement transfusion" OR "substitution transfusion") OR AB=("replacement transfusion" OR "substitution transfusion")) OR (TI=("exchange transfusion" OR autotransfusion) OR AB=("exchange transfusion" OR autotransfusion)) OR (TI=("transfusion blood" OR "transfusion therapy") OR AB=("transfusion blood" OR "transfusion therapy")) OR (TI=(multitransfusion OR polytransfusion OR retransfusion) OR AB=(multitransfusion OR polytransfusion OR retransfusion)) OR (TI=(haemotherapy OR haematherapy OR haematotherapy) OR AB=(haemotherapy OR haematherapy OR haematotherapy)) OR (TI=(hemotherapy OR hematherapy OR hematotherapy) OR AB=(hemotherapy OR hematherapy OR hematotherapy)) OR (TI=("blood replacement" OR "blood retransfusion") OR AB=("blood replacement" OR "blood retransfusion")) OR (TI=("blood exchange" OR "blood infusion") OR AB=("blood exchange" OR "blood infusion")) OR (TI=(blood %1 transfusion*) OR AB=(blood %1 transfusion*)) OR ((MH_PHRASE="Blood Transfusion, Intrauterine" OR MH_PHRASE="Platelet Transfusion" OR MH_PHRASE="Erythrocyte Transfusion" OR MH_PHRASE="Leukocyte Transfusion" OR MH_PHRASE="Blood Transfusion, Autologous" OR MH_PHRASE="Lymphocyte Transfusion" OR MH_PHRASE="Blood Transfusion" OR MH_PHRASE="Blood Component Transfusion" OR MH_PHRASE="Exchange Transfusion, Whole Blood" OR MH_PHRASE="Plasma Exchange")))	512
#13	SUBJECT=(blood transfusion)	354
#12	TI=("lymphocyte transfusion" OR "thrombocytic transfusion") OR AB=("lymphocyte transfusion" OR "thrombocytic transfusion")	0
#11	TI=("erythrocyte transfusion" OR "leukocyte transfusion") OR AB=("erythrocyte transfusion" OR "leukocyte transfusion")	0
#10	TI=("replacement transfusion" OR "substitution transfusion") OR AB=("replacement transfusion" OR "substitution transfusion")	0
#9	TI=("exchange transfusion" OR autotransfusion) OR AB=("exchange transfusion" OR autotransfusion)	18
#8	TI=("transfusion blood" OR "transfusion therapy") OR AB=("transfusion blood" OR "transfusion therapy")	5
#7	TI=(multitransfusion OR polytransfusion OR retransfusion) OR AB=(multitransfusion OR polytransfusion OR retransfusion)	0
#6	TI=(haemotherapy OR haematherapy OR haematotherapy) OR AB=(haemotherapy OR haematherapy OR haematotherapy)	0
#5	TI=(hemotherapy OR hematherapy OR hematotherapy) OR AB=(hemotherapy OR hematherapy OR hematotherapy)	0
#4	TI=("blood replacement" OR "blood retransfusion") OR AB=("blood replacement" OR "blood retransfusion")	1
#3	TI=("blood exchange" OR "blood infusion") OR AB=("blood exchange" OR "blood infusion")	0
#2	TI=(blood %1 transfusion*) OR AB=(blood %1 transfusion*)	194

No.	Query	Results
#1	(MH_PHRASE="Blood Transfusion, Intrauterine" OR MH_PHRASE="Platelet Transfusion" OR MH_PHRASE="Erythrocyte Transfusion" OR MH_PHRASE="Leukocyte Transfusion" OR MH_PHRASE="Blood Transfusion, Autologous" OR MH_PHRASE="Lymphocyte Transfusion" OR MH_PHRASE="Blood Transfusion" OR MH_PHRASE="Blood Component Transfusion" OR MH_PHRASE="Exchange Transfusion, Whole Blood" OR MH_PHRASE="Plasma Exchange")	263

* The search was conducted using Informit online platform on 11 June 2009

A6 Literature searches, Question 6

In patients undergoing surgery, what is the effect of non-transfusion interventions to increase haemoglobin concentration on morbidity, mortality and need for RBC blood transfusion?

EMBASE.com: search conducted 27 May 2009

No.	Query	Results
#1	'anemia'/exp OR anaemia:ab,ti OR anemia:ab,ti	170,860
#2	'perioperative period'/exp OR 'perioperative nursing'/exp OR 'perioperative complication'/exp OR 'preoperative period'/exp OR 'preoperative complication'/exp OR 'intraoperative period'/exp OR perioperative:ab,ti OR 'peri operative':ab,ti OR preoperative:ab,ti OR 'pre operative':ab,ti OR intraoperative:ab,ti OR 'intra operative':ab,ti OR peroperative:ab,ti OR 'per operative':ab,ti OR 'postoperative period'/exp OR 'postoperative complication'/exp OR postoperative:ab,ti OR 'post operative':ab,ti	865,643
#3	'injury'/exp OR injur*:ab,ti OR trauma*:ab,ti	1,263,038
#4	'shock'/exp OR shock:ab,ti OR 'cardiovascular collapse':ab,ti OR 'circulatory collapse':ab,ti	135,548
#5	'blood transfusion'/exp OR ('bleeding'/exp AND 'transfusion'/exp) AND massive:ab,ti OR 'massive transfusion':ab,ti OR 'massive blood transfusion':ab,ti OR 'massive transfusion protocol':ab,ti OR ('massive' NEAR/3 'transfusion'):ab,ti OR ('massive' NEAR/3 'transfusions'):ab,ti OR 'massive infusion':ab,ti OR 'massively transfused':ab,ti OR 'massive bleeding':ab,ti OR 'massive haemorrhage':ab,ti OR 'massive hemorrhage':ab,ti	8,411
#6	'thorax surgery'/exp OR 'heart surgery'/exp OR 'cardiothoracic surgery':ab,ti OR 'chest surgery':ab,ti OR 'cardiothoracic patient':ab,ti OR 'cardiothoracic patients':ab,ti OR 'thoracic operation':ab,ti OR 'thoracic surgery':ab,ti OR thoracoplasty:ab,ti OR 'thoracic procedure':ab,ti OR 'thoracic procedures':ab,ti	285,419
#7	'surgery'/exp OR 'surgical ward'/exp OR 'surgical patient'/exp OR surgical:ab,ti OR surgery:ab,ti OR operation:ab,ti OR resection:ab,ti	2,728,593
#8	'orthopedic surgery'/exp OR 'orthopedic surgery':ab,ti OR 'orthopaedic surgery':ab,ti OR 'bone surgery':ab,ti OR orthopaedics:ab,ti OR orthopedics:ab,ti OR 'orthopedic patient':ab,ti OR 'orthopedic patients':ab,ti OR 'orthopaedic patient':ab,ti OR 'orthopaedic patients':ab,ti OR 'orthopedic operation':ab,ti OR 'orthopedic procedures':ab,ti OR 'orthopaedic operation':ab,ti OR 'orthopaedic procedures':ab,ti OR 'orthopedic procedure':ab,ti OR 'orthopaedic procedure':ab,ti	258,328
#9	'antianemic agent'/exp OR 'antianemic agent':ab,ti OR 'antianemic agents':ab,ti OR 'anti anemic agent':ab,ti OR 'anti anemic agents':ab,ti OR 'antianaemic agent':ab,ti OR 'antianaemic agents':ab,ti OR 'anti anaemic agent':ab,ti OR 'anti anaemic agents':ab,ti OR 'erythropoiesis stimulating agent':ab,ti OR 'hematinics':ab,ti OR 'erythropoiesis stimulating agents':ab,ti OR 'haematinics':ab,ti OR 'hematinic agent':ab,ti OR 'hematinic agents':ab,ti OR 'haematinic agent':ab,ti OR 'haematinic agents':ab,ti OR 'hematopoietic agent':ab,ti OR 'hematopoietic agents':ab,ti OR 'haematopoietic agent':ab,ti OR 'haematopoietic agents':ab,ti OR 'hemopoietic agent':ab,ti OR 'hemopoietic agents':ab,ti OR 'haemopoietic agent':ab,ti OR 'haemopoietic agents':ab,ti	61,198

No.	Query	Results
#10	'erythropoietin'/de OR 'recombinant erythropoietin'/de OR erthropoietin:tn,ab,ti OR 'erythropoiesis stimulating factor':tn,ab,ti OR 'erythropoietic factor':tn,ab,ti OR hematopoietin:tn,ab,ti OR hemopoietin:tn,ab,ti OR haematopoietin:tn,ab,ti OR haemopoietin:tn,ab,ti OR dynepo OR epoch OR epoconn OR epoetin OR epog?n OR epoietin:tn,ab,ti OR epoxitin:tn,ab,ti OR eprex:tn,ab,ti OR erantin:tn,ab,ti OR erypo:tn,ab,ti OR espo:tn,ab,ti OR exprex:tn,ab,ti OR globuren:tn,ab,ti OR hemax:tn,ab,ti OR marogen:tn,ab,ti OR neorecormon:tn,ab,ti OR procrit:tn,ab,ti OR recormon:tn,ab,ti OR recormone:tn,ab,ti OR 'krn 5702':tn,ab,ti OR krn5702:tn,ab,ti OR 'snb 5001':tn,ab,ti OR snb5001:tn,ab,ti OR 'tyb 5220':tn,ab,ti OR tyb5220:tn,ab,ti OR rhuepo:tn,ab,ti OR 'rhu epo':tn,ab,ti OR 'r hu epo':tn,ab,ti OR '11096 26 7':rn OR (113427:rn AND 24:rn AND 0:rn) OR '122312 54 3':rn OR '130455 76 4':rn	32,022
#11	'iron therapy'/de OR 'iron'/dd_dt OR 'iron'/dd_ad OR 'iron therapy':an,ab OR 'iron treatment':an,ab OR 'iron supplement':ab,ti OR 'iron supplements':ab,ti	9,262
#12	'folic acid'/de OR 'cyanocobalamin'/de OR 'ascorbic acid'/exp OR 'folic acid':tn,ab,ti OR folacin:tn,ab,ti OR folate:tn,ab,ti OR foldine:tn,ab,ti OR foliamin:tn,ab,ti OR folicet:tn,ab,ti OR 'folium acid':tn,ab,ti OR folsan:tn,ab,ti OR folvite:tn,ab,ti OR lafol:tn,ab,ti OR 'lactobacillus casei factor':tn,ab,ti OR 'mission prenatal':tn,ab,ti OR 'vitamin bc':tn,ab,ti OR 'vitamin m':tn,ab,ti OR 'pteroyl glutamate':tn,ab,ti OR 'pteroyl l glutamic acid':tn,ab,ti OR 'pteroyl monoglutamate':tn,ab,ti OR pteroylglutamate:tn,ab,ti OR 'pteroylglutamic acid':tn,ab,ti OR pteroylmonoglutamate:tn,ab,ti OR 'pteroylmonoglutamic acid':tn,ab,ti OR cyanobalamin:tn,ab,ti OR cobalamin:tn,ab,ti OR cobalamins:tn,ab,ti OR 'vitamin b12':tn,ab,ti OR 'vitamin b 12':tn,ab,ti OR berubigen:tn,ab,ti OR docibin:tn,ab,ti OR bevidox:tn,ab,ti OR ducobee:tn,ab,ti OR sytobex:ab,ti OR eritron:ab,ti OR 'ascorbic acid':tn,ab,ti OR 'cevitamic acid':tn,ab,ti OR 'vitamin c':tn,ab,ti OR ascorbate:tn,ab,ti OR 'magnesium ascorbicum':tn,ab,ti OR magnorbin:tn,ab,ti OR '59 30 3':rn OR '6484 89 5':rn OR '53570 76 6':rn OR '68 19 9':rn OR '8064 09 3':rn OR '134 03 2':rn OR '15421 15 5':rn OR '50 81 7':rn	107,291
#13	'erythrocyte transfusion'/exp OR 'erythrocyte transfusion':ab,ti OR 'erythrocyte transfusions':ab,ti OR 'red blood cell transfusion':ab,ti OR 'rbc transfusion':ab,ti OR 'red blood cell transfusions':ab,ti OR 'rbc transfusions':ab,ti OR 'red cell transfusion':ab,ti OR 'normocyte transfusion':ab,ti OR 'red cell transfusions':ab,ti OR 'normocyte transfusions':ab,ti OR 'red blood cell exchange':ab,ti OR 'rbc exchange':ab,ti OR ('red cell' NEAR/3 'exchange'):ab,ti OR ('red cells' NEAR/3 'exchange'):ab,ti	8,413
#14	'perioperative complication'/exp	451
#15	'preoperative period'/exp	135,378
#16	preoperative:ab,ti OR 'pre operative':ab,ti	140,998
#17	'adverse outcome'/exp OR 'outcome assessment'/exp OR 'morbidity'/exp OR 'mortality'/exp OR morbidity:ab,ti OR incidence:ab,ti OR prevalence:ab,ti OR occurrence:ab,ti OR mortality:ab,ti OR death:ab,ti OR survival:ab,ti	1,926,742
#18	'quality of life'/exp OR qol:ab,ti OR 'quality of life':ab,ti OR 'quality of wellbeing':ab,ti OR 'health related quality':ab,ti OR hrqol:ab,ti OR qaly*:ab,ti OR 'quality adjusted':ab,ti OR 'adjusted life':ab,ti	159,858

No.	Query	Results
#19	'blood component therapy'/exp AND ('dose response'/exp OR 'drug dose'/exp) OR 'fresh frozen plasma'/exp/dd_do OR 'recombinant erythropoietin'/exp/dd_do OR 'transfusion frequency':ab,ti OR ('frequency' NEAR/5 'transfusion'):ab,ti OR ('frequency' NEAR/5 'transfusions'):ab,ti OR 'transfusion rate':ab,ti OR 'transfusion rates':ab,ti OR ('rate' NEAR/5 'transfusion'):ab,ti OR ('rates' NEAR/5 'transfusion'):ab,ti OR 'transfusion requirement':ab,ti OR 'transfusion requirements':ab,ti OR 'transfusion indication':ab,ti OR 'transfusion indications':ab,ti OR ('indications' NEAR/5 'transfusion'):ab,ti OR ('indications' NEAR/5 'transfusions'):ab,ti OR ('indication' NEAR/5 'transfusion'):ab,ti OR ('indication' NEAR/5 'transfusions'):ab,ti OR 'transfusion interval':ab,ti OR 'transfusion intervals':ab,ti OR ('need' NEAR/3 'transfusion'):ab,ti OR ('need' NEAR/3 'transfusions'):ab,ti OR 'transfusion need':ab,ti OR 'transfusion needs':ab,ti OR ('dose' NEAR/3 'transfusion'):ab,ti OR ('dose' NEAR/3 'transfusions'):ab,ti OR ('dose' NEAR/3 'transfused'):ab,ti OR ('transfusions' NEAR/3 'dose'):ab,ti OR 'transfusion dose':ab,ti OR ('transfused' NEAR/3 'dose'):ab,ti OR 'platelet dose':ab,ti OR ('dose' NEAR/3 'platelets'):ab,ti OR (dose:ab,ti AND transfus*:ab,ti)	17,399
#20	'hemoglobin'/de OR 'hemoglobin determination'/de OR 'hemoglobin blood level'/de OR 'mean corpuscular volume'/de OR 'blood haemoglobin':ab,ti OR 'blood hemoglobin':ab,ti OR 'haemoglobin level':ab,ti OR 'hemoglobin level':ab,ti OR 'haemoglobin levels':ab,ti OR 'hemoglobin levels':ab,ti OR 'hb level':ab,ti OR 'hb levels':ab,ti OR 'haemoglobin determination':ab,ti OR 'hemoglobin determination':ab,ti OR 'hemoglobin assay':ab,ti OR 'haemoglobin assay':ab,ti OR 'hemoglobin estimation':ab,ti OR 'haemoglobin estimation':ab,ti OR 'hb determination':ab,ti OR 'hb estimation':ab,ti OR 'hb assay':ab,ti OR 'hemoglobin content':ab,ti OR 'hemoglobin concentration':ab,ti OR 'haemoglobin content':ab,ti OR 'haemoglobin concentration':ab,ti OR 'hb content':ab,ti OR 'hb concentration':ab,ti OR hemoglobinometry:ab,ti OR haemoglobinometry:ab,ti OR 'plasma haemoglobin':ab,ti OR 'plasma hemoglobin':ab,ti OR 'serum haemoglobin':ab,ti OR 'serum hemoglobin':ab,ti OR 'mean corpuscular haemoglobin':ab,ti OR 'mean corpuscular hemoglobin':ab,ti OR 'mean cell haemoglobin':ab,ti OR 'mean cell hemoglobin':ab,ti OR 'erythrocyte indices':ab,ti OR 'erythrocyte index':ab,ti OR 'erythrocyte indexes':ab,ti OR 'red cell indices':ab,ti OR 'red cell index':ab,ti OR 'red cell indexes':ab,ti OR 'rbc indices':ab,ti OR 'rbc index':ab,ti OR 'rbc indexes':ab,ti	86,870
#21	'health economics'/exp OR 'economic aspect'/exp OR 'economics'/exp OR 'finance'/exp OR 'biomedical technology assessment'/exp OR 'economic evaluation'/exp OR 'health care cost'/exp OR economic*:ab,ti OR pharmacoeconomic*:ab,ti OR cost*:ab,ti OR price*:ab,ti OR pricing:ab,ti OR 'burden of illness':ab,ti OR 'value money':ab,ti OR (resource*:ab,ti AND utili*:ab,ti) OR 'technology assessment':ab,ti OR 'technology assessments':ab,ti OR 'technology appraisal':ab,ti OR 'technology appraisals':ab,ti	996,491
#22	'hospitalization'/exp OR 'length of stay'/exp OR hospitaliz*:ab,ti OR hospitalis*:ab,ti OR ('length' NEAR/3 'stay'):ab,ti OR 'hospital stay':ab,ti	244,661
#23	'intensive care unit'/exp OR 'intensive care unit':ab,ti OR icu:ab,ti OR 'intensive care units':ab,ti OR 'close attention unit':ab,ti OR 'close attention units':ab,ti OR 'intensive care department':ab,ti OR 'intensive care departments':ab,ti OR 'special care unit':ab,ti OR 'special care units':ab,ti OR 'critical care unit':ab,ti OR 'critical care units':ab,ti	76,701
#24	'hospital admission'/exp OR 'hospital readmission'/exp OR 'hospital admission':ab,ti OR 'hospital admittance':ab,ti OR 'patient admission':ab,ti OR readmission:ab,ti OR rehospitalization:ab,ti OR rehospitalisation:ab,ti	77,581
#25	#2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8	3,685,139
#26	#1 AND #25	38,858
#27	#14 OR #15 OR #16	228,489

No.	Query	Results
#28	#13 AND #27	506
#29	#9 OR #10 OR #11 OR #12 OR #28	171,905
#30	#26 AND #29	5,622
#31	#17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24	3,138,584
#32	#30 AND #31	3,301

Cochrane Library Database: search conducted 21 May 2009

No.	Query	Results
#1	MeSH descriptor Erythrocyte Transfusion explode all trees	346
#2	"erythrocyte transfusion" OR "erythrocyte transfusions"	432
#3	("red blood cell" OR rbc) NEAR/1 transfusion*	142
#4	"red cell" NEAR/1 transfusion*	3
#5	"normocyte transfusion" OR "normocyte transfusions"	0
#6	("red blood cell" OR rbc) NEAR/1 exchange	2
#7	("red cell" OR "red cells") NEAR/3 exchange	3
#8	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7	1916
#9	MeSH descriptor Anemia explode all trees	2505
#10	(anaemia OR anemia)	5050
#11	#9 or #10	1473
#12	#8 AND #11	1296
#13	MeSH descriptor Perioperative Care explode all trees	4254
#14	MeSH descriptor Preoperative Care explode all trees	4098
#15	MeSH descriptor Postoperative Complications explode all trees	21418
#16	MeSH descriptor Postoperative Period explode all trees	3483
#17	MeSH descriptor Intraoperative Complications explode all trees	2476
#18	MeSH descriptor Intraoperative Period explode all trees	919
#19	(perioperative OR "peri operative")	5196

No.	Query	Results
#20	(preoperative OR "pre operative")	11093
#21	(intraoperative OR "intra operative")	8039
#22	(peroperative OR "per operative")	474
#23	(postoperative OR "post operative")	40236
#24	#13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23	1268
#25	#12 AND #24	550
#26	MeSH descriptor Wounds and Injuries explode all trees	10953
#27	(injur* OR trauma*)	20750
#28	#26 OR #27	499
#29	#12 AND #28	417
#30	MeSH descriptor Shock explode all trees	930
#31	(shock OR "cardiovascular collapse" OR "circulatory collapse")	3179
#32	#30 OR #31	381
#33	#12 AND #32	316
#34	MeSH descriptor Blood Transfusion explode all trees	2628
#35	(massive)	599
#36	#34 AND #35	265
#37	(massive NEAR/3 transfusion*)	20
#38	"massive infusion" OR "massively transfused"	3
#39	(massive NEAR/1 (bleeding OR haemorrhage OR hemorrhage))	47
#40	#36 OR #37 OR #38 OR #39	284
#41	#12 AND #40	203
#42	MeSH descriptor Thoracic Surgical Procedures explode all trees	10297
#43	MeSH descriptor Thoracic Surgery explode all trees	130
#44	MeSH descriptor Cardiovascular Surgical Procedures explode all trees	10930
#45	"cardiothoracic surgery" OR (chest NEAR/1 surgery)	675

No.	Query	Results
#46	(cardiothoracic NEAR/1 patient*)	4
#47	"thoracic operation" OR "thoracic surgery" OR thoracoplasty	2131
#48	(thoracic NEAR/1 procedure*)	16
#49	#42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48	253
#50	#12 AND #49	127
#51	MeSH descriptor Surgical Procedures, Operative explode all trees	68578
#52	MeSH descriptor General Surgery explode all trees	167
#53	MeSH descriptor Surgery Department, Hospital explode all trees	68
#54	(surgical OR surgery OR operation OR resection)	91783
#55	#51 OR #52 OR #53 OR #54	121
#56	#12 AND #55	87
#57	MeSH descriptor Orthopedic Procedures explode all trees	5335
#58	MeSH descriptor Orthopedics explode all trees	272
#59	"orthopedic surgery" OR "orthopaedic surgery"	2339
#60	"bone surgery" OR orthopaedics or orthopedics	7975
#61	(orthopedic OR orthopaedic) NEAR/1 patient*	223
#62	"orthopedic operation" OR "orthopaedic operation"	6
#63	(orthopedic OR orthopaedic) NEAR/1 procedure*	638
#64	#57 OR #58 OR #59 OR #60 OR #61 OR #62 OR #63	98
#65	#12 AND #64	63
#66	#25 OR #29 OR #33 OR #41 OR #50 OR #56 OR #65	556
#67	MeSH descriptor Hematinics explode all trees	1418
#68	"antianemic agent" OR "antianemic agents"	9
#69	"anti anemic agent" OR "anti anemic agents"	0
#70	"antianaemic agent" OR "antianaemic agents"	0
#71	"anti anaemic agent" OR "anti anaemic agents"	0

No.	Query	Results
#72	"erythropoiesis stimulating agent" OR "hematinics"	394
#73	"erythropoiesis stimulating agents" OR "haematinics"	34
#74	"hematinic agent" OR "hematinic agents"	0
#75	"haematinic agent" OR "haematinic agents"	0
#76	"hematopoietic agent" OR "hematopoietic agents"	2
#77	"haematopoietic agent" OR "haematopoietic agents"	0
#78	"hemopoietic agent" OR "hemopoietic agents"	0
#79	"haemopoietic agent" OR "haemopoietic agents"	0
#80	#67 OR #68 OR #69 OR #70 OR #71 OR #72 OR #73 OR #74 OR #75 OR #76 OR #77 OR #78 OR #79	76
#81	#66 AND #80	40
#82	MeSH descriptor Erythropoietin explode all trees	1234
#83	(erthropoietin OR "erythropoiesis stimulating factor")	4
#84	"erythropoietic NEAR/1 factor"	0
#85	(hematopoietin OR hemopoietin)	2
#86	(haematopoietin OR haemopoietin)	1
#87	(dynepo OR epoch OR epoconn OR epoetin OR epog?n)	789
#88	(epoietin OR epoxitin OR eprex OR erantin OR erypo)	55
#89	(espo OR exprex OR globuren OR hemax OR marogen)	35
#90	(neorecormon OR procrit OR recormon OR recormone)	45
#91	"krn 5702" OR krn5702 OR "snb 5001" OR snb5001	10
#92	"tyb 5220" OR tyb5220	3
#93	(rHuEPO OR "rHu EPO" OR "r Hu EPO")	381
#94	#82 OR #83 OR #84 OR #85 OR #86 OR #87 OR #88 OR #89 OR #90 OR #91 OR #92 OR #93	59
#95	#66 AND #94	23
#96	MeSH descriptor Iron explode all trees with qualifier: TU	311

No.	Query	Results
#97	MeSH descriptor Iron explode all trees with qualifier: AD	448
#98	"iron therapy" OR "iron treatment"	320
#99	"iron supplement" OR "iron supplements"	194
#100	#96 OR #97 OR #98 OR #99	29
#101	#66 AND #100	16
#102	MeSH descriptor Folic Acid explode all trees	1615
#103	MeSH descriptor Vitamin B 12 explode all trees	439
#104	MeSH descriptor Ascorbic Acid explode all trees	1185
#105	MeSH descriptor Anencephaly explode all trees	8
#106	(folicet OR "folium acid" OR folsan OR folvite OR lafol)	5
#107	"lactobacillus casei factor" OR "mission prenatal"	0
#108	"vitamin bc" OR "vitamin m"	0
#109	"pteroyl glutamate" OR "pteroyl l glutamic acid"	0
#110	"pteroyl monoglutamate" OR pteroylglutamate	0
#111	"pteroylglutamic acid" OR pteroylmonoglutamate	5
#112	"pteroylmonoglutamic acid"	0
#113	(cyanobalamin OR cobalamin OR cobalamins)	89
#114	"vitamin B12" OR "vitamin b 12"	792
#115	(Berubigen OR Docibin OR Bevidox OR Ducobee)	0
#116	(Sytobex OR Eritron)	0
#117	"ascorbic acid" OR "cevitamic acid" OR "vitamin C"	2183
#118	(ascorbate OR "Magnesium Ascorbicum" OR Magnorbin)	151
#119	#102 OR #103 OR #104 OR #105 OR #106 OR #107 OR #108 OR #109 OR #110 OR #111 OR #112 OR #113 OR #114 OR #115 OR #116 OR #117 OR #118	46
#120	#66 AND #119	9
#121	#14 OR #20	1116
#122	#8 AND #121	9

No.	Query	Results
#123	#66 AND #122	9
#124	#81 OR #95 OR #101 OR 120 OR #123	14575
#125	MeSH descriptor Morbidity explode all trees	8475
#126	MeSH descriptor Mortality explode all trees	7946
#127	(morbidity OR incidence OR prevalence OR occurrence)	62784
#128	(mortality OR death OR survival)	55325
#129	#125 OR #126 OR #127 OR #128	11
#130	#124 AND #129	9
#131	MeSH descriptor Quality of Life explode all trees	9425
#132	MeSH descriptor Quality-Adjusted Life Years explode all trees	2062
#133	(qol OR "quality of life" OR "quality of wellbeing")	21521
#134	"health related quality" or hrqol	2898
#135	(qaly* or "quality adjusted" or "adjusted life")	3802
#136	#131 OR #132 OR #133 OR #134 OR #135	11
#137	#124 AND #136	8
#138	MeSH descriptor Blood Component Transfusion explode all trees with qualifier: MT	99
#139	(frequency NEAR/5 transfusion*)	84
#140	(rate* NEAR/5 transfusion*)	324
#141	"transfusion requirement" OR "transfusion requirements"	949
#142	(indication* NEAR/5 transfusion*)	45
#143	"transfusion interval" OR "transfusion intervals"	13
#144	(need NEAR/3 transfusion*) OR "transfusion needs"	623
#145	(dose NEAR/3 transfus*)	86
#146	"platelet dose" OR (dose NEAR/3 platelets)	185
#147	(dose and transfus*):ti	72
#148	#138 or #139 or #140 or #141 OR #142 OR #143 OR #144 OR #145 OR #146 OR #147	16

No.	Query	Results
#149	#124 AND #148	2
#150	MeSH descriptor Hemoglobins explode all trees	4487
#151	MeSH descriptor Hemoglobinometry explode all trees	152
#152	MeSH descriptor Erythrocyte Indices explode all trees	110
#153	"blood haemoglobin" OR "blood hemoglobin"	241
#154	(haemoglobin OR hemoglobin) NEAR/1 level*	1228
#155	"hb level" OR "hb levels"	236
#156	"haemoglobin determination" OR "hemoglobin determination"	120
#157	"hemoglobin assay" OR "haemoglobin assay"	4
#158	"hemoglobin estimation" OR "haemoglobin estimation"	5
#159	"hb determination" OR "hb estimation" OR "hb assay"	2
#160	(hemoglobin NEAR/1 (content OR concentration))	904
#161	(haemoglobin NEAR/1 (content OR concentration))	904
#162	"hb content" OR "hb concentration"	110
#163	(hemoglobinometry OR haemoglobinometry)	166
#164	"plasma haemoglobin" OR "plasma hemoglobin"	65
#165	"serum haemoglobin" OR "serum hemoglobin"	47
#166	"mean corpuscular volume" OR mcv OR mch OR mchc	350
#167	"mean corpuscular haemoglobin" OR "mean corpuscular hemoglobin"	41
#168	"Mean Cell" NEAR/1 (Haemoglobin OR Hemoglobin)	2
#169	"erythrocyte indices" OR "Erythrocyte Index" OR "Erythrocyte Indexes"	121
#170	(red NEAR/1 ("cell indices" OR "Cell Index" OR "Cell Indexes"))	14
#171	"rbc indices" OR "RBC Index" OR "RBC Indexes"	2
#172	(#150 OR #151 OR #152 OR #153 OR #154 OR #155 OR #156 OR #157 OR #158 OR #159 OR #160 OR #161 OR #162 OR #163 OR #164 OR #165 OR #166 OR #167 OR #168 OR #169 OR #170 OR #171)	6494
#173	(#124 AND #172)	310

No.	Query	Results
#174	MeSH descriptor Costs and Cost Analysis explode all trees	26772
#175	MeSH descriptor Economics explode all trees	28552
#176	MeSH descriptor Models, Economic explode all trees	1853
#177	MeSH descriptor Value of Life explode all trees	274
#178	MeSH descriptor Utilization Review explode all trees	420
#179	MeSH descriptor Delivery of Health Care explode all trees with qualifiers: EM,UT	762
#180	(economic* or pharmacoeconomic*)	37332
#181	(cost* or price* or pricing)	48938
#182	(resource* near utili*)	1537
#183	"burden of illness" or (value NEAR/1 money)	87
#184	#174 OR #175 OR #176 OR #177 OR #178 OR #179 OR #180 OR #181 OR #182 OR #183	13
#185	#124 AND #184	0
#186	MeSH descriptor Hospitalization explode all trees	10690
#187	MeSH descriptor Child, Hospitalized explode all trees	82
#188	(hospitaliz* OR hospitalis*)	16298
#189	(length NEAR/3 stay) OR "hospital stay"	11735
#190	#186 OR #187 OR #188 OR #189	3
#191	#124 AND #190	0
#192	MeSH descriptor Intensive Care Units explode all trees	1978
#193	"intensive care unit" OR icu OR "intensive care units"	6712
#194	"close attention unit" OR "close attention units"	0
#195	"intensive care department" OR "intensive care departments"	56
#196	"special care unit" OR "special care units"	63
#197	"critical care unit" OR "critical care units"	108
#198	#192 OR #193 OR #194 OR #195 OR #196 OR #197	1
#199	#124 AND #198	0

No.	Query	Results
#200	MeSH descriptor Patient Admission explode all trees	604
#201	MeSH descriptor Patient Readmission explode all trees	593
#202	"hospital admission" OR "hospital admittance"	1727
#203	"patient admission" OR readmission	2327
#204	(rehospitalization OR rehospitalisation)	504
#205	#200 OR #201 OR #202 OR #203 OR #204	19
#206	#124 AND #205	0
#207	#130 OR #137 OR #149 OR #173 OR #185 OR #191 OR #199 OR #206	15

PreMedline: search conducted 28 May 2009

No.	Query	Result
1	"erythrocyte transfusion"[tw] OR "erythrocyte transfusions"[tw]	
2	("red blood cell"[tw] OR rbc[tw]) AND transfusion*[tw]	
3	"red cell"[tw] AND transfusion*[tw]	
4	"normocyte transfusion"[tw] OR "normocyte transfusions"[tw]	
5	("red blood cell[tw] OR rbc[tw]) AND exchange	
6	("red cell"[tw] OR "red cells"[tw]) AND exchange[tw]	
7	#1 OR #2 OR #3 OR #4 OR #5 OR #6	
8	anaemia[tw] OR anemia [tw]	
9	#7 AND #8	
10	perioperative[tw] OR "peri operative"[tw]	
11	preoperative[tw] OR "pre operative"[tw]	
12	intraoperative[tw] OR "intra operative"[tw]	
13	peroperative[tw] OR "per operative"[tw]	
14	postoperative[tw] OR "post operative"[tw]	
15	#10 OR #11 OR #12 OR #13 OR #14	
16	#9 AND #15	
17	injur*[tw] OR trauma*[tw]	
18	#9 AND #17	
19	shock[tw] OR "cardiovascular collapse"[tw] OR "circulatory collapse"[tw]	
20	#9 AND #19	
21	massive[tw] AND transfusion*[tw]	

No.	Query	Result
22	"massive infusion"[tw] OR "massively transfused"[tw]	
23	massive[tw] AND bleeding[tw]	
24	massive[tw] AND hemorrhage[tw]	
25	massive[tw] AND haemorrhage[tw]	
26	#21 OR #22 OR #23 OR #24 OR #25	
27	#9 AND #26	
28	"cardiothoracic surgery"[tw] OR (chest[tw] AND surgery[tw])	
29	cardiothoracic[tw] AND patient*[tw]	
30	"thoracic operation"[tw] OR "thoracic surgery"[tw] OR thoracoplasty[tw]	
31	thoracic[tw] AND procedure*[tw]	
32	#28 OR #29 OR #30 OR #31	
33	#9 AND #32	
34	surgical[tw] OR surgery[tw] OR operation[tw] OR resection[tw]	
35	#9 AND #34	
36	"orthopedic surgery"[tw] OR "orthopaedic surgery"[tw]	
37	"bone surgery"[tw] OR orthopaedics[tw] or orthopedics[tw]	
38	orthopedic[tw] AND patient*[tw]	
39	orthopaedic[tw] AND patient*[tw]	
40	"orthopedic operation"[tw] OR "orthopaedic operation"[tw]	
41	orthopaedic[tw] AND procedure*[tw]	
42	orthopedic[tw] AND procedure*[tw]	
43	#36 OR #37 OR #38 OR #39 OR #40	
44	#9 AND #43	
45	#16 OR #18 OR #20 OR #27 OR #33 OR #35 OR #44	
46	#45 NOT (medline[SB] OR oldmedline[sb])	
47	#45 AND in process[sb]	
48	#45 AND pubmednotmedline[sb]	
49	#46 OR #47 OR #48	314

Note: Search results for individual search strands (1 to 48) were not recorded.

CINAHL: search conducted 14 May 2009

No.	Query	Results
S133	s89 OR s103 OR s109 OR s128 OR s132	28
S132	s74 AND s131	11
S131	s11 AND s130	39
S130	s18 OR s24 OR s129	12618
S129	(MH "Preoperative Care+")	6893
S128	s74 AND s127	0
S127	s110 OR s111 OR s112 OR s113 OR s114 OR s119 OR s120 OR s121 OR s122 OR s123 OR s125 OR s126	6054
S126	TI (ascorbate OR "Magnesium Ascorbicum" OR Magnorbin) OR AB (ascorbate OR "Magnesium Ascorbicum" OR Magnorbin)	86
S125	TI ("ascorbic acid" OR "cevitamic acid" OR "vitamin C") OR AB ("ascorbic acid" OR "cevitamic acid" OR "vitamin C")	1323
S124	TI (Sytobex OR Eritron) OR AB (Sytobex OR Eritron)	0
S123	TI (Berubigen OR Docibin OR Bevidox OR Ducobee) OR AB (Berubigen OR Docibin OR Bevidox OR Ducobee)	1
S122	TI ("vitamin B12" OR "vitamin b 12") OR AB ("vitamin B12" OR "vitamin b 12")	719
S121	TI (cyanobalamin OR cobalamin OR cobalamins) OR AB (cyanobalamin OR cobalamin OR cobalamins)	123
S120	TI ("pteroylmonoglutamic acid") OR AB ("pteroylmonoglutamic acid")	1
S119	TI ("pteroylglutamic acid" OR pteroylmonoglutamate) OR AB ("pteroylglutamic acid" OR pteroylmonoglutamate)	3
S118	TI ("pteroyl monoglutamate" OR pteroylglutamate) OR AB ("pteroyl monoglutamate" OR pteroylglutamate)	0
S117	TI ("pteroyl glutamate" OR "pteroyl l glutamic acid") OR AB ("pteroyl glutamate" OR "pteroyl l glutamic acid")	0
S116	TI ("vitamin bc" OR "vitamin m") OR AB ("vitamin bc" OR "vitamin m")	0
S115	TI ("lactobacillus casei factor" OR "mission prenatal") OR AB ("lactobacillus casei factor" OR "mission prenatal")	0
S114	TI (folicet OR "folium acid" OR folsan OR folvite OR lafol) OR AB (folicet OR "folium acid" OR folsan OR folvite OR lafol)	2
S113	TI ("folic acid" OR folacin OR folate OR foldine OR foliamin) OR AB ("folic acid" OR folacin OR folate OR foldine OR foliamin)	2168

No.	Query	Results
S112	(MH "Ascorbic Acid")	1785
S111	(MH "Vitamin B12")	1181
S110	(MH "Folic Acid+")	2731
S109	s74 AND s108	3
S108	s104 OR s105 OR s106	429
S107	TI ("iron supplement" OR "iron supplements") OR AB "iron supplement" OR "iron supplements")	0
S106	TI ("iron therapy" OR "iron treatment") OR AB ("iron therapy" OR "iron treatment")	98
S105	(MH "Iron/AD")	219
S104	(MH "Iron/TU")	174
S103	s74 AND s102	20
S102	s90 OR s91 OR s95 OR s96 OR s97 OR s98 OR s101	1711
S101	TI (rHuEPO OR "rHu EPO" OR "r Hu EPO") OR AB (rHuEPO OR "rHu EPO" OR "r Hu EPO")	72
S100	TI ("tyb 5220" OR tyb5220) OR AB ("tyb 5220" OR tyb5220)	0
S99	TI ("krn 5702" OR krn5702 OR "snb 5001" OR snb5001) OR AB ("krn 5702" OR krn5702 OR "snb 5001" OR snb5001)	0
S98	TI (neorecormon OR procrit OR recormon OR recormone) OR AB (neorecormon OR procrit OR recormon OR recormone)	29
S97	TI (espo OR exprex OR globuren OR hemax OR marogen) OR AB (espo OR exprex OR globuren OR hemax OR marogen)	1
S96	TI (epoietin OR epoxitin OR eprex OR erantin OR erypo) OR AB (epoietin OR epoxitin OR eprex OR erantin OR erypo)	12
S95	TI (dynepo OR epoch OR epoconn OR epoetin OR epogen OR epogin) OR AB (dynepo OR epoch OR epoconn OR epoetin OR epogen OR epogin)	475
S94	TI (haematopoietin OR haemopoietin) OR AB (haematopoietin OR haemopoietin)	0
S93	TI (hematopoietin OR hemopoietin) OR AB (hematopoietin OR hemopoietin)	0
S92	TI ("erythropoietic N1 factor") OR AB ("erythropoietic N1 factor")	0
S91	TI (erthropoietin OR "erythropoiesis stimulating factor") OR AB (erthropoietin OR "erythropoiesis stimulating factor")	4
S90	(MH "Erythropoietin")	1592
S89	s74 AND s88	2

No.	Query	Results
S88	S75 OR S80 OR S81 OR S84 OR S85	262
S87	TI ("haemopoietic agent" OR "haemopoietic agents") OR AB ("haemopoietic agent" OR "haemopoietic agents")	0
S86	TI ("hemopoietic agent" OR "hemopoietic agents") OR AB ("hemopoietic agent" OR "hemopoietic agents")	0
S85	TI ("haematopoietic agent" OR "haematopoietic agents") OR AB ("haematopoietic agent" OR "haematopoietic agents")	1
S84	TI ("hematopoietic agent" OR "hematopoietic agents") OR AB ("hematopoietic agent" OR "hematopoietic agents")	2
S83	TI ("haematinic agent" OR "haematinic agents") OR AB ("haematinic agent" OR "haematinic agents")	0
S82	TI ("hematinic agent" OR "hematinic agents") OR AB ("hematinic agent" OR "hematinic agents")	0
S81	TI ("erythropoiesis stimulating agents" OR "haematinics") OR AB ("erythropoiesis stimulating agents" OR "haematinics")	92
S80	TI ("erythropoiesis stimulating agent" OR "hematinics") OR AB ("erythropoiesis stimulating agent" OR "hematinics")	25
S79	TI ("anti anemic agent" OR "anti anemic agents") OR AB ("anti anemic agent" OR "anti anemic agents")	0
S78	TI ("anti anaemic agent" OR "anti anaemic agents") OR AB ("anti anaemic agent" OR "anti anaemic agents")	0
S77	TI ("antianaemic agent" OR "antianaemic agents") OR AB ("antianaemic agent" OR "antianaemic agents")	0
S76	TI ("antianemic agent" OR "antianemic agents") OR AB ("antianemic agent" OR "antianemic agents")	0
S75	(MH "Hematinics")	175
S74	s29 OR s35 OR s39 OR s47 OR s56 OR s61 OR s73	76
S73	s15 and s72	6
S72	S62 or S63 or S64 or S65 or S66 OR S67 OR S68 OR S69 OR s70 OR s71	25842
S71	TI (orthopaedic N1 procedure*) or AB (orthopeadic N1 procedure*)	14
S70	TI (orthopedic N1 procedure*) or AB (orthopedic N1 procedure*)	115
S69	TI ("orthopedic operation" OR "orthopaedic operation") or AB ("orthopedic operation" OR "orthopaedic operation")	6
S68	TI (orthopaedic N1 patient*) or AB (orthopaedic N1 patient*)	355

No.	Query	Results
S67	TI (orthopedic N1 patient*) or AB (orthopedic N1 patient*)	245
S66	TI ("bone surgery" OR orthopaedics or orthopedics) or AB ("bone surgery" OR orthopaedics or orthopedics)	911
S65	TI ("orthopedic surgery" OR "orthopaedic surgery") or AB ("orthopedic surgery" OR "orthopaedic surgery")	790
S64	(MH "Orthopedic Nursing")	1422
S63	(MH "Orthopedics")	3289
S62	(MH "Orthopedic Surgery+")	21259
S61	s15 and s60	53
S60	S57 or S58 OR S59	170781
S59	TI (surgical OR surgery OR operation OR resection) or AB (surgical OR surgery OR operation OR resection)	69889
S58	(MH "Medical-Surgical Nursing")	2427
S57	(MH "Surgery, Operative+")	136639
S56	s15 and s55	13
S55	S48 or S49 or S50 or S51 or S52 or S53 OR S54	23228
S54	TI (thoracic N1 procedure*) or AB (thoracic N1 procedure*)	32
S53	TI ("thoracic operation" OR "thoracic surgery" OR thoracoplasty) or AB ("thoracic operation" OR "thoracic surgery" OR thoracoplasty)	253
S52	TI (cardiothoracic N1 patient*) or AB (cardiothoracic N1 patient*)	56
S51	TI ("cardiothoracic surgery" OR (chest N1 surgery)) or AB ("cardiothoracic surgery" OR (chest N1 surgery))	166
S50	(MH "Cardiovascular Nursing+")	2655
S49	(MH "Surgery, Cardiovascular+")	16879
S48	(MH "Thoracic Surgery+")	16901
S47	s15 and s46	8
S46	S42 or S43 or S44 OR S45	5121
S45	TI (massive N1 (bleeding OR haemorrhage OR hemorrhage)) or AB (massive N1 (bleeding OR haemorrhage OR hemorrhage))	5042
S44	TI ("massive infusion" OR "massively transfused") or AB ("massive infusion" OR "massively transfused")	10

No.	Query	Results
S43	TI (massive N3 transfusion*) or AB (massive N3 transfusion*)	87
S42	S40 and S41	74
S41	TI (massive) or AB (massive)	1888
S40	(MH "Blood Transfusion")	3427
S39	s15 and s38	4
S38	S36 or S37	6687
S37	TI (shock OR "cardiovascular collapse" OR "circulatory collapse") or AB (shock OR "cardiovascular collapse" OR "circulatory collapse")	5193
S36	(MH "Shock+")	3242
S35	S15 and S34	18
S34	S30 OR S31 or S32 OR S33	121361
S33	TI (injur* OR trauma*) or AB (injur* OR trauma*)	67640
S32	(MH "Trauma Nursing")	526
S31	(MH "Trauma+")	5857
S30	(MH "Wounds and Injuries+")	90837
S29	S15 AND S28	33
S28	S16 or S17 or S18 or S19 or S20 or S21 or S22 or S23 or S24 or S25 OR S26 OR S27	54117
S27	TI (postoperative OR "post operative") or AB (postoperative OR "post operative")	14379
S26	TI (peroperative OR "per operative") or AB (peroperative OR "per operative")	51
S25	TI (intraoperative OR "intra operative") or AB (intraoperative OR "intra operative")	2954
S24	TI (preoperative OR "pre operative") or AB (preoperative OR "pre operative")	7186
S23	TI (perioperative OR "peri operative") or AB (perioperative OR "peri operative")	5307
S22	(MH "Postoperative Period")	1898
S21	(MH "Postoperative Complications+")	21107
S20	(MH "Intraoperative Period")	364
S19	(MH "Intraoperative Complications+")	1795
S18	(MH "Preoperative Period+")	719
S17	(MH "Perioperative Nursing")	8787
S16	(MH "Perioperative Care+")	16023

No.	Query	Results
S15	S11 and S14	235
S14	S12 or S13	7549
S13	TI (anaemia OR anemia) or AB (anaemia OR anemia)	3956
S12	(MH "Anemia+")	6210
S11	s1 OR s2 OR s3 OR s4 OR s5 OR s7 OR s8 OR s9	1014
S10	TI ("red cells" N3 exchange) OR AB ("red cells" N3 exchange)	0
S9	TI ("red cell" N3 exchange) OR AB ("red cell" N3 exchange)	5
S8	TI (rbc N1 exchange) OR AB (rbc N1 exchange)	3
S7	TI ("red blood cell" N1 exchange) OR AB ("red blood cell" N1 exchange)	5
S6	TI ("normocyte transfusion" OR "normocyte transfusions") OR AB ("normocyte transfusion" OR "normocyte transfusions")	0
S5	TI ("red cell" N1 transfusion*) OR AB ("red cell" N1 transfusion*)	63
S4	TI (rbc N1 transfusion*) OR AB (rbc N1 transfusion*)	121
S3	TI ("red blood cell" N1 transfusion*) OR AB ("red blood cell" N1 transfusion*)	212
S2	TI ("erythrocyte transfusion" OR "erythrocyte transfusions") OR AB ("erythrocyte transfusion" OR "erythrocyte transfusions")	16
S1	(MH "Blood Component Transfusion")	820

* The search was conducted using EBSCOhost on 14 May 2009

AMI: search conducted 14 May 2009

No.	Query	Results
#13	((((SUBJECT=(anemia)) OR (TI=(anaemia OR anemia) OR AB=(anaemia OR anemia)) OR ((MH_PHRASE="Anemia" OR MH_PHRASE="Anemia, Hemolytic" OR MH_PHRASE="Anemia, Hemolytic, Congenital" OR MH_PHRASE="Anemia, Aplastic" OR MH_PHRASE="Anemia, Myelophthisic" OR MH_PHRASE="Anemia, Iron-Deficiency" OR MH_PHRASE="Anemia, Neonatal" OR MH_PHRASE="Anemia, Sideroblastic" OR MH_PHRASE="Anemia, Hypoplastic, Congenital" OR MH_PHRASE="Anemia, Megaloblastic" OR MH_PHRASE="Anemia, Refractory" OR MH_PHRASE="Anemia, Macrocytic" OR MH_PHRASE="Anemia, Dyserythropoietic, Congenital" OR MH_PHRASE="Anemia, Diamond-Blackfan" OR MH_PHRASE="Anemia, Pernicious" OR MH_PHRASE="Anemia, Hemolytic, Congenital Nonspherocytic" OR MH_PHRASE="Fanconi Anemia" OR MH_PHRASE="Anemia, Sickle Cell" OR MH_PHRASE="Anemia, Hemolytic, Autoimmune" OR MH_PHRASE="Anemia, Hypochromic" OR MH_PHRASE="Anemia, Refractory, with Excess of Blasts")))) AND (((TI=(("red cell" OR "red cells") %3 exchange) OR AB=(("red cell" OR "red cells") %3 exchange)) OR (TI=(("red blood cell" OR rbc) %1 exchange) OR AB=(("red blood cell" OR rbc) %1 exchange)) OR (TI=("normocyte transfusion" OR "normocyte transfusions") OR AB=("normocyte transfusion" OR "normocyte transfusions")) OR (TI=("red cell" %1 transfusion*) OR AB=("red cell" %1 transfusion*)) OR (TI=(("red blood cell" OR rbc) %1 transfusion*) OR AB=(("red blood cell" OR rbc) %1 transfusion*)) OR (TI=("erythrocyte transfusion" OR "erythrocyte transfusions") OR AB=("erythrocyte transfusion" OR "erythrocyte transfusions")) OR ((MH_PHRASE="Erythrocyte Transfusion")))))	41
#12	((SUBJECT=(anemia)) OR (TI=(anaemia OR anemia) OR AB=(anaemia OR anemia)) OR ((MH_PHRASE="Anemia" OR MH_PHRASE="Anemia, Hemolytic" OR MH_PHRASE="Anemia, Hemolytic, Congenital" OR MH_PHRASE="Anemia, Aplastic" OR MH_PHRASE="Anemia, Myelophthisic" OR MH_PHRASE="Anemia, Iron-Deficiency" OR MH_PHRASE="Anemia, Neonatal" OR MH_PHRASE="Anemia, Sideroblastic" OR MH_PHRASE="Anemia, Hypoplastic, Congenital" OR MH_PHRASE="Anemia, Megaloblastic" OR MH_PHRASE="Anemia, Refractory" OR MH_PHRASE="Anemia, Macrocytic" OR MH_PHRASE="Anemia, Dyserythropoietic, Congenital" OR MH_PHRASE="Anemia, Diamond-Blackfan" OR MH_PHRASE="Anemia, Pernicious" OR MH_PHRASE="Anemia, Hemolytic, Congenital Nonspherocytic" OR MH_PHRASE="Fanconi Anemia" OR MH_PHRASE="Anemia, Sickle Cell" OR MH_PHRASE="Anemia, Hemolytic, Autoimmune" OR MH_PHRASE="Anemia, Hypochromic" OR MH_PHRASE="Anemia, Refractory, with Excess of Blasts")))	594
#11	SUBJECT=(anemia)	437
#10	TI=(anaemia OR anemia) OR AB=(anaemia OR anemia)	393
#9	(MH_PHRASE="Anemia" OR MH_PHRASE="Anemia, Hemolytic" OR MH_PHRASE="Anemia, Hemolytic, Congenital" OR MH_PHRASE="Anemia, Aplastic" OR MH_PHRASE="Anemia, Myelophthisic" OR MH_PHRASE="Anemia, Iron-Deficiency" OR MH_PHRASE="Anemia, Neonatal" OR MH_PHRASE="Anemia, Sideroblastic" OR MH_PHRASE="Anemia, Hypoplastic, Congenital" OR MH_PHRASE="Anemia, Megaloblastic" OR MH_PHRASE="Anemia, Refractory" OR MH_PHRASE="Anemia, Macrocytic" OR MH_PHRASE="Anemia, Dyserythropoietic, Congenital" OR MH_PHRASE="Anemia, Diamond-Blackfan" OR MH_PHRASE="Anemia, Pernicious" OR MH_PHRASE="Anemia, Hemolytic, Congenital Nonspherocytic" OR MH_PHRASE="Fanconi Anemia" OR MH_PHRASE="Anemia, Sickle Cell" OR MH_PHRASE="Anemia, Hemolytic, Autoimmune" OR MH_PHRASE="Anemia, Hypochromic" OR MH_PHRASE="Anemia, Refractory, with Excess of Blasts")	34

No.	Query	Results
#8	((TI=(("red cell" OR "red cells") %3 exchange) OR AB=(("red cell" OR "red cells") %3 exchange)) OR (TI=(("red blood cell" OR rbc) %1 exchange) OR AB=(("red blood cell" OR rbc) %1 exchange)) OR (TI=("normocyte transfusion" OR "normocyte transfusions") OR AB=("normocyte transfusion" OR "normocyte transfusions")) OR (TI=("red cell" %1 transfusion*) OR AB=("red cell" %1 transfusion*)) OR (TI=(("red blood cell" OR rbc) %1 transfusion*) OR AB=(("red blood cell" OR rbc) %1 transfusion*)) OR (TI=("erythrocyte transfusion" OR "erythrocyte transfusions") OR AB=("erythrocyte transfusion" OR "erythrocyte transfusions")) OR ((MH_PHRASE="Erythrocyte Transfusion")))	43
#7	TI=(("red cell" OR "red cells") %3 exchange) OR AB=(("red cell" OR "red cells") %3 exchange)	2
#6	TI=(("red blood cell" OR rbc) %1 exchange) OR AB=(("red blood cell" OR rbc) %1 exchange)	0
#5	TI=("normocyte transfusion" OR "normocyte transfusions") OR AB=("normocyte transfusion" OR "normocyte transfusions")	0
#4	TI=("red cell" %1 transfusion*) OR AB=("red cell" %1 transfusion*)	13
#3	TI=(("red blood cell" OR rbc) %1 transfusion*) OR AB=(("red blood cell" OR rbc) %1 transfusion*)	11
#2	TI=("erythrocyte transfusion" OR "erythrocyte transfusions") OR AB=("erythrocyte transfusion" OR "erythrocyte transfusions")	1
#1	(MH_PHRASE="Erythrocyte Transfusion")	24

* The search was conducted using Informit online platform on 14 May 2009

A7 Literature searches, Question 7

In patients undergoing surgery, what is the effect of recombinant activated factor VII (rFVIIa) (prophylaxis or treatment) on morbidity, mortality and transfusion rate?

EMBASE.com: search conducted 24 June 2009

ID	Query	Results
#1	'recombinant blood clotting factor 7a'/exp	2,756
#2	'blood clotting factor 7a'/exp	1,850
#3	'recombinant protein'/exp	189,913
#4	#2 AND #3	465
#5	'recombinant fviia':de	170
#6	'nn 1731':de	12
#7	'recombinant activated factor vii':ab,ti,tn	791
#8	'recombinant *2 viia':ab,ti,tn OR 'recombinant *2 fviia':ab,ti,tn	1,133
#9	'recombinant f viia':ab,ti,tn	3
#10	rfviia:ab,ti,tn OR 'r fviia':ab,ti,tn OR 'r f viia':ab,ti,tn OR rf7a:ab,ti,tn	1,070
#11	'eptacog alfa':ab,ti,tn OR niastase:ab,ti,tn OR 'novo seven':ab,ti,tn OR novoseven:ab,ti,tn	1,272
#12	'nn 1731':ab,ti,tn OR nn1731:ab,ti,tn	12
#13	'blood clotting factor viia':ab,ti,tn OR 'coagulation factor viia':ab,ti,tn	133
#14	'activated *2 factor vii':ab,ti,tn OR 'activated *2 fvii':ab,ti,tn OR acset:ab,ti,tn	1,301
#15	'activated *2 factor 7':ab,ti,tn OR 'activated *2 f7':ab,ti,tn	2
#16	'98982 74 2':rn	1,850
#17	#13 OR #14 OR #15 OR #16	2,949
#18	recombinant:ab,ti	166,319
#19	#17 AND #18	1,275
#20	#1 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #19	3,550
#21	(('perioperative period'/exp) OR ('perioperative nursing'/exp) OR ('perioperative complication'/exp) OR ('preoperative period'/exp) OR ('preoperative complication'/exp) OR ('intraoperative period'/exp) OR (perioperative:ab,ti OR 'peri operative':ab,ti) OR (preoperative:ab,ti OR 'pre operative':ab,ti) OR (intraoperative:ab,ti OR 'intra operative':ab,ti) OR (peroperative:ab,ti OR 'per operative':ab,ti)) OR ('postoperative period'/exp) OR ('postoperative complication'/exp) OR (postoperative:ab,ti OR 'post operative':ab,ti)	869,935
#22	('injury'/exp) OR (injur*:ab,ti OR trauma*:ab,ti)	1,268,915
#23	('shock'/exp) OR (shock:ab,ti OR 'cardiovascular collapse':ab,ti OR 'circulatory collapse':ab,ti)	136,163
#24	((('blood transfusion'/exp) OR (('bleeding'/exp) AND ('transfusion'/exp))) AND (massive:ab,ti)) OR ('massive transfusion':ab,ti) OR ('massive blood transfusion':ab,ti) OR ('massive transfusion protocol':ab,ti) OR ('massive *3 transfusion':ab,ti OR 'massive *3 transfusions':ab,ti) OR ('massive infusion':ab,ti OR 'massively transfused':ab,ti) OR ('massive *1 bleeding':ab,ti) OR ('massive *1 haemorrhage':ab,ti OR 'massive *1 hemorrhage':ab,ti)	8,445

ID	Query	Results
#25	('thorax surgery'/exp) OR ('heart surgery'/exp) OR ('cardiothoracic surgery':ab,ti OR 'chest *1 surgery':ab,ti) OR ('cardiothoracic *1 patient':ab,ti OR 'cardiothoracic *1 patients':ab,ti) OR ('thoracic operation':ab,ti OR 'thoracic surgery':ab,ti OR thoracoplasty:ab,ti) OR ('thoracic *1 procedure':ab,ti OR 'thoracic *1 procedures':ab,ti)	286,765
#26	('surgery'/exp) OR ('surgical ward'/exp) OR ('surgical patient'/exp) OR (surgical:ab,ti OR surgery:ab,ti OR operation:ab,ti OR resection:ab,ti)	2,740,539
#27	('orthopedic surgery'/exp) OR ('orthopedic surgery':ab,ti OR 'orthopaedic surgery':ab,ti) OR ('bone surgery':ab,ti OR orthopaedics:ab,ti OR orthopedics:ab,ti) OR ('orthopedic *1 patient':ab,ti OR 'orthopedic *1 patients':ab,ti) OR ('orthopaedic *1 patient':ab,ti OR 'orthopaedic *1 patients':ab,ti) OR ('orthopedic operation':ab,ti OR 'orthopedic *1 procedures':ab,ti) OR ('orthopaedic operation':ab,ti OR 'orthopaedic *1 procedures':ab,ti) OR ('orthopedic *1 procedure':ab,ti OR 'orthopaedic *1 procedure':ab,ti)	259,726
#28	#21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27	3,700,992
#29	#20 AND #28	2,351
#30	('adverse outcome'/exp) OR ('outcome assessment'/exp) OR ('morbidity'/exp) OR ('mortality'/exp) OR (morbidity:ab,ti OR incidence:ab,ti OR prevalence:ab,ti OR occurrence:ab,ti) OR (mortality:ab,ti OR death:ab,ti OR survival:ab,ti)	1,938,636
#31	('quality of life'/exp) OR (qol:ab,ti OR 'quality of life':ab,ti OR 'quality of wellbeing':ab,ti) OR ('health related quality':ab,ti OR hrqol:ab,ti) OR (qaly*:ab,ti OR 'quality adjusted':ab,ti OR 'adjusted life':ab,ti)	161,033
#31	('quality of life'/exp) OR (qol:ab,ti OR 'quality of life':ab,ti OR 'quality of wellbeing':ab,ti) OR ('health related quality':ab,ti OR hrqol:ab,ti) OR (qaly*:ab,ti OR 'quality adjusted':ab,ti OR 'adjusted life':ab,ti)	161,033
#32	(('blood component therapy'/exp) AND (('dose response'/exp) OR ('drug dose'/exp))) OR ('fresh frozen plasma'/exp/dd_do) OR ('recombinant erythropoietin'/exp/dd_do) OR ('transfusion frequency':ab,ti) OR ('frequency *5 transfusion':ab,ti OR 'frequency *5 transfusions':ab,ti) OR ('transfusion rate':ab,ti OR 'transfusion rates':ab,ti) OR ('rate *5 transfusion':ab,ti OR 'rates *5 transfusion':ab,ti) OR ('transfusion requirement':ab,ti OR 'transfusion requirements':ab,ti) OR ('transfusion indication':ab,ti OR 'transfusion indications':ab,ti) OR ('indications *5 transfusion':ab,ti OR 'indications *5 transfusions':ab,ti) OR ('indication *5 transfusion':ab,ti OR 'indication *5 transfusions':ab,ti) OR ('transfusion interval':ab,ti OR 'transfusion intervals':ab,ti) OR ('need *3 transfusion':ab,ti OR 'need *3 transfusions':ab,ti) OR ('transfusion need':ab,ti OR 'transfusion needs':ab,ti) OR ('dose *3 transfusion':ab,ti OR 'dose *3 transfusions':ab,ti) OR ('dose *3 transfused':ab,ti OR 'transfusions *3 dose':ab,ti) OR ('transfusion dose':ab,ti OR 'transfused *3 dose':ab,ti) OR ('platelet dose':ab,ti OR 'dose *3 platelets':ab,ti) OR (dose:ab,ti AND transfus*:ab,ti)	17,470

ID	Query	Results
#33	('hemoglobin'/de) OR ('hemoglobin determination'/de) OR ('hemoglobin blood level'/de) OR ('mean corpuscular volume'/de) OR ('blood haemoglobin':ab,ti OR 'blood hemoglobin':ab,ti) OR ('haemoglobin *1 level':ab,ti OR 'hemoglobin *1 level':ab,ti) OR ('haemoglobin *1 levels':ab,ti OR 'hemoglobin *1 levels':ab,ti) OR ('hb level':ab,ti OR 'hb levels':ab,ti) OR ('haemoglobin determination':ab,ti OR 'hemoglobin determination':ab,ti) OR ('hemoglobin assay':ab,ti OR 'haemoglobin assay':ab,ti) OR ('hemoglobin estimation':ab,ti OR 'haemoglobin estimation':ab,ti) OR ('hb determination':ab,ti OR 'hb estimation':ab,ti OR 'hb assay':ab,ti) OR ('hemoglobin *1 content':ab,ti OR 'hemoglobin *1 concentration':ab,ti) OR ('haemoglobin *1 content':ti,ab OR 'haemoglobin *1 concentration':ti,ab) OR ('hb content':ab,ti OR 'hb concentration':ab,ti) OR (hemoglobinometry:ab,ti OR haemoglobinometry:ab,ti) OR ('plasma haemoglobin':ab,ti OR 'plasma hemoglobin':ab,ti) OR ('serum haemoglobin':ab,ti OR 'serum hemoglobin':ab,ti) OR ('mean corpuscular haemoglobin':ab,ti OR 'mean corpuscular hemoglobin':ab,ti) OR ('mean cell *1 haemoglobin':ab,ti OR 'mean cell *1 hemoglobin':ab,ti) OR ('erythrocyte indices':ti,ab OR 'erythrocyte index':ti,ab OR 'erythrocyte indexes':ti,ab) OR ('red *1 cell indices':ab,ti OR 'red *1 cell index':ab,ti OR 'red *1 cell indexes':ab,ti) OR ('rbc indices':ab,ti OR 'rbc index':ab,ti OR 'rbc indexes':ab,ti)	87,280
#34	('re-operation'/de) OR ('bleeding'/de) OR ('postoperative hemorrhage'/de) OR (('bleeding'/de) OR ('postoperative hemorrhage'/de)) OR (('re-operation'/de) OR ('postoperative hemorrhage'/de)) OR (re-operation*:ti AND (bleeding:ti OR 'blood loss':ti)) OR (re-operation*:ti AND (hemorrhag*:ti OR haemorrhag*:ti)) OR (('re operation':ti OR 're operations':ti) AND bleeding:ti) OR (('re operation':ti OR 're operations':ti) AND 'blood loss':ti) OR (('re operation':ti OR 're operations':ti) AND hemorrhag*:ti) OR (('re operation':ti OR 're operations':ti) AND haemorrhag*:ti) OR (re-operation*:ab AND (bleeding:ab OR 'blood loss':ab)) OR (re-operation*:ab AND (hemorrhag*:ab OR haemorrhag*:ab)) OR (('re operation':ab OR 're operations':ab) AND bleeding:ab) OR (('re operation':ab OR 're operations':ab) AND 'blood loss':ab) OR (('re operation':ab OR 're operations':ab) AND hemorrhag*:ab) OR (('re operation':ab OR 're operations':ab) AND haemorrhag*:ab) OR ('repeat surgery':ab,ti OR 'surgical revision':ab,ti)	135,567
#35	('disseminated intravascular clotting'/de) OR ('consumption coagulopathy':ab,ti OR 'consumptive coagulopathy':ab,ti) OR ('defibrination syndrome':ab,ti OR 'sanarelli shwartzman syndrome':ab,ti) OR ('disseminated fibrin thromboembolism':ab,ti) OR ('disseminated intravasal thromboembolism':ab,ti) OR ('intravasal agglutination':ab,ti OR 'intravasal *1 clotting':ab,ti) OR ('intravascular *1 clotting':ab,ti OR 'intravascular *1 coagulation':ab,ti) OR ('intravascular *1 coagulopathy':ti,ab OR 'intravenous *1 coagulation':ti,ab)	18,502
#36	('health economics'/exp) OR ('economic aspect'/exp) OR ('economics'/exp) OR ('finance'/exp) OR ('biomedical technology assessment'/exp) OR ('economic evaluation'/exp) OR ('health care cost'/exp) OR (economic*:ab,ti OR pharmacoeconomic*:ab,ti) OR (cost*:ab,ti OR price*:ab,ti OR pricing:ab,ti) OR ('burden of illness':ab,ti OR 'value *1 money':ab,ti) OR (resource*:ab,ti AND utili*:ab,ti) OR (resource*:ab,ti AND utili*:ab,ti) OR ('technology assessment':ab,ti OR 'technology assessments':ab,ti) OR ('technology appraisal':ab,ti OR 'technology appraisals':ab,ti)	1,001,267
#37	('hospitalization'/exp) OR ('length of stay'/exp) OR (hospitaliz*:ab,ti OR hospitalis*:ab,ti) OR ('length *3 stay':ab,ti OR 'hospital stay':ab,ti)	246,178
#38	('intensive care unit'/exp) OR ('intensive care unit':ab,ti OR icu:ab,ti OR 'intensive care units':ab,ti) OR ('close attention unit':ab,ti OR 'close attention units':ab,ti) OR ('intensive care department':ab,ti OR 'intensive care departments':ab,ti) OR ('special care unit':ab,ti OR 'special care units':ab,ti) OR ('critical care unit':ab,ti OR 'critical care units':ab,ti)	77,229

ID	Query	Results
#39	('hospital admission'/exp) OR ('hospital readmission'/exp) OR ('hospital admission':ab,ti OR 'hospital admittance':ab,ti) OR ('patient admission':ab,ti OR readmission:ab,ti) OR (rehospitalization:ab,ti OR rehospitalisation:ab,ti)	78,138
#40	#30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39	3,250,321
#41	#29 AND #40	1,835

Cochrane Library Database: search conducted 24 June 2009

No.	Query	Results
#1	MeSH descriptor Factor VIIa explode all trees	126
#2	MeSH descriptor Recombinant Proteins explode all trees	5962
#3	#1 AND #2	1738
#4	"recombinant activated factor VII"	69
#5	"recombinant *2 VIIa" OR "Recombinant *2 FVIIa"	0
#6	"recombinant F VIIa"	0
#7	rFVIIa OR "r FVIIa" OR "r F VIIa" OR rf7a	111
#8	"eptacog alfa" OR niastase OR "Novo Seven" OR Novoseven	60
#9	"nn 1731" OR nn1731	0
#10	"blood clotting factor viia" OR "coagulation factor viia"	3
#11	Activated NEAR/2 ("Factor VII" OR FVII")	142
#12	Activated NEAR/2 ("Factor 7" OR "F7")	1
#13	acset	1
#14	#10 OR #11 OR #12 OR #13	1422
#15	recombinant	8146
#16	#14 AND #15	1020
#17	#3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #16	1836
#18	MeSH descriptor Perioperative Care explode all trees	4254
#19	MeSH descriptor Preoperative Care explode all trees	4098
#20	MeSH descriptor Postoperative Complications explode all trees	21418
#21	MeSH descriptor Postoperative Period explode all trees	3483
#22	MeSH descriptor Intraoperative Complications explode all trees	2476
#23	MeSH descriptor Intraoperative Period explode all trees	919
#24	perioperative OR "peri operative"	5196

No.	Query	Results
#25	preoperative OR "pre operative"	11093
#26	intraoperative OR "intra operative"	8039
#27	peroperative OR "per operative"	474
#28	postoperative OR "post operative"	40236
#29	#18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28	933
#30	#17 AND #29	385
#31	MeSH descriptor Wounds and Injuries explode all trees	10953
#32	injur* OR trauma*	20750
#33	#31 OR #32	356
#34	#17 AND #33	284
#35	MeSH descriptor Shock explode all trees	930
#36	shock OR "cardiovascular collapse" OR "circulatory collapse"	3179
#37	#35 OR #36	281
#38	#17 AND #37	241
#39	MeSH descriptor Blood Transfusion explode all trees	2628
#40	massive	599
#41	#39 AND #40	205
#42	massive NEAR/3 transfusion*	20
#43	"massive infusion" OR "massively transfused"	3
#44	massive NEAR/1 (bleeding OR haemorrhage OR hemorrhage)	47
#45	#41 OR #42 OR #43 OR #44	254
#46	#17 AND #45	159
#47	MeSH descriptor Thoracic Surgical Procedures explode all trees	10297
#48	MeSH descriptor Thoracic Surgery explode all trees	130
#49	MeSH descriptor Cardiovascular Surgical Procedures explode all trees	10930
#50	"cardiothoracic surgery" OR (chest NEAR/1 surgery)	675
#51	cardiothoracic NEAR/1 patient*	4
#52	"thoracic operation" OR "thoracic surgery" OR thoracoplasty	2131
#53	thoracic NEAR/1 procedure*	16
#54	#47 OR #48 OR #49 OR #50 OR #51 OR #52 OR #53	164

No.	Query	Results
#55	#17 AND #54	91
#56	MeSH descriptor Surgical Procedures, Operative explode all trees	68578
#57	MeSH descriptor General Surgery, this term only	167
#58	MeSH descriptor Surgery Department, Hospital, this term only	68
#59	surgical OR surgery OR operation OR resection	91783
#60	#56 OR #57 OR #58 OR #59	88
#61	#17 AND #60	69
#62	MeSH descriptor Orthopedic Procedures explode all trees	5335
#63	MeSH descriptor Orthopedics, this term only	272
#64	"orthopedic surgery" OR "orthopaedic surgery"	2339
#65	"bone surgery" OR orthopaedics or orthopedics	7975
#66	(orthopedic OR orthopaedic) NEAR/1 patient*	223
#67	"orthopedic operation" OR "orthopaedic operation"	6
#68	(orthopedic OR orthopaedic) NEAR/1 procedure*	638
#69	#62 OR #63 OR #64 OR #65 OR #66 OR #67 OR #68	79
#70	#17 AND #69	51
#71	#30 OR #34 OR #38 OR #46 OR #55 OR #61 OR #70	466
#72	MeSH descriptor Morbidity explode all trees	8475
#73	MeSH descriptor Mortality explode all trees	7946
#74	morbidity OR incidence OR prevalence OR occurrence	62784
#75	mortality OR death OR survival	55325
#76	#72 OR #73 OR #74 OR #75	54
#77	#71 AND #76	43
#78	MeSH descriptor Quality of Life, this term only	9425
#79	MeSH descriptor Quality-Adjusted Life Years, this term only	2062
#80	qol OR "quality of life" OR "quality of wellbeing"	21521
#81	"health related quality" or hrqol	2898
#82	qaly* or "quality adjusted" or "adjusted life"	3802
#83	#78 OR #79 OR #80 OR #81 OR #82	49
#84	#71 AND #83	37

No.	Query	Results
#85	MeSH descriptor Blood Component Transfusion explode all trees with qualifier: MT	99
#86	frequency NEAR/5 transfusion*	84
#87	rate* NEAR/5 transfusion*	324
#88	"transfusion requirement" OR "transfusion requirements"	949
#89	indication* NEAR/5 transfusion*	45
#90	"transfusion interval" OR "transfusion intervals"	13
#91	(need NEAR/3 transfusion*) OR "transfusion needs"	623
#92	dose NEAR/3 transfus*	86
#93	"platelet dose" OR (dose NEAR/3 platelets)	185
#94	(dose and transfus*):ti	72
#95	#85 OR #86 OR #87 OR #88 OR #89 OR #90 OR #91 OR #92 OR #93 OR #94	56
#96	#71 AND #95	22
#97	MeSH descriptor Hemoglobins, this term only	1990
#98	MeSH descriptor Hemoglobinometry, this term only	152
#99	MeSH descriptor Erythrocyte Indices, this term only	110
#100	"blood haemoglobin" OR "blood hemoglobin"	241
#101	(haemoglobin OR hemoglobin) NEAR/1 level*	1228
#102	"hb level" OR "hb levels"	236
#103	"haemoglobin determination" OR "hemoglobin determination"	120
#104	"hemoglobin assay" OR "haemoglobin assay"	4
#105	"hemoglobin estimation" OR "haemoglobin estimation"	5
#106	"hb determination" OR "hb estimation" OR "hb assay"	2
#107	hemoglobin NEAR/1 (content OR concentration)	904
#108	haemoglobin NEAR/1 (content OR concentration)	904
#109	"hb content" OR "hb concentration"	110
#110	hemoglobinometry OR haemoglobinometry	166
#111	"plasma haemoglobin" OR "plasma hemoglobin"	65
#112	"serum haemoglobin" OR "serum hemoglobin"	47
#113	"mean corpuscular volume" OR mcv OR mch OR mchc	350
#114	"mean corpuscular haemoglobin" OR "mean corpuscular hemoglobin"	41

No.	Query	Results
#115	"Mean Cell" NEAR/1 (Haemoglobin OR Hemoglobin)	2
#116	"erythrocyte indices" OR "Erythrocyte Index" OR "Erythrocyte Indexes"	121
#117	red NEAR/1 ("cell indices" OR "Cell Index" OR "Cell Indexes")	14
#118	"rbc indices" OR "RBC Index" OR "RBC Indexes"	2
#119	#97 OR #98 OR #99 OR #100 OR #101 OR #102 OR #103 OR #104 OR #105 OR #106 OR #107 OR #108 OR #109 OR #110 OR #111 OR #112 OR #113 OR #114 OR #115 OR #116 OR #117 OR #118	62
#120	#71 AND #119	9
#121	MeSH descriptor Re-operation, this term only	1199
#122	MeSH descriptor Hemorrhage, this term only	1471
#123	MeSH descriptor Postoperative Hemorrhage, this term only	485
#124	MeSH descriptor Blood Loss, Surgical, this term only	1399
#125	#122 OR #123 OR #124	13
#126	#121 AND #125	9
#127	re-operation* NEAR/15 (bleeding or "blood loss")	136
#128	re-operation* NEAR/15 (hemorrhag* OR haemorrhag*)	69
#129	("re operation" OR "re operations") NEAR/15 bleeding	31
#130	("re operation" OR "re operations") NEAR/15 "blood loss"	15
#131	("re operation" OR "re operations") NEAR/15 hemorrhag*	2
#132	("re operation" OR "re operations") NEAR/15 haemorrhag*	9
#133	"Repeat Surgery" OR "Surgical Revision"	110
#134	#126 OR #127 OR #128 OR #129 OR #130 OR #131 OR #132 OR #133	13
#135	#71 AND #134	8
#136	MeSH descriptor Disseminated Intravascular Coagulation, this term only	75
#137	"consumption coagulopathy" OR "consumptive coagulopathy"	12
#138	"defibrination syndrome" OR "sanarelli shwartzman syndrome"	1
#139	"disseminated fibrin thromboembolism"	0
#140	"disseminated intravasal thromboembolism"	0
#141	"intravasal agglutination" OR (intravasal NEAR/1 clotting)	0
#142	intravascular NEAR/1 (clotting OR coagulation OR coagulopathy)	237
#143	intravenous NEAR/1 coagulation	1

No.	Query	Results
#144	#136 OR #137 OR #138 OR #139 OR #140 OR #141 OR #142 OR #143	14
#145	#71 AND #144	7
#146	MeSH descriptor Costs and Cost Analysis explode all trees	26772
#147	MeSH descriptor Economics, this term only	65
#148	MeSH descriptor Models, Economic explode all trees	1853
#149	MeSH descriptor Value of Life, this term only	274
#150	MeSH descriptor Utilization Review explode all trees	420
#151	MeSH descriptor Delivery of Health Care, this term only with qualifier: UT	62
#152	economic* OR pharmacoeconomic*	37332
#153	cost* OR price* OR pricing	48938
#154	resource* NEAR utili*	1537
#155	"burden of illness" OR (value NEAR/1 money)	87
#156	#146 OR #147 OR #148 OR #149 OR #150 OR #151 OR #152 OR #153 OR #154 OR #155	8
#157	#71 AND #156	1
#158	MeSH descriptor Hospitalization explode all trees	10690
#159	MeSH descriptor Child, Hospitalized, this term only	82
#160	hospitaliz* OR hospitalis*	16298
#161	(length NEAR/3 stay) OR "hospital stay"	11735
#162	#158 OR #159 OR #160 OR #161	1
#163	#71 AND #162	1
#164	MeSH descriptor Intensive Care Units explode all trees	1978
#165	"intensive care unit" OR icu OR "intensive care units"	6712
#166	"close attention unit" OR "close attention units"	0
#167	"intensive care department" OR "intensive care departments"	56
#168	"special care unit" OR "special care units"	63
#169	"critical care unit" OR "critical care units"	108
#170	#164 OR #165 OR #166 OR #167 OR #168 OR #169	5
#171	#71 AND #170	0
#172	MeSH descriptor Patient Admission, this term only	604
#173	MeSH descriptor Patient Readmission, this term only	593

No.	Query	Results
#174	"hospital admission" OR "hospital admittance"	1727
#175	"patient admission" OR readmission	2327
#176	rehospitalization OR rehospitalisation	504
#177	#172 OR #173 OR #174 OR #175 OR #176	9
#178	#71 AND #177	0
#179	#77 OR #84 OR #96 OR #120 OR #135 OR #145 OR #157 OR #163 OR #171 OR #178	55

PreMedline: search conducted 24 June 2009

No.	Query	Results
#54	Search #51 OR #52 OR #53	57
#53	Search #50 AND pubmednotmedline[sb]	5
#52	Search #50 AND in process[sb]	34
#51	Search #50 NOT (medline[SB] OR oldmedline[sb])	57
#50	Search #21 OR #23 OR #25 OR #32 OR #38 OR #40 OR #49	812
#49	Search #14 AND #48	47
#48	Search #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47	43020
#47	Search orthopedic[tw] AND procedure*[tw]	11166
#46	Search orthopaedic[tw] AND procedure*[tw]	3376
#45	Search "orthopedic operation"[tw] OR "orthopaedic operation"[tw]	75
#44	Search orthopaedic[tw] AND patient*[tw]	8162
#43	Search orthopedic[tw] AND patient*[tw]	15187
#42	Search "bone surgery"[tw] OR orthopaedics[tw] or orthopedics[tw]	17665
#41	Search "orthopedic surgery"[tw] OR "orthopaedic surgery"[tw]	6028
#40	Search #14 AND #39	585
#39	Search surgical[tw] OR surgery[tw] OR operation[tw] OR resection[tw]	1882022
#38	Search #14 AND #37	32
#37	Search #33 OR #34 OR #35 OR #36	54299
#36	Search thoracic[tw] AND procedure*[tw]	19240
#35	Search "thoracic operation"[tw] OR "thoracic surgery"[tw] OR thoracoplasty[tw]	16763

No.	Query	Results
#34	Search cardiothoracic[tw] AND patient*[tw]	2288
#33	Search "cardiothoracic surgery"[tw] OR (chest[tw] AND surgery[tw])	24500
#32	Search #14 AND #31	149
#31	Search #26 OR #27 OR #28 OR #29 OR #30	11339
#30	Search "massive infusion"[tw] OR "massively transfused"[tw]	102
#29	Search massive[tw] AND haemorrhage[tw]	1184
#28	Search massive[tw] AND hemorrhage[tw]	7719
#27	Search massive[tw] AND bleeding[tw]	4968
#26	Search massive[tw] AND transfusion*[tw]	2323
#25	Search #14 AND #24	70
#24	Search shock[tw] OR "cardiovascular collapse"[tw] OR "circulatory collapse"[tw]	135235
#23	Search #14 AND #22	293
#22	Search injur*[tw] OR trauma*[tw]	720615
#21	Search #14 AND #20	293
#20	Search #15 OR #16 OR #17 OR #18 OR #19	613621
#19	Search postoperative[tw] OR "post operative"[tw]	469400
#18	Search peroperative[tw] OR "per operative"[tw]	3711
#17	Search intraoperative[tw] OR "intra operative"[tw]	88480
#16	Search preoperative[tw] OR "pre operative"[tw]	149999
#15	Search perioperative[tw] OR "peri operative"[tw]	43061
#14	Search #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #13	1479
#13	Search #11 AND #12	1076
#12	Search recombinant[tw]	314925
#11	Search #7 OR #8 OR #9 OR #10	2061
#10	Search acset[tw]	0
#9	Search Activated[tw] AND ("Factor 7"[tw] OR "F7"[tw])	178
#8	Search Activated[tw] AND ("Factor VII"[tw] OR "FVII"[tw])	1775
#7	Search "blood clotting factor viia"[tw] OR "coagulation factor viia"[tw]	132
#6	Search "nn 1731"[tw] OR nn1731[tw]	8
#5	Search "eptacog alfa"[tw] OR niastase[tw] OR "Novo Seven"[tw] OR Novoseven[tw]	335

No.	Query	Results
#4	Search rFVIIa[tw] OR "r FVIIa"[tw] OR "r F VIIa"[tw] OR rf7a[tw]	921
#3	Search "recombinant F VIIa" [tw]	0
#2	Search "recombinant *2 VIIa"[tw] OR "Recombinant *2 FVIIa"[tw]	0
#1	Search "recombinant activated factor VII"[tw]	679

CINAHL: search conducted 23 June 2009

No.	Query	Results
S14	S1 or S2 or S3 or S4 or S5 or S6 or S13	199
S13	S11 and S12	84
S12	TI recombinant or AB recombinant	2345
S11	S7 or S8 or S9 or S10	145
S10	TI acset or AB acset	0
S9	TI (Activated N2 ("Factor 7" OR F7)) or AB (Activated N2 ("Factor 7" OR F7))	37
S8	TI (Activated N2 ("Factor VII" OR FVII)) or AB (Activated N2 ("Factor VII" OR FVII))	105
S7	TI ("blood clotting factor viia" OR "coagulation factor viia") or AB ("blood clotting factor viia" OR "coagulation factor viia")	3
S6	TI ("nn 1731" OR nn1731) or AB ("nn 1731" OR nn1731)	0
S5	TI ("eptacog alfa" OR niastase OR "Novo Seven" OR Novoseven) or AB ("eptacog alfa" OR niastase OR "Novo Seven" OR Novoseven)	14
S4	TI (rFVIIa OR "r FVIIa" OR "r F VIIa" OR rf7a) or AB (rFVIIa OR "r FVIIa" OR "r F VIIa" OR rf7a)	72
S3	TI "recombinant F VIIa" or AB "recombinant F VIIa"	0
S2	TI (recombinant N2 (VIIa OR FVIIa)) or AB (recombinant N2 (VIIa OR FVIIa))	117
S1	TI "recombinant activated factor VII" or AB "recombinant activated factor VII"	71

* The search was conducted using EBSCOhost on 23 June 2009

A8 Literature searches, Question 8

In patients undergoing surgery, what is the effect of fresh frozen plasma (FFP), cryoprecipitate, fibrinogen concentrate, and/or platelet transfusion on patient outcomes?

EMBASE.com: search conducted 25 June 2009

Transfusion therapy

#	Query	Results
#1	'blood component therapy'/exp	42,649
#2	'blood transfusion'/exp	108,198
#3	'transfusion'/exp	171,322
#4	transfusion:ab,ti	52,679
#5	'blood exchange':ab,ti OR 'blood infusion':ab,ti	512
#6	'blood replacement':ab,ti OR 'blood retransfusion':ab,ti	645
#7	hemotherapy:ab,ti OR hematherapy:ab,ti OR hematotherapy:ab,ti	449
#8	haemotherapy:ab,ti OR haematherapy:ab,ti OR haematotherapy:ab,ti	109
#9	multitransfusion:ab,ti OR polytransfusion:ab,ti OR retransfusion:ab,ti	536
#10	'transfusion blood':ab,ti OR 'transfusion therapy':ab,ti	1,732
#11	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10	188,592

Blood component

#	Query	Results
#1	'blood component'/exp	1,318
#2	'blood component':ab,ti OR 'blood components':ab,ti	4,118
#3	'blood product':ab,ti OR 'blood products':ab,ti	6,910
#4	'transfusion product':ab,ti OR 'transfusion products':ab,ti	83
#5	'blood constituent':ab,ti OR 'blood constituents':ab,ti	679
#6	#1 OR #2 OR #3 OR #4 OR #5	11,898

Fresh frozen plasma

#	Query	Results
#1	'fresh frozen plasma'/exp	3,856
#2	'plasma'/exp	51,785
#3	'fresh frozen plasma':ab,ti OR ffp:ab,ti	3,545
#4	#1 OR #2 OR #3	57,199

Plasma transfusion

#	Query	Results
#1	'plasma transfusion'/exp	1,485
#2	'plasma transfusion':ab,ti	240
#3	'plasma infusion':ab,ti OR 'serum transfusion':ab,ti	386
#4	#1 OR #2 OR #3	1,886

Cryoprecipitate

#	Query	Results
#1	'cryoprecipitate'/exp	1,125
#2	'cryoprecipitate coagulum':de	75
#3	cryoprecipitate:ab,ti OR 'cryo precipitate':ab,ti	1,521
#4	#1 OR #2 OR #3	2,268

Fibrinogen

#	Query	Results
#1	'fibrinogen'/exp	33,677
#2	fibrinogen:ab,ti OR 'factor 1':ab,ti OR 'factor i':ab,ti	69,267
#3	'9001 32 5':rn	33,687
#4	#1 OR #2 OR #3	82,495

Platelet

#	Query	Results
#1	'thrombocyte transfusion'/exp	6,564
#2	'thrombocyte'/exp	53,469
#3	'blood transfusion'/exp	108,198
#4	'transfusion'/exp	171,322
#5	#3 OR #4	171,322
#6	#2 AND #5	3,307
#7	'platelet *1 transfusion':ab,ti OR 'platelet *1 transfusions':ab,ti	2,966
#8	'transfusion *3 platelet':ab,ti OR 'transfusion *3 platelets':ab,ti	700
#9	'thrombocyte transfusion':ab,ti OR 'thrombocytic transfusion':ab,ti	42
#10	#1 OR #6 OR #7 OR #8 OR #9	10,225

Complete EMBASE search

No.	Query	Results
#1	('blood component therapy'/exp) OR ('blood transfusion'/exp) OR ('transfusion'/exp) OR (transfusion:ab,ti) OR ('blood exchange':ab,ti OR 'blood infusion':ab,ti) OR ('blood replacement':ab,ti OR 'blood retransfusion':ab,ti) OR (hemotherapy:ab,ti OR hematherapy:ab,ti OR hematotherapy:ab,ti) OR (haemotherapy:ab,ti OR haematherapy:ab,ti OR haematotherapy:ab,ti) OR (multitransfusion:ab,ti OR polytransfusion:ab,ti OR retransfusion:ab,ti) OR ('transfusion blood':ab,ti OR 'transfusion therapy':ab,ti)	188,592
#2	('blood component'/exp) OR ('blood component':ab,ti OR 'blood components':ab,ti) OR ('blood product':ab,ti OR 'blood products':ab,ti) OR ('transfusion product':ab,ti OR 'transfusion products':ab,ti) OR ('blood constituent':ab,ti OR 'blood constituents':ab,ti)	11,898
#3	('fresh frozen plasma'/exp) OR ('plasma'/exp) OR ('fresh frozen plasma':ab,ti OR ffp:ab,ti)	57,199
#4	('plasma transfusion'/exp) OR ('plasma transfusion':ab,ti) OR ('plasma infusion':ab,ti OR 'serum transfusion':ab,ti)	1,886
#5	('cryoprecipitate'/exp) OR ('cryoprecipitate coagulum':de) OR (cryoprecipitate:ab,ti OR 'cryo precipitate':ab,ti)	2,268
#6	('fibrinogen'/exp) OR (fibrinogen:ab,ti OR 'factor 1':ab,ti OR 'factor i':ab,ti) OR ('9001 32 5':rn)	82,495
#7	('thrombocyte transfusion'/exp) OR (('thrombocyte'/exp) AND (('blood transfusion'/exp) OR ('transfusion'/exp))) OR ('platelet *1 transfusion':ab,ti OR 'platelet *1 transfusions':ab,ti) OR ('transfusion *3 platelet':ab,ti OR 'transfusion *3 platelets':ab,ti) OR ('thrombocyte transfusion':ab,ti OR 'thrombocytic transfusion':ab,ti)	10,225
#8	#2 OR #3 OR #5 OR #6	149,046
#9	#1 AND #8	12,970
#10	#4 OR #7 OR #9	21,876
#11	(('perioperative period'/exp) OR ('perioperative nursing'/exp) OR ('perioperative complication'/exp) OR ('preoperative period'/exp) OR ('preoperative complication'/exp) OR ('intraoperative period'/exp) OR (perioperative:ab,ti OR 'peri operative':ab,ti) OR (preoperative:ab,ti OR 'pre operative':ab,ti) OR (intraoperative:ab,ti OR 'intra operative':ab,ti) OR (peroperative:ab,ti OR 'per operative':ab,ti)) OR ('postoperative period'/exp) OR ('postoperative complication'/exp) OR (postoperative:ab,ti OR 'post operative':ab,ti)	870,294
#12	injur*:ab,ti OR trauma*:ab,ti	554,730
#13	('shock'/exp) OR (shock:ab,ti OR 'cardiovascular collapse':ab,ti OR 'circulatory collapse':ab,ti)	136,201
#14	((('blood transfusion'/exp) OR (('bleeding'/exp) AND ('transfusion'/exp))) AND (massive:ab,ti)) OR ('massive transfusion':ab,ti) OR ('massive blood transfusion':ab,ti) OR ('massive transfusion protocol':ab,ti) OR ('massive *3 transfusion':ab,ti OR 'massive *3 transfusions':ab,ti) OR ('massive infusion':ab,ti OR 'massively transfused':ab,ti) OR ('massive *1 bleeding':ab,ti) OR ('massive *1 haemorrhage':ab,ti OR 'massive *1 hemorrhage':ab,ti)	8,451

No.	Query	Results
#15	('thorax surgery'/exp) OR ('heart surgery'/exp) OR ('cardiothoracic surgery':ab,ti OR 'chest *1 surgery':ab,ti) OR ('cardiothoracic *1 patient':ab,ti OR 'cardiothoracic *1 patients':ab,ti) OR ('thoracic operation':ab,ti OR 'thoracic surgery':ab,ti OR thoracoplasty:ab,ti) OR ('thoracic *1 procedure':ab,ti OR 'thoracic *1 procedures':ab,ti)	286,869
#16	('surgery'/exp) OR ('surgical ward'/exp) OR ('surgical patient'/exp) OR (surgical:ab,ti OR surgery:ab,ti OR operation:ab,ti OR resection:ab,ti)	2,741,599
#17	('orthopedic surgery'/exp) OR ('orthopedic surgery':ab,ti OR 'orthopaedic surgery':ab,ti) OR ('bone surgery':ab,ti OR orthopaedics:ab,ti OR orthopedics:ab,ti) OR ('orthopedic *1 patient':ab,ti OR 'orthopedic *1 patients':ab,ti) OR ('orthopaedic *1 patient':ab,ti OR 'orthopaedic *1 patients':ab,ti) OR ('orthopedic operation':ab,ti OR 'orthopedic *1 procedures':ab,ti) OR ('orthopaedic operation':ab,ti OR 'orthopaedic *1 procedures':ab,ti) OR ('orthopedic *1 procedure':ab,ti OR 'orthopaedic *1 procedure':ab,ti)	259,925
#18	#11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17	3,294,948
#19	#10 AND #18	10,104
#20	('adverse outcome'/exp) OR ('outcome assessment'/exp) OR ('morbidity'/exp) OR ('mortality'/exp) OR (morbidity:ab,ti OR incidence:ab,ti OR prevalence:ab,ti OR occurrence:ab,ti) OR (mortality:ab,ti OR death:ab,ti OR survival:ab,ti)	1,939,842
#21	('quality of life'/exp) OR (qol:ab,ti OR 'quality of life':ab,ti OR 'quality of wellbeing':ab,ti) OR ('health related quality':ab,ti OR hrqol:ab,ti) OR (qaly*:ab,ti OR 'quality adjusted':ab,ti OR 'adjusted life':ab,ti)	161,171
#22	(('blood component therapy'/exp) AND (('dose response'/exp) OR ('drug dose'/exp))) OR ('fresh frozen plasma'/exp/dd_do) OR ('recombinant erythropoietin'/exp/dd_do) OR ('transfusion frequency':ab,ti) OR ('frequency *5 transfusion':ab,ti OR 'frequency *5 transfusions':ab,ti) OR ('transfusion rate':ab,ti OR 'transfusion rates':ab,ti) OR ('rate *5 transfusion':ab,ti OR 'rates *5 transfusion':ab,ti) OR ('transfusion requirement':ab,ti OR 'transfusion requirements':ab,ti) OR ('transfusion indication':ab,ti OR 'transfusion indications':ab,ti) OR ('indications *5 transfusion':ab,ti OR 'indications *5 transfusions':ab,ti) OR ('indication *5 transfusion':ab,ti OR 'indication *5 transfusions':ab,ti) OR ('transfusion interval':ab,ti OR 'transfusion intervals':ab,ti) OR ('need *3 transfusion':ab,ti OR 'need *3 transfusions':ab,ti) OR ('transfusion need':ab,ti OR 'transfusion needs':ab,ti) OR ('dose *3 transfusion':ab,ti OR 'dose *3 transfusions':ab,ti) OR ('dose *3 transfused':ab,ti OR 'transfusions *3 dose':ab,ti) OR ('transfusion dose':ab,ti OR 'transfused *3 dose':ab,ti) OR ('platelet dose':ab,ti OR 'dose *3 platelets':ab,ti) OR (dose:ab,ti AND transfus*:ab,ti)	17,482

No.	Query	Results
#23	('hemoglobin'/de) OR ('hemoglobin determination'/de) OR ('hemoglobin blood level'/de) OR ('mean corpuscular volume'/de) OR ('blood haemoglobin':ab,ti OR 'blood hemoglobin':ab,ti) OR ('haemoglobin *1 level':ab,ti OR 'hemoglobin *1 level':ab,ti) OR ('haemoglobin *1 levels':ab,ti OR 'hemoglobin *1 levels':ab,ti) OR ('hb level':ab,ti OR 'hb levels':ab,ti) OR ('haemoglobin determination':ab,ti OR 'hemoglobin determination':ab,ti) OR ('hemoglobin assay':ab,ti OR 'haemoglobin assay':ab,ti) OR ('hemoglobin estimation':ab,ti OR 'haemoglobin estimation':ab,ti) OR ('hb determination':ab,ti OR 'hb estimation':ab,ti OR 'hb assay':ab,ti) OR ('hemoglobin *1 content':ab,ti OR 'hemoglobin *1 concentration':ab,ti) OR ('haemoglobin *1 content':ti,ab OR 'haemoglobin *1 concentration':ti,ab) OR ('hb content':ab,ti OR 'hb concentration':ab,ti) OR (hemoglobinometry:ab,ti OR haemoglobinometry:ab,ti) OR ('plasma haemoglobin':ab,ti OR 'plasma hemoglobin':ab,ti) OR ('serum haemoglobin':ab,ti OR 'serum hemoglobin':ab,ti) OR ('mean corpuscular haemoglobin':ab,ti OR 'mean corpuscular hemoglobin':ab,ti) OR ('mean cell *1 haemoglobin':ab,ti OR 'mean cell *1 hemoglobin':ab,ti) OR ('erythrocyte indices':ti,ab OR 'erythrocyte index':ti,ab OR 'erythrocyte indexes':ti,ab) OR ('red *1 cell indices':ab,ti OR 'red *1 cell index':ab,ti OR 'red *1 cell indexes':ab,ti) OR ('rbc indices':ab,ti OR 'rbc index':ab,ti OR 'rbc indexes':ab,ti)	87,312
#24	('re-operation'/de) OR ('bleeding'/de) OR ('postoperative hemorrhage'/de) OR (('bleeding'/de) OR ('postoperative hemorrhage'/de)) OR (('re-operation'/de) OR ('postoperative hemorrhage'/de)) OR (re-operation*:ti AND (bleeding:ti OR 'blood loss':ti)) OR (re-operation*:ti AND (hemorrhag*:ti OR haemorrhag*:ti)) OR (('re operation':ti OR 're operations':ti) AND bleeding:ti) OR (('re operation':ti OR 're operations':ti) AND 'blood loss':ti) OR (('re operation':ti OR 're operations':ti) AND hemorrhag*:ti) OR (('re operation':ti OR 're operations':ti) AND haemorrhag*:ti) OR (re-operation*:ab AND (bleeding:ab OR 'blood loss':ab)) OR (re-operation*:ab AND (hemorrhag*:ab OR haemorrhag*:ab)) OR (('re operation':ab OR 're operations':ab) AND bleeding:ab) OR (('re operation':ab OR 're operations':ab) AND 'blood loss':ab) OR (('re operation':ab OR 're operations':ab) AND hemorrhag*:ab) OR (('re operation':ab OR 're operations':ab) AND haemorrhag*:ab) OR ('repeat surgery':ab,ti OR 'surgical revision':ab,ti)	135,633
#25	('disseminated intravascular clotting'/de) OR ('consumption coagulopathy':ab,ti OR 'consumptive coagulopathy':ab,ti) OR ('defibrination syndrome':ab,ti OR 'sanarelli shwartzman syndrome':ab,ti) OR ('disseminated fibrin thromboembolism':ab,ti) OR ('disseminated intravasal thromboembolism':ab,ti) OR ('intravasal agglutination':ab,ti OR 'intravasal *1 clotting':ab,ti) OR ('intravascular *1 clotting':ab,ti OR 'intravascular *1 coagulation':ab,ti) OR ('intravascular *1 coagulopathy':ti,ab OR 'intravenous *1 coagulation':ti,ab)	18,505
#26	('health economics'/exp) OR ('economic aspect'/exp) OR ('economics'/exp) OR ('finance'/exp) OR ('biomedical technology assessment'/exp) OR ('economic evaluation'/exp) OR ('health care cost'/exp) OR (economic*:ab,ti OR pharmacoeconomic*:ab,ti) OR (cost*:ab,ti OR price*:ab,ti OR pricing:ab,ti) OR ('burden of illness':ab,ti OR 'value *1 money':ab,ti) OR (resource*:ab,ti AND utili*:ab,ti) OR (resource*:ab,ti AND utili*:ab,ti) OR ('technology assessment':ab,ti OR 'technology assessments':ab,ti) OR ('technology appraisal':ab,ti OR 'technology appraisals':ab,ti)	1,001,779
#27	('hospitalization'/exp) OR ('length of stay'/exp) OR (hospitaliz*:ab,ti OR hospitalis*:ab,ti) OR ('length *3 stay':ab,ti OR 'hospital stay':ab,ti)	246,361
#28	('intensive care unit'/exp) OR ('intensive care unit':ab,ti OR icu:ab,ti OR 'intensive care units':ab,ti) OR ('close attention unit':ab,ti OR 'close attention units':ab,ti) OR ('intensive care department':ab,ti OR 'intensive care departments':ab,ti) OR ('special care unit':ab,ti OR 'special care units':ab,ti) OR ('critical care unit':ab,ti OR 'critical care units':ab,ti)	77,297

No.	Query	Results
#29	('hospital admission'/exp) OR ('hospital readmission'/exp) OR ('hospital admission':ab,ti OR 'hospital admittance':ab,ti) OR ('patient admission':ab,ti OR readmission:ab,ti) OR (rehospitalization:ab,ti OR rehospitalisation:ab,ti)	78,194
#30	#20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29	3,252,157
#31	#19 AND #30	6,327

Cochrane Library Database: search conducted 25 June 2009

No.	Query	Results
#1	MeSH descriptor Blood Component Transfusion, this term only	94
#2	MeSH descriptor Blood Transfusion, this term only	1519
#3	transfusion	6598
#4	"blood exchange" OR "blood infusion"	42
#5	"blood replacement" OR "blood retransfusion"	73
#6	hemotherapy OR hematherapy OR hematotherapy	55
#7	haemotherapy OR haematherapy OR haematotherapy	5
#8	multitransfusion OR polytransfusion OR retransfusion	66
#9	"transfusion blood" OR "transfusion therapy"	224
#10	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9	1930
#11	"blood component" OR "blood components"	429
#12	"blood product" OR "blood products"	639
#13	"transfusion product" OR "transfusion products"	6
#14	"blood constituent" OR "blood constituents"	14
#15	#11 OR #12 OR #13 OR #14	1340
#16	#10 AND #15	1020
#17	MeSH descriptor Plasma, this term only	236
#18	"fresh frozen plasma" OR FFP	348
#19	#17 OR #18	924
#20	#10 AND #19	762

No.	Query	Results
#21	"plasma transfusion"	30
#22	"plasma infusion" OR "serum transfusion"	17
#23	#20 OR #21 OR #22	761
#24	cryoprecipitate	65
#25	cryoprecipitate OR "cryo precipitate"	65
#26	#24 OR #25	580
#27	#10 AND #26	477
#28	Fibrinogen	2831
#29	fibrinogen OR "factor 1" OR "factor I"	4401
#30	#28 OR #29	437
#31	#10 AND #30	360
#32	MeSH descriptor Platelet Transfusion, this term only	208
#33	MeSH descriptor Blood Platelets, this term only	1366
#34	#2 AND #33	286
#35	platelet* NEAR/3 transfusion*	552
#36	"thrombocyte transfusion" OR "thrombocytic transfusion"	40
#37	#32 OR #34 OR #35 OR #36	412
#38	#16 OR #23 OR #27 OR #31 OR #37	1004
#39	MeSH descriptor Perioperative Care explode all trees	4254
#40	MeSH descriptor Preoperative Care explode all trees	4098
#41	MeSH descriptor Postoperative Complications explode all trees	21418
#42	MeSH descriptor Postoperative Period explode all trees	3483
#43	MeSH descriptor Intraoperative Complications explode all trees	2476
#44	MeSH descriptor Intraoperative Period, this term only	919
#45	perioperative OR "peri operative"	5196
#46	preoperative OR "pre operative"	11093

No.	Query	Results
#47	intraoperative OR "intra operative"	8039
#48	peroperative OR "per operative"	474
#49	postoperative OR "post operative"	40236
#50	#39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49	303
#51	#38 AND #50	117
#52	MeSH descriptor Wounds and Injuries explode all trees	10953
#53	injur* OR trauma*	20750
#54	#52 OR #53	113
#55	#38 AND #54	89
#56	MeSH descriptor Shock explode all trees	930
#57	shock OR "cardiovascular collapse" OR "circulatory collapse"	3179
#58	#56 OR #57	86
#59	#38 AND #58	75
#60	MeSH descriptor Blood Transfusion, this term only	1519
#61	massive	599
#62	#60 AND #61	66
#63	massive NEAR/3 transfusion*	20
#64	"massive infusion" OR "massively transfused"	3
#65	massive NEAR/1 (bleeding OR haemorrhage OR hemorrhage)	47
#66	#62 OR #63 OR #64 OR #65	74
#67	#38 AND #66	56
#68	MeSH descriptor Thoracic Surgical Procedures explode all trees	10297
#69	MeSH descriptor Thoracic Surgery, this term only	130
#70	MeSH descriptor Cardiovascular Surgical Procedures explode all trees	10930
#71	"cardiothoracic surgery" OR (chest NEAR/1 surgery)	675
#72	cardiothoracic NEAR/1 patient*	4

No.	Query	Results
#73	"thoracic operation" OR "thoracic surgery" OR thoracoplasty	2131
#74	thoracic NEAR/1 procedure*	16
#75	#68 OR #69 OR #70 OR #71 OR #72 OR #73 OR #74	62
#76	#38 AND #75	45
#77	MeSH descriptor Surgical Procedures, Operative explode all trees	68578
#78	MeSH descriptor General Surgery, this term only	167
#79	MeSH descriptor Surgery Department, Hospital, this term only	68
#80	surgical OR surgery OR operation OR resection	91783
#81	#77 OR #78 OR #79 OR #80	51
#82	#38 AND #81	37
#83	MeSH descriptor Orthopedic Procedures explode all trees	5335
#84	MeSH descriptor Orthopedics, this term only	272
#85	"orthopedic surgery" OR "orthopaedic surgery"	2339
#86	"bone surgery" OR orthopaedics or orthopedics	7975
#87	(orthopedic OR orthopaedic) NEAR/1 patient*	223
#88	"orthopedic operation" OR "orthopaedic operation"	6
#89	(orthopedic OR orthopaedic) NEAR/1 procedure*	638
#90	#83 OR #84 OR #85 OR #86 OR #87 OR #88 OR #89	51
#91	#38 AND #90	26
#92	#51 OR #55 OR #59 OR #67 OR #76 OR #82 OR #91	122
#93	MeSH descriptor Morbidity explode all trees	8475
#94	MeSH descriptor Mortality explode all trees	7946
#95	morbidity OR incidence OR prevalence OR occurrence	62784
#96	mortality OR death OR survival	55325
#97	#93 OR #94 OR #95 OR #96	34
#98	#92 AND #97	20

No.	Query	Results
#99	MeSH descriptor Quality of Life, this term only	9425
#100	MeSH descriptor Quality-Adjusted Life Years, this term only	2062
#101	qol OR "quality of life" OR "quality of wellbeing"	21521
#102	"health related quality" or hrqol	2898
#103	qaly* or "quality adjusted" or "adjusted life"	3802
#104	#99 OR #100 OR #101 OR #102 OR #103	34
#105	#92 AND #104	15
#106	MeSH descriptor Blood Component Transfusion explode all trees with qualifier: MT	99
#107	frequency NEAR/5 transfusion*	84
#108	rate* NEAR/5 transfusion*	324
#109	"transfusion requirement" OR "transfusion requirements"	949
#110	indication* NEAR/5 transfusion*	45
#111	"transfusion interval" OR "transfusion intervals"	13
#112	(need NEAR/3 transfusion*) OR "transfusion needs"	623
#113	dose NEAR/3 transfus*	86
#114	"platelet dose" OR (dose NEAR/3 platelets)	185
#115	(dose and transfus*):ti	72
#116	#106 OR #107 OR #108 OR #109 OR #110 OR #111 OR #112 OR #113 OR #114 OR #115	29
#117	#92 AND #116	11
#118	MeSH descriptor Hemoglobins, this term only	1990
#119	MeSH descriptor Hemoglobinometry, this term only	152
#120	MeSH descriptor Erythrocyte Indices, this term only	110
#121	"blood haemoglobin" OR "blood hemoglobin"	241
#122	(haemoglobin OR hemoglobin) NEAR/1 level*	1228
#123	"hb level" OR "hb levels"	236
#124	"haemoglobin determination" OR "hemoglobin determination"	120

No.	Query	Results
#125	"hemoglobin assay" OR "haemoglobin assay"	4
#126	"hemoglobin estimation" OR "haemoglobin estimation"	5
#127	"hb determination" OR "hb estimation" OR "hb assay"	2
#128	hemoglobin NEAR/1 (content OR concentration)	904
#129	haemoglobin NEAR/1 (content OR concentration)	904
#130	"hb content" OR "hb concentration"	110
#131	hemoglobinometry OR haemoglobinometry	166
#132	"plasma haemoglobin" OR "plasma hemoglobin"	65
#133	"serum haemoglobin" OR "serum hemoglobin"	47
#134	"mean corpuscular volume" OR mcv OR mch OR mchc	350
#135	"mean corpuscular haemoglobin" OR "mean corpuscular hemoglobin"	41
#136	"Mean Cell" NEAR/1 (Haemoglobin OR Hemoglobin)	2
#137	"erythrocyte indices" OR "Erythrocyte Index" OR "Erythrocyte Indexes"	121
#138	red NEAR/1 ("cell indices" OR "Cell Index" OR "Cell Indexes")	14
#139	"rbc indices" OR "RBC Index" OR "RBC Indexes"	2
#140	#118 OR #119 OR #120 OR #121 OR #122 OR #123 OR #124 OR #125 OR #126 OR #127 OR #128 OR #129 OR #130 OR #131 OR #132 OR #133 OR #134 OR #135 OR #136 OR #137 OR #138 OR #139	33
#141	#92 AND #140	8
#142	MeSH descriptor Re-operation, this term only	1199
#143	MeSH descriptor Hemorrhage, this term only	1471
#144	MeSH descriptor Postoperative Hemorrhage, this term only	485
#145	MeSH descriptor Blood Loss, Surgical, this term only	1399
#146	#143 OR #144 OR #145	10
#147	#142 AND #146	5
#148	re-operation* NEAR/15 (bleeding or "blood loss")	136
#149	re-operation* NEAR/15 (hemorrhag* OR haemorrhag*)	69

No.	Query	Results
#150	("re operation" OR "re operations") NEAR/15 bleeding	31
#151	("re operation" OR "re operations") NEAR/15 "blood loss"	15
#152	("re operation" OR "re operations") NEAR/15 hemorrhag*	2
#153	("re operation" OR "re operations") NEAR/15 haemorrhag*	9
#154	"Repeat Surgery" OR "Surgical Revision"	110
#155	#147 OR #148 OR #149 OR #150 OR #151 OR #152 OR #153 OR #154	5
#156	#92 AND #155	1
#157	MeSH descriptor Disseminated Intravascular Coagulation, this term only	75
#158	"consumption coagulopathy" OR "consumptive coagulopathy"	12
#159	"defibrination syndrome" OR "sanarelli shwartzman syndrome"	1
#160	"disseminated fibrin thromboembolism"	0
#161	"disseminated intravasal thromboembolism"	0
#162	"intravasal agglutination" OR (intravasal NEAR/1 clotting)	0
#163	intravascular NEAR/1 (clotting OR coagulation OR coagulopathy)	237
#164	intravenous NEAR/1 coagulation	1
#165	#157 OR #158 OR #159 OR #160 OR #161 OR #162 OR #163 OR #164	2
#166	#92 AND #165	1
#167	MeSH descriptor Costs and Cost Analysis explode all trees	26772
#168	MeSH descriptor Economics, this term only	65
#169	MeSH descriptor Models, Economic explode all trees	1853
#170	MeSH descriptor Value of Life, this term only	274
#171	MeSH descriptor Utilization Review explode all trees	420
#172	MeSH descriptor Delivery of Health Care, this term only with qualifier: UT	62
#173	economic* or pharmacoeconomic*	37332
#174	cost* or price* or pricing	48938
#175	resource* near utili*	1537

No.	Query	Results
#176	"burden of illness" or (value NEAR/1 money)	87
#177	#167 OR #168 OR #169 OR #170 OR #171 OR #172 OR #173 OR #174 OR #175 OR #176	13
#178	#92 and #177	0
#179	MeSH descriptor Hospitalization explode all trees	10690
#180	MeSH descriptor Hospitalization, this term only	4328
#181	hospitaliz* OR hospitalis*	16298
#182	(length NEAR/3 stay) OR "hospital stay"	11735
#183	#179 OR #180 OR #181 OR #182	6
#184	#92 AND #183	0
#185	MeSH descriptor Intensive Care Units explode all trees	1978
#186	"intensive care unit" OR icu OR "intensive care units"	6712
#187	"close attention unit" OR "close attention units"	0
#188	"intensive care department" OR "intensive care departments"	56
#189	"special care unit" OR "special care units"	63
#190	"critical care unit" OR "critical care units"	108
#191	#185 OR #186 OR #187 OR #188 OR #189 OR #190	3
#192	#92 AND #191	0
#193	MeSH descriptor Patient Admission, this term only	604
#194	MeSH descriptor Patient Readmission, this term only	593
#195	"hospital admission" OR "hospital admittance"	1727
#196	"patient admission" OR readmission	2327
#197	rehospitalization OR rehospitalisation	504
#198	#193 OR #194 OR #195 OR #196 OR #197	1
#199	#92 AND #198	0
#200	#98 OR #105 OR #117 OR #141 OR #156 OR #166 OR #178 OR #184 OR #192 OR #199	23

PreMedline: search conducted 25 June 2009

No.	Query	Results
#66	Search #37 OR #39 OR #41 OR #48 OR #54 OR #56 OR #65	168
#65	Search #30 AND #64	3
#64	Search #57 OR #58 OR #59 OR #60 OR #61 OR #62 OR #63	43030
#63	Search orthopedic[tw] AND procedure*[tw]	11166
#62	Search orthopaedic[tw] AND procedure*[tw]	3378
#61	Search "orthopedic operation"[tw] OR "orthopaedic operation"[tw]	75
#60	Search orthopaedic[tw] AND patient*[tw]	8166
#59	Search orthopedic[tw] AND patient*[tw]	15190
#58	Search "bone surgery"[tw] OR orthopaedics[tw] or orthopedics[tw]	17668
#57	Search "orthopedic surgery"[tw] OR "orthopaedic surgery"[tw]	6029
#56	Search #30 AND #55	114
#55	Search surgical[tw] OR surgery[tw] OR operation[tw] OR resection[tw]	1882237
#54	Search #30 AND #53	9
#53	Search #49 OR #50 OR #51 OR #52	54307
#52	Search thoracic[tw] AND procedure*[tw]	19247
#51	Search "thoracic operation"[tw] OR "thoracic surgery"[tw] OR thoracoplasty[tw]	16764
#50	Search cardiothoracic[tw] AND patient*[tw]	2289
#49	Search "cardiothoracic surgery"[tw] OR (chest[tw] AND surgery[tw])	24504
#48	Search #30 AND #47	27
#47	Search #42 OR #43 OR #44 OR #45 OR #46	11341
#46	Search "massive infusion"[tw] OR "massively transfused"[tw]	102
#45	Search massive[tw] AND haemorrhage[tw]	1185
#44	Search massive[tw] AND hemorrhage[tw]	7720
#43	Search massive[tw] AND bleeding[tw]	4969
#42	Search massive[tw] AND transfusion*[tw]	2325
#41	Search #30 AND #40	17
#40	Search shock[tw] OR "cardiovascular collapse"[tw] OR "circulatory collapse"[tw]	135260
#39	Search #30 AND #38	49
#38	Search injur*[tw] OR trauma*[tw]	720728

No.	Query	Results
#37	Search #30 AND #36	73
#36	Search #31 OR #32 OR #33 OR #34 OR #35	613700
#35	Search postoperative[tw] OR "post operative"[tw]	469454
#34	Search peroperative[tw] OR "per operative"[tw]	3712
#33	Search intraoperative[tw] OR "intra operative"[tw]	88495
#32	Search preoperative[tw] OR "pre operative"[tw]	150018
#31	Search perioperative[tw] OR "peri operative"[tw]	43074
#30	Search #27 OR #28 OR #29	391
#29	Search #26 AND pubmednotmedline[sb]	59
#28	Search #26 AND in process[sb]	216
#27	Search #26 NOT (medline[SB] OR oldmedline[sb])	391
#26	Search #14 OR #19 OR #21 OR #23 OR #24 OR #25	17790
#25	Search "thrombocyte transfusion"[tw] OR "thrombocytic transfusion"[tw]	37
#24	Search platelet*[tw] AND transfusion*[tw]	11149
#23	Search #8 AND #22	1327
#22	Search fibrinogen[tw] OR "factor 1"[tw] OR "factor I"[tw]	99755
#21	Search #8 AND #20	423
#20	Search cryoprecipitate[tw] OR "cryo precipitate"[tw]	1449
#19	Search #16 OR #17 OR #18	1957
#18	Search "plasma infusion"[tw] OR "serum transfusion"[tw]	344
#17	Search "plasma transfusion"[tw]	243
#16	Search #8 AND #15	1477
#15	Search "fresh frozen plasma"[tw] OR FFP[tw]	3202
#14	Search #8 AND #13	7052
#13	Search #9 OR #10 OR #11 OR #12	14015
#12	Search "blood constituent"[tw] OR "blood constituents"[tw]	683
#11	Search "transfusion product"[tw] OR "transfusion products"[tw]	67
#10	Search "blood product"[tw] OR "blood products"[tw]	6061
#9	Search "blood component"[tw] OR "blood components"[tw]	7960

No.	Query	Results
#8	Search #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7	89994
#7	Search "transfusion blood"[tw] OR "transfusion therapy"[tw]	1482
#6	Search multitransfusion[tw] OR polytransfusion[tw] OR retransfusion[tw]	478
#5	Search haemotherapy[tw] OR haematherapy[tw] OR haematotherapy[tw]	67
#4	Search hemotherapy[tw] OR hematherapy[tw] OR hematotherapy[tw]	513
#3	Search "blood replacement"[tw] OR "blood retransfusion"[tw]	569
#2	Search "blood exchange"[tw] OR "blood infusion"[tw]	485
#1	Search transfusion[tw]	89172

CINAHL: search conducted 26 June 2009

No.	Query	Results
S221	S101 or S107 or S121 or S151 or S172 or S185 or S197 or S204 or S213 or S220	529[a]
S220	S95 and S219	6
S219	S214 or S215 or S216 or S217 or S218	8367
S218	TI (rehospitalization OR rehospitalisation) or AB (rehospitalization OR rehospitalisation)	440
S217	TI ("patient admission" OR readmission) or AB ("patient admission" OR readmission)	1129
S216	TI ("hospital admission" OR "hospital admittance") or AB ("hospital admission" OR "hospital admittance")	1934
S215	(MH "Readmission")	1926
S214	(MH "Patient Admission")	4308
S213	S95 and S212	57
S212	S205 or S206 or S207 or S208 or S209 or S210 or S211	32811
S211	TI ("critical care unit" OR "critical care units") or AB ("critical care unit" OR "critical care units")	868
S210	TI ("special care unit" OR "special care units") or AB ("special care unit" OR "special care units")	264
S209	TI ("intensive care department" OR "intensive care departments") or AB ("intensive care department" OR "intensive care departments")	33
S208	TI ("close attention unit" OR "close attention units") or AB ("close attention unit" OR "close attention units")	0
S207	TI ("intensive care unit" OR icu OR "intensive care units") or AB ("intensive care unit" OR icu OR "intensive care units")	13701
S206	(MH "Critical Care Nursing+")	15472
S205	(MH "Intensive Care Units+")	14710

No.	Query	Results
S204	S95 and S203	46
S203	S198 or S199 or S200 or S201 or S202	42095
S202	TI ("hospital stay") or AB ("hospital stay")	3313
S201	TI (length N3 stay) or AB (length N3 stay)	5843
S200	TI (hospitaliz* OR hospitalis*) or AB (hospitaliz* OR hospitalis*)	18171
S199	(MH "Child, Hospitalized")	2176
S198	(MH "Hospitalization+")	20839
S197	S95 and S196	40
S196	S186 or S187 or S188 or S189 or S190 or S191 or S192 or S193 or S194 or S195	82178
S195	TI (value N1 money) or AB (value N1 money)	214
S194	TI ("burden of illness") or AB ("burden of illness")	175
S193	TI (resource* and utili*) or AB (resource* and utili*)	3155
S192	TI (cost* or price* or pricing) or AB (cost* or price* or pricing)	45979
S191	TI (economic* or pharmacoeconomic*) or AB (economic* or pharmacoeconomic*)	16293
S190	(MH "Health Care Delivery/UT")	65
S189	(MH "Utilization Review+")	3417
S188	(MH "Economic Value of Life")	236
S187	(MH "Economics")	2517
S186	(MH "Costs and Cost Analysis+")	32852
S185	S95 and S184	19
S184	S173 or S174 or S175 or S180 or S181 or S182	636
S183	TI (intravenous N1 coagulation) OR AB (intravenous N1 coagulation)	0
S182	TI (intravascular N1 coagulopathy) OR AB (intravascular N1 coagulopathy)	36
S181	TI (intravascular N1 coagulation) OR AB (intravascular N1 coagulation)	262
S180	TI (intravascular N1 clotting) OR AB (intravascular N1 clotting)	1
S179	TI (intravasal N1 clotting) OR AB (intravasal N1 clotting)	0
S178	TI ("intravasal agglutination") OR AB ("intravasal agglutination")	0
S177	TI ("disseminated intravasal thromboembolism") OR AB ("disseminated intravasal thromboembolism")	0
S176	TI ("disseminated fibrin thromboembolism") OR AB ("disseminated fibrin thromboembolism")	0
S175	TI ("defibrination syndrome" OR "sanarelli shwartzman syndrome") OR AB ("defibrination syndrome" OR "sanarelli shwartzman syndrome")	1
S174	TI ("consumption coagulopathy" OR "consumptive coagulopathy") OR AB ("consumption coagulopathy" OR "consumptive coagulopathy")	18
S173	(MH "Disseminated Intravascular Coagulation")	494

No.	Query	Results
S172	S95 and S171	7
S171	S157 or S158 or S159 or S160 or S161 or S162 or S164 or S166 or S168 or S170	213
S170	TI ("Repeat Surgery" OR "Surgical Revision") OR AB ("Repeat Surgery" OR "Surgical Revision")	92
S169	TI ("re operations" N15 haemorrhag*) OR AB ("re operations" N15 haemorrhag*)	0
S168	TI ("re operation" N15 haemorrhag*) OR AB ("re operation" N15 haemorrhag*)	1
S167	TI ("re operations" N15 hemorrhag*) OR AB ("re operations" N15 hemorrhag*)	0
S166	TI ("re operation" N15 hemorrhag*) OR AB ("re operation" N15 hemorrhag*)	1
S165	TI ("re operations" N15 "blood loss") OR AB ("re operations" N15 "blood loss")	0
S164	TI ("re operation" N15 "blood loss") OR AB ("re operation" N15 "blood loss")	4
S163	TI ("re operations" N15 bleeding) OR AB ("re operations" N15 bleeding)	0
S162	TI ("re operation" N15 bleeding) OR AB ("re operation" N15 bleeding)	5
S161	TI (re-operation* N15 haemorrhag*) OR AB (re-operation* N15 haemorrhag*)	2
S160	TI (re-operation* N15 hemorrhag) OR AB (re-operation* N15 hemorrhag*)	9
S159	TI (re-operation* N15 "blood loss") OR AB (re-operation* N15 "blood loss")	5
S158	TI (re-operation* N15 bleeding) OR AB (re-operation* N15 bleeding)	41
S157	S152 and S156	63
S156	S153 or S154 or S155	4145
S155	(MH "Blood Loss, Surgical")	626
S154	(MH "postoperative hemorrhage")	501
S153	(MH "hemorrhage")	3116
S152	(MH "Repeat Procedures+")	3142
S151	S95 and S150	37
S150	S122 or S123 or S124 or S125 or S126 or S127 or S128 or S129 or S130 or S131 or S132 or S133 or S134 or S135 or S136 or S137 or S138 or S139 or S140 or S141 or S142 or S143 or S144 or S145 or S146 or S148 or S149	3661
S149	TI ("rbc indices" OR "RBC Index" OR "RBC Indexes") OR AB ("rbc indices" OR "RBC Index" OR "RBC Indexes")	8
S148	TI (red N1 "Cell Indexes") OR AB (red N1 "Cell Indexes")	6
S147	TI (red N1 "Cell Index") OR AB (red N1 "Cell Index")	0
S146	TI (red N1 "cell indices") OR AB (red N1 "cell indices")	24
S145	TI ("erythrocyte indices" OR "Erythrocyte Index" OR "Erythrocyte Indexes") OR AB ("erythrocyte indices" OR "Erythrocyte Index" OR "Erythrocyte Indexes")	8
S144	TI ("Mean Cell" N1 Haemoglobin) OR AB ("Mean Cell" N1 Haemoglobin)	3
S143	TI ("Mean Cell" N1 Hemoglobin) OR AB ("Mean Cell" N1 Hemoglobin)	10
S142	TI ("mean corpuscular haemoglobin" OR "mean corpuscular hemoglobin") OR AB	30

No.	Query	Results
	("mean corpuscular haemoglobin" OR "mean corpuscular hemoglobin")	
S141	TI ("mean corpuscular volume" OR mcv OR mch OR mchc) OR AB ("mean corpuscular volume" OR mcv OR mch OR mchc)	358
S140	TI ("serum haemoglobin" OR "serum hemoglobin") OR AB ("serum haemoglobin" OR "serum hemoglobin")	15
S139	TI ("plasma haemoglobin" OR "plasma hemoglobin") OR AB ("plasma haemoglobin" OR "plasma hemoglobin")	30
S138	TI (hemoglobinometry OR haemoglobinometry) OR AB (hemoglobinometry OR haemoglobinometry)	2
S137	TI ("hb content" OR "hb concentration") OR AB ("hb content" OR "hb concentration")	50
S136	TI (haemoglobin N1 concentration) OR AB (haemoglobin N1 concentration)	70
S135	TI (haemoglobin N1 content) OR AB (haemoglobin N1 content)	4
S134	TI (hemoglobin N1 concentration) OR AB (hemoglobin N1 concentration)	275
S133	TI (hemoglobin N1 content) OR AB (hemoglobin N1 content)	26
S132	TI ("hb determination" OR "hb estimation" OR "hb assay") OR AB ("hb determination" OR "hb estimation" OR "hb assay")	3
S131	TI ("hemoglobin estimation" OR "haemoglobin estimation") OR AB ("hemoglobin estimation" OR "haemoglobin estimation")	3
S130	TI ("hemoglobin assay" OR "haemoglobin assay") OR AB ("hemoglobin assay" OR "haemoglobin assay")	6
S129	TI ("haemoglobin determination" OR "hemoglobin determination") OR AB ("haemoglobin determination" OR "hemoglobin determination")	7
S128	TI ("hb level" OR "hb levels") OR AB ("hb level" OR "hb levels")	170
S127	TI (haemoglobin N1 level*) OR AB (haemoglobin N1 level*)	152
S126	TI (hemoglobin N1 level*) OR AB (hemoglobin N1 level*)	673
S125	TI ("blood haemoglobin" OR "blood hemoglobin") OR AB ("blood haemoglobin" OR "blood hemoglobin")	45
S124	(MH "Erythrocyte Indices")	97
S123	(MH "Hemoglobinometry")	22
S122	(MH "Hemoglobins")	2525
S121	S95 and S120	121
S120	S108 or S109 or S110 or S111 or S112 or S113 or S114 or S115 or S116 or S117 or S118 or S119	809
S119	TI (dose and transfus*)	7
S118	TI (dose N3 platelets) or AB (dose N3 platelets)	3
S117	TI ("platelet dose") or AB ("platelet dose")	3
S116	TI (dose N3 transfus*) or AB (dose N3 transfus*)	14
S115	TI ("transfusion needs") or AB ("transfusion needs")	25

No.	Query	Results
S114	TI (need N3 transfusion*) or AB (need N3 transfusion*)	236
S113	TI ("transfusion interval" OR "transfusion intervals") or AB ("transfusion interval" OR "transfusion intervals")	4
S112	TI (indication* N5 transfusion*) or AB (indication* N5 transfusion*)	34
S111	TI ("transfusion requirement" OR "transfusion requirements") or AB ("transfusion requirement" OR "transfusion requirements")	255
S110	TI (rate* N5 transfusion*) or AB (rate* N5 transfusion*)	169
S109	TI (frequency N5 transfusion*) or AB (frequency N5 transfusion*)	19
S108	(MH "Blood Component Transfusion+/MT")	143
S107	S95 and S106	2
S106	S102 or S103 or S104 or S105	37397
S105	TI (qaly* or "quality adjusted" or "adjusted life") or AB (qaly* or "quality adjusted" or "adjusted life")	834
S104	TI ("health related quality" or hrqol) or AB ("health related quality" or hrqol)	3433
S103	TI (qol OR "quality of life" OR "quality of wellbeing") or AB (qol OR "quality of life" OR "quality of wellbeing")	23773
S102	(MH "Quality of Life+")	26875
S101	S95 and S100	194
S100	S96 or S97 or S98 or S99	152334
S99	TI (mortality OR death OR survival) or AB (mortality OR death OR survival)	72235
S98	TI (morbidity OR incidence OR prevalence OR occurrence) or AB (morbidity OR incidence OR prevalence OR occurrence)	78734
S97	(MH "Mortality+")	18757
S96	(MH "Morbidity+")	28062
S95	S50 or S56 or S60 or S68 or S77 or S82 or S94	505
S94	S36 and S93	32
S93	S83 or S84 or S85 or S86 or S87 or S88 or S89 or S90 or S91 or S92	26353
S92	TI (orthopaedic N1 procedure*) or AB (orthopaedic N1 procedure*)	88
S91	TI (orthopedic N1 procedure*) or AB (orthopedic N1 procedure*)	116
S90	TI ("orthopedic operation" OR "orthopaedic operation") or AB ("orthopedic operation" OR "orthopaedic operation")	6
S89	TI (orthopaedic N1 patient*) or AB (orthopaedic N1 patient*)	359
S88	TI (orthopedic N1 patient*) or AB (orthopedic N1 patient*)	247
S87	TI ("bone surgery" OR orthopaedics or orthopedics) or AB ("bone surgery" OR orthopaedics or orthopedics)	924
S86	TI ("orthopedic surgery" OR "orthopaedic surgery") or AB ("orthopedic surgery" OR "orthopaedic surgery")	803

No.	Query	Results
S85	(MH "Orthopedic Nursing")	1426
S84	(MH "Orthopedics")	3401
S83	(MH "Orthopedic Surgery+")	21657
S82	S36 and S81	344
S81	S78 or S79 or S80	173634
S80	TI (surgical OR surgery OR operation OR resection) or AB (surgical OR surgery OR operation OR resection)	70928
S79	(MH "Medical-Surgical Nursing")	2449
S78	(MH "Surgery, Operative+")	139091
S77	S36 and S76	85
S76	S69 or S70 or S71 or S72 or S73 or S74 or S75	23580
S75	TI (thoracic N1 procedure*) or AB (thoracic N1 procedure*)	34
S74	TI ("thoracic operation" OR "thoracic surgery" OR thoracoplasty) or AB ("thoracic operation" OR "thoracic surgery" OR thoracoplasty)	255
S73	TI (cardiothoracic N1 patient*) or AB (cardiothoracic N1 patient*)	57
S72	TI ("cardiothoracic surgery" OR (chest N1 surgery)) or AB ("cardiothoracic surgery" OR (chest N1 surgery))	170
S71	(MH "Cardiovascular Nursing+")	2682
S70	(MH "Surgery, Cardiovascular+")	17133
S69	(MH "Thoracic Surgery+")	17176
S68	S36 and S67	96
S67	S63 or S64 or S65 or S66	5213
S66	TI (massive N1 (bleeding OR haemorrhage OR hemorrhage)) or AB (massive N1 (bleeding OR haemorrhage OR hemorrhage))	5133
S65	TI ("massive infusion" OR "massively transfused") or AB ("massive infusion" OR "massively transfused")	10
S64	TI (massive N3 transfusion*) or AB (massive N3 transfusion*)	88
S63	S61 and S62	74
S62	TI (massive) or AB (massive)	1910
S61	(MH "Blood Transfusion")	3485
S60	S36 and S59	43
S59	S57 or S58	6769
S58	TI (shock OR "cardiovascular collapse" OR "circulatory collapse") or AB (shock OR "cardiovascular collapse" OR "circulatory collapse")	5247
S57	(MH "Shock+")	3312
S56	S36 and S55	179

No.	Query	Results
S55	S51 or S52 or S53 or S54	122929
S54	TI (injur* OR trauma*) or AB (injur* OR trauma*)	68513
S53	(MH "Trauma Nursing")	532
S52	(MH "Trauma+")	5939
S51	(MH "Wounds and Injuries+")	91987
S50	S36 and S49	192
S49	S37 or S38 or S39 or S40 or S41 or S42 or S43 or S44 or S45 or S46 or S47 or S48	54968
S48	TI (postoperative OR "post operative") or AB (postoperative OR "post operative")	14568
S47	TI (peroperative OR "per operative") or AB (peroperative OR "per operative")	51
S46	TI (intraoperative OR "intra operative") or AB (intraoperative OR "intra operative")	3001
S45	TI (preoperative OR "pre operative") or AB (preoperative OR "pre operative")	7282
S44	TI (perioperative OR "peri operative") or AB (perioperative OR "peri operative")	5369
S43	(MH "Postoperative Period")	1926
S42	(MH "Postoperative Complications+")	21543
S41	(MH "Intraoperative Period")	367
S40	(MH "Intraoperative Complications+")	1832
S39	(MH "Preoperative Period+")	726
S38	(MH "Perioperative Nursing")	8865
S37	(MH "Perioperative Care+")	16246
S36	S16 or S23 or S25 or S29 or S35	1186
S35	S30 or S32 or S33 or S34	482
S34	TI ("thrombocyte transfusion" OR "thrombocytic transfusion") or AB ("thrombocyte transfusion" OR "thrombocytic transfusion")	0
S33	TI platelet* N3 transfusion* or AB platelet* N3 transfusion*	186
S32	S2 and S31	86
S31	(MH "Blood Platelets")	1345
S30	(MH "Platelet Transfusion")	320
S29	S10 and S28	53
S28	S26 or S27	1893
S27	TI (fibrinogen OR "factor 1" OR "factor I") or AB (fibrinogen OR "factor 1" OR "factor I")	1665
S26	(MH "Fibrinogen")	529
S25	S10 and S24	27
S24	TI (cryoprecipitate OR "cryo precipitate") or AB (cryoprecipitate OR "cryo precipitate")	41
S23	S20 or S21 or S22	273
S22	TI ("plasma infusion" OR "serum transfusion") or AB ("plasma infusion" OR "serum	6

No.	Query	Results
	transfusion")	
S21	TI "plasma transfusion"	14
S20	S10 and S19	267
S19	S17 or S18	856
S18	TI ("fresh frozen plasma" OR FFP) or AB ("fresh frozen plasma" OR FFP)	224
S17	(MH "Plasma")	709
S16	S10 and S15	583
S15	S11 or S12 or S13 or S14	966
S14	TI ("blood constituent" OR "blood constituents") or AB ("blood constituent" OR "blood constituents")	11
S13	TI ("transfusion product" OR "transfusion products") or AB ("transfusion product" OR "transfusion products")	5
S12	TI ("blood product" OR "blood products") or AB ("blood product" OR "blood products")	700
S11	TI ("blood component" OR "blood components") or AB ("blood component" OR "blood components")	298
S10	S1 or S2 or S3 or S4 or S5 or S6 or S7 or S8 or S9	5951
S9	TI ("transfusion blood" OR "transfusion therapy") or AB ("transfusion blood" OR "transfusion therapy")	143
S8	TI (multitransfusion OR polytransfusion OR retransfusion) or AB (multitransfusion OR polytransfusion OR retransfusion)	23
S7	TI (haemotherapy OR haematherapy OR haematotherapy) or AB (haemotherapy OR haematherapy OR haematotherapy)	0
S6	TI (hemotherapy OR hematherapy OR hematotherapy) or AB (hemotherapy OR hematherapy OR hematotherapy)	14
S5	TI ("blood replacement" OR "blood retransfusion") or AB ("blood replacement" OR "blood retransfusion")	18
S4	TI ("blood exchange" OR "blood infusion") or AB ("blood exchange" OR "blood infusion")	16
S3	TI transfusion or AB transfusion	3686
S2	(MH "Blood Transfusion")	3485
S1	(MH "Blood Component Transfusion")	843

* The search was conducted using EBSCOhost on 26 June 2009

[a] The records from each of these search statements were exported separately owing to technical difficulties experienced with EBSCOhost when processing this search statement. Consequently there were duplicated records in this number

AMI: search conducted 30 June 2009

No.	Query	Results
#18	((TI=("thrombocyte transfusion" OR "thrombocytic transfusion") OR AB=("thrombocyte transfusion" OR "thrombocytic transfusion")) OR (TI=(platelet* %3 transfusion*) OR AB=(platelet* %3 transfusion*)) OR ((MH_PHRASE="Platelet Transfusion")) OR (((TI=(concentrat*) OR AB=(concentrat*)) AND (((TI=(fibrinogen OR "factor 1" OR "factor I") OR AB=(fibrinogen OR "factor 1" OR "factor I")) OR (MH_PHRASE="Fibrinogen"))))) OR (TI=("plasma infusion" OR "serum transfusion") OR AB=("plasma infusion" OR "serum transfusion")) OR (TI=("plasma transfusion") OR AB=("plasma transfusion")) OR (TI=("fresh frozen plasma" OR FFP) OR AB=("fresh frozen plasma" OR FFP)) OR (TI=("blood constituent" OR "blood constituents") OR AB=("blood constituent" OR "blood constituents")) OR (TI=("transfusion product" OR "transfusion products") OR AB=("transfusion product" OR "transfusion products")) OR (TI=("blood product" OR "blood products") OR AB=("blood product" OR "blood products")) OR (TI=("blood component" OR "blood components") OR AB=("blood component" OR "blood components")) OR ((MH_PHRASE="Blood Component Transfusion")))	191
#17	TI=("thrombocyte transfusion" OR "thrombocytic transfusion") OR AB=("thrombocyte transfusion" OR "thrombocytic transfusion")	0
#16	TI=(platelet* %3 transfusion*) OR AB=(platelet* %3 transfusion*)	13
#15	(MH_PHRASE="Platelet Transfusion")	9
#14	((TI=(concentrat*) OR AB=(concentrat*)) AND (((TI=(fibrinogen OR "factor 1" OR "factor I") OR AB=(fibrinogen OR "factor 1" OR "factor I")) OR (MH_PHRASE="Fibrinogen"))))	31
#13	TI=(concentrat*) OR AB=(concentrat*)	2952
#12	((TI=(fibrinogen OR "factor 1" OR "factor I") OR AB=(fibrinogen OR "factor 1" OR "factor I")) OR (MH_PHRASE="Fibrinogen"))	206
#11	TI=(fibrinogen OR "factor 1" OR "factor I") OR AB=(fibrinogen OR "factor 1" OR "factor I")	204
#10	MH_PHRASE="Fibrinogen"	4
#9	TI=(cryoprecipitate OR "cryo precipitate") OR AB=(cryoprecipitate OR "cryo precipitate")	14
#8	TI=("plasma infusion" OR "serum transfusion") OR AB=("plasma infusion" OR "serum transfusion")	3
#7	TI=("plasma transfusion") OR AB=("plasma transfusion")	0
#6	TI=("fresh frozen plasma" OR FFP) OR AB=("fresh frozen plasma" OR FFP)	29
#5	TI=("blood constituent" OR "blood constituents") OR AB=("blood constituent" OR "blood constituents")	2
#4	TI=("transfusion product" OR "transfusion products") OR AB=("transfusion product" OR "transfusion products")	0
#3	TI=("blood product" OR "blood products") OR AB=("blood product" OR "blood products")	100
#2	TI=("blood component" OR "blood components") OR AB=("blood component" OR "blood components")	18
#1	(MH_PHRASE="Blood Component Transfusion")	23

* The search was conducted using Informit online platform on 30 June 2009

A9 Literature searches, Question 9

In patients undergoing surgery, at what international normalised ratio (INR (prothrombin time/activated partial thromboplastin time [PT/ APTT]) for FFP, fibrinogen level for cryoprecipitate and platelet count for platelet concentrates should patients be transfused to avoid risks of significant adverse events?

EMBASE.com: search conducted 28 June 2009

#	Query	Results
#1	'transfusion'/exp	171,390
#2	'blood transfusion'/exp	108,244
#3	transfus*:ab,ti	68,100
#4	'blood exchange':ab,ti OR 'blood infusion':ab,ti	512
#5	'blood replacement':ab,ti OR 'blood retransfusion':ab,ti	646
#6	hemotherapy:ab,ti OR hematherapy:ab,ti OR hematotherapy:ab,ti	449
#7	haemotherapy:ab,ti OR haematherapy:ab,ti OR haematotherapy:ab,ti	109
#8	multitransfusion:ab,ti OR polytransfusion:ab,ti OR retransfusion:ab,ti	536
#9	'transfusion blood':ab,ti OR 'transfusion therapy':ab,ti	1,732
#10	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9	195,155
#11	'fresh frozen plasma'/exp	3,863
#12	'plasma'/exp	51,796
#13	'plasma transfusion'/exp	1,487
#14	'fresh frozen plasma':ab,ti OR ffp:ab,ti	3,549
#15	'plasma infusion':ab,ti OR 'serum transfusion':ab,ti	386
#16	#11 OR #12 OR #13 OR #14 OR #15	58,271
#17	'international normalized ratio'/exp	2,883
#18	'prothrombin time'/exp	11,644
#19	'partial thromboplastin time'/exp	8,140
#20	'thromboplastin time'/exp	984
#21	'thrombotest'/exp	182
#22	'international standard unit'/exp	2,270
#23	'international sensitivity index':de	4
#24	'dilute russell viper venom time test':de	1
#25	'russell viper venom time':de	8
#26	'dilute russell viper venom time':de	4
#27	'diluted russell viper venom time':de	1
#28	'russell viper venom':de	127

#29	'international normalized ratio':ab,ti OR inr:ab,ti	4,786
#30	'international normalised ratio':ab,ti	320
#31	'international sensitivity index':ab,ti OR isi:ab,ti	2,871
#32	'prothrombin *1 time':ab,ti OR pt:ab,ti OR thrombotest:ab,ti	28,896
#33	'prothrombin test':ab,ti OR 'prothrombine time':ab,ti OR 'protrombin time':ab,ti	91
#34	'howell test':ab,ti OR 'smith test':ab,ti OR 'quick test':ab,ti	345
#35	'russell viper venom time':ab,ti OR drvvt:ab,ti OR rvvt:ab,ti	197
#36	'partial thromboplastin time':ab,ti OR ptt:ab,ti OR aptt:ab,ti	8,527
#37	#17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36	52,753
#38	#16 AND #37	1,674
#39	#10 AND #38	638
#40	'cryoprecipitation'/exp	1,839
#41	'cryoprecipitate coagulum':de	75
#42	cryoprecipitate:ab,ti OR 'cryo precipitate':ab,ti	1,521
#43	#16 OR #40 OR #41 OR #42	60,043
#44	'fibrinogen'/exp	33,692
#45	'fibrinogen blood level'/exp	4,032
#46	fibrinogen:ab,ti OR 'factor 1':ab,ti OR 'factor i':ab,ti	69,316
#47	'9001 32 5':rn	33,702
#48	#44 OR #45 OR #46 OR #47	82,850
#49	#43 AND #48	2,384
#50	#10 AND #49	615
#51	'thrombocyte concentrate'/exp	1,760
#52	'thrombocyte transfusion'/exp	6,565
#53	'thrombocyte'/exp	53,484
#54	#2 OR #3	133,476
#55	#53 AND #54	3,041
#56	'thrombocyte concentrate':ab,ti OR 'thrombocyte concentrates':ab,ti	100
#57	'platelet concentrate':ab,ti OR 'platelet concentrates':ab,ti	2,198
#58	'platelet *1 transfusion':ab,ti OR 'platelet *1 transfusions':ab,ti	2,968
#59	'transfusion *3 platelet':ab,ti OR 'transfusion *3 platelets':ab,ti	701
#60	'thrombocyte transfusion':ab,ti OR 'thrombocytic transfusion':ab,ti	42
#61	#51 OR #52 OR #54 OR #55 OR #56 OR #57 OR #58 OR #59 OR #60	134,760
#62	'thrombocyte count'/exp	21,426
#63	'thrombocyte count':ab,ti OR 'thrombocytic count':ab,ti	414

#64	'thrombocyte counts':ab,ti OR 'thrombocytic counts':ab,ti	236
#65	'thrombocyte number':ab,ti OR 'thrombocyte numbers':ab,ti	56
#66	'thrombocyte counting':ab,ti OR 'platelet counting':ab,ti	237
#67	'platelet count':ab,ti OR 'platelet counts':ab,ti	16,635
#68	'platelet number':ab,ti OR 'platelet numbers':ab,ti	906
#69	#62 OR #63 OR #64 OR #65 OR #66 OR #67 OR #68	30,335
#70	#61 AND #69	4,484
#71	#10 AND #70	4,336
#72	#39 OR #50 OR #71	5,178
#73	(('perioperative period'/exp) OR ('perioperative nursing'/exp) OR ('perioperative complication'/exp) OR ('preoperative period'/exp) OR ('preoperative complication'/exp) OR ('intraoperative period'/exp) OR (perioperative:ab,ti OR 'peri operative':ab,ti) OR (preoperative:ab,ti OR 'pre operative':ab,ti) OR (intraoperative:ab,ti OR 'intra operative':ab,ti) OR (peroperative:ab,ti OR 'per operative':ab,ti)) OR ('postoperative period'/exp) OR ('postoperative complication'/exp) OR (postoperative:ab,ti OR 'post operative':ab,ti)	870,712
#74	('injury'/exp) OR (injur*:ab,ti OR trauma*:ab,ti)	1,270,020
#75	('shock'/exp) OR (shock:ab,ti OR 'cardiovascular collapse':ab,ti OR 'circulatory collapse':ab,ti)	136,258
#76	((('blood transfusion'/exp) OR (('bleeding'/exp) AND ('transfusion'/exp))) AND (massive:ab,ti)) OR ('massive transfusion':ab,ti) OR ('massive blood transfusion':ab,ti) OR ('massive transfusion protocol':ab,ti) OR ('massive *3 transfusion':ab,ti OR 'massive *3 transfusions':ab,ti) OR ('massive infusion':ab,ti OR 'massively transfused':ab,ti) OR ('massive *1 bleeding':ab,ti) OR ('massive *1 haemorrhage':ab,ti OR 'massive *1 hemorrhage':ab,ti)	8,454
#77	('thorax surgery'/exp) OR ('heart surgery'/exp) OR ('cardiothoracic surgery':ab,ti OR 'chest *1 surgery':ab,ti) OR ('cardiothoracic *1 patient':ab,ti OR 'cardiothoracic *1 patients':ab,ti) OR ('thoracic operation':ab,ti OR 'thoracic surgery':ab,ti OR thoracoplasty:ab,ti) OR ('thoracic *1 procedure':ab,ti OR 'thoracic *1 procedures':ab,ti)	286,978
#78	('surgery'/exp) OR ('surgical ward'/exp) OR ('surgical patient'/exp) OR (surgical:ab,ti OR surgery:ab,ti OR operation:ab,ti OR resection:ab,ti)	2,742,947
#79	('orthopedic surgery'/exp) OR ('orthopedic surgery':ab,ti OR 'orthopaedic surgery':ab,ti) OR ('bone surgery':ab,ti OR orthopaedics:ab,ti OR orthopedics:ab,ti) OR ('orthopedic *1 patient':ab,ti OR 'orthopedic *1 patients':ab,ti) OR ('orthopaedic *1 patient':ab,ti OR 'orthopaedic *1 patients':ab,ti) OR ('orthopedic operation':ab,ti OR 'orthopedic *1 procedures':ab,ti) OR ('orthopaedic operation':ab,ti OR 'orthopaedic *1 procedures':ab,ti) OR ('orthopedic *1 procedure':ab,ti OR 'orthopaedic *1 procedure':ab,ti)	260,054
#80	#73 OR #74 OR #75 OR #76 OR #77 OR #78 OR #79	3,704,145
#81	#72 AND #80	3,018
#82	('adverse outcome'/exp) OR ('outcome assessment'/exp) OR ('morbidity'/exp) OR ('mortality'/exp) OR (morbidity:ab,ti OR incidence:ab,ti OR prevalence:ab,ti OR occurrence:ab,ti) OR (mortality:ab,ti OR death:ab,ti OR survival:ab,ti)	1,941,273
#83	('quality of life'/exp) OR (qol:ab,ti OR 'quality of life':ab,ti OR 'quality of wellbeing':ab,ti) OR ('health related quality':ab,ti OR hrqol:ab,ti) OR (qaly*:ab,ti OR 'quality adjusted':ab,ti OR	161,320

	'adjusted life':ab,ti)	
#84	(('blood component therapy'/exp) AND (('dose response'/exp) OR ('drug dose'/exp))) OR ('fresh frozen plasma'/exp/dd_do) OR ('recombinant erythropoietin'/exp/dd_do) OR ('transfusion frequency':ab,ti) OR ('frequency *5 transfusion':ab,ti OR 'frequency *5 transfusions':ab,ti) OR ('transfusion rate':ab,ti OR 'transfusion rates':ab,ti) OR ('rate *5 transfusion':ab,ti OR 'rates *5 transfusion':ab,ti) OR ('transfusion requirement':ab,ti OR 'transfusion requirements':ab,ti) OR ('transfusion indication':ab,ti OR 'transfusion indications':ab,ti) OR ('indications *5 transfusion':ab,ti OR 'indications *5 transfusions':ab,ti) OR ('indication *5 transfusion':ab,ti OR 'indication *5 transfusions':ab,ti) OR ('transfusion interval':ab,ti OR 'transfusion intervals':ab,ti) OR ('need *3 transfusion':ab,ti OR 'need *3 transfusions':ab,ti) OR ('transfusion need':ab,ti OR 'transfusion needs':ab,ti) OR ('dose *3 transfusion':ab,ti OR 'dose *3 transfusions':ab,ti) OR ('dose *3 transfused':ab,ti OR 'transfusions *3 dose':ab,ti) OR ('transfusion dose':ab,ti OR 'transfused *3 dose':ab,ti) OR ('platelet dose':ab,ti OR 'dose *3 platelets':ab,ti) OR (dose:ab,ti AND transfus*:ab,ti)	17,493
#85	#82 OR #83 OR #84	2,063,307
#86	#81 AND #85	1,366

EMBASE.com: search conducted 4 January 2010

#	Query	Results
#232	#84 OR #96 OR #108 OR #115 OR #119 OR #125 OR #141 OR #145 OR #160 OR #165 OR #173 OR #182 OR #187 OR #191 OR #197 OR #203 OR #210 OR #215 OR #224 OR #229 OR #231	716
#231	#72 AND #230	178
#230	'nonsurgical invasive therapy'/exp	200,774
#229	#72 AND #228	11
#228	#225 OR #226 OR #227	86,814
#227	neuroradiography OR neuroroentgenology:ab,ti	29
#226	neuroradiology OR neuroradiological:ab,ti	86,802
#225	'neuroradiology'/exp	57,931
#224	#72 AND #223	5
#223	#216 OR #219 OR #220 OR #221 OR #222	2,622
#222	'subarachnoid pressure monitoring':ab,ti	2
#221	'brain pressure monitoring' OR 'intracerebral pressure monitoring':ab,ti	4
#220	'intracranial pressure monitoring' OR 'intracranial tension monitoring':ab,ti	1,161
#219	#217 AND #218	1,772
#218	'monitoring'/exp	247,179
#217	'intracranial pressure'/de	14,460
#216	'intracranial pressure monitoring'/de	524
#215	#72 AND #214	0

#214	#211 OR #212 OR #213	694
#213	'peribulbar block' OR 'peribulbar blockade':ab,ti	173
#212	'peribulbar anesthesia' OR 'peribulbar anaesthesia':ab,ti	636
#211	'peribulbar anesthesia'/de	436
#210	#72 AND #209	0
#209	#204 OR #205 OR #206 OR #207 OR #208	1,053
#208	'retro ocular block' OR 'retro ocular blockade':ab,ti	1
#207	'retroocular block' OR 'retroocular blockade':ab,ti	0
#206	'retrobulbar block' OR 'retrobulbar blockade':ab,ti	228
#205	'retrobulbar anesthesia' OR 'retrobulbar anaesthesia':ab,ti	981
#204	'retrobulbar anesthesia'/de	785
#203	#72 AND #202	75
#202	#198 OR #199 OR #200 OR #201	262,689
#201	'blood vessel radiography' OR vasography:ab,ti	162
#200	'peripheral vasculography' OR 'rheoacroangiography':ab,ti	1
#199	angiography OR angioradiology OR arteriography:ab,ti	262,568
#198	'angiography'/exp	230,856
#197	#72 AND #196	8
#196	#192 OR #193 OR #194 OR #195	18,509
#195	tips OR tipss:ab,ti	17,723
#194	('transjugular intrahepatic' NEXT/3 (stent OR stents OR stenting)):ab,ti	336
#193	('transjugular intrahepatic' NEXT/3 (shunt OR shunts OR shunting)):ab,ti	1,974
#192	'transjugular intrahepatic portosystemic shunt'/de	325
#191	#72 AND #190	3
#190	#188 OR #189	4,899
#189	polypectomy:ab,ti	3,418
#188	'polypectomy'/de	2,856
#187	#72 AND #186	0
#186	#183 OR #184 OR #185	75
#185	'central nerve blockade' OR 'central nerve block':ab,ti	20
#184	'central neural blockade' OR 'central neural block':ab,ti	56
#183	'central neural blockade':de	1
#182	#72 AND #181	21
#181	#174 OR #175 OR #176 OR #177 OR #178 OR #179 OR #180	28,415
#180	regional NEXT/2 analgesia OR 'bier block':ab,ti	755

#179	'anesthesia regionalis' OR 'anaesthesia regionalis':ab,ti	0
#178	'region anesthesia' OR 'region anaesthesia':ab,ti	4
#177	'block anesthesia' OR 'block anaesthesia':ab,ti	619
#176	'conduction anesthesia' OR 'conduction anaesthesia':ab,ti	366
#175	(regional NEXT/2 (anesthesia OR anaesthesia)):ab,ti	6,392
#174	'regional anesthesia'/exp	25,544
#173	#72 AND #172	8
#172	#166 OR #167 OR #168 OR #169 OR #170 OR #171	3,490
#171	'pleural punction' OR 'pleural puncture':ab,ti	166
#170	'pleura punction' OR 'pleura puncture':ab,ti	7
#169	'pleura aspiration' OR 'pleural aspiration':ab,ti	80
#168	pleurocantensis OR pleuracentesis OR pleurocentesis:ab,ti	65
#167	thoracentesis OR thoracocentesis:ab,ti	1,571
#166	'thoracocentesis'/de	2,575
#165	#72 AND #164	15
#164	#161 OR #162 OR #163	6,839
#163	'spinal puncture' OR 'spinal tap':ab,ti	522
#162	'lumbar punction' OR 'thecal puncture' OR rachiocentesis:ab,ti	65
#161	'lumbar puncture'/de	6,356
#160	#72 AND #159	1
#159	#146 OR #156 OR #157 OR #158	415
#158	'endo luminal stent' OR 'endo luminal stents' OR 'endo luminal stenting':ab,ti	1
#157	'endoluminal stent' OR 'endoluminal stents' OR 'endoluminal stenting':ab,ti	408
#156	#154 AND #155	10
#155	'stent'/exp	52,095
#154	#147 OR #148 OR #149 OR #150 OR #151 OR #152 OR #153	15
#153	'endoluminal treatment':de	3
#152	'endoluminal repair':de	3
#151	'endoluminal stent graft':de	3
#150	'endoluminal grafting':de	1
#149	'endoluminal therapy':de	3
#148	'endoluminal flow disrupting device':de	1
#147	'endoluminal aortic stent grafting':de	1
#146	'endoluminal stent':de	7
#145	#72 AND #144	49

#144	#142 OR #143	58,694
#143	angioplasty OR 'endoluminal repair' OR 'endo luminal repair':ab,ti	58,694
#142	'angioplasty'/exp	47,959
#141	#72 AND #140	81
#140	#126 OR #127 OR #128 OR #129 OR #130 OR #131 OR #132 OR #133 OR #134 OR #135 OR #136 OR #137 OR #138 OR #139	112,103
#139	(cardiac NEXT/2 ablation):ab,ti	112
#138	'coronary arteriogram' OR 'coronary arteriography':ab,ti	4,911
#137	'coronary angiography' OR coronarography:ab,ti	21,398
#136	'transluminal coronary artery dilatation':ab,ti	4
#135	(coronary NEXT/2 (angioplasty OR balloon)):ab,ti	13,750
#134	'percutaneous coronary intervention' OR 'percutaneous coronary stent':ab,ti	34,295
#133	'interventional cardiology' OR 'p t c a' OR ptca:ab,ti	12,844
#132	'thoracoscopic microwave epicardial ablation':de	1
#131	'percutaneous epicardial ablation':de	1
#130	'heart ablation':de	1
#129	'epicardial ablation':de	4
#128	'epicardial high intensity focused ultrasound cardiac ablation':de	1
#127	'angiocardiography'/exp	55,931
#126	'interventional cardiovascular procedure'/exp	51,294
#125	#72 AND #124	16
#124	#120 OR #121 OR #122 OR #123	5,270
#123	'pericardial aspiration' OR 'pericardium puncture':ab,ti	49
#122	paracentesis OR pericardicentesis OR pericardiocentesis:ab,ti	5,227
#121	pericardiocentesis:ab,ti	1,475
#120	'paracentesis'/de	2,605
#119	#72 AND #118	7
#118	#116 OR #117	7,432
#117	(('central venous' OR 'central vein') NEXT/2 catheteri?ation):ab,ti	5,219
#116	'central venous catheterization'/de	5,344
#115	#72 AND #114	364
#114	#109 OR #110 OR #111 OR #112 OR #113	414,673
#113	'kidney puncture' OR 'renal puncture' OR 'pyelocalycial puncture':ab,ti	190
#112	'hepatic puncture' OR 'liver puncture':ab,ti	282
#111	'bronchus brushing' OR 'tracheobronchial smear':ab,ti	2
#110	biopsy OR biopsies OR biopsied:ab,ti	414,521

#109	'biopsy'/exp	305,255
#108	#72 AND #107	127
#107	#97 OR #98 OR #99 OR #100 OR #101 OR #102 OR #103 OR #104 OR #105 OR #106	315,571
#106	uteroscopy:ab,ti	9
#105	hysteroscopy OR hysteroscopies OR hysteroscopic:ab,ti	6,028
#104	proctosigmoidoscopy OR rectoromanoscopy OR rectosigmoidoscopy:ab,ti	515
#103	sigmoidoscopy OR sigmoideoscopy OR sigmoidoscopic:ab,ti	7,732
#102	colonoscopy OR coloscopy OR colonoscopic:ab,ti	27,898
#101	cardioendoscopy OR pylorobulboscopy:ab,ti	1
#100	gastroscopic OR fibergastroscopy OR fibrogastroscopy:ab,ti	1,091
#99	gastroscopy OR gastrofibroscopy OR 'stomach endoscopy':ab,ti	15,886
#98	endoscopy OR endoscopies OR endoscopic:ab,ti	310,900
#97	'endoscopy'/exp	249,520
#96	#72 AND #95	24
#95	#85 OR #86 OR #87 OR #88 OR #89 OR #90 OR #91 OR #92 OR #93 OR #94	26,433
#94	'peridural analgesia' OR 'peridural block' OR 'peridural blocking':ab,ti	405
#93	'peridural anesthesia' OR 'peridural anaesthesia':ab,ti	1,296
#92	'extradural analgesia' OR 'extradural block':ab,ti	402
#91	'extradural anesthesia' OR 'extradural anaesthesia':ab,ti	219
#90	'caudal block' OR 'caudal blocking' OR 'dural blocking':ab,ti	371
#89	'caudal anesthesia' OR 'caudal anaesthesia':ab,ti	1,192
#88	'epidural analgesia' OR 'epidural block' OR 'epidural blockade':ab,ti	7,205
#87	'epidural anesthetic' OR 'epidural anaesthetic':ab,ti	207
#86	'epidural anesthesia' OR 'epidural anaesthesia':ab,ti	24,383
#85	'epidural anesthesia'/exp	22,947
#84	#72 AND #83	22
#83	#73 OR #74 OR #75 OR #76 OR #77 OR #78 OR #79 OR #80 OR #81 OR #82	15,395
#82	'intraspinal anesthesia' OR 'intraspinal anaesthesia':ab,ti	4
#81	'subarachnoidal anesthesia' OR 'subarachnoidal anaesthesia':ab,ti	22
#80	'subarachnoid anesthesia' OR 'subarachnoid anaesthesia':ab,ti	302
#79	'spinal block' OR 'subarachnoid block' OR 'intraspinal block':ab,ti	949
#78	'spinal cord anesthesia' OR 'spinal cord anaesthesia':ab,ti	7
#77	'spinal anesthetic' OR 'spinal anesthaetic':ab,ti	221
#76	'lumbar anaesthesia' OR 'lumbar anesthesia':ab,ti	113
#75	'spinal analgesia' OR 'lumbar extradural blockade':ab,ti	607

#74	'spinal anesthesia' OR 'spinal anaesthesia':ab,ti	14,832
#73	'spinal anesthesia'/de	13,606
#72	#39 OR #50 OR #71	5,252
#71	#10 AND #70	4,353
#70	#61 AND #69	4,586
#69	#62 OR #63 OR #64 OR #65 OR #66 OR #67 OR #68	33,564
#68	'platelet number' OR 'platelet numbers':ab,ti	1,067
#67	'platelet count' OR 'platelet counts':ab,ti	20,358
#66	'thrombocyte counting' OR 'platelet counting':ab,ti	275
#65	'thrombocyte number' OR 'thrombocyte numbers':ab,ti	65
#64	'thrombocyte counts' OR 'thrombocytic counts':ab,ti	269
#63	'thrombocyte count' OR 'thrombocytic count':ab,ti	23,025
#62	'thrombocyte count'/de	22,733
#61	#51 OR #54 OR #55 OR #56 OR #57 OR #58 OR #59 OR #60	120,664
#60	'thrombocyte transfusion' OR 'thrombocytic transfusion':ab,ti	6,894
#59	'transfusion' NEAR/3 'platelet' OR ('transfusion' NEAR/3 'platelets'):ab,ti	2,717
#58	'platelet' NEAR/1 'transfusion' OR ('platelet' NEAR/1 'transfusions'):ab,ti	3,345
#57	'platelet concentrate' OR 'platelet concentrates':ab,ti	2,495
#56	'thrombocyte concentrate' OR 'thrombocyte concentrates':ab,ti	1,978
#55	#53 AND #54	3,198
#54	#2 OR #3	119,286
#53	'thrombocyte'/exp	56,400
#52	'thrombocyte transfusion'/de	6,879
#51	'thrombocyte concentrate'/de	1,883
#50	#10 AND #49	671
#49	#43 AND #48	2,709
#48	#44 OR #45 OR #46 OR #47	127,083
#47	'9001 32 5':rn	35,032
#46	fibrinogen OR 'factor 1' OR 'factor i':ab,ti	127,083
#45	'fibrinogen blood level'/de	4,212
#44	'fibrinogen'/de	35,268
#43	#16 OR #40 OR #41 OR #42	61,824
#42	cryoprecipitate OR 'cryo precipitate':ab,ti	2,522
#41	'cryoprecipitate coagulum':de	72
#40	'cryoprecipitation'/exp	1,951

#39	#10 AND #38	698
#38	#16 AND #37	1,922
#37	#17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36	139,210
#36	'partial thromboplastin time' OR ptt OR aptt:ab,ti	14,190
#35	'russell viper venom time' OR drvvt OR rvvt:ab,ti	228
#34	'howell test' OR 'smith test' OR 'quick test':ab,ti	397
#33	'prothrombin test' OR 'prothrombine time' OR 'protrombin time':ab,ti	107
#32	prothrombin NEXT/2 time OR pt OR thrombotest:ab,ti	120,615
#31	'international sensitivity index' OR isi:ab,ti	3,140
#30	'international normalised ratio':ab,ti	344
#29	'international normalized ratio' OR inr:ab,ti	7,233
#28	'russell viper venom':de	129
#27	'diluted russell viper venom time':de	1
#26	'dilute russell viper venom time':de	4
#25	'russell viper venom time':de	8
#24	'dilute russell viper venom time test':de	1
#23	'international sensitivity index':de	4
#22	'international standard unit'/de	2,042
#21	'thrombotest'/de	183
#20	'thromboplastin time'/de	1,006
#19	'partial thromboplastin time'/de	8,542
#18	'prothrombin time'/de	12,623
#17	'international normalized ratio'/de	3,670
#16	#11 OR #12 OR #13 OR #14 OR #15	59,927
#15	'plasma infusion' OR 'serum transfusion':ab,ti	421
#14	'fresh frozen plasma' OR ffp:ab,ti	6,533
#13	'plasma transfusion'/de	1,596
#12	'plasma'/de	52,860
#11	'fresh frozen plasma'/de	4,278
#10	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9	120,967
#9	'transfusion blood' OR 'transfusion therapy':ab,ti	1,894
#8	multitransfusion OR polytransfusion OR retransfusion:ab,ti	592
#7	haemotherapy OR haematherapy OR haematotherapy:ab,ti	200
#6	hemotherapy OR hematherapy OR hematotherapy:ab,ti	1,317
#5	'blood replacement'/exp OR 'blood retransfusion':ab,ti	91,098

#4	'blood exchange' OR 'blood infusion':ab,ti	589
#3	transfus*:ab,ti	76,034
#2	'blood transfusion'/exp	91,090
#1	'transfusion'/de	2,411

Cochrane Library Database: search conducted 28 June 2009

#	Query	Results
#1	MeSH descriptor Blood Transfusion explode all trees	2628
#2	transfus*	6897
#3	"blood exchange" OR "blood infusion"	42
#4	"blood replacement" OR "blood retransfusion"	73
#5	hemotherapy OR hematherapy OR hematotherapy	55
#6	haemotherapy OR haematherapy OR haematotherapy	5
#7	multitransfusion OR polytransfusion OR retransfusion	66
#8	"transfusion blood" OR "transfusion therapy"	224
#9	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8	1922
#10	MeSH descriptor Plasma, this term only	236
#11	"fresh frozen plasma" OR FFP	348
#12	"plasma transfusion"	30
#13	"plasma infusion" OR "serum transfusion"	17
#14	#10 OR #11 OR #12 OR #13	1422
#15	MeSH descriptor International Normalized Ratio, this term only	263
#16	MeSH descriptor Prothrombin Time, this term only	362
#17	MeSH descriptor Partial Thromboplastin Time, this term only	376
#18	"international normalized ratio" OR inr	728
#19	"international normalised ratio"	123
#20	"International Sensitivity Index" OR isi	723
#21	(prothrombin NEAR/1 time) OR pt OR Thrombotest	13024
#22	"prothrombin test" OR "prothrombine time" OR "protrombin time"	13
#23	"howell test" OR "smith test" OR "Quick Test"	19
#24	"Russell Viper Venom Time" OR dRVVT OR RVVT	9
#25	"partial thromboplastin time" OR ptt OR aptt	1096
#26	#15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25	1129
#27	#14 AND #26	479
#28	#9 AND #27	452

#29	cryoprecipitate	65
#30	cryoprecipitate OR "cryo precipitate"	65
#31	#14 OR #29 OR #30	1122
#32	MeSH descriptor Fibrinogen, this term only	954
#33	fibrinogen OR "factor 1" OR "factor I"	4401
#34	#32 OR #33	335
#35	#31 AND #34	280
#36	#9 AND #35	260
#37	MeSH descriptor Platelet Transfusion, this term only	208
#38	MeSH descriptor Blood Platelets, this term only	1366
#39	MeSH descriptor Blood Transfusion, this term only	1519
#40	#38 AND #39	217
#41	"thrombocyte concentrate" OR "thrombocyte concentrates"	16
#42	"platelet concentrate" OR "platelet concentrates"	176
#43	platelet* NEAR/3 transfusion*	552
#44	"thrombocyte transfusion" OR "thrombocytic transfusion"	40
#45	#37 OR #40 OR #41 OR #42 OR #43 OR #44	317
#46	MeSH descriptor Platelet Count, this term only	955
#47	"thrombocyte count" OR "thrombocytic count"	133
#48	"thrombocyte counts" OR "thrombocytic counts"	11
#49	"thrombocyte number" OR "thrombocyte numbers"	1
#50	"thrombocyte counting" OR "platelet counting"	9
#51	"platelet count" OR "platelet counts"	2114
#52	"platelet number" OR "platelet numbers"	75
#53	#46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52	177
#54	#45 AND #53	99
#55	#9 AND #54	92
#56	#28 OR #36 OR #55	442
#57	MeSH descriptor Perioperative Care explode all trees	4254
#58	MeSH descriptor Preoperative Care explode all trees	4098
#59	MeSH descriptor Postoperative Complications explode all trees	21418
#60	MeSH descriptor Postoperative Period explode all trees	3483
#61	MeSH descriptor Intraoperative Complications explode all trees	2476
#62	MeSH descriptor Intraoperative Period, this term only	919
#63	perioperative OR "peri operative"	5196

#64	preoperative OR "pre operative"	11093
#65	intraoperative OR "intra operative"	8039
#66	peroperative OR "per operative"	474
#67	postoperative OR "post operative"	40236
#68	#57 OR #58 OR #59 OR #60 OR #61 OR #62 OR #63 OR #64 OR #65 OR #66 OR #67	106
#69	#56 AND #68	51
#70	MeSH descriptor Wounds and Injuries explode all trees	10953
#71	injur* OR trauma*	20750
#72	#70 OR #71	54
#73	#56 AND #72	48
#74	MeSH descriptor Shock explode all trees	930
#75	shock OR "cardiovascular collapse" OR "circulatory collapse"	3179
#76	#74 OR #75	50
#77	#56 AND #76	41
#78	MeSH descriptor Blood Transfusion, this term only	1519
#79	massive	599
#80	#78 AND #79	39
#81	massive NEAR/3 transfusion*	20
#82	"massive infusion" OR "massively transfused"	3
#83	massive NEAR/1 (bleeding OR haemorrhage OR hemorrhage)	47
#84	#80 OR #81 OR #82 OR #83	43
#85	#56 AND #84	35
#86	MeSH descriptor Thoracic Surgical Procedures explode all trees	10297
#87	MeSH descriptor Thoracic Surgery, this term only	130
#88	MeSH descriptor Cardiovascular Surgical Procedures explode all trees	10930
#89	"cardiothoracic surgery" OR (chest NEAR/1 surgery)	675
#90	cardiothoracic NEAR/1 patient*	4
#91	"thoracic operation" OR "thoracic surgery" OR thoracoplasty	2131
#92	thoracic NEAR/1 procedure*	16
#93	#86 OR #87 OR #88 OR #89 OR #90 OR #91 OR #92	47
#94	#56 AND #93	24
#95	MeSH descriptor Surgical Procedures, Operative explode all trees	68578
#96	MeSH descriptor General Surgery, this term only	167
#97	MeSH descriptor Surgery Department, Hospital, this term only	68
#98	surgical OR surgery OR operation OR resection	91783

#99	#95 OR #96 OR #97 OR #98	27
#100	#56 AND #99	17
#101	MeSH descriptor Orthopedic Procedures explode all trees	5335
#102	MeSH descriptor Orthopedics, this term only	272
#103	"orthopedic surgery" OR "orthopaedic surgery"	2339
#104	"bone surgery" OR orthopaedics or orthopedics	7975
#105	(orthopedic OR orthopaedic) NEAR/1 patient*	223
#106	"orthopedic operation" OR "orthopaedic operation"	6
#107	(orthopedic OR orthopaedic) NEAR/1 procedure*	638
#108	#101 OR #102 OR #103 OR #104 OR #105 OR #106 OR #107	30
#109	#56 AND #108	13
#110	#69 OR #73 OR #77 OR #85 OR #94 OR #100 OR #109	74
#111	MeSH descriptor Morbidity explode all trees	8475
#112	MeSH descriptor Mortality explode all trees	7946
#113	morbidity OR incidence OR prevalence OR occurrence	62784
#114	mortality OR death OR survival	55325
#115	#111 OR #112 OR #113 OR #114	20
#116	#110 AND #115	11
#117	MeSH descriptor Quality of Life, this term only	9425
#118	MeSH descriptor Quality-Adjusted Life Years, this term only	2062
#119	qol OR "quality of life" OR "quality of wellbeing"	21521
#120	"health related quality" or hrqol	2898
#121	qaly* or "quality adjusted" or "adjusted life"	3802
#122	#117 OR #118 OR #119 OR #120 OR #121	25
#123	#110 AND #122	9
#124	MeSH descriptor Blood Component Transfusion explode all trees with qualifier: MT	99
#125	frequency NEAR/5 transfusion*	84
#126	rate* NEAR/5 transfusion*	324
#127	"transfusion requirement" OR "transfusion requirements"	949
#128	indication* NEAR/5 transfusion*	45
#129	"transfusion interval" OR "transfusion intervals"	13
#130	(need NEAR/3 transfusion*) OR "transfusion needs"	623
#131	dose NEAR/3 transfus*	86
#132	"platelet dose" OR (dose NEAR/3 platelets)	185
#133	(dose and transfus*):ti	72

#134	#124 OR #125 OR #126 OR #127 OR #128 OR #129 OR #130 OR #131 OR #132 OR #133	15
#135	#110 AND #134	8
#136	#116 OR #123 OR #135	15

Cochrane Library Database: search conducted 4 January 2010

#	Query	Results
#1	MeSH descriptor Blood Transfusion explode all trees	2,756
#2	transfus*	7,133
#3	"blood exchange" OR "blood infusion"	43
#4	"blood replacement" OR "blood retransfusion"	73
#5	hemotherapy OR hematherapy OR hematotherapy	56
#6	haemotherapy OR haematherapy OR haematotherapy	7
#7	multitransfusion OR polytransfusion OR retransfusion	69
#8	"transfusion blood" OR "transfusion therapy"	233
#9	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8	2,074
#10	MeSH descriptor Plasma, this term only	255
#11	"fresh frozen plasma" OR FFP	360
#12	"plasma transfusion"	31
#13	"plasma infusion" OR "serum transfusion"	17
#14	#10 OR #11 OR #12 OR #13	1,547
#15	MeSH descriptor International Normalized Ratio, this term only	278
#16	MeSH descriptor Prothrombin Time, this term only	368
#17	MeSH descriptor Partial Thromboplastin Time, this term only	385
#18	"international normalized ratio" OR inr	771
#19	"international normalised ratio"	132
#20	"International Sensitivity Index" OR isi	819
#21	(prothrombin NEAR/1 time) OR pt OR Thrombotest	14,153
#22	"prothrombin test" OR "prothrombine time" OR "protrombin time"	13
#23	"howell test" OR "smith test" OR "Quick Test"	23
#24	"Russell Viper Venom Time" OR dRVVT OR RVVT	9
#25	"partial thromboplastin time" OR ptt OR aptt	1,127
#26	#15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25	1,227
#27	#14 AND #26	512
#28	#9 AND #27	481

#29	cryoprecipitate	66
#30	cryoprecipitate OR "cryo precipitate"	66
#31	#14 OR #29 OR #30	1,228
#32	MeSH descriptor Fibrinogen, this term only	988
#33	fibrinogen OR "factor 1" OR "factor I"	4,567
#34	#32 OR #33	352
#35	#31 AND #34	296
#36	#9 AND #35	277
#37	MeSH descriptor Platelet Transfusion, this term only	217
#38	MeSH descriptor Blood Platelets, this term only	1,401
#39	MeSH descriptor Blood Transfusion, this term only	1,588
#40	#38 AND #39	230
#41	"thrombocyte concentrate" OR "thrombocyte concentrates"	16
#42	"platelet concentrate" OR "platelet concentrates"	179
#43	platelet* NEAR/3 transfusion*	580
#44	"thrombocyte transfusion" OR "thrombocytic transfusion"	41
#45	#37 OR #40 OR #41 OR #42 OR #43 OR #44	334
#46	MeSH descriptor Platelet Count, this term only	987
#47	"thrombocyte count" OR "thrombocytic count"	146
#48	"thrombocyte counts" OR "thrombocytic counts"	11
#49	"thrombocyte number" OR "thrombocyte numbers"	1
#50	"thrombocyte counting" OR "platelet counting"	10
#51	"platelet count" OR "platelet counts"	2,178
#52	"platelet number" OR "platelet numbers"	77
#53	#46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52	185
#54	#45 AND #53	102
#55	#9 AND #54	97
#56	#28 OR #36 OR #55	468
#57	MeSH descriptor Anesthesia, Spinal, this term only	1,534
#58	"spinal anesthesia" OR "spinal anaesthesia"	2,104
#59	"spinal analgesia" OR "lumbar extradural blockade"	144
#60	"lumbar anaesthesia" OR "lumbar anesthesia"	9
#61	"spinal anesthetic" OR "spinal anesthaetic"	68
#62	"spinal cord anesthesia" OR "spinal cord anaesthesia"	0
#63	"spinal block" OR "subarachnoid block" OR "intraspinal block"	295

#64	"subarachnoid anesthesia" OR "subarachnoid anaesthesia"	81
#65	"subarachnoidal anesthesia" OR "subarachnoidal anaesthesia"	3
#66	"intraspinal anesthesia" OR "intraspinal anaesthesia"	1
#67	#57 OR #58 OR #59 OR #60 OR #61 OR #62 OR #63 OR #64 OR #65 OR #66	111
#68	#56 AND #67	54
#69	MeSH descriptor Anesthesia, Epidural explode all trees	1,559
#70	"epidural anesthesia" OR "epidural anaesthesia"	2,281
#71	"epidural anesthetic" OR "epidural anaesthetic"	36
#72	"epidural analgesia" OR "epidural block" OR "epidural blockade"	2,268
#73	"caudal anesthesia" OR "caudal anaesthesia"	144
#74	"caudal block" OR "caudal blocking" OR "dural blocking"	150
#75	"extradural anesthesia" OR "extradural anaesthesia"	69
#76	"extradural analgesia" OR "extradural block"	140
#77	"peridural anesthesia" OR "peridural anaesthesia"	60
#78	"peridural analgesia" OR "peridural block" OR "peridural blocking"	42
#79	#69 OR #70 OR #71 OR #72 OR #73 OR #74 OR #75 OR #76 OR #77 OR #78	69
#80	#56 AND #79	37
#81	MeSH descriptor Endoscopy explode all trees	10,541
#82	endoscopy OR endoscopies OR endoscopic	9,762
#83	gastroscopy OR gastrofibroscopy OR "stomach endoscopy"	982
#84	Gastroscopic OR fibergastroscopy OR fibrogastroscopy	77
#85	cardioendoscopy OR pylorobulboscopy	0
#86	colonoscopy OR coloscopy OR Colonoscopic	1,407
#87	sigmoidoscopy OR sigmoideoscopy OR Sigmoidoscopic	575
#88	proctosigmoidoscopy OR rectoromanoscopy OR rectosigmoidoscopy	29
#89	hysteroscopy OR hysteroscopies OR hysteroscopic	460
#90	Uteroscopy	1
#91	#81 OR #82 OR #83 OR #84 OR #85 OR #86 OR #87 OR #88 OR #89 OR #90	54
#92	#56 AND #91	23
#93	MeSH descriptor Biopsy explode all trees	3,351
#94	biopsy OR biopsies OR biopsied	9,727
#95	"bronchus brushing" OR "tracheobronchial smear"	0
#96	"hepatic puncture" OR "liver puncture"	1
#97	"kidney puncture" OR "renal puncture" OR "pyelocalycial puncture"	3
#98	#93 OR #94 OR #95 OR #96 OR #97	33

#99	#56 AND #98	17
#100	MeSH descriptor Catheterization, Central Venous, this term only	615
#101	("central venous" OR "central vein") NEAR/1 catheteri?ation	641
#102	#100 OR #101	21
#103	#56 AND #102	15
#104	MeSH descriptor Paracentesis explode all trees	203
#105	pericardiocentesis	16
#106	paracentesis OR pericardicentesis OR pericardiocentesis	261
#107	"pericardial aspiration" OR "pericardium puncture"	0
#108	#104 OR #105 OR #106 OR #107	20
#109	#56 AND #108	12
#110	MeSH descriptor Coronary Angiography, this term only	2,529
#111	MeSH descriptor Angioplasty, Transluminal, Percutaneous Coronary, this term only	2,841
#112	"interventional cardiology" OR "p t c a" OR ptca	1,265
#113	|"percutaneous coronary intervention" OR "percutaneous coronary stent"	1,419
#114	coronary NEAR/1 (angioplasty OR balloon)	1,771
#115	"transluminal coronary artery dilatation"	0
#116	"coronary angiography" OR coronarography	3,267
#117	"coronary arteriogram" OR "coronary arteriography"	237
#118	cardiac NEAR/1 ablation	3
#119	#110 OR #111 OR #112 OR #113 OR #114 OR #115 OR #116 OR #117 OR #118	25
#120	#56 AND #119	9
#121	MeSH descriptor Angioplasty explode all trees	3,510
#122	angioplasty OR "Endoluminal Repair" OR "Endo luminal Repair"	4,856
#123	#121 OR #122	11
#124	#56 AND #123	9
#125	"endoluminal stent" OR "endoluminal stents" OR "endoluminal stenting"	12
#126	"endo luminal stent" OR "endo luminal stents" OR "endo luminal stenting"	0
#127	#125 OR #126	10
#128	#56 AND #127	9
#129	MeSH descriptor Spinal Puncture, this term only	212
#130	"lumbar punction" OR "thecal puncture" OR rachiocentesis	3
#131	"spinal puncture" OR "spinal tap"	268
#132	#129 OR #130 OR #131	11
#133	#56 AND #132	9

#134	thoracentesis OR thoracocentesis	49
#135	pleurocantensis OR pleuracentesis OR pleurocentesis	3
#136	"pleura aspiration" OR "pleural aspiration"	3
#137	"pleura punction" OR "pleura puncture"	0
#138	"pleural punction" OR "pleural puncture"	4
#139	#134 OR #135 OR #136 OR #137 OR #138	10
#140	#56 AND #139	8
#141	MeSH descriptor Anesthesia, Conduction explode all trees	6,062
#142	regional NEAR/1 (anesthesia OR anaesthesia)	1,554
#143	"conduction anesthesia" OR "conduction anaesthesia"	131
#144	"block anesthesia" OR "block anaesthesia"	84
#145	"region anesthesia" OR "region anaesthesia"	1
#146	"anesthesia regionalis" OR "anaesthesia regionalis"	0
#147	(regional NEAR/1 analgesia) OR "Bier block"	135
#148	#141 OR #142 OR #143 OR #144 OR #145 OR #146 OR #147	13
#149	#56 AND #148	3
#150	"central neural blockade" OR "central neural block"	3
#151	"central nerve blockade" OR "central nerve block"	1
#152	#150 OR #151	4
#153	#56 AND #152	2
#154	MeSH descriptor Polyps explode all trees with qualifier: SU	152
#155	polypectomy	175
#156	#154 OR #155	3
#157	#56 AND #156	2
#158	MeSH descriptor Portasystemic Shunt, Transjugular Intrahepatic, this term only	86
#159	"transjugular intrahepatic" NEAR/2 (shunt OR shunts OR shunting)	96
#160	"transjugular intrahepatic" NEAR/2 (stent OR stents OR stenting)	2
#161	TIPS OR TIPSS	1,850
#162	#158 OR #159 OR #160 OR #161	2
#163	#56 AND #162	2
#164	MeSH descriptor Angiography explode all trees	4,680
#165	angiography OR angioradiology OR Arteriography	6,605
#166	"peripheral vasculography" OR"rheoacroangiography"	0
#167	"blood vessel radiography" OR vasography	2
#168	#164 OR #165 OR #166 OR #167	4

#169	#56 AND #168	1
#170	"retrobulbar anesthesia" OR "retrobulbar anaesthesia"	155
#171	"retrobulbar block" OR "retrobulbar blockade"	98
#172	"retroocular block" OR "retroocular blockade"	0
#173	"retro ocular block" OR "retro ocular blockade"	0
#174	#170 OR #171 OR #172 OR #173	5
#175	#56 AND #174	0
#176	"peribulbar anesthesia" OR "peribulbar anaesthesia"	149
#177	"peribulbar block" OR "peribulbar blockade"	88
#178	#176 OR #177	2
#179	#56 AND #178	0
#180	MeSH descriptor Intracranial Pressure, this term only	239
#181	MeSH descriptor Monitoring, Physiologic explode all trees	6,816
#182	#180 AND #181	0
#183	"intracranial pressure monitoring" OR "intracranial tension monitoring"	25
#184	"brain pressure monitoring" OR "intracerebral pressure monitoring"	0
#185	"subarachnoid pressure monitoring"	0
#186	#182 OR #183 OR #184 OR #185	3
#187	#56 AND #186	0
#188	MeSH descriptor Neuroradiography explode all trees	641
#189	neuroradiology OR neuroradiological	381
#190	neuroradiography OR neuroroentgenology	10
#191	#188 OR #189 OR #190	0
#192	#56 AND #191	0
#193	#68 OR #80 OR #92 OR #99 OR #103 OR #109 OR #120 OR #124 OR #128 OR #133 OR #140 OR #149 OR #153 OR #157 OR #163 OR #169 OR #175 OR #179 OR #187 OR #192	87

PreMedline: search conducted 28 June 2009

#	Query	Results
#48	Search #45 OR #46 OR #47	86
#47	Search #44 AND pubmednotmedline[sb]	9
#46	Search #44 AND in process[sb]	53
#45	Search #44 NOT (medline[SB] OR oldmedline[sb])	86
#44	Search #24 OR #29 OR #43	3463
#43	Search #8 AND #42	3081

#42	Search #34 AND #41	3311
#41	Search #35 OR #36 OR #37 OR #38 OR #39 OR #40	26433
#40	Search "platelet number"[tw] OR "platelet numbers"[tw]	924
#39	Search "platelet count"[tw] OR "platelet counts"[tw]	25512
#38	Search "thrombocyte counting"[tw] OR "platelet counting"[tw]	214
#37	Search "thrombocyte number"[tw] OR "thrombocyte numbers"[tw]	48
#36	Search "thrombocyte counts"[tw] OR "thrombocytic counts"[tw]	200
#35	Search "thrombocyte count"[tw] OR "thrombocytic count"[tw]	377
#34	Search #30 OR #31 OR #32 OR #33	12050
#33	Search "thrombocyte transfusion"[tw] OR "thrombocytic transfusion"[tw]	37
#32	Search platelet*[tw] AND transfusion*[tw]	11154
#31	Search "platelet concentrate"[tw] OR "platelet concentrates"[tw]	2075
#30	Search "thrombocyte concentrate"[tw] OR "thrombocyte concentrates"[tw]	93
#29	Search #8 AND #28	294
#28	Search #26 AND #27	726
#27	Search fibrinogen[tw] OR "factor 1"[tw] OR "factor I"[tw]	99797
#26	Search #12 OR #25	4787
#25	Search cryoprecipitate[tw] OR "cryo precipitate"[tw]	1449
#24	Search #8 AND #23	272
#23	Search #12 AND #22	529
#22	Search #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21	43935
#21	Search "partial thromboplastin time"[tw] OR ptt[tw] OR aptt[tw]	9935
#20	Search "Russell Viper Venom Time"[tw] OR dRVVT[tw] OR RVVT[tw]	198
#19	Search "howell test"[tw] OR "smith test"[tw] OR "Quick Test"[tw]	322
#18	Search "prothrombin test"[tw] OR "prothrombine time"[tw] OR "protrombin time"[tw]	79
#17	Search pt[tw] OR Thrombotest[tw]	19741
#16	Search prothrombin[tw] AND time[tw]	14153
#15	Search "International Sensitivity Index"[tw] OR isi[tw]	2672
#14	Search "international normalised ratio"[tw]	302
#13	Search "international normalized ratio"[tw] OR inr[tw]	5087
#12	Search #9 OR #10 OR #11	3638
#11	Search "plasma infusion"[tw] OR "serum transfusion"[tw]	344
#10	Search "plasma transfusion"[tw]	243
#9	Search "fresh frozen plasma"[tw] OR FFP[tw]	3203
#8	Search #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7	98504

#7	Search "transfusion blood"[tw] OR "transfusion therapy"[tw]	1482
#6	Search multitransfusion[tw] OR polytransfusion[tw] OR retransfusion[tw]	478
#5	Search haemotherapy[tw] OR haematherapy[tw] OR haematotherapy[tw]	67
#4	Search hemotherapy[tw] OR hematherapy[tw] OR hematotherapy[tw]	513
#3	Search "blood replacement"[tw] OR "blood retransfusion"[tw]	569
#2	Search "blood exchange"[tw] OR "blood infusion"[tw]	485
#1	Search transfus*[tw]	97701

CINAHL: search conducted 30 June 2009

#	Query	Results
S56	S29 or S36 or S55	137
S55	S9 and S54	83
S54	S45 and S53	93
S53	S46 or S47 or S48 or S49 or S50 or S51 or S52	989
S52	TI ("platelet number" OR "platelet numbers") or AB ("platelet number" OR "platelet numbers")	22
S51	TI ("platelet count" OR "platelet counts") or AB ("platelet count" OR "platelet counts")	662
S50	TI ("thrombocyte counting" OR "platelet counting") or AB ("thrombocyte counting" OR "platelet counting")	5
S49	TI ("thrombocyte number" OR "thrombocyte numbers") or AB ("thrombocyte number" OR "thrombocyte numbers")	0
S48	TI ("thrombocyte counts" OR "thrombocytic counts") or AB ("thrombocyte counts" OR "thrombocytic counts")	5
S47	TI ("thrombocyte count" OR "thrombocytic count") or AB ("thrombocyte count" OR "thrombocytic count")	4
S46	(MH "Platelet Count")	462
S45	S37 or S40 or S41 or S42 or S43 or S44	570
S44	TI ("thrombocyte transfusion" OR "thrombocytic transfusion") or AB ("thrombocyte transfusion" OR "thrombocytic transfusion")	0
S43	TI platelet* N3 transfusion* or AB platelet* N3 transfusion*	186
S42	TI ("platelet concentrate" OR "platelet concentrates") or AB ("platelet concentrate" OR "platelet concentrates")	143
S41	TI ("thrombocyte concentrate" OR "thrombocyte concentrates") or AB ("thrombocyte concentrate" OR "thrombocyte concentrates")	1
S40	S38 and S39	86
S39	(MH "Blood Transfusion")	3490
S38	(MH "Blood Platelets")	1349

S37	(MH "Platelet Transfusion")	320
S36	S9 and S35	19
S35	S31 and S34	41
S34	S32 or S33	1899
S33	TI (fibrinogen OR "factor 1" OR "factor I") or AB (fibrinogen OR "factor 1" OR "factor I")	1671
S32	(MH "Fibrinogen")	531
S31	S14 or S30	876
S30	TI (cryoprecipitate OR "cryo precipitate") or AB (cryoprecipitate OR "cryo precipitate")	41
S29	S9 and S28	42
S28	S14 and S27	1917
S27	S15 or S16 or S17 or S18 or S19 or S20 or S21 or S23 or S24 or S25 or S26	1917
S26	TI ("partial thromboplastin time" OR ptt OR aptt) or AB ("partial thromboplastin time" OR ptt OR aptt)	355
S25	TI ("Russell Viper Venom Time" OR dRVVT OR RVVT) or AB ("Russell Viper Venom Time" OR dRVVT OR RVVT)	6
S24	TI ("howell test" OR "smith test" OR "Quick Test") or AB ("howell test" OR "smith test" OR "Quick Test")	30
S23	TI ("prothrombin test" OR "prothrombine time" OR "protrombin time") or AB ("prothrombin test" OR "prothrombine time" OR "protrombin time")	1
S22	TI (pt OR Thrombotest) or AB (pt OR Thrombotest)	0
S21	TI prothrombin N1 time or AB prothrombin N1 time	293
S20	TI ("International Sensitivity Index" OR isi) or AB ("International Sensitivity Index" OR isi)	341
S19	TI "international normalised ratio" or AB "international normalised ratio"	31
S18	TI ("international normalized ratio" OR inr) or AB ("international normalized ratio" OR inr)	479
S17	(MH "Partial Thromboplastin Time")	190
S16	(MH "Prothrombin Time")	204
S15	(MH "International Normalized Ratio")	696
S14	S10 or S11 or S12 or S13	864
S13	TI ("plasma infusion" OR "serum transfusion") or AB ("plasma infusion" OR "serum transfusion")	6
S12	TI "plasma transfusion" or AB "plasma transfusion"	27
S11	TI ("fresh frozen plasma" OR FFP) or AB ("fresh frozen plasma" OR FFP)	224
S10	(MH "Plasma")	710
S9	S1 or S2 or S3 or S4 or S5 or S6 or S7 or S8	7007
S8	TI ("transfusion blood" OR "transfusion therapy") or AB ("transfusion blood" OR "transfusion therapy")	143
S7	TI (multitransfusion OR polytransfusion OR retransfusion) or AB (multitransfusion OR polytransfusion OR retransfusion)	23

S6	TI (haemotherapy OR haematherapy OR haematotherapy) or AB (haemotherapy OR haematherapy OR haematotherapy)	0
S5	TI (hemotherapy OR hematherapy OR hematotherapy) or AB (hemotherapy OR hematherapy OR hematotherapy)	14
S4	TI ("blood replacement" OR "blood retransfusion") or AB ("blood replacement" OR "blood retransfusion")	18
S3	TI ("blood exchange" OR "blood infusion") or AB ("blood exchange" OR "blood infusion")	16
S2	TI transfus* or AB transfus*	4524
S1	(MH "Blood Transfusion+")	5098

CINAHL: search conducted 6 January 2010

#	Query	Results
S56	S29 or S36 or S55	151
S55	S9 and S54	92
S54	S45 and S53	103
S53	S46 or S47 or S48 or S49 or S50 or S51 or S52	1,072
S52	TI ("platelet number" OR "platelet numbers") or AB ("platelet number" OR "platelet numbers")	22
S51	TI ("platelet count" OR "platelet counts") or AB ("platelet count" OR "platelet counts")	718
S50	TI ("thrombocyte counting" OR "platelet counting") or AB ("thrombocyte counting" OR "platelet counting")	5
S49	TI ("thrombocyte number" OR "thrombocyte numbers") or AB ("thrombocyte number" OR "thrombocyte numbers")	0
S48	TI ("thrombocyte counts" OR "thrombocytic counts") or AB ("thrombocyte counts" OR "thrombocytic counts")	6
S47	TI ("thrombocyte count" OR "thrombocytic count") or AB ("thrombocyte count" OR "thrombocytic count")	5
S46	(MH "Platelet Count")	497
S45	S37 or S40 or S41 or S42 or S43 or S44	612
S44	TI ("thrombocyte transfusion" OR "thrombocytic transfusion") or AB ("thrombocyte transfusion" OR "thrombocytic transfusion")	0
S43	TI platelet* N3 transfusion* or AB platelet* N3 transfusion*	202
S42	TI ("platelet concentrate" OR "platelet concentrates") or AB ("platelet concentrate" OR "platelet concentrates")	150
S41	TI ("thrombocyte concentrate" OR "thrombocyte concentrates") or AB ("thrombocyte concentrate" OR "thrombocyte concentrates")	1
S40	S38 and S39	87
S39	(MH "Blood Transfusion")	3,608

S38	(MH "Blood Platelets")	1,429
S37	(MH "Platelet Transfusion")	342
S36	S9 and S35	23
S35	S31 and S34	48
S34	S32 or S33	2,019
S33	TI (fibrinogen OR "factor 1" OR "factor I") or AB (fibrinogen OR "factor 1" OR "factor I")	1,781
S32	(MH "Fibrinogen")	565
S31	S14 or S30	941
S30	TI (cryoprecipitate OR "cryo precipitate") or AB (cryoprecipitate OR "cryo precipitate")	45
S29	S9 and S28	44
S28	S14 and S27	62
S27	S15 or S16 or S17 or S18 or S19 or S20 or S21 or S23 or S24 or S25 or S26	2,058
S26	TI ("partial thromboplastin time" OR ptt OR aptt) or AB ("partial thromboplastin time" OR ptt OR aptt)	371
S25	TI ("Russell Viper Venom Time" OR dRVVT OR RVVT) or AB ("Russell Viper Venom Time" OR dRVVT OR RVVT)	6
S24	TI ("howell test" OR "smith test" OR "Quick Test") or AB ("howell test" OR "smith test" OR "Quick Test")	30
S23	TI ("prothrombin test" OR "prothrombine time" OR "protrombin time") or AB ("prothrombin test" OR "prothrombine time" OR "protrombin time")	1
S22	"TI (pt OR Thrombotest) or AB (pt OR Thrombotest)"	0
S21	TI prothrombin N1 time or AB prothrombin N1 time	307
S20	TI ("International Sensitivity Index" OR isi) or AB ("International Sensitivity Index" OR isi)	383
S19	TI "international normalised ratio" or AB "international normalised ratio"	32
S18	TI ("international normalized ratio" OR inr) or AB ("international normalized ratio" OR inr)	524
S17	(MH "Partial Thromboplastin Time")	203
S16	(MH "Prothrombin Time")	217
S15	(MH "International Normalized Ratio")	748
S14	S10 or S11 or S12 or S13	928
S13	TI ("plasma infusion" OR "serum transfusion") or AB ("plasma infusion" OR "serum transfusion")	6
S12	TI "plasma transfusion" or AB "plasma transfusion"	27
S11	TI ("fresh frozen plasma" OR FFP) or AB ("fresh frozen plasma" OR FFP)	240
S10	(MH "Plasma")	764
S9	S1 or S2 or S3 or S4 or S5 or S6 or S7 or S8	7,330
S8	TI ("transfusion blood" OR "transfusion therapy") or AB ("transfusion blood" OR "transfusion therapy")	150

S7	TI (multitransfusion OR polytransfusion OR retransfusion) or AB (multitransfusion OR polytransfusion OR retransfusion)	23
S6	TI (haemotherapy OR haematherapy OR haematotherapy) or AB (haemotherapy OR haematherapy OR haematotherapy)	0
S5	TI (hemotherapy OR hematherapy OR hematotherapy) or AB (hemotherapy OR hematherapy OR hematotherapy)	14
S4	TI ("blood replacement" OR "blood retransfusion") or AB ("blood replacement" OR "blood retransfusion")	18
S3	TI ("blood exchange" OR "blood infusion") or AB ("blood exchange" OR "blood infusion")	18
S2	TI transfus* or AB transfus*	4,751
S1	(MH "Blood Transfusion+")	5,317

The search was conducted using EBSCOhost on 6 January 2010

AMI: search conducted 30 June 2009

#	Query	Results
#43	((((((TI=("platelet number" OR "platelet numbers") OR AB=("platelet number" OR "platelet numbers")) OR (TI=("platelet count" OR "platelet counts") OR AB=("platelet count" OR "platelet counts")) OR (TI=("thrombocyte counting" OR "platelet counting") OR AB=("thrombocyte counting" OR "platelet counting")) OR (TI=("thrombocyte number" OR "thrombocyte numbers") OR AB=("thrombocyte number" OR "thrombocyte numbers")) OR (TI=("thrombocyte counts" OR "thrombocytic counts") OR AB=("thrombocyte counts" OR "thrombocytic counts")) OR (TI=("thrombocyte count" OR "thrombocytic count") OR AB=("thrombocyte count" OR "thrombocytic count")) OR ((MH_PHRASE="Platelet Count")))) AND (((TI=("thrombocyte transfusion" OR "thrombocytic transfusion") OR AB=("thrombocyte transfusion" OR "thrombocytic transfusion")) OR (TI=(platelet* %3 transfusion*) OR AB=(platelet* %3 transfusion*)) OR (TI=("platelet concentrate" OR "platelet concentrates") OR AB=("platelet concentrate" OR "platelet concentrates")) OR (TI=("thrombocyte concentrate" OR "thrombocyte concentrates") OR AB=("thrombocyte concentrate" OR "thrombocyte concentrates")) OR ((((MH_PHRASE="Blood Transfusion")) AND ((MH_PHRASE="Blood Platelets")))) OR ((MH_PHRASE="Platelet Transfusion")))))) OR (((((TI=(fibrinogen OR "factor 1" OR "factor I") OR AB=(fibrinogen OR "factor 1" OR "factor I")) OR (MH_PHRASE="Fibrinogen"))) AND (((TI=(cryoprecipitate OR "cryo precipitate") OR AB=(cryoprecipitate OR "cryo precipitate")) OR (((TI=("plasma infusion" OR "serum transfusion") OR AB=("plasma infusion" OR "serum transfusion")) OR (TI=("plasma transfusion") OR AB=("plasma transfusion")) OR (TI=("fresh frozen plasma" OR FFP) OR AB=("fresh frozen plasma" OR FFP)) OR (MH_PHRASE="Plasma"))))))) OR (((((TI=("partial thromboplastin time" OR ptt OR aptt) OR AB=("partial thromboplastin time" OR ptt OR aptt)) OR (TI=("Russell Viper Venom Time" OR dRVVT OR RVVT) OR AB=("Russell Viper Venom Time" OR dRVVT OR RVVT)) OR (TI=("howell test" OR "smith test" OR "Quick Test") OR AB=("howell test" OR "smith test" OR "Quick Test")) OR (TI=("prothrombin test" OR "prothrombine time" OR "protrombin time") OR AB=("prothrombin test" OR "prothrombine time" OR "protrombin time")) OR (TI=((prothrombin %1 time) OR pt OR Thrombotest) OR AB=((prothrombin %1 time) OR pt OR Thrombotest)) OR (TI=("International Sensitivity Index" OR isi) OR AB=("International Sensitivity Index" OR isi)) OR (TI=("international normalised ratio") OR AB=("international normalised ratio")) OR (TI=("international normalized ratio" OR inr) OR AB=("international normalized ratio" OR inr)) OR	56

	((MH_PHRASE="Partial Thromboplastin Time")) OR ((MH_PHRASE="Prothrombin Time")) OR ((MH_PHRASE="International Normalized Ratio")))) AND (((TI=("plasma infusion" OR "serum transfusion") OR AB=("plasma infusion" OR "serum transfusion")) OR (TI=("plasma transfusion") OR AB=("plasma transfusion")) OR (TI=("fresh frozen plasma" OR FFP) OR AB=("fresh frozen plasma" OR FFP)) OR (MH_PHRASE="Plasma"))))))	
#42	((((TI=("platelet number" OR "platelet numbers") OR AB=("platelet number" OR "platelet numbers")) OR (TI=("platelet count" OR "platelet counts") OR AB=("platelet count" OR "platelet counts")) OR (TI=("thrombocyte counting" OR "platelet counting") OR AB=("thrombocyte counting" OR "platelet counting")) OR (TI=("thrombocyte number" OR "thrombocyte numbers") OR AB=("thrombocyte number" OR "thrombocyte numbers")) OR (TI=("thrombocyte counts" OR "thrombocytic counts") OR AB=("thrombocyte counts" OR "thrombocytic counts")) OR (TI=("thrombocyte count" OR "thrombocytic count") OR AB=("thrombocyte count" OR "thrombocytic count")) OR ((MH_PHRASE="Platelet Count")))) AND (((TI=("thrombocyte transfusion" OR "thrombocytic transfusion") OR AB=("thrombocyte transfusion" OR "thrombocytic transfusion")) OR (TI=(platelet* %3 transfusion*) OR AB=(platelet* %3 transfusion*)) OR (TI=("platelet concentrate" OR "platelet concentrates") OR AB=("platelet concentrate" OR "platelet concentrates")) OR (TI=("thrombocyte concentrate" OR "thrombocyte concentrates") OR AB=("thrombocyte concentrate" OR "thrombocyte concentrates")) OR ((((MH_PHRASE="Blood Transfusion")) AND ((MH_PHRASE="Blood Platelets")))) OR ((MH_PHRASE="Platelet Transfusion")))))	17
#41	((TI=("platelet number" OR "platelet numbers") OR AB=("platelet number" OR "platelet numbers")) OR (TI=("platelet count" OR "platelet counts") OR AB=("platelet count" OR "platelet counts")) OR (TI=("thrombocyte counting" OR "platelet counting") OR AB=("thrombocyte counting" OR "platelet counting")) OR (TI=("thrombocyte number" OR "thrombocyte numbers") OR AB=("thrombocyte number" OR "thrombocyte numbers")) OR (TI=("thrombocyte counts" OR "thrombocytic counts") OR AB=("thrombocyte counts" OR "thrombocytic counts")) OR (TI=("thrombocyte count" OR "thrombocytic count") OR AB=("thrombocyte count" OR "thrombocytic count")) OR ((MH_PHRASE="Platelet Count")))	104
#40	TI=("platelet number" OR "platelet numbers") OR AB=("platelet number" OR "platelet numbers")	2
#39	TI=("platelet count" OR "platelet counts") OR AB=("platelet count" OR "platelet counts")	67
#38	TI=("thrombocyte counting" OR "platelet counting") OR AB=("thrombocyte counting" OR "platelet counting")	1
#37	TI=("thrombocyte number" OR "thrombocyte numbers") OR AB=("thrombocyte number" OR "thrombocyte numbers")	0
#36	TI=("thrombocyte counts" OR "thrombocytic counts") OR AB=("thrombocyte counts" OR "thrombocytic counts")	0
#35	TI=("thrombocyte count" OR "thrombocytic count") OR AB=("thrombocyte count" OR "thrombocytic count")	0
#34	(MH_PHRASE="Platelet Count")	48
#33	((TI=("thrombocyte transfusion" OR "thrombocytic transfusion") OR AB=("thrombocyte transfusion" OR "thrombocytic transfusion")) OR (TI=(platelet* %3 transfusion*) OR AB=(platelet* %3 transfusion*)) OR (TI=("platelet concentrate" OR "platelet concentrates") OR AB=("platelet concentrate" OR "platelet concentrates")) OR (TI=("thrombocyte concentrate" OR "thrombocyte concentrates") OR AB=("thrombocyte concentrate" OR "thrombocyte concentrates")) OR ((((MH_PHRASE="Blood Transfusion")) AND ((MH_PHRASE="Blood Platelets")))) OR ((MH_PHRASE="Platelet Transfusion")))	34
#32	TI=("thrombocyte transfusion" OR "thrombocytic transfusion") OR AB=("thrombocyte	0

	transfusion" OR "thrombocytic transfusion")	
#31	TI=(platelet* %3 transfusion*) OR AB=(platelet* %3 transfusion*)	13
#30	TI=("platelet concentrate" OR "platelet concentrates") OR AB=("platelet concentrate" OR "platelet concentrates")	16
#29	TI=("thrombocyte concentrate" OR "thrombocyte concentrates") OR AB=("thrombocyte concentrate" OR "thrombocyte concentrates")	0
#28	(((MH_PHRASE="Blood Transfusion")) AND ((MH_PHRASE="Blood Platelets")))	1
#27	(MH_PHRASE="Blood Transfusion")	179
#26	(MH_PHRASE="Blood Platelets")	40
#25	(MH_PHRASE="Platelet Transfusion")	9
#24	((((TI=(fibrinogen OR "factor 1" OR "factor I") OR AB=(fibrinogen OR "factor 1" OR "factor I")) OR (MH_PHRASE="Fibrinogen"))) AND (((TI=(cryoprecipitate OR "cryo precipitate") OR AB=(cryoprecipitate OR "cryo precipitate")) OR (((TI=("plasma infusion" OR "serum transfusion") OR AB=("plasma infusion" OR "serum transfusion")) OR (TI=("plasma transfusion") OR AB=("plasma transfusion")) OR (TI=("fresh frozen plasma" OR FFP) OR AB=("fresh frozen plasma" OR FFP)) OR (MH_PHRASE="Plasma"))))))	5
#23	((TI=(fibrinogen OR "factor 1" OR "factor I") OR AB=(fibrinogen OR "factor 1" OR "factor I")) OR (MH_PHRASE="Fibrinogen"))	206
#22	TI=(fibrinogen OR "factor 1" OR "factor I") OR AB=(fibrinogen OR "factor 1" OR "factor I")	204
#21	MH_PHRASE="Fibrinogen"	4
#20	((TI=(cryoprecipitate OR "cryo precipitate") OR AB=(cryoprecipitate OR "cryo precipitate")) OR (((TI=("plasma infusion" OR "serum transfusion") OR AB=("plasma infusion" OR "serum transfusion")) OR (TI=("plasma transfusion") OR AB=("plasma transfusion")) OR (TI=("fresh frozen plasma" OR FFP) OR AB=("fresh frozen plasma" OR FFP)) OR (MH_PHRASE="Plasma"))))	69
#19	TI=(cryoprecipitate OR "cryo precipitate") OR AB=(cryoprecipitate OR "cryo precipitate")	14
#18	((((TI=("partial thromboplastin time" OR ptt OR aptt) OR AB=("partial thromboplastin time" OR ptt OR aptt)) OR (TI=("Russell Viper Venom Time" OR dRVVT OR RVVT) OR AB=("Russell Viper Venom Time" OR dRVVT OR RVVT)) OR (TI=("howell test" OR "smith test" OR "Quick Test") OR AB=("howell test" OR "smith test" OR "Quick Test")) OR (TI=("prothrombin test" OR "prothrombine time" OR "protrombin time") OR AB=("prothrombin test" OR "prothrombine time" OR "protrombin time")) OR (TI=((prothrombin %1 time) OR pt OR Thrombotest) OR AB=((prothrombin %1 time) OR pt OR Thrombotest)) OR (TI=("International Sensitivity Index" OR isi) OR AB=("International Sensitivity Index" OR isi)) OR (TI=("international normalised ratio") OR AB=("international normalised ratio")) OR (TI=("international normalized ratio" OR inr) OR AB=("international normalized ratio" OR inr)) OR ((MH_PHRASE="Partial Thromboplastin Time")) OR ((MH_PHRASE="Prothrombin Time")) OR ((MH_PHRASE="International Normalized Ratio")))) AND (((TI=("plasma infusion" OR "serum transfusion") OR AB=("plasma infusion" OR "serum transfusion")) OR (TI=("plasma transfusion") OR AB=("plasma transfusion")) OR (TI=("fresh frozen plasma" OR FFP) OR AB=("fresh frozen plasma" OR FFP)) OR (MH_PHRASE="Plasma"))))	54
#17	((TI=("partial thromboplastin time" OR ptt OR aptt) OR AB=("partial thromboplastin time" OR ptt OR aptt)) OR (TI=("Russell Viper Venom Time" OR dRVVT OR RVVT) OR AB=("Russell Viper Venom Time" OR dRVVT OR RVVT)) OR (TI=("howell test" OR "smith test" OR "Quick Test") OR AB=("howell test" OR "smith test" OR "Quick Test")) OR (TI=("prothrombin test" OR "prothrombine time" OR "protrombin time") OR AB=("prothrombin test" OR	270

	"prothrombine time" OR "protrombin time")) OR (TI=((prothrombin %1 time) OR pt OR Thrombotest) OR AB=((prothrombin %1 time) OR pt OR Thrombotest)) OR (TI=("International Sensitivity Index" OR isi) OR AB=("International Sensitivity Index" OR isi)) OR (TI=("international normalised ratio") OR AB=("international normalised ratio")) OR (TI=("international normalized ratio" OR inr) OR AB=("international normalized ratio" OR inr)) OR ((MH_PHRASE="Partial Thromboplastin Time")) OR ((MH_PHRASE="Prothrombin Time")) OR ((MH_PHRASE="International Normalized Ratio")))	
#16	TI=("partial thromboplastin time" OR ptt OR aptt) OR AB=("partial thromboplastin time" OR ptt OR aptt)	57
#15	TI=("Russell Viper Venom Time" OR dRVVT OR RVVT) OR AB=("Russell Viper Venom Time" OR dRVVT OR RVVT)	2
#14	TI=("howell test" OR "smith test" OR "Quick Test") OR AB=("howell test" OR "smith test" OR "Quick Test")	5
#13	TI=("prothrombin test" OR "prothrombine time" OR "protrombin time") OR AB=("prothrombin test" OR "prothrombine time" OR "protrombin time")	1
#12	TI=((prothrombin %1 time) OR pt OR Thrombotest) OR AB=((prothrombin %1 time) OR pt OR Thrombotest)	77
#11	TI=("International Sensitivity Index" OR isi) OR AB=("International Sensitivity Index" OR isi)	13
#10	TI=("international normalised ratio") OR AB=("international normalised ratio")	23
#9	TI=("international normalized ratio" OR inr) OR AB=("international normalized ratio" OR inr)	53
#8	(MH_PHRASE="Partial Thromboplastin Time")	65
#7	(MH_PHRASE="Prothrombin Time")	56
#6	(MH_PHRASE="International Normalized Ratio")	79
#5	((TI=("plasma infusion" OR "serum transfusion") OR AB=("plasma infusion" OR "serum transfusion")) OR (TI=("plasma transfusion") OR AB=("plasma transfusion")) OR (TI=("fresh frozen plasma" OR FFP) OR AB=("fresh frozen plasma" OR FFP)) OR (MH_PHRASE="Plasma"))	62
#4	TI=("plasma infusion" OR "serum transfusion") OR AB=("plasma infusion" OR "serum transfusion")	3
#3	TI=("plasma transfusion") OR AB=("plasma transfusion")	0
#2	TI=("fresh frozen plasma" OR FFP) OR AB=("fresh frozen plasma" OR FFP)	29
#1	MH_PHRASE="Plasma"	50

AMI: search conducted 6 January 2010

#	Query	Results
#43	(#18 OR #24 OR #42)	23
#42	(#33 AND #41)	8
#41	(#34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40)	107
#40	(TI=("platelet number" OR "platelet numbers") OR AB=("platelet number" OR "platelet numbers"))	2

#39	(TI=("platelet count" OR "platelet counts") OR AB=("platelet count" OR "platelet counts"))	70
#38	(TI=("thrombocyte counting" OR "platelet counting") OR AB=("thrombocyte counting" OR "platelet counting"))	1
#37	(TI=("thrombocyte number" OR "thrombocyte numbers") OR AB=("thrombocyte number" OR "thrombocyte numbers"))	0
#36	(TI=("thrombocyte counts" OR "thrombocytic counts") OR AB=("thrombocyte counts" OR "thrombocytic counts"))	0
#35	(TI=("thrombocyte count" OR "thrombocytic count") OR AB=("thrombocyte count" OR "thrombocytic count"))	0
#34	((MH_PHRASE="Platelet Count"))	49
#33	(#25 OR #28 OR #29 OR #30 OR #31 OR #32)	34
#32	(TI=("thrombocyte transfusion" OR "thrombocytic transfusion") OR AB=("thrombocyte transfusion" OR "thrombocytic transfusion"))	0
#31	(TI=(platelet* %3 transfusion*) OR AB=(platelet* %3 transfusion*))	13
#30	(TI=("platelet concentrate" OR "platelet concentrates") OR AB=("platelet concentrate" OR "platelet concentrates"))	16
#29	(TI=("thrombocyte concentrate" OR "thrombocyte concentrates") OR AB=("thrombocyte concentrate" OR "thrombocyte concentrates"))	0
#28	(#26 AND #27)	1
#27	((MH_PHRASE="Blood Transfusion"))	181
#26	((MH_PHRASE="Blood Platelets"))	40
#25	((MH_PHRASE="Platelet Transfusion"))	9
#24	(#20 AND #23)	4
#23	(#21 OR #22)	212
#22	(TI=(fibrinogen OR "factor 1" OR "factor I") OR AB=(fibrinogen OR "factor 1" OR "factor I"))	209
#21	MH_PHRASE="Fibrinogen"	5
#20	(#5 OR #14)	69
#19	(TI=(cryoprecipitate OR "cryo precipitate") OR AB=(cryoprecipitate OR "cryo precipitate"))	14
#18	(#5 AND #17)	14
#17	(#6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16)	280
#16	(TI=("partial thromboplastin time" OR ptt OR aptt) OR AB=("partial thromboplastin time" OR ptt OR aptt))	57
#15	(TI=("Russell Viper Venom Time" OR dRVVT OR RVVT) OR AB=("Russell Viper Venom Time" OR dRVVT OR RVVT))	2
#14	(TI=("howell test" OR "smith test" OR "Quick Test") OR AB=("howell test" OR "smith test" OR "Quick Test"))	5
#13	(TI=("prothrombin test" OR "prothrombine time" OR "protrombin time") OR AB=("prothrombin test" OR "prothrombine time" OR "protrombin time"))	1
#12	(TI=((prothrombin %1 time) OR pt OR Thrombotest) OR AB=((prothrombin %1 time) OR pt	79

	OR Thrombotest))	
#11	(TI=("International Sensitivity Index" OR isi) OR AB=("International Sensitivity Index" OR isi))	13
#10	(TI=("international normalised ratio") OR AB=("international normalised ratio"))	26
#9	(TI=("international normalized ratio" OR inr) OR AB=("international normalized ratio" OR inr))	56
#8	((MH_PHRASE="Partial Thromboplastin Time"))	65
#7	((MH_PHRASE="Prothrombin Time"))	57
#6	((MH_PHRASE="International Normalized Ratio"))	83
#5	(#1 OR #2 OR #3 OR #4)	64
#4	(TI=("plasma infusion" OR "serum transfusion") OR AB=("plasma infusion" OR "serum transfusion"))	3
#3	(TI=("plasma transfusion") OR AB=("plasma transfusion"))	0
#2	(TI=("fresh frozen plasma" OR FFP) OR AB=("fresh frozen plasma" OR FFP))	31
#1	MH_PHRASE="Plasma"	51

Appendix B: Excluded studies

This appendix documents studies that met inclusion criteria determined by PICO, PPO or PRO criteria, but were later excluded. These studies, and their reasons for exclusion, are listed below.

B1 Excluded studies, Question 1

What is the effect of a multidisciplinary, multimodal, programmatic approach to perioperative patient blood management on patient blood management on patient outcomes?

No studies that met inclusion criteria were later excluded.

B2 Excluded studies, Question 2

In patients undergoing surgery or invasive procedures, what effect does the cessation and timing of cessation of medications that affect haemostasis have on morbidity, mortality and transfusion requirements?

Excluded non-comparative Level IV (cardiac and noncardiac) studies

Al Rashid M, Parker MJ. Anticoagulation management in hip fracture patients on warfarin. Injury. 2005;36(11):1311–1315.

Alcalay J. Cutaneous surgery in patients receiving warfarin therapy. Dermatol Surg. 2001;27(8):756–758.

Alcalay J, Alkalay R. Controversies in perioperative management of blood thinners in dermatologic surgery: continue or discontinue? Dermatol Surg. 2004;30(8):1091–1094.

Ang-Lee MK, Moss J, Yuan CS. Herbal medicines and perioperative care. J Am Med Assoc. 2001;286(2):208–216.

Annala AP, Karjalainen PP, Porela P, Nyman K, Ylitalo A, Airaksinen J. Safety of diagnostic coronary angiography during uninterrupted therapeutic warfarin treatment. Am J Cardiol 2008; 102:386-390.

Bigalke B, Seizer P, Geisler T, Lindemann S, Gawaz M, May AE. Perioperative antiplatelet therapy in patients at risk for coronary stent thrombosis undergoing noncardiac surgery. Clin Res Cardiol. 2009;98(5):335–339.

Chakravarti A, MacDermott S. Transurethral resection of the prostate in the anticoagulated patient. Br J Urol. 1998;81(4):520–522.

D'Urbano M, Barlocco F, Poli A, Fetiveau R, Vandoni P, Savonitto S, et al. Unplanned surgery after drug eluting stent implantation: a strategy for safe temporary withdrawal of dual oral antiplatelet therapy. J Cardiovasc Med (Hagerstown). 2008;9(7):737–741.

Daly DM, Myles PS, Smith JA, et al. Anticoagulation, bleeding and blood transfusion practices in Australasian cardiac surgical practice. Anaesth Intensive Care. 2007;35(5):760–8.

Dotan ZA, Mor Y, Leibovitch I, Varon D, Golomb J, Duvdevan M, et al. The efficacy and safety of perioperative low molecular weight heparin substitution in patients on chronic oral anticoagulant therapy undergoing transurethral prostatectomy for bladder outlet obstruction. J Urol. 2002;168(2):610–614.

Douketis JD, Berger PB, Dunn AS, Jaffer AK, Spyropoulos AC, Becker RC, et al. The perioperative management of antithrombotic therapy: American College of Chest Physicians evidence-based clinical practice guidelines (8th edition). Chest. 2008;133(6 SUPPL. 6):299S–339S.

Dunn AS, Spyropoulos AC, Turpie AGG. Bridging therapy in patients on long-term oral anticoagulants who require surgery: The Prospective Perioperative Enoxaparin Cohort Trial (PROSPECT). J Thromb Haemost. 2007;5(11):2211–2218.

Dunning J, Versteegh M, Fabbri A, Pavie A, Kolh P, Lockowandt U, et al. Guideline on antiplatelet and anticoagulation management in cardiac surgery. Eur J Cardio-thorac Surg. 2008;34(1):73–92.

Fauno P, Petersen KD, Husted SE. Increased blood loss after preoperative NSAID. Retrospective study of 186 hip arthroplasties. Acta Orthop Scand. 1993;64(5):522–524.

Ferrieri GB, Castiglioni S, Carmagnola D, Cargnel M, Strohmenger L, Abati S. Oral surgery in patients on anticoagulant treatment without therapy interruption. J Oral Maxillofac Surg. 2007;65(6):1149–1154.

Hirschman DR, Morby LJ. A study of the safety of continued anticoagulation for cataract surgery patients. Nursing forum. 2006;41(1):30–37.

Jaffer AK, Ahmed M, Brotman DJ, Bragg L, Seshadri N, Qadeer MA, et al. Low-molecular-weight-heparins as periprocedural anticoagulation for patients on long-term warfarin therapy: A standardized bridging therapy protocol. J Thromb Trombolysis. 2005;20(1):11–16.

Kaluza GL, Joseph J, Lee JR, Raizner ME, Raizner AE. Catastrophic outcomes of noncardiac surgery soon after coronary stenting. J Am Coll Cardiol. 2000;35(5):1288–1294.

Kefer JC, Turna B, Stein RJ, Desai MM. Safety and Efficacy of Percutaneous Nephrostolithotomy in Patients on Anticoagulant Therapy. J Urol. 2009;181(1):144–148.

Kim YH, Suh JS. Low incidence of deep-vein thrombosis after cementless total hip replacement. J Bone Jt Surg Ser A. 1988;70(6):878–882.

Larson BJG, Zumberg MS, Kitchens CS. A feasibility study of continuing dose-reduced warfarin for invasive procedures in patients with high thromboembolic risk. Chest. 2005;127(3):922–927.

Lazio BE, Simard JM. Anticoagulation in neurosurgical patients. Neurosurgery. 1999;45(4):838–848.

Madan GA, Madan SG, Madan G, Madan AD. Minor oral surgery without stopping daily low-dose aspirin therapy: A study of 51 patients. J Oral Maxillofac Surg. 2005;63(9):1262–1265.

McCormack P, Simcock PR, Tullo AB. Management of the anticoagulated patient for ophthalmic surgery. Eye. 1993;7(6):749–750.

Morris CD, Vega JD, Levy JH, Buist NN, Smith AL, Despotis GJ, et al. Warfarin therapy does not increase bleeding in patients undergoing heart transplantation. Ann Thorac Surg. 2001;72(3):714–718.

Mortada ME, Chandrasekaran K, Nangia V, Dhala A, Blanck Z, Cooley R, et al. Periprocedural anticoagulation for atrial fibrillation ablation. J Cardiovasc Electrophysiol. 2008;19(4):362–366.

Narendran N, Williamson TH. The effects of aspirin and warfarin therapy on haemorrhage in vitreoretinal surgery. Acta Ophthalmol Scand. 2003;81(1):38–40.

Robinson M, Healey JS, Eikelboom J, Schulman S, Morillo CA, Nair GM, et al. Postoperative low-molecular-weight heparin bridging is associated with an increase in wound hematoma following surgery for pacemakers and implantable defibrillators. PACE Pacing Clin Electrophysiol. 2009;32(3):378–382.

Sargi Z, Casiano R. Endoscopic sinus surgery in patients receiving anticoagulant or antiplatelet therapy. Am J Rhinol. 2007;21(3):335–338.

Smith W, Merkonidis C, Yung M. Endoscopic dacryocystorhinostomy in patients taking aspirin perioperatively. Am J Otolaryngol Head Neck Med Surg. 2006;27(5):323–326.

Spyropoulos AC, Jenkins P, Bornikova L. A disease management protocol for outpatient perioperative bridge therapy with enoxaparin in patients requiring temporary interruption of long-term oral anticoagulation. pharmacotherapy. 2004;24(5 I):649–658.

Timothy SKC, Hicks TC, Opelka FG, Timmcke AE, Beck DE, Church J. Colonoscopy in the patient requiring anticoagulation. Dis Colon Rectum. 2001;44(12):1845–1849.

Tinmouth AH, Morrow BH, Cruickshank MK, Moore PM, Kovacs MJ. Dalteparin as periprocedure anticoagulation for patients on warfarin and at high risk of thrombosis. Ann Pharmacother. 2001;35(6):669–674.

Vicenzi MN, Meislitzer T, Heitzinger B, Halaj M, Fleisher LA, Metzler H. Coronary artery stenting and noncardiac surgery—a prospective outcome study. Br J Anaesth. 2006;96(6):686–693.

Excluded duplicate evidence

Study excluded as it contained a subset of the publications included in the systematic review by Burger, et al (2005):

Armstrong MJ, Schneck MJ, Biller J. Discontinuation of perioperative and anticoagulant therapy in stroke patients. Neuro Clin 2006; 24:607-630.

B3 Excluded studies, Question 3

In patients undergoing surgery, what is the effect of perioperative strategies that minimise blood loss on morbidity, mortality, and blood transfusion?

The body of evidence found by the systematic literature review and associated appendixes for Perioperative Foreground Question 3 are presented in a separate report.

B4 Excluded studies, Question 4

Is anaemia an independent risk factor for adverse outcomes?

Excluded non-comparative Level IV studies

Gruson KI, Accousti KJ, Parsons BO, Pillai G, Flatow EL. Transfusion after shoulder arthroplasty: an analysis of rates and risk factors. J Shoulder Elbow Surg. 2009;18(2):225–230.

Kable A, Gibberd R, Spigelman A. Predictors of adverse events in surgical admissions in Australia. Int J Qual Healthcare. 2008;20(6):406–411.

Nelson AH, Fleisher LA, Rosenbaum SH. Relationship between postoperative anaemia and cardiac morbidity in high-risk vascular patients in the intensive care unit. Crit Care Med. 1993;21(6):860–866.

Patil CG, Lad EM, Lad SP, Ho C, Boakye M. Visual loss after spine surgery: a population-based study. Spine. 2009;33(13):1491–1496.

Rawstron RE. Anaemia and surgery: a retrospective clinical study. Aust N Z J Surg. 1970;39(4):425–432.

Spence RK, Carson JA, Poses R, McCoy S, Pello M, Alexander J, et al. Elective surgery without transfusion: influence of preoperative hemoglobin level and blood loss on mortality. Am J Surg. 1990;159:320–324.

B5 Excluded studies, Question 5

What is the effect of red blood cell transfusion on patient outcomes?

No studies that met inclusion criteria were later excluded.

B6 Excluded studies, Question 6

What is the effect of interventions to increase haemoglobin concentration on morbidity, mortality and need for red blood cell transfusion?

Effect of intravenous iron

Excluded non-comparative Level IV studies

Theusinger OM, Leyvraz P-F, Schanz U, Seifert B, Spahn DR. Treatment of iron deficiency anaemia in orthopaedic surgery with intravenous iron: Efficacy and limits—A prospective study. Anaesthesiol 2007;107:923–927

Effect of erythropoietin

Excluded Level III studies

Atabek U, Alvarez R, Pello, MJ, Alexander JB, Camishion RC, Curry C, Spence RK. Erythropoietin accelerates hematocrit recovery in post-surgical anemia. Am Surg 1995; 61:74–77.

Garcia-Erce JA, Cuenca J, Munoz M, Izuel M, Martinez AA, Herrera A, Solano VM, Martinez F. Perioperative stimulation of erythropoiesis with intravenous iron and erythropoietin reduces transfusion requirements in patients with hip fracture. A prospective observational study. Vox Sang 2005; 88:235–243.

Laffosse J-M, Minville V, Chiron P, Colombani A, Gris C, Pourrut J-C, Eychenne B, Fourcade O. Preoperative use of epoietin beta in total hip replacement: a prospective study. Arch Orthop Trauma Surg Mar 31, 2009. [Epub ahead of print]

Ootaki Y, Yamaguchi M, Yoshimura N, Oka S, Yoshida M, Hasegawa T. The efficacy of preoperative administration of a single dose of recombinant human erythropoietin in pediatric cardiac surgery. Heart Surg Forum 2007; 10:86–90.

Santoro JE, Eastlack RK, Mirocha JM, Bugbee WD. Impact of erythropoietin on allogenic blood exposure in orthopaedic surgery. Am J Orthop 2007; 36(11):600–604.

Sesti F, Ticconi C, Bonifacio S, Piccione E. Preoperative administration of recombinant erythropoietin in patients undergoing gynaecologic surgery. Gynecol Obstet Invest 2002; 54:1–5.

Excluded non-comparative Level IV studies

Garcia-Erce JA, Cuenca J, Martinez F, Cardona R, Perez-Serrano L, Munoz M. Perioperative intravenous iron preserves iron stores and may hasten the recovery from postoperative anaemia after knee replacement surgery. Transfus Med 2006; 16:335–341.

Gall RM, Kerr PD. Use of preoperative erythropoietin in head and neck surgery. J Otolaryngol 2000; 29(3):131–134.

Ging AL, Onge S, Fitzgerald DC, Collazo LR, Bower LS, Shen I. Bloodless cardiac surgery and the pediatric patient: a case study. Perfusion 2008; 23:131–134.

Konishi T, Ohbayashi T, Kaneko T, Ohki T, Saitou Y, Yamato Y. Preoperative use of erythropoietin for cardiovascular operations in anemia. Ann Thorac Surg 1993; 56:101–103.

Kourounis GS, Michail GD, Adonakis GL. Managing anemia in gynaecologic surgery with postoperative administration of recombinant human epoetins. Clin Exp Obst & Gyn 2005; 32:68–70.

Perez-Ferrer A, De Vincente J, Gredilla E, Garcia-Vega MI, Bourgeois P, Goldman LJ. Case report: use of erythropoietin for bloodless surgery in a Jehovah's Witness infant. Paediatr Anaesth 2003; 13:633–636.

Podesta A, Parodi E, Dottori V, Crivellari R, Passerone GC. Epoetin alpha in elective coronary and valve surgery in Jehovah's Witness patients. Experience in 45 patients. Minerva Cardioangiol 2002; 50:125–131.

Sparling E, Nelson CL, Lavender R, Smith J. The use of erythropoietin in the management of Jehovah's Witnesses who have revision total hip arthroplasty. J Bone Jt Surg Ser A1996; 78:1548–1552.

Wolff M, Fandrey J, Hirner A, Jelkmann W. Perioperative use of recombinant human erythropoietin in patients refusing blood transfusions. Pathological considerations based on 5 cases. Eur J Haematol 1997; 58:154–159.

B7 Excluded studies, Question 7

What is the effect of rFVIIa (prophylaxis or treatment) on morbidity, mortality and transfusion rate?

Excluded systematic reviews, reporting data from non-perioperative as well as perioperative studies

Hsia CC, Chin-Yee IH, McAlister VC. Use of recombinant activated factor VII in patients without hemophilia: a meta-analysis of randomized control trials. Ann Surg. 2008;248(1):61–68.

Johansson PI. Off-label use of recombinant factor VIIa for treatment of haemorrhage: Results from randomized clinical trials. Vox Sang. 2008;95(1):1–7.

Lam MSH, Sims-McCallum RP. Recombinant factor VIIa in the treatment of non-hemophiliac bleeding. Ann Pharmacother. 2005;39(5):885–891.

Moltzan CJ, Anderson DA, Callum J, Fremes S, Hume H, Mazer CD, et al. The evidence for the use of recombinant factor VIIa in massive bleeding: Development of a transfusion policy framework. Transfus Med. 2008;18(2):112–120.

Squizzato A, Ageno W. Recombinant activated factor VII as a general haemostatic agent: Evidence-based efficacy and safety. Curr Drug Saf. 2007;2(2):155–161.

Stanworth SJ, Birchall J, Doree CJ, Hyde C. Recombinant factor VIIa for the prevention and treatment of bleeding in patients without haemophilia. Cochrane Database Syst Rev. 2007 Apr 18;(2): CD005011.

Excluded Level II studies, reported in included systematic reviews

Diprose P, Herbertson MJ, O'Shaughnessy DO, Gill RS. Activated recombinant factor VII after cardiopulmonary bypass reduces allogeneic transfusion in complex non-coronary cardiac surgery: Randomized double-blind placebo-controlled pilot study. Br J Anaesth. 2005;95(5):596–602.

Ekert H, Brizard C, Eyers R, Cochrane A, Henning R. Elective administration in infants of low-dose recombinant activated factor VII (rFVIIa) in cardiopulmonary bypass surgery for congenital heart disease does not shorten time to chest closure or reduce blood loss and need for transfusions. Blood Coagul Fibrinolysis. 2006;17(5):389–395.

Friederich PW, Henny CP, Messelink EJ, Geerdink MG, Keller T, Kurth KH, et al. Effect of recombinant activated factor VII on perioperative blood loss in patients undergoing retropubic prostatectomy: A double-blind placebo-controlled randomised trial. Lancet. 2003;361(9353):201–205.

Lodge JPA, Jonas S, Oussoultzoglou E, Malago M, Jayr C, Cherqui D, et al. Recombinant coagulation factor VIIa in major liver resection: A randomized, placebo-controlled, double-blind clinical trial. Anesthesiology. 2005;102(2):269–275.

Lodge JPA, Jonas S, Jones RM, Olausson M, Mir-Pallardo J, Soefelt S, et al. Efficacy and safety of repeated perioperative doses of recombinant factor VIIa in liver transplantation. Liver Transplant. 2005;11(8):973–979.

Planinsic RM, van der Meer J, Testa G, Grande L, Candela A, Porte RJ, et al. Safety and efficacy of a single bolus administration of recombinant factor VIIa in liver transplantation due to chronic liver disease. Liver Transplant. 2005;11(8):895–900.

Raobaikady R, Redman J, Ball JAS, Maloney G, Grounds RM. Use of activated recombinant coagulation factor VII in patients undergoing reconstruction surgery for traumatic fracture of pelvis or pelvis and acetabulum: A double-blind, randomized, placebo-controlled trial. Br J Anaesth. 2005;94(5):586–591.

Shao YF, Yang JM, Chau GY, Sirivatanauksorn Y, Zhong SX, Erhardtsen E, et al. Safety and hemostatic effect of recombinant activated factor VII in cirrhotic patients undergoing partial hepatectomy: A multicenter, randomized, double-blind, placebo-controlled trial. Am J Surg. 2006;191(2):245–249.

Excluded Level III studies

Gelsomino S, Lorusso R, Romagnoli S, Bevilacqua S, De Cicco G, Bille G, et al. Treatment of refractory bleeding after cardiac operations with low-dose recombinant activated factor VII (NovoSeven(registered trademark)): a propensity score analysis. Eur J Cardiothorac Surg. 2008;33(1):64–71.

Hendriks HGD, Meijer K, De Wolf JT, Klompmaker IJ, Porte RJ, De Kam PJ, et al. Reduced transfusion requirements by recombinant factor VIIa in orthotopic liver transplantation. Transplantation. 2001;71(3):402–405.

Kalicinski P, Markiewicz M, Kaminski A, Laniewski P, Ismail H, Drewniak T, et al. Single pretransplant bolus of recombinant activated factor VII ameliorates influence of risk factors for blood loss during orthotopic liver transplantation. Pediatr Transplant. 2005;9(3):299–304.

Karkouti K, Beattie WS, Wijeysundera DN, Yau TM, McCluskey SA, Ghannam M, et al. Recombinant factor VIIa for intractable blood loss after cardiac surgery: A propensity score-matched case-control analysis. Transfusion. 2005;45(1):26–34.

Karkouti K, Yau TM, Riazi S, Dattilo KM, Wasowicz M, Meineri M, et al. Determinants of complications with recombinant factor VIIa for refractory blood loss in cardiac surgery. Can J Anesth. 2006;53(8):802–809.

Kolban M, Balachowska-Kosciolek I, Chmielnicki M. Recombinant coagulation factor VIIa—a novel haemostatic agent in scoliosis surgery? Eur Spine J. 2006;15(6):944–952.

McMorrow RCN, Ryan SM, Blunnie WP, Bowen M, Carton EG, Gardiner J, et al. Use of recombinant factor VIIa in massive post-partum haemorrhage. Eur J Anaesthesiol. 2008;25(4):293–298.

Niemann CU, Behrends M, Quan D, Eilers H, Gropper MA, Roberts JP, et al. Recombinant factor VIIa reduces transfusion requirements in liver transplant patients with high MELD scores. Transfus Med. 2006;16(2):93–100.

Niles SD, Burkhart HM, Duffey DA, Buhrman K, Burzynski J, Holt DW. Use of recombinant factor VIIa (NovoSeven) in pediatric cardiac surgery. J Extra Corpor Technol. 2008;40(4):241–248.

Romagnoli S, Bevilacqua S, Gelsomino S, Pradella S, Ghilli L, Rostagno C, et al. Small-dose recombinant activated factor VII (NovoSeven(registered trademark)) in cardiac surgery. Anesth Analg. 2006;102(5):1320–1326.

Tritapepe L, De Santis V, Vitale D, Nencini C, Pellegrini F, Landoni G, et al. Recombinant activated factor VII for refractory bleeding after acute aortic dissection surgery: A propensity score analysis. Crit Care Med. 2007;35(7):1685–1690.

Trowbridge C, Stammers A, Klayman M, Brindisi N, Woods E. Characteristics of uncontrolled hemorrhage in cardiac surgery. J Extra Corpor Technol. 2008;40(2):89–93.

von Heymann C, Redlich U, Jain U, Kastrup M, Schroeder T, Sander M, et al. Recombinant activated factor VII for refractory bleeding after cardiac surgery—a retrospective analysis of safety and efficacy. Crit Care Med. 2005;33(10):2241–2246.

Excluded Level IV studies

Aggarwal A, Malkovska V, Catlett JP, Alcorn K. Recombinant activated factor VII (rFVIIa) as salvage treatment for intractable hemorrhage. Thromb J. 2004;2(1):9.

Beltran de Heredia S, Bisbe E, Rojo A, Gracia MP, Lopez M, Escolano F. Usefulness of activated recombinant factor VII for controlling massive bleeding: 4 years' experience in a university hospital. Rev Esp Anestesiol Reanim. 2008;55(6):355–359.

Berkhof FF, Eikenboom JC. Efficacy of recombinant activated factor VII in patients with massive uncontrolled bleeding: A retrospective observational analysis. Transfusion. 2008;49(3):570–577.

Brown JB, Emerick KM, Brown DL, Whitington PF, Alonso EM. Recombinant factor VIIa improves coagulopathy caused by liver failure. J Pediatr Gastroenterol Nutr. 2003;37(3):268–272.

Deveras RAE, Kessler CM. Reversal of warfarin-induced excessive anticoagulation with recombinant human factor VIIa concentrate. Ann Intern Med. 2002;137(11):884–888.

Egan JR, Lammi A, Schell DN, Gillis J, Nunn GR. Recombinant activated factor VII in paediatric cardiac surgery. Intensive Care Med. 2004;30(4):682–685.

Eikelboom JW, Bird R, Blythe D, Coyle L, Gan E, Harvey M, et al. Recombinant activated factor VII for the treatment of life-threatening haemorrhage. Blood Coagul Fibrinolysis. 2003;14(8):713–717.

Hendriks HGD, Van der Maaten JMAA, De Wolf J, Waterbolk TW, Slooff MJH, van der Meer J. An effective treatment of severe intractable bleeding after valve repair by one single dose of activated recombinant factor VII. Anesth Analg. 2001;93(2):287–289.

Kapapa T, Konig K, Heissler HE, Schatzmann C, Tschan CA, Perl M, et al. The use of recombinant activated factor VII in neurosurgery. Surg Neurol. 2009;71(2):172–179.

Lacheva A, Georgiev S, Pilossoff V, Lazarov S, Mitev P. Administration of recombinant factor VIIA for the management of massive postoperative blood loss in children with congenital heart defects. Anaesthesiol Intensive Care. 2008;35(2):3–8.

Karkouti K, Beattie WS. Pro: The role of recombinant factor VIIa in cardiac surgery. J Cardiothorac Vasc Anesth. 2008;22(5):779–782.

Laffan M, O'Connell NM, Perry DJ, Hodgson AJ, O'Shaughnessy D, Smith OP. Analysis and results of the recombinant factor VIIa extended-use registry. Blood Coagul Fibrinolysis. 2003;14 Suppl 1:S35–S38.

Markiewicz M, Kalicinski P, Kaminski A, Laniewski P, Ismail H, Drewniak T, et al. Acute coagulopathy after reperfusion of the liver graft in children correction with recombinant activated factor VII. Transplant Proc. 2003;35(6):2318–2319.

O'Connell NM, Perry DJ, Hodgson AJ, O'Shaughnessy DF, Laffan MA, Smith OP. Recombinant FVIIa in the management of uncontrolled hemorrhage. Transfusion. 2003;43(12):1711–1716.

Raivio P, Suojaranta-Ylinen R, Kuitunen AH. Recombinant factor VIIa in the treatment of postoperative hemorrhage after cardiac surgery. Ann Thorac Surg. 2005;80(1):66–71.

Reiter PD, Valuck RJ, Taylor RS. Evaluation of off-label recombinant activated factor VII for multiple indications in children. Clin Appl Thromb Hemost. 2007;13(3):233–240.

Rizoli SB, Nascimento J, Osman F, Netto FS, Kiss A, Callum J, et al. Recombinant activated coagulation factor VII and bleeding trauma patients. J Trauma Inj Infect Crit Care. 2006;61(6):1419–1425.

Tobias JD, Simsic JM, Weinstein S, Schechter W, Kartha V, Michler R. Recombinant factor VIIa to control excessive bleeding following surgery for congenital heart disease in pediatric patients. J Intensive Care Med. 2004;19(5):270–273.

von Heymann C, Jonas S, Spies C, Wernecke KD, Ziemer S, Janssen D, et al. Recombinant activated factor VIIa for the treatment of bleeding in major abdominal surgery including vascular and urological surgery: a review and meta-analysis of published data. Crit Care. 2008;12(1):R14.

Wittenstein B, Ng C, Ravn H, Goldman A. Recombinant factor VII for severe bleeding during extracorporeal membrane oxygenation following open heart surgery. Pediatr Crit Care Med. 2005;6(4):473–476.

B8 Excluded studies, Question 8

What is the effect of fresh frozen plasma, cryoprecipitate, fibrinogen concentrate, and/or platelet transfusion on patient outcome?

Excluded non-comparative Level IV studies

Premaratne S, Razzuk AM, Premaratne DR, Mugiishi MM, Hasaniya NW, Behling AF. Effects of platelet transfusion on post cardiopulmonary bypass bleeding. Jpn Heart J. 2001; 42(4):425–433.

B9 Excluded studies, Question 9

At what INR (or PT/APTT) for fresh frozen plasma, fibrinogen level for cryoprecipitate, platelet count for platelets concentrates should patients be transfused to avoid risks of significant adverse events?

Excluded, no usable data

Farrell TA, Hicks ME. A review of radiologically guided percutaneous nephrostomies in 303 patients. J Vasc Interv Radiol. 1997;8:769–774.

Excluded non-comparative Level IV studies

Piccinino F, Sagnelli E, Pasquale G, Giusti G. Complications following percutaneous liver biopsy. A multicentre retrospective study on 68 276 biopsies. J Hepatol. 1986;2:165–173.

Rasmus KT, Rottman RL, Kotelko DM, Wright WC, Stone JJ, Rosenblatt RM. Unrecognised thrombocytopenia and regional anaesthesia in parturients: a retrospective review. Obstet Gynecol. 1989;73:943–946.

B10 Late Exclusions

After the technical report was written, and during drafting of the recommendations and practice points, each chapter underwent an internal clinical peer review by a member of the Clinical Reference Group and some late exclusions from studies in Generic Questions 3 and 4 were made.

Question 6 Late Exclusions:

Andrews et al (1997) [149] – only level IV evidence reported for oral iron (i.e. the intervention in question). Level IV evidence was excluded for this intervention as higher level evidence was available.

Several studies[163,164,165,168,170,177,178] were late exclusions because the study populations were found not to be anaemic at baseline.

Question 7 Late Exclusion:

Pihusch (2005) [189] was excluded because the study population did not undergo surgery or invasive procedure.

As a consequence of this internal peer review and quality assurance process, the above studies have not been used to inform any of the recommendations for the clinical questions affected, however the data extraction and appraisal of these studies have been retained in the technical report as the data were considered informative.

Appendix C: Literature search results

C1 Literature search results, Question 1

What is the effect of a multidisciplinary, multimodal, programmatic approach to perioperative patient blood management on patient outcomes?

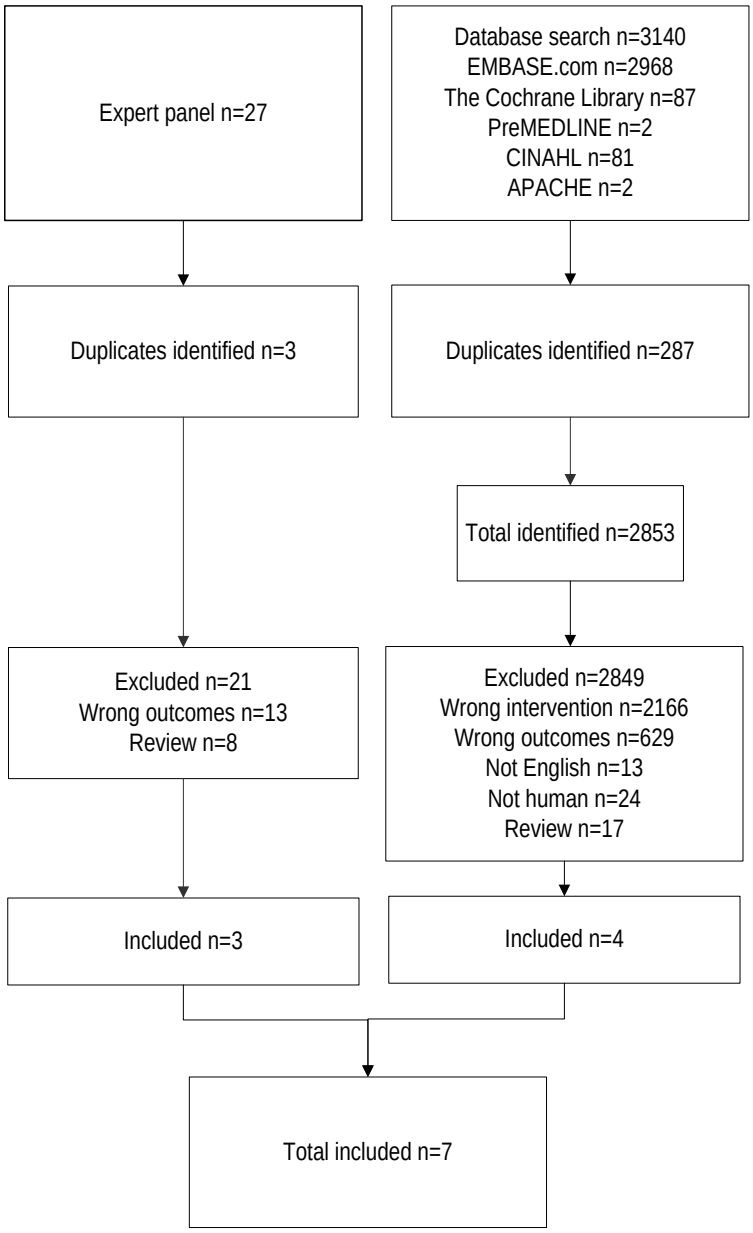

Figure 1 Literature search results, Question 1

C2 Literature search results, Question 2

In patients undergoing surgery or invasive procedures, what effect does the cessation and timing of cessation of medications that affect haemostasis have on morbidity, mortality and transfusion requirements?

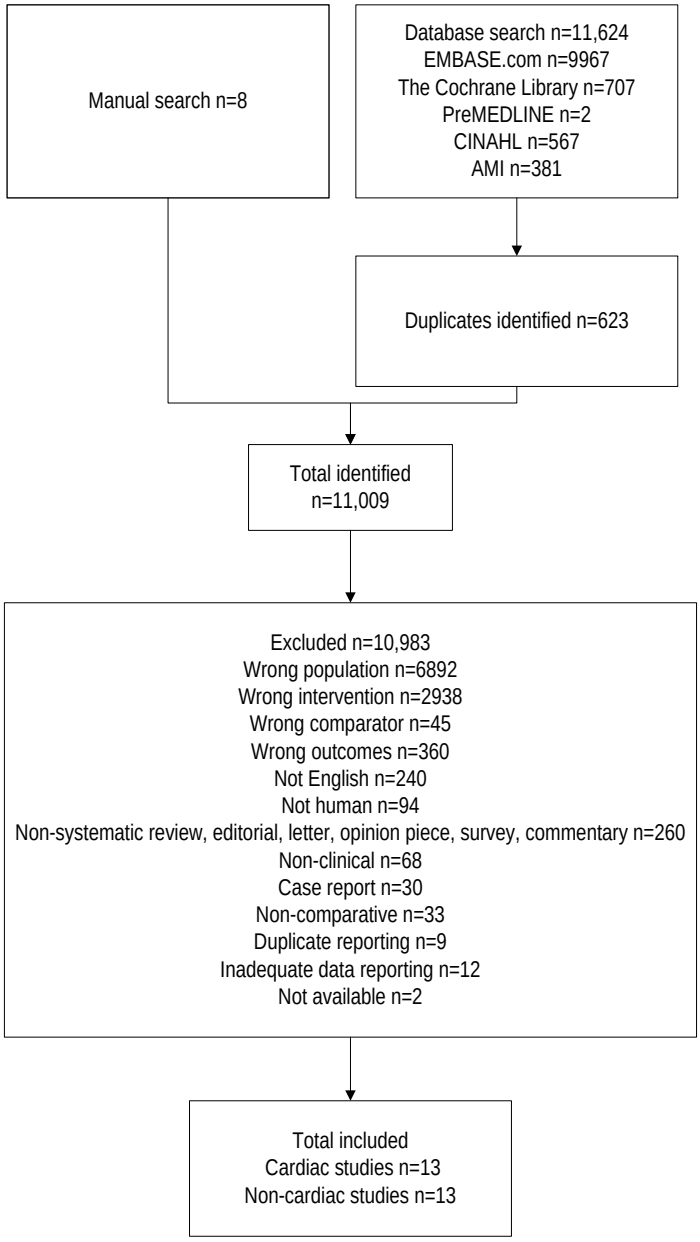

Figure 2 Literature search results, Question 2

C3 Literature search results, Question 3

In patients undergoing surgery, what is the effect of perioperative strategies that minimise blood loss on morbidity, mortality, and blood transfusion?

The body of evidence found by the systematic literature review and associated appendixes for Perioperative Foreground Question 3 are presented in a separate report.

C4 Literature search results, Question 4

Is anaemia an independent risk factor for adverse outcomes?

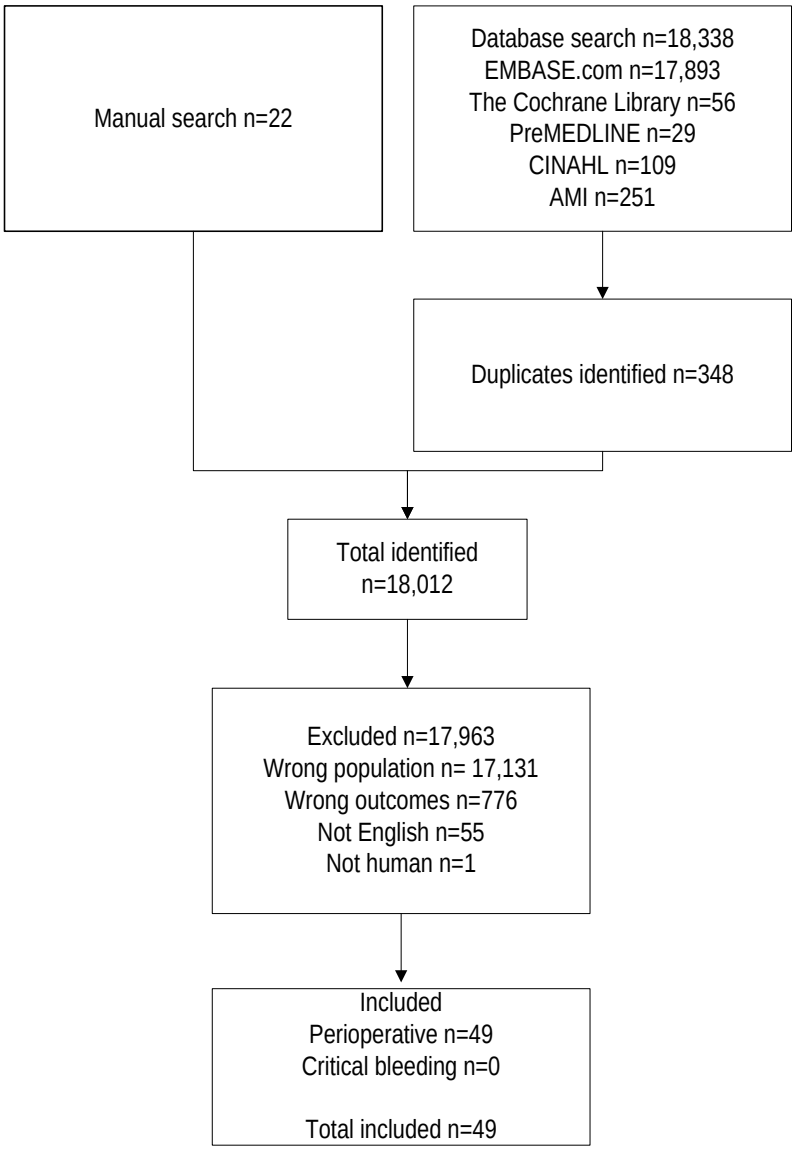

Figure 3 Literature search results, Question 4

C5 Literature search results, Question 5

What is the effect of red blood cell transfusion on patient outcomes?

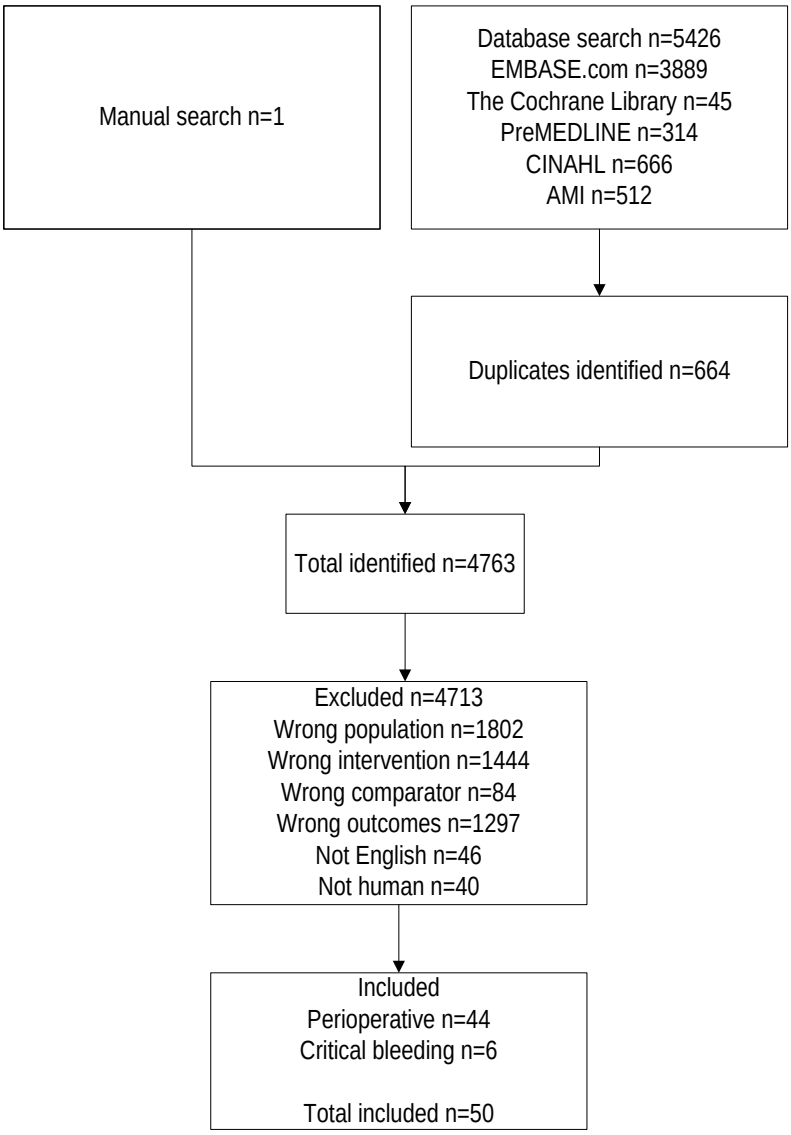

Figure 4 Literature search results, Question 5

C6 Literature search results, Question 6

What is the effect of interventions to increase haemoglobin concentration on morbidity, mortality and need for red blood cell transfusion?

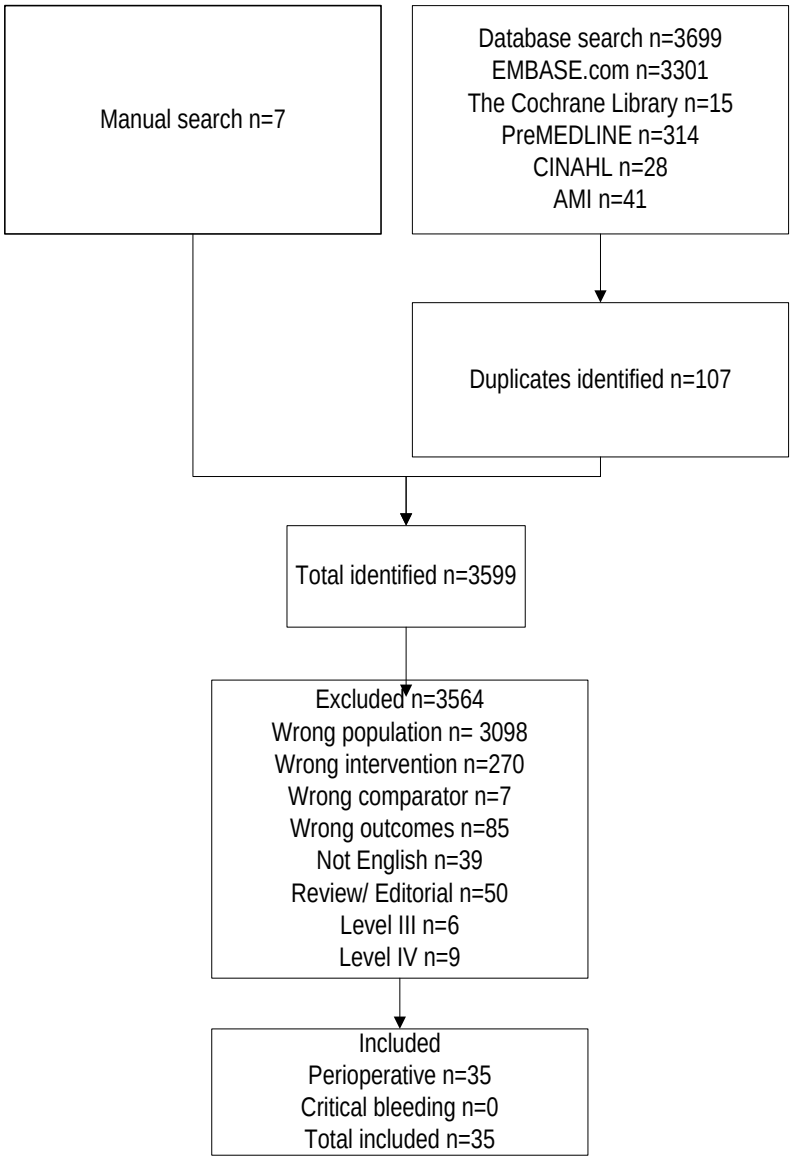

Figure 5 Literature search results, Question 6

C7 Literature search results, Question 7

What is the effect of rFVIIa (prophylaxis or treatment) on morbidity, mortality and transfusion rate?

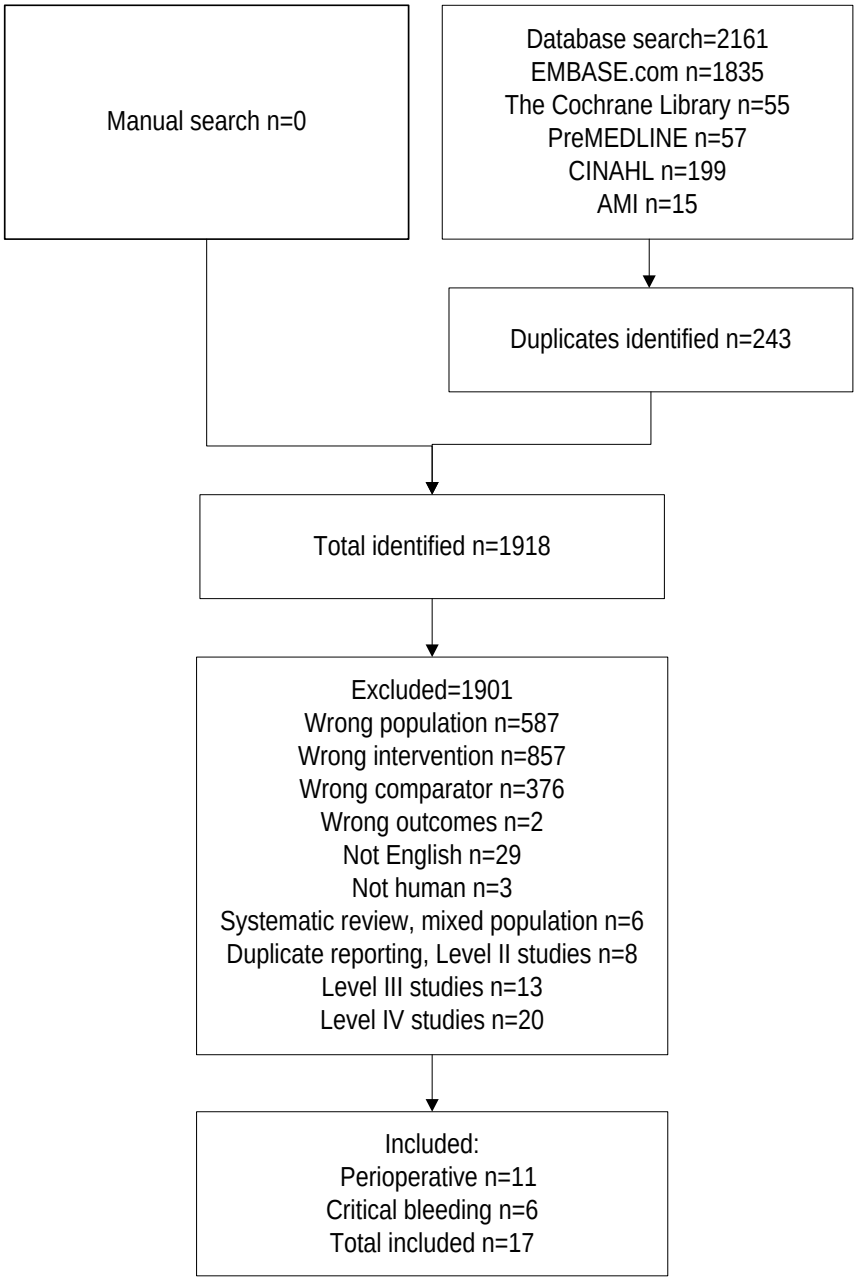

Figure 6 Literature search results, Question 7

C8 Literature search results, Question 8

What is the effect of fresh frozen plasma, cryoprecipitate, fibrinogen concentrate, and/or platelet transfusion on patient outcome?

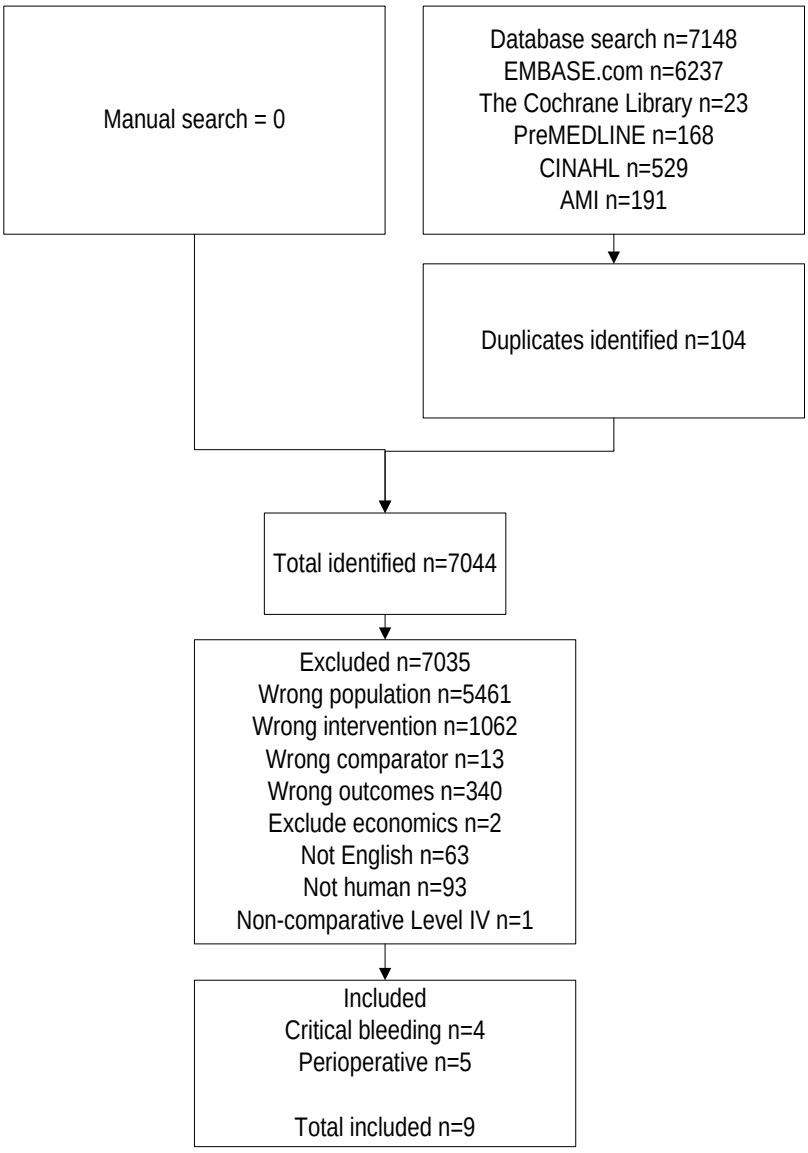

Figure 7 Literature search results, Question 8

C9 Literature search results, Question 9

At what INR (or PT/APTT) for fresh frozen plasma, fibrinogen level for cryoprecipitate, platelet count for platelet concentrates should patients be transfused to avoid risks of significant adverse events?

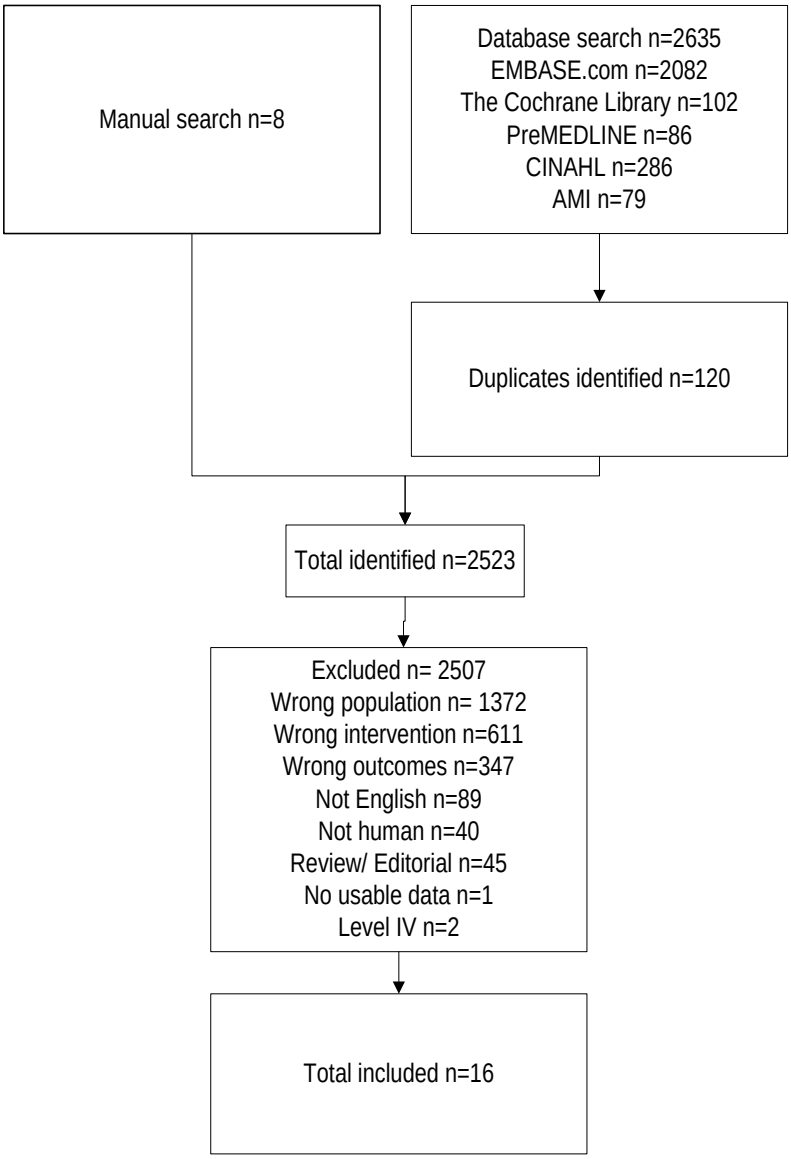

Figure 8 Literature search results, Question 9

Appendix D: Evidence matrixes

D1 Evidence matrix, Question 1

What is the effect of a multidisciplinary, multimodal, programmatic approach to perioperative patient blood management on patient outcomes?

Key question What is the effect of a multidisciplinary, multimodal, programmatic approach to perioperative patient blood management on patient outcomes?	Evidence table ref: Ferraris et al (2007)[27], Freedman et al (2005)[28], DeAnda et al (2006)[29], Freedman et al (2008)[30], Brevig et al (2009)[31], Bui et al (2002)[32], Bolan et al (2001)[33]	
1. Evidence base *(quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)*		
One Level I study[27], five Level III studies,[28–32] and one Level IV[33] study, all with a high level of bias	A	Excellent (One or more Level I studies with a low risk of bias or several Level II studies with a low risk of bias)
	B	Good (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	Satisfactory (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	Poor (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. Consistency *(the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)*		
In general, consistent findings were made in all studies, but the measured outcomes differed slightly and there was some inconsistency on the effect for mortality	A	Excellent (all studies consistent)
	B	Good (most studies consistent and inconsistency can be explained)
	C	Satisfactory (some inconsistency, reflecting genuine uncertainty around question)
	D	Poor (evidence is inconsistent)
	NA	Not applicable (one study only)
3. Clinical impact *(the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)*		
A multidisciplinary, multimodal programmatic approach to perioperative blood management is associated with decreases in morbidity, blood loss, transfusion requirements and length of stay in hospital. The impact on mortality is unclear	A	Excellent (very large clinical impact)
	B	Good (substantial clinical impact)
	C	Satisfactory (moderate clinical impact)
	D	Poor (slight or restricted clinical impact)
4. Generalisability *(how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?)*		
Population/s studied in the body of evidence are similar to the target population for the guideline	A	Excellent (directly generalisable to target population)
	B	Good (directly generalisable to target population with some caveats)
	C	Satisfactory (not directly generalisable to the target population but could be sensibly applied)
	D	Poor (not directly generalisable to target population and hard to judge whether it is sensible to apply)

5. Applicability *(the extent to which the body of evidence is directly applicable to Australian healthcare context)*		
Satisfactory (C): Most studies were conducted in the USA. Because the health system is dissimilar to Australia's, applicability is reduced	A	**Excellent** (directly applicable to Australian healthcare context)
	B	**Good** (applicable to Australian healthcare context with few caveats)
	C	**Satisfactory** (probably applicable to Australian healthcare context with some caveats)
	D	**Poor** (not applicable to Australian healthcare context)

6. Other factors (*Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation)*

EVIDENCE STATEMENT *Please summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account. Please indicate any dissenting opinions.*

A multidisciplinary, multimodal programmatic approach to perioperative blood management is associated with a reduction in transfusion requirements during cardiac or noncardiac surgery. The effect of such programs on morbidity and mortality is uncertain (Grade C)[29–33]

Component	Rating	Description
Evidence base	D	Poor
Consistency	B	Good
Clinical impact	B	Good
Generalisability	B	Good
Applicability	C	Satisfactory

Indicate any dissenting opinions

RECOMMENDATION *What recommendation (s) does the guideline development group draw from this evidence?*	GRADE OF RECOMMENDATION *(A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B)*	C

Health-care services should establish a multidisciplinary, multimodal perioperative patient blood management program (Grade C). This should include preoperative optimisation of red cell mass and coagulation status, meticulous attention to surgical haemostasis and minimisation of perioperative blood loss.

UNRESOLVED ISSUES

If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up

IMPLEMENTATION OF RECOMMENDATION

Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline.

Will this recommendation result in changes in usual care? Improved organisation of perioperative care	Yes	No
Are there any resource implications associated with the implementing this recommendation? Large resourcing implications: Use the same as above (money, people, logistics implementation)	Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized? Yes, requires a paradigm shift	Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation? NBA have produced a report on barriers to the uptake of several patient blood management approaches that included financial reasons, current regulations, availability of products, Medicare regulations/remunerations, politics, awareness of and willingness to implement program. This report is available upon request.	Yes	No

D2 Evidence matrix, Question 2

In patients undergoing surgery or invasive procedures, what effect does the cessation and timing of cessation of medications that affect haemostasis have on morbidity, mortality and transfusion requirements?

Key question In patients undergoing surgery or invasive procedures, what effect does the cessation and timing of cessation of medications that affect haemostasis have on morbidity, mortality, and RBC transfusion? This evidence matrix pertains to cardiac surgery patients who have been receiving aspirin monotherapy (PO2.1)		**Evidence table ref:** Ghaffarinejad et al (2007)[35]; Gerrah et al (2005)[36]; Gulbins et al (2009)[37]; Kamran et al (2008)[38]; and Weightman et al (2002)[47]
1. **Evidence base** *(quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)*		
One Level II study[35] with a moderate risk of bias; two Level III studies[36,37] with a moderate risk of bias; and two Level III studies with a high risk of bias[38,47]	A	**Excellent** (One or more Level I studies with a low risk of bias or several Level II studies with a low risk of bias)
	B	**Good** (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	**Satisfactory** (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	**Poor** (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. **Consistency** *(the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)*		
Most studies were consistent. Inconsistency can be explained by differences in study quality	A	**Excellent** (all studies consistent)
	B	**Good** (most studies consistent and inconsistency can be explained)
	C	**Satisfactory** (some inconsistency, reflecting genuine uncertainty around question)
	D	**Poor** (evidence is inconsistent)
	NA	**Not applicable** (one study only)
3. **Clinical impact** *(the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)*		
Slight clinical impact. The impact of the timing of cessation of aspirin therapy on mortality, morbidity (MI and pericardial effusion), and hospital and ICU LOS, blood loss and transfusion requirements is uncertain. The reduction in blood loss is not considered clinically meaningful.	A	**Excellent** (very large clinical impact)
	B	**Good** (substantial clinical impact)
	C	**Satisfactory** (moderate clinical impact)
	D	**Poor** (slight or restricted clinical impact)
4. **Generalisability** *(how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?)*		
All studies were in coronary artery bypass surgery populations with or without cardiopulmonary bypass.	A	**Excellent** (directly generalisable to target population)
	B	**Good** (directly generalisable to target population with some caveats)
	C	**Satisfactory** (not directly generalisable to the target population but could be sensibly applied)

	D	**Poor** (not directly generalisable to target population and hard to judge whether it is sensible to apply)
5. **Applicability** *(the extent to which the body of evidence is directly applicable to Australian healthcare context)*		
One included study from Europe[37] and one from Australia[47]. There are differences between the healthcare systems of Australian/NZ and other included studies[35,36,38]	A	**Excellent** (directly applicable to Australian healthcare context)
	B	**Good** (applicable to Australian healthcare context with few caveats)
	C	**Satisfactory** (probably applicable to Australian healthcare context with some caveats)
	D	**Poor** (not applicable to Australian healthcare context)
6. **Other factors** (*Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation)*		
EVIDENCE STATEMENT *Please summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account. Please indicate any dissenting opinions* In patients undergoing undergoing coronary artery bypass surgery, the effect of continuing aspirin monotherapy until the day of surgery on mortality[35,36], morbidity[35,37] (myocardial infarction and pericardial effusion), ICU LOS[37,38] , hospital LOS[36,38,47], perioperative blood loss and transfusion requirement is uncertain (Grade C)[35–38,47]		

Component	Rating	Description
Evidence base	B	Good
Consistency	C	Satisfactory
Clinical impact	D	Poor
Generalisability	A	Excellent
Applicability	C	Satisfactory

Indicate any dissenting opinions

RECOMMENDATION *What recommendation (s) does the guideline development group draw from this evidence?*	GRADE OF RECOMMENDATION *(A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B)*	NA
No recommendation was made on the basis of this uncertain evidence.		

UNRESOLVED ISSUES *If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up*

IMPLEMENTATION OF RECOMMENDATION *Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline*

Will this recommendation result in changes in usual care?	Yes	No
Are there any resource implications associated with the implementing this recommendation?	Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized?	Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation?	Yes	No

Key question In patients undergoing surgery or invasive procedures, what effect does the cessation and timing of cessation of medications that affect haemostasis have on morbidity, mortality, and RBC transfusion? This evidence matrix pertains to cardiac surgery patients who have been receiving clopidogrel monotherapy (PO2.2)		**Evidence table ref:** Ascione et al (2005)[39] Berger et al (2008) [470]; Chu et al (2004) [471]
1. **Evidence base** *(quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)*		
Three Level III studies: two with a moderate risk of bias[40,41]and one with a high risk of bias[39]	A	**Excellent** (One or more Level I studies with a low risk of bias or several Level II studies with a low risk of bias)
	B	**Good** (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	**Satisfactory** (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	**Poor** (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. **Consistency** *(the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)*		
Some conflicting findings: mortality was increased in one study[39], but unaffected in others[40,41]. There were also some differences in morbidity findings[40,41]. Inconsistencies may be explained due to study quality, selection bias and a lack of power	A	**Excellent** (all studies consistent)
	B	**Good** (most studies consistent and inconsistency can be explained)
	C	**Satisfactory** (some inconsistency, reflecting genuine uncertainty around question)
	D	**Poor** (evidence is inconsistent)
	NA	**Not applicable** (one study only)
3. **Clinical impact** *(the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)*		
Substantial clinical impact. Stopping clopidogrel closer to the time of surgery has negative consequences, including increased transfusion requirements and re-operation for bleeding	A	**Excellent** (very large clinical impact)
	B	**Good** (substantial clinical impact)
	C	**Satisfactory** (moderate clinical impact)
	D	**Poor** (slight or restricted clinical impact)
4. **Generalisability** *(how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?)*		
Study populations are the same as the target population	A	**Excellent** (directly generalisable to target population)
	B	**Good** (directly generalisable to target population with some caveats)
	C	**Satisfactory** (not directly generalisable to the target population but could be sensibly applied)
	D	**Poor** (not directly generalisable to target population and hard to judge whether it is sensible to apply)

5. Applicability *(the extent to which the body of evidence is directly applicable to Australian healthcare context)*		
One study was performed in the UK[39]; one in Canada[41], and another in the USA[40] where the healthcare system has some differences to Australia/NZ	A	**Excellent** (directly applicable to Australian healthcare context)
	B	**Good** (applicable to Australian healthcare context with few caveats)
	C	**Satisfactory** (probably applicable to Australian healthcare context with some caveats)
	D	**Poor** (not applicable to Australian healthcare context)

6. Other factors (*Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation)*

EVIDENCE STATEMENT *Please summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account. Please indicate any dissenting opinions*

In patients undergoing coronary artery bypass surgery there may be an increased risk of bleeding, transfusion requirement and re-operation for bleeding if clopidogrel is not ceased at least 5 days before surgery. The impact on morbidity and mortality is uncertain (Grade C)[39–41].

Component	Rating	Description
Evidence base	D	Poor
Consistency	C	Satisfactory
Clinical impact	B	Good
Generalisability	A	Excellent
Applicability	B	Good

Indicate any dissenting opinions

RECOMMENDATION *What recommendation (s) does the guideline development group draw from this evidence?*	GRADE OF RECOMMENDATION *(A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B)*	C

In patients undergoing coronary artery bypass surgery (CABG), either with cardiopulmonary bypass (CPB) or without (OPCAB), clopidogrel should be stopped, where possible, at least 5 days before surgery (Grade C) (Recommendation 2.1)

UNRESOLVED ISSUES *If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up*

IMPLEMENTATION OF RECOMMENDATION *Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline*

Will this recommendation result in changes in usual care?	Yes	No
Are there any resource implications associated with the implementing this recommendation?	Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized?	Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation?	Yes	No

Key question In patients undergoing surgery or invasive procedures, what effect does the cessation and timing of cessation of medications that affect haemostasis have on morbidity, mortality, and RBC transfusion? This evidence matrix pertains to cardiac surgery patients, undergoing coronary artery bypass surgery with cardiopulmonary bypass who have been receiving combination antiplatelet medication (PO2.3)		Evidence table ref: Kang et al (2007)[45]; Picker et al(2007) [46]
1. Evidence base *(quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)*		
Two Level III studies with a high risk of bias[45,46]	A	**Excellent** (One or more Level I studies with a low risk of bias or several Level II studies with a low risk of bias)
	B	**Good** (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	**Satisfactory** (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	**Poor** (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. Consistency *(the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)*		
Results are fairly similar across the studies	A	**Excellent** (all studies consistent)
	B	**Good** (most studies consistent and inconsistency can be explained)
	C	**Satisfactory** (some inconsistency, reflecting genuine uncertainty around question)
	D	**Poor** (evidence is inconsistent)
	NA	**Not applicable** (one study only)
3. Clinical impact *(the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)*		
There is moderate clinical impact (units transfused)	A	**Excellent** (very large clinical impact)
	B	**Good** (substantial clinical impact)
	C	**Satisfactory** (moderate clinical impact)
	D	**Poor** (slight or restricted clinical impact)
4. Generalisability *(how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?)*		
Study population is the same as the target population	A	**Excellent** (directly generalisable to target population)
	B	**Good** (directly generalisable to target population with some caveats)
	C	**Satisfactory** (not directly generalisable to the target population but could be sensibly applied)
	D	**Poor** (not directly generalisable to target population and hard to judge whether it is sensible to apply)

5. Applicability *(the extent to which the body of evidence is directly applicable to Australian healthcare context)*		
Satisfactory (C): One study was performed in the USA where the healthcare system has some differences to Australia/NZ[45]. One study was performed in Germany[46]	A	**Excellent** (directly applicable to Australian healthcare context)
	B	**Good** (applicable to Australian healthcare context with few caveats)
	C	**Satisfactory** (probably applicable to Australian healthcare context with some caveats)
	D	**Poor** (not applicable to Australian healthcare context)

6. Other factors (*Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation)*

EVIDENCE STATEMENT *Please summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account. Please indicate any dissenting opinions*

In patients undergoing coronary artery bypass graft surgery with cardiopulmonary bypass who are receiving combination antiplatelet medication, the continuation of clopidogrel up until the time of surgery may be associated with an increase in volume of transfusion; however, the available evidence is poor (Grade D)[45,46].

Component	Rating	Description
Evidence base	D	Poor
Consistency	C	Satisfactory
Clinical impact	C	Moderate
Generalisability	A	Excellent
Applicability	C	Satisfactory

Indicate any dissenting opinions

RECOMMENDATION *What recommendation (s) does the guideline development group draw from this evidence?*	GRADE OF RECOMMENDATION *(A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B)*	NA
No Recommendation was made (Grade D evidence).		

UNRESOLVED ISSUES *If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up*

IMPLEMENTATION OF RECOMMENDATION *Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline*

Will this recommendation result in changes in usual care? Greater flexibility in surgical options; may lead to an improvement in patient outcomes	Yes	No
Are there any resource implications associated with the implementing this recommendation?	Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized?	Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation?	Yes	No

Key question In patients undergoing surgery or invasive procedures, what effect does the cessation and timing of cessation of medications that affect haemostasis have on morbidity, mortality, and RBC transfusion? This evidence matrix pertains to cardiac surgery patients, undergoing coronary bypass surgery, who have been receiving combination antiplatelet medication (PO2.4)		**Evidence table ref:** Kapetanakis et al (2006)[42]; Shim et al (2007)[43]; Song et al (2008)[44]
1. **Evidence base** *(quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)*		
Three Level III studies, one with a moderate risk of bias[42] and two with a high risk of bias[43,44]	A	**Excellent** (One or more Level I studies with a low risk of bias or several Level II studies with a low risk of bias)
	B	**Good** (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	**Satisfactory** (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	**Poor** (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. **Consistency** *(the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)*		
Consistent evidence for most outcomes, inconsistent finding for intraoperative blood loss, transfusion and re-operation for bleeding. Explained by inter-study heterogeneity and variation in statistical analyses	A	**Excellent** (all studies consistent)
	B	**Good** (most studies consistent and inconsistency can be explained)
	C	**Satisfactory** (some inconsistency, reflecting genuine uncertainty around question)
	D	**Poor** (evidence is inconsistent)
	NA	**Not applicable** (one study only)
3. **Clinical impact** *(the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)*		
Timing of combination anti-platelet cessation does not have negative consequences for the majority of relevant outcomes. However, there may be an increased likelihood of intraoperative blood loss, transfusion and re-operation for bleeding	A	**Excellent** (very large clinical impact)
	B	**Good** (substantial clinical impact)
	C	**Satisfactory** (moderate clinical impact)
	D	**Poor** (slight or restricted clinical impact)
4. **Generalisability** *(how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?)*		
All study populations were off-pumpcardiac surgery.	A	**Excellent** (directly generalisable to target population)
	B	**Good** (directly generalisable to target population with some caveats)
	C	**Satisfactory** (not directly generalisable to the target population but could be sensibly applied)
	D	**Poor** (not directly generalisable to target population and hard to judge whether it is sensible to apply)

5. Applicability *(the extent to which the body of evidence is directly applicable to Australian healthcare context)*		
Two studies were from Korea[43,44] the other from the USA[42]. Healthcare systems in both countries differ from the Australian and New Zealand healthcare systems	A	**Excellent** (directly applicable to Australian healthcare context)
	B	**Good** (applicable to Australian healthcare context with few caveats)
	C	**Satisfactory** (probably applicable to Australian healthcare context with some caveats)
	D	**Poor** (not applicable to Australian healthcare context)

6. Other factors (*Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation)*

EVIDENCE STATEMENT *Please summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account. Please indicate any dissenting opinions*

In patients undergoing off-pump coronary artery bypass graft surgery who are receiving combination antiplatelet therapy, continuing clopidogrel within the 7-day period before surgery may be associated with an increased likelihood of red blood cell transfusion, and re-operation for bleeding (Grade C)[42–44]. The effect on mortality[42,44], ICU LOS[42,44] or hospital LOS[42,43] is uncertain (Grade C)[42–44].

Component	Rating	Description
Evidence base	D	Poor
Consistency	C	Satisfactory
Clinical impact	B	Good
Generalisability	A	Excellent
Applicability	C	Satisfactory

Indicate any dissenting opinions

RECOMMENDATION *What recommendation (s) does the guideline development group draw from this evidence?*	GRADE OF RECOMMENDATION *(A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B)*	C

In patients undergoing coronary artery bypass surgery (CABG), either with cardiopulmonary bypass (CPB) or without (OPCAB), clopidogrel should be stopped, where possible, at least 5 days before surgery (Grade C)

UNRESOLVED ISSUES *If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up*

IMPLEMENTATION OF RECOMMENDATION *Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline*

Will this recommendation result in changes in usual care? Greater flexibility in surgical options; may lead to an improvement in patient outcomes	Yes	No
Are there any resource implications associated with the implementing this recommendation?	Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized?	Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation?	Yes	No

Key question What is the perioperative management strategy for patients undergoing noncardiac surgery or invasive procedures receiving aspirin therapy? (PO2.5)	Evidence table ref: Burger et al (2005)[48]; Krishnan et al (2008)[51]	
1. Evidence base *(quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)*		
One systematic review made up mostly of Level III studies[48] and one Level III study with a moderate risk of bias[51]	A	Excellent (One or more Level I studies with a low risk of bias or several Level II studies with a low risk of bias)
	B	Good (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	Satisfactory (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	Poor (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. Consistency *(the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)*		
Results are generally consistent	A	Excellent (all studies consistent)
	B	Good (most studies consistent and inconsistency can be explained)
	C	Satisfactory (some inconsistency, reflecting genuine uncertainty around question)
	D	Poor (evidence is inconsistent)
	NA	Not applicable (one study only)
3. Clinical impact *(the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)*		
Moderate clinical impact. Overall study and sample size is relatively large and the evidence comes from a range of different procedures. In most cases, low dose aspirin use increased the frequency of bleeding, although this was not reflected in the severity of bleeding or bleeding complications (with the possible exception of intracranial surgery and prostatectomy). The balance between the risk of bleeding and of thrombotic cardiovascular events should be considered.	A	Excellent (very large clinical impact)
	B	Good (substantial clinical impact)
	C	Satisfactory (moderate clinical impact)
	D	Poor (slight or restricted clinical impact)
4. Generalisability *(how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?)*		
The studies included a range of different non-cardac surgeries and invasive procedures and is generalisable to this patient population	A	Excellent (directly generalisable to target population)
	B	Good (directly generalisable to target population with some caveats)
	C	Satisfactory (not directly generalisable to the target population but could be sensibly applied)
	D	Poor (not directly generalisable to target population and hard to judge whether it is sensible to apply)
5. Applicability *(the extent to which the body of evidence is directly applicable to Australian healthcare context)*		
The results of these studies are most likely applicable to the Australian healthcare system	A	Excellent (directly applicable to Australian healthcare context)
	B	Good (applicable to Australian healthcare context with few caveats)

	C	Satisfactory (probably applicable to Australian healthcare context with some caveats)
	D	Poor (not applicable to Australian healthcare context)

6. Other factors (*Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation)*

EVIDENCE STATEMENT

Please summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account. Please indicate any dissenting opinions.

In patients undergoing noncardiac surgery or invasive procedures, the effect of continuing aspirin therapy on morbidity, mortality and transfusion is uncertain given the heterogeneity of the populations studied[48,51] (Grade C).

Component	Rating	Description
Evidence base	C	Satisfactory
Consistency	B	Good
Clinical impact	C	Satisfactory
Generalisability	B	Good
Applicability	B	Good

RECOMMENDATION *What recommendation (s) does the guideline development group draw from this evidence?*	GRADE OF RECOMMENDATION *(A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B).*	C

In patients undergoing noncardiac surgery, it is reasonable to continue low dose aspirin therapy. This may require specific evaluation in neurosurgery and intraocular surgery (Grade C).

UNRESOLVED ISSUES

If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up

IMPLEMENTATION OF RECOMMENDATION

Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline.

Will this recommendation result in changes in usual care?	Yes	No
Are there any resource implications associated with the implementing this recommendation?	Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized?	Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation?	Yes	No

Key question What is the perioperative management strategy for patients undergoing noncardiac surgery or invasive procedures receiving NSAID therapy? (PO2.6)		Evidence table ref: Slappendel et al (2002)[52]; Robinson et al (1993)[53]; An et al (1991)[54]
1. Evidence base *(quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)*		
One Level II study with a low risk of bias[52] and two Level III studies with a moderate risk of bias[53,54]	A	Excellent (One or more Level I studies with a low risk of bias or several Level II studies with a low risk of bias)
	B	Good (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	Satisfactory (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	Poor (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. Consistency *(the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)*		
Results were consistent	A	Excellent (all studies consistent)
	B	Good (most studies consistent and inconsistency can be explained)
	C	Satisfactory (some inconsistency, reflecting genuine uncertainty around question)
	D	Poor (evidence is inconsistent)
	NA	Not applicable (one study only)
3. Clinical impact *(the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)*		
Moderate clinical impact	A	Excellent (very large clinical impact)
	B	Good (substantial clinical impact)
	C	Satisfactory (moderate clinical impact)
	D	Poor (slight or restricted clinical impact)
4. Generalisability *(how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?)*		
All studies were performed in orthopaedic patients, specifically hip arthroplasty, and may be generalisable to orthopaedic patient populations	A	Excellent (directly generalisable to target population)
	B	Good (directly generalisable to target population with some caveats)
	C	Satisfactory (not directly generalisable to the target population but could be sensibly applied)
	D	Poor (not directly generalisable to target population and hard to judge whether it is sensible to apply)
5. Applicability *(the extent to which the body of evidence is directly applicable to Australian healthcare context)*		
One study was performed in the USA, one in the UK, and one in the Netherlands	A	Excellent (directly applicable to Australian healthcare context)
	B	Good (applicable to Australian healthcare context with few caveats)

	C	**Satisfactory** (probably applicable to Australian healthcare context with some caveats)
	D	**Poor** (not applicable to Australian healthcare context)

6. Other factors (*Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation)*

No information regarding the timing of the cessation of NSAIDs was available. The evidence statement and recommendation was therefore downgraded to a C, despite the quality of the evidence base.

EVIDENCE STATEMENT

Please summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account. Please indicate any dissenting opinions.

In patients undergoing orthopaedic surgery receiving NSAID therapy, blood loss and transfusion requirements are increased when NSAID therapy is continued until the day of surgery[52–54] (Grade C). There is insufficient evidence to determine the effect of the timing of cessation of NSAID therapy.

Component	Rating	Description
Evidence base	B	Good
Consistency	B	Good
Clinical impact	C	Satisfactory
Generalisability	B	Good
Applicability	B	Good

RECOMMENDATION *What recommendation (s) does the guideline development group draw from this evidence?*	GRADE OF RECOMMENDATION *(A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B).*	B

In patients undergoing elective orthopaedic surgery, NSAID therapy should be ceased preoperatively to reduce blood loss and transfusion (Grade C). The timing of the cessation should reflect the agent's pharmacology. (Recommendaton PO2.3)

UNRESOLVED ISSUES

If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up

IMPLEMENTATION OF RECOMMENDATION

Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline.

Will this recommendation result in changes in usual care?	Yes	No
Are there any resource implications associated with the implementing this recommendation?	Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized?	Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation?	Yes	No

Key question What is the perioperative management strategy for patients undergoing noncardiac surgery or invasive procedures receiving clopidogrel therapy? (PO2.7)	Evidence table ref: Ozao-Choy et al (2008)[55]	
1. Evidence base *(quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)*		
One Level III study with a moderate risk of bias[55]	A	Excellent (One or more Level I studies with a low risk of bias or several Level II studies with a low risk of bias)
	B	Good (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	Satisfactory (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	Poor (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. Consistency *(the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)*		
Only one study	A	Excellent (all studies consistent)
	B	Good (most studies consistent and inconsistency can be explained)
	C	Satisfactory (some inconsistency, reflecting genuine uncertainty around question)
	D	Poor (evidence is inconsistent)
	NA	Not applicable (one study only)
3. Clinical impact *(the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)*		
This is a small study with slight or restricted clinical impact	A	Excellent (very large clinical impact)
	B	Good (substantial clinical impact)
	C	Satisfactory (moderate clinical impact)
	D	Poor (slight or restricted clinical impact)
4. Generalisability *(how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?)*		
The study included patients undergoing a range of different noncardiac surgeries and is probably generalisable to this patient population	A	Excellent (directly generalisable to target population)
	B	Good (directly generalisable to target population with some caveats)
	C	Satisfactory (not directly generalisable to the target population but could be sensibly applied)
	D	Poor (not directly generalisable to target population and hard to judge whether it is sensible to apply)
5. Applicability *(the extent to which the body of evidence is directly applicable to Australian healthcare context)*		
The one study was from the USA	A	Excellent (directly applicable to Australian healthcare context)
	B	Good (applicable to Australian healthcare context with few caveats)

	C	**Satisfactory** (probably applicable to Australian healthcare context with some caveats)
	D	**Poor** (not applicable to Australian healthcare context)

6. Other factors (*Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation)*

EVIDENCE STATEMENT

Please summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account. Please indicate any dissenting opinions.

In patients undergoing noncardiac surgery, the effect of continuing clopidogrel on morbidity, mortality and transfusion is uncertain (Grade D)[55]

Component	Rating	Description
Evidence base	D	Poor
Consistency	NA	Not Applicable
Clinical impact	D	Poor
Generalisability	B	Good
Applicability	C	Satisfactory

RECOMMENDATION *What recommendation (s) does the guideline development group draw from this evidence?*	GRADE OF RECOMMENDATION *(A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B).*	NA

No recommendation was made due to imbalance between study arms. The results were unable to be relied on.

UNRESOLVED ISSUES

If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up

IMPLEMENTATION OF RECOMMENDATION

Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline.

Will this recommendation result in changes in usual care?	Yes	No
Are there any resource implications associated with the implementing this recommendation?	Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized?	Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation?	Yes	No

Key question What is the perioperative management strategy for patients undergoing noncardiac surgery or invasive procedures receiving warfarin therapy? (PO2.8)	Evidence table ref: Dunn et al (2003)[49]; Nematullah et al (2009)[50]; Devani et al (1998)[56]; Campbell et al (20000)[57]; El-Jack et al (2006)[58]; Wysokinski et al (2008)[59]; McLemore et al (2006)[60]	
1. Evidence base *(quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)*		
One Level I study[50] and one Level III study[59] with a low risk of bias; one Level I study[49] and two Level II studies[58,60] with a moderate risk of bias; and two Level II studies[56,57] with a high risk of bias.	A	Excellent (One or more Level I studies with a low risk of bias or several Level II studies with a low risk of bias)
	B	Good (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	Satisfactory (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	Poor (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. Consistency *(the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)*		
Studies are generally all consistent	A	Excellent (all studies consistent)
	B	Good (most studies consistent and inconsistency can be explained)
	C	Satisfactory (some inconsistency, reflecting genuine uncertainty around question)
	D	Poor (evidence is inconsistent)
	NA	Not applicable (one study only)
3. Clinical impact *(the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)*		
Ovrall there was a substantial clinical impact	A	Excellent (very large clinical impact)
	B	Good (substantial clinical impact)
	C	Satisfactory (moderate clinical impact)
	D	Poor (slight or restricted clinical impact)
4. Generalisability *(how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?)*		
The results are directly generalisable to patients undergoing noncardiac surgery or invasive procedures	A	Excellent (directly generalisable to target population)
	B	Good (directly generalisable to target population with some caveats)
	C	Satisfactory (not directly generalisable to the target population but could be sensibly applied)
	D	Poor (not directly generalisable to target population and hard to judge whether it is sensible to apply)
5. Applicability *(the extent to which the body of evidence is directly applicable to Australian healthcare context)*		
Results of the included studies are most likely applicable to the Australian healthcare system	A	Excellent (directly applicable to Australian healthcare context)
	B	Good (applicable to Australian healthcare context with few caveats)

	C	**Satisfactory** (probably applicable to Australian healthcare context with some caveats)
	D	**Poor** (not applicable to Australian healthcare context)

6. Other factors (*Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation)*

EVIDENCE STATEMENT

Please summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account. Please indicate any dissenting opinions.

In patients undergoing minor dental procedures, arthrocentesis, cataract surgery, upper gastrointestinal endoscopy or colonoscopy with or without biopsy, morbidity and mortality are unaffected when warfarin is continued[49,50,56–59] (Grade B). In patients undergoing more complex procedures, the effect on mortality and morbidity is unclear when warfarin is continued or when bridging therapy is administered[49] (Grade B)

Component	Rating	Description
Evidence base	A	Excellent
Consistency	B	Good
Clinical impact	B	Good
Generalisability	A	Excellent
Applicability	B	Good

RECOMMENDATION *What recommendation (s) does the guideline development group draw from this evidence?*	GRADE OF RECOMMENDATION *(A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B).*	B

In patients undergoing minor dental procedures, arthrocentesis, cataract surgery, upper gastrointestinal endoscopy without biopsy or colonoscopy without biopsy, warfarin may be continued (Grade B).

UNRESOLVED ISSUES

If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up

IMPLEMENTATION OF RECOMMENDATION

Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline.

Will this recommendation result in changes in usual care?	Yes	No
Are there any resource implications associated with the implementing this recommendation?	Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized?	Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation?	Yes	No

D3 Evidence matrix, Question 3

In patients undergoing surgery, what is the effect of perioperative strategies that minimise blood loss on morbidity, mortality, and blood transfusion?

The body of evidence found by the systematic literature review and associated appendixes for Perioperative Foreground Question 3 are presented in a separate report.

D4 Evidence matrix, Question 4

Is anaemia an independent risk factor for adverse outcomes?

Key question Is preoperative anaemia an independent risk factor for morbidity and mortality in patients undergoing cardiac surgery? (GN1.1)	Evidence table ref: Koch et al (2003)[64]; Kulier et al (2007)[65]; Zindrou et al (2002)[71]; Bell et al (2008)[79]; Cladellas et al (2006)[80]; Ferraris et al (1996)[82]; Higgins et al (1992)[85]; Karkouti et al (2008a)[87]; Karkouti et al (2009)[86]	
1. Evidence base *(quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)*		
One good quality Level II study[65], three good quality[79,80,85] and three fair quality[82,87,86] Level III studies for morbidity; two good quality Level II[64,71] and three good quality Level III studies[79,80,85] for mortality	A	Excellent (One or more Level I studies with a low risk of bias or several Level II studies with a low risk of bias)
	B	Good (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	Satisfactory (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	Poor (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. Consistency *(the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)*		
A relationship between anaemia and mortality was consistent; the relationship between morbidity and anaemia was mostly consistent	A	Excellent (all studies consistent)
	B	Good (most studies consistent and inconsistency can be explained)
	C	Satisfactory (some inconsistency, reflecting genuine uncertainty around question)
	D	Poor (evidence is inconsistent)
	NA	Not applicable (one study only)
3. Clinical impact *the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)*		
Overall study and sample size is large but there was some discrepancy around the definition of mortality	A	Excellent (very large clinical impact)
	B	Good (substantial clinical impact)
	C	Satisfactory (moderate clinical impact)
	D	Poor (slight or restricted clinical impact)
4. Generalisability *(how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?)*		
All results were from patients undergoing cardiac surgery	A	Excellent (directly generalisable to target population)
	B	Good (directly generalisable to target population with some caveats)
	C	Satisfactory (not directly generalisable to the target population but could be sensibly applied)
	D	Poor (not directly generalisable to target population and hard to judge whether it is sensible to apply)

5. Applicability *(the extent to which the body of evidence is directly applicable to Australian healthcare context)*		
Seven studies were from the USA, three from Europe (Spain and the UK) and one from Canada	A	**Excellent** (directly applicable to Australian healthcare context)
	B	**Good** (applicable to Australian healthcare context with few caveats)
	C	**Satisfactory** (probably applicable to Australian healthcare context with some caveats)
	D	**Poor** (not applicable to Australian healthcare context)

6. Other factors (*Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation)*
The Kulier et al (2007) study performed a multivariate analysis. The adjusted results from this study underpin the evidence base.

EVIDENCE STATEMENT
Please summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account. Please indicate any dissenting opinions.

In patients undergoing cardiac surgery, preoperative anaemia is associated with an increased risk of morbidity and mortality[64,65,71,79,80,82,85,86,,87] (Grade B)

Component	Rating	Description
Evidence base	B	Good
Consistency	B	Good
Clinical impact	C	Satisfactory
Generalisability	B	Good
Applicability	C	Satisfactory

Indicate any dissenting opinions

RECOMMENDATION *What recommendation (s) does the guideline development group draw from this evidence?*	GRADE OF RECOMMENDATION *(A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B).*	NA
No recommendation was made because this was a risk question. It did not examine the effect of an intervention.		

UNRESOLVED ISSUES *If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up*

IMPLEMENTATION OF RECOMMENDATION *Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline*

Will this recommendation result in changes in usual care?	Yes	No
Are there any resource implications associated with the implementing this recommendation?	Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized?	Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation?	Yes	No

Key question Is preoperative anaemia an independent risk factor for increased risk of transfusion in patients undergoing cardiac surgery? (GN1.2)		Evidence table ref: Parr et al (2003)[67]; Litmathe et al (2003)[90]; Gombotz et al (2007)[63]
1. Evidence base *(quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)*		
Two good quality[63,67] Level II studies; one fair quality Level III study[90]	A	Excellent (One or more Level I studies with a low risk of bias or several Level II studies with a low risk of bias)
	B	Good (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	Satisfactory (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	Poor (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. Consistency *(the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)*		
All consistent	A	Excellent (all studies consistent)
	B	Good (most studies consistent and inconsistency can be explained)
	C	Satisfactory (some inconsistency, reflecting genuine uncertainty around question)
	D	Poor (evidence is inconsistent)
	NA	Not applicable (one study only)
3. Clinical impact *(the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)*		
Substantial clinical impact	A	Excellent (very large clinical impact)
	B	Good (substantial clinical impact)
	C	Satisfactory (moderate clinical impact)
	D	Poor (slight or restricted clinical impact)
4. Generalisability *(how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?)*		
Can be applied to cardiac patients; need to take into consideration the procedure being completed	A	Excellent (directly generalisable to target population)
	B	Good (directly generalisable to target population with some caveats)
	C	Satisfactory (not directly generalisable to the target population but could be sensibly applied)
	D	Poor (not directly generalisable to target population and hard to judge whether it is sensible to apply)
5. Applicability *(the extent to which the body of evidence is directly applicable to Australian healthcare context)*		
One study was from the USA and two from Europe	A	Excellent (directly applicable to Australian healthcare context)
	B	Good (applicable to Australian healthcare context with few caveats)
	C	Satisfactory (probably applicable to Australian healthcare context with some caveats)
	D	Poor (not applicable to Australian healthcare context)
6. Other factors (*Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation)*		

EVIDENCE STATEMENT *Please summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account. Please indicate any dissenting opinions.*				
In patients undergoing cardiac surgery, preoperative anaemia is associated with an increased likelihood of transfusion (Grade B) [63,67,90].				
Component	Rating	Description		
Evidence base	B	Good		
Consistency	A	Excellent		
Clinical impact	B	Good		
Generalisability	B	Good		
Applicability	C	Satisfactory		
Indicate any dissenting opinions				
RECOMMENDATION *What recommendation (s) does the guideline development group draw from this evidence?* No recommendation was made because this was a risk question. It did not examine the effect of an intervention.			GRADE OF RECOMMENDATION *(A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B).*	NA
UNRESOLVED ISSUES *If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up*				
IMPLEMENTATION OF RECOMMENDATION *Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline.*				
Will this recommendation result in changes in usual care?			Yes	No
Are there any resource implications associated with the implementing this recommendation?			Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized?			Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation?			Yes	No

Key question Are preoperative and intraoperative anaemia independent risk factors for increased hospital length of stay in patients undergoing cardiac surgery? (GN1.3)		Evidence table ref: Ferraris et al (1996)[82], Habib et al (2003)[83]
1. Evidence base *(quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)*		
Two fair quality Level III studies[82,83]	A	**Excellent** (One or more Level I studies with a low risk of bias or several Level II studies with a low risk of bias)
	B	**Good** (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	**Satisfactory** (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	**Poor** (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. Consistency *(the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)*		
Some inconsistency, reflecting genuine uncertainty around the question	A	**Excellent** (all studies consistent)
	B	**Good** (most studies consistent and inconsistency can be explained)
	C	**Satisfactory** (some inconsistency, reflecting genuine uncertainty around question)
	D	**Poor** (evidence is inconsistent)
	NA	**Not applicable** (one study only)
3. Clinical impact (*the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)*		
Slight or restricted clinical impact	A	**Excellent** (very large clinical impact)
	B	**Good** (substantial clinical impact)
	C	**Satisfactory** (moderate clinical impact)
	D	**Poor** (slight or restricted clinical impact)
4. Generalisability *(how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?)*		
May be applied to all cardiac surgical patients	A	**Excellent** (directly generalisable to target population)
	B	**Good** (directly generalisable to target population with some caveats)
	C	**Satisfactory** (not directly generalisable to the target population but could be sensibly applied)
	D	**Poor** (not directly generalisable to target population and hard to judge whether it is sensible to apply)
5. Applicability *(the extent to which the body of evidence is directly applicable to Australian healthcare context)*		
Both studies were conducted in the USA	A	**Excellent** (directly applicable to Australian healthcare context)
	B	**Good** (applicable to Australian healthcare context with few caveats)
	C	**Satisfactory** (probably applicable to Australian healthcare context with some caveats)

	D	Poor (not applicable to Australian healthcare context)

6. Other factors (*Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation)*		
EVIDENCE STATEMENT *Please summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account. Please indicate any dissenting opinions.*		
In patients undergoing cardiac surgery, preoperative and intraoperative anaemia are associated with increased hospital length of stay (Grade D)		
Component	Rating	Description
Evidence base	D	Poor
Consistency	C	Satisfactory
Clinical impact	D	Poor
Generalisability	C	Satisfactory
Applicability	C	Satisfactory
Indicate any dissenting opinions		

RECOMMENDATION *What recommendation (s) does the guideline development group draw from this evidence?*	GRADE OF RECOMMENDATION *(A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B)*	NA
No recommendation was made because this was a risk question. It did not examine the effect of an intervention.		
UNRESOLVED ISSUES *If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up*		
IMPLEMENTATION OF RECOMMENDATION *Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline*		

Will this recommendation result in changes in usual care?	Yes	No
Are there any resource implications associated with the implementing this recommendation?	Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized?	Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation?	Yes	No

Key question Is intraoperative anaemia an independent risk factor for morbidity and mortality in patients undergoing cardiac surgery? (GN1.4)	**Evidence table ref:** DeFoe et al (2001)[62]; Habib et al (2003)[83]; Habib et al (2005)[84]Fang et al (1997[81])	
1. **Evidence base** *(quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)*		
One good quality[62] Level II study; two good quality[81, 84]and one fair quality[83] Level III study	A	**Excellent** (One or more Level I studies with a low risk of bias or several Level II studies with a low risk of bias)
	B	**Good** (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	**Satisfactory** (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	**Poor** (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. **Consistency** *(the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)*		
The studies demonstrated a relationship between intraoperative anaemia and mortality and mobidity	A	**Excellent** (all studies consistent)
	B	**Good** (most studies consistent and inconsistency can be explained)
	C	**Satisfactory** (some inconsistency, reflecting genuine uncertainty around question)
	D	**Poor** (evidence is inconsistent)
	NA	**Not applicable** (one study only)
3. **Clinical impact** *(the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)*		
Overall there was a moderate clinical impact	A	**Excellent** (very large clinical impact)
	B	**Good** (substantial clinical impact)
	C	**Satisfactory** (moderate clinical impact)
	D	**Poor** (slight or restricted clinical impact)
4. **Generalisability** *(how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?)*		
All studies were from groups having cardiac surgery	A	**Excellent** (directly generalisable to target population)
	B	**Good** (directly generalisable to target population with some caveats)
	C	**Satisfactory** (not directly generalisable to the target population but could be sensibly applied)
	D	**Poor** (not directly generalisable to target population and hard to judge whether it is sensible to apply)
5. **Applicability** *(the extent to which the body of evidence is directly applicable to Australian healthcare context)*		
All studies were conducted in the USA	A	**Excellent** (directly applicable to Australian healthcare context)
	B	**Good** (applicable to Australian healthcare context with few caveats)
	C	**Satisfactory** (probably applicable to Australian healthcare context with some caveats)
	D	**Poor** (not applicable to Australian healthcare context)
6. **Other factors** (*Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation)*		

EVIDENCE STATEMENT *Please summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account. Please indicate any dissenting opinions.*		
In patients undergoing cardiac surgery, an intraoperative/operative haematocrit level of less than 20% is associated with an increased risk of morbidity and mortality (Grade C) [62,81, 83,84]		
Component	Rating	Description
Evidence base	C	Satisfactory
Consistency	B	Good
Clinical impact	C	Satisfactory
Generalisability	B	Good
Applicability	C	Satisfactory
Indicate any dissenting opinions		

RECOMMENDATION *What recommendation (s) does the guideline development group draw from this evidence?*	GRADE OF RECOMMENDATION *(A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B).*	NA
No recommendation was made because this was a risk question. It did not examine the effect of an intervention.		
UNRESOLVED ISSUES *If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up*		
IMPLEMENTATION OF RECOMMENDATION *Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline*		
Will this recommendation result in changes in usual care?	Yes	No
Are there any resource implications associated with the implementing this recommendation?	Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized?	Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation?	Yes	No

Key question Is preoperative anaemia an independent risk factor for adverse outcomes (mortality and morbidity) in patients undergoing noncardiac surgery? (GN1.5)	**Evidence table ref:** Halm et al (2004)[74]; Myers et al (2004)[76]; Wolters et al (1997)[78]; Beattie et al (2009)[93]; Carson et al (2002)[94]; Dunkelgrun et al 2008 [95]; Gruson et al (2002)[96]; Lawrence et al (2003)[97]; Lunn and Elwood (1970)[98]; Marcantonio et al (1998)[99]; Wu et al (2007)[103]; Rogers et al 2007a[100]	
1. **Evidence base** *(quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)*		
One good quality[74] Level II study, and two good quality[93,103], one fair quality[99] and one poor quality Level III study[98] for mortality. Two good quality[74,78] and one poor quality[76] Level II study, and two good quality[103,95], three fair quality[94,96,100] and two poor quality[97,98] Level III studies for morbidity	A	**Excellent** (One or more Level I studies with a low risk of bias or several Level II studies with a low risk of bias)
	B	**Good** (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	**Satisfactory** (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	**Poor** (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. **Consistency** *(the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)*		
Mortality results consistent; some consistency among morbidity results	A	**Excellent** (all studies consistent)
	B	**Good** (most studies consistent and inconsistency can be explained)
	C	**Satisfactory** (some inconsistency, reflecting genuine uncertainty around question)
	D	**Poor** (evidence is inconsistent)
	NA	**Not applicable** (one study only)
3. **Clinical impact** *(the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)*		
Reasonable samples; however, each applies to different outcomes for morbidity, and there is a question around the definition of mortality	A	**Excellent** (very large clinical impact)
	B	**Good** (substantial clinical impact)
	C	**Satisfactory** (moderate clinical impact)
	D	**Poor** (slight or restricted clinical impact)
4. **Generalisability** *(how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?)*		
The results are generalisable to some extent, given they are from preoperative populations. The results, however, may depend on the type of surgery undergone	A	**Excellent** (directly generalisable to target population)
	B	**Good** (directly generalisable to target population with some caveats)
	C	**Satisfactory** (not directly generalisable to the target population but could be sensibly applied)
	D	**Poor** (not directly generalisable to target population and hard to judge whether it is sensible to apply)

5. Applicability *(the extent to which the body of evidence is directly applicable to Australian healthcare context)*		
Seven studies were conducted in the USA, two in the UK, and one each in Canada,Germany and the Netherlands.	A	**Excellent** (directly applicable to Australian healthcare context)
	B	**Good** (applicable to Australian healthcare context with few caveats)
	C	**Satisfactory** (probably applicable to Australian healthcare context with some caveats)
	D	**Poor** (not applicable to Australian healthcare context)

6. Other factors (*Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation)*
The Halm et al (2004) study performed a multivariate analysis. The adjusted results from this study underpin the evidence base.

EVIDENCE STATEMENT *Please summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account. Please indicate any dissenting opinions.*

In patients undergoing noncardiac surgery, preoperative anaemia is associated with an increased risk of postoperative morbidity and mortality (Grade B) [74,76,78,93, 95,96,98,100,103]

Component	Rating	Description
Evidence base	B	Good
Consistency	B	Good
Clinical impact	C	Satisfactory
Generalisability	B	Good
Applicability	C	Satisfactory

Indicate any dissenting opinions

RECOMMENDATION *What recommendation (s) does the guideline development group draw from this evidence?*	GRADE OF RECOMMENDATION *(A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B)*	NA

No recommendation was made because this was a risk question. It did not examine the effect of an intervention.

UNRESOLVED ISSUES *If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up*

IMPLEMENTATION OF RECOMMENDATION *Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline*

Will this recommendation result in changes in usual care?	Yes	No
Are there any resource implications associated with the implementing this recommendation?	Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized?	Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation?	Yes	No

Key question Is preoperative anaemia an independent risk factor for increased length of stay and likelihood of transfusion in patients undergoing noncardiac surgery? (GN1.6)		Evidence table ref: Gombotz et al (2007)[63]; Halm et al (2004)[74]; Myers et al (2004)[76]; Gruson et al (2002)[96]; Stoller et al (1994)[101]; Saleh et al (2007)[102]
1. Evidence base *(quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)*		
One good quality[74] and one poor quality Level II[76] study, one fair quality[96] Level III study for length of stay; one good quality Level II[63], one fair quality[101] and one poor quality[102] Level III study for likelihood of transfusion	A	**Excellent** (One or more Level I studies with a low risk of bias or several Level II studies with a low risk of bias)
	B	**Good** (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	**Satisfactory** (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	**Poor** (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. Consistency *(the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)*		
All results were consistent	A	**Excellent** (all studies consistent)
	B	**Good** (most studies consistent and inconsistency can be explained)
	C	**Satisfactory** (some inconsistency, reflecting genuine uncertainty around question)
	D	**Poor** (evidence is inconsistent)
	NA	**Not applicable** (one study only)
3. Clinical impact *(the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)*		
Good sample size	A	**Excellent** (very large clinical impact)
	B	**Good** (substantial clinical impact)
	C	**Satisfactory** (moderate clinical impact)
	D	**Poor** (slight or restricted clinical impact)
4. Generalisability *(how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?)*		
Not directly generalisable	A	**Excellent** (directly generalisable to target population)
	B	**Good** (directly generalisable to target population with some caveats)
	C	**Satisfactory** (not directly generalisable to the target population but could be sensibly applied)
	D	**Poor** (not directly generalisable to target population and hard to judge whether it is sensible to apply)
5. Applicability *(the extent to which the body of evidence is directly applicable to Australian healthcare context)*		
Three studies wre conducted in the USA, and three in Europe	A	**Excellent** (directly applicable to Australian healthcare context)
	B	**Good** (applicable to Australian healthcare context with few caveats)
	C	**Satisfactory** (probably applicable to Australian healthcare context with some caveats)
	D	**Poor** (not applicable to Australian healthcare context)

6. Other factors (*Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation)*		
EVIDENCE STATEMENT *Please summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account. Please indicate any dissenting opinions.*		
In patients undergoing noncardiac surgery, preoperative anaemia is associated with an increased likelihood of transfusion and increased hospital length of stay (Grade C) [63,74,76,96,101,102]		
Component	Rating	Description
Evidence base	C	Satisfactory
Consistency	A	Excellent
Clinical impact	B	Good
Generalisability	D	Poor
Applicability	C	Good
Indicate any dissenting opinions		

RECOMMENDATION *What recommendation (s) does the guideline development group draw from this evidence?*	GRADE OF RECOMMENDATION *(A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B)*	NA
No recommendation was made because this was a risk question. It did not examine the effect of an intervention.		
UNRESOLVED ISSUES *If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up*		
IMPLEMENTATION OF RECOMMENDATION *Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline*		
Will this recommendation result in changes in usual care?	Yes	No
Are there any resource implications associated with the implementing this recommendation?	Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized?	Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation?	Yes	No

Key question Is postoperative anaemia an independent risk factor for adverse outcomes (mortality) in patients undergoing noncardiac surgery? (GN1.7a)		Evidence table ref: Halm et al (2004)[74]; Carson et al (2002)[94]
1. Evidence base *(quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)*		
One good quality[74] Level II study, and one fair quality[94] Level III study	A	Excellent (One or more Level I studies with a low risk of bias or several Level II studies with a low risk of bias)
	B	Good (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	Satisfactory (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	Poor (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. Consistency *(the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)*		
All studies report a link with intraoperative anaemia and mortality outcomes	A	Excellent (all studies consistent)
	B	Good (most studies consistent and inconsistency can be explained)
	C	Satisfactory (some inconsistency, reflecting genuine uncertainty around question)
	D	Poor (evidence is inconsistent)
	NA	Not applicable (one study only)
3. Clinical impact *(the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)*		
The review demonstrates moderate clinical impact	A	Excellent (very large clinical impact)
	B	Good (substantial clinical impact)
	C	Satisfactory (moderate clinical impact)
	D	Poor (slight or restricted clinical impact)
4. Generalisability *(how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?)*		
Main study is from a hip fracture population, which is not generalisable to the noncardiac perioperative population	A	Excellent (directly generalisable to target population)
	B	Good (directly generalisable to target population with some caveats)
	C	Satisfactory (not directly generalisable to the target population but could be sensibly applied)
	D	Poor (not directly generalisable to target population and hard to judge whether it is sensible to apply)
5. Applicability *(the extent to which the body of evidence is directly applicable to Australian healthcare context)*		
Two studies were conducted in the USA and one in the UK	A	Excellent (directly applicable to Australian healthcare context)
	B	Good (applicable to Australian healthcare context with few caveats)
	C	Satisfactory (probably applicable to Australian healthcare context with some caveats)
	D	Poor (not applicable to Australian healthcare context)

6. Other factors (*Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation)*		
EVIDENCE STATEMENT *Please summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account. Please indicate any dissenting opinions*		
GN1.7a In patients undergoing noncardiac surgery, postoperative anaemia is associated with an increased risk of mortality (Grade C) [74,94]. Overall Evidence Statement for GN1.7 incorporating 1.7a and 1.7b In patients undergoing noncardiac surgery, postoperative anaemia is associated with an increased risk of morbidity (Grade B) [72–75,77,94,97,99] and mortality (Grade C) [74,94].		
Component	Rating	Description
Evidence base	B	Good
Consistency	B	Good
Clinical impact	C	Satisfactory
Generalisability	D	Poor
Applicability	C	Satisfactory
Indicate any dissenting opinions		

RECOMMENDATION *What recommendation (s) does the guideline development group draw from this evidence?*	GRADE OF RECOMMENDATION *(A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B)*	NA
No recommendation was made because this was a risk question. It did not examine the effect of an intervention.		
UNRESOLVED ISSUES *If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up*		
IMPLEMENTATION OF RECOMMENDATION *Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline*		
Will this recommendation result in changes in usual care?	Yes	No
Are there any resource implications associated with the implementing this recommendation?	Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized?	Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation?	Yes	No

Key question Is postoperative anaemia an independent risk factor for adverse outcomes (morbidity) in patients undergoing noncardiac surgery? (GN1.7b)	**Evidence table ref:** Conlon et al (2008)[72]; Foss et al (2008)[73]; Halm et al (2004)[74]; Meltomaa et al (2005)[75]; Wallis et al (2005)[77]; Carson et al (2002)[94]; Lawrence et al (2003)[97]; Marcantonio et al (1998)[99];	
1. **Evidence base** *(quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)*		
Three good quality[72–74], one fair quality[75] and one poor quality[77] Level II study; one fair quality[94] and two poor quality[97,99,] Level III studies	A	**Excellent** (One or more Level I studies with a low risk of bias or several Level II studies with a low risk of bias)
	B	**Good** (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	**Satisfactory** (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	**Poor** (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. **Consistency** *(the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)*		
All studies report a link between intraoperative anaemia and morbidity outcomes; however, the outcomes are different	A	**Excellent** (all studies consistent)
	B	**Good** (most studies consistent and inconsistency can be explained)
	C	**Satisfactory** (some inconsistency, reflecting genuine uncertainty around question)
	D	**Poor** (evidence is inconsistent)
	NA	**Not applicable** (one study only)
3. **Clinical impact** *(the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)*		
Reasonable samples; however, they apply to different outcomes for morbidity	A	**Excellent** (very large clinical impact)
	B	**Good** (substantial clinical impact)
	C	**Satisfactory** (moderate clinical impact)
	D	**Poor** (slight or restricted clinical impact)
4. **Generalisability** *(how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?)*		
Studies are made up of differing types of noncardiac surgery	A	**Excellent** (directly generalisable to target population)
	B	**Good** (directly generalisable to target population with some caveats)
	C	**Satisfactory** (not directly generalisable to the target population but could be sensibly applied)
	D	**Poor** (not directly generalisable to target population and hard to judge whether it is sensible to apply)

5. Applicability *(the extent to which the body of evidence is directly applicable to Australian healthcare context)*		
Four studies were conducted in the USA, two in the UK, and one each in New Zealand, Denmark and Finland	A	**Excellent** (directly applicable to Australian healthcare context)
	B	**Good** (applicable to Australian healthcare context with few caveats)
	C	**Satisfactory** (probably applicable to Australian healthcare context with some caveats)
	D	**Poor** (not applicable to Australian healthcare context)

6. Other factors (*Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation)*

EVIDENCE STATEMENT *Please summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account. Please indicate any dissenting opinions.*

GN 1.7b In patients undergoing noncardiac surgery, postoperative anaemia is associated with an increased risk of morbidity (Grade B) [72–75,77,94,97,99]

Overall Evidence Statement for GN1.7 incorporating 1.7a and 1.7b

In patients undergoing noncardiac surgery, postoperative anaemia is associated with an increased risk of morbidity (Grade B) [72–75,77,94,97,99] and mortality (Grade C) [74,94].

Component	Rating	Description
Evidence base	B	Good
Consistency	B	Good
Clinical impact	C	Satisfactory
Generalisability	C	Satisfactory
Applicability	C	Satisfactory

Indicate any dissenting opinions

RECOMMENDATION *What recommendation (s) does the guideline development group draw from this evidence?*	GRADE OF RECOMMENDATION *(A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B)*	NA
No recommendation was made because this was a risk question. It did not examine the effect of an intervention.		

UNRESOLVED ISSUES *If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up*

IMPLEMENTATION OF RECOMMENDATION *Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline*

Will this recommendation result in changes in usual care?	Yes	No
Are there any resource implications associated with the implementing this recommendation?	Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized?	Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation?	Yes	No

Key question Is postoperative anaemia associated with an increased likelihood of transfusion in patients undergoing noncardiac surgery? (GN1.8)		Evidence table ref: Gombotz et al (2007)[63]
1. Evidence base *(quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)*		
One good quality[63] Level II study	A	Excellent (One or more Level I studies with a low risk of bias or several Level II studies with a low risk of bias)
	B	Good (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	Satisfactory (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	Poor (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. Consistency *(the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)*		
Only one study	A	Excellent (all studies consistent)
	B	Good (most studies consistent and inconsistency can be explained)
	C	Satisfactory (some inconsistency, reflecting genuine uncertainty around question)
	D	Poor (evidence is inconsistent)
	NA	Not applicable (one study only)
3. Clinical impact *(the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)*		
Moderate clinical impact	A	Excellent (very large clinical impact)
	B	Good (substantial clinical impact)
	C	Satisfactory (moderate clinical impact)
	D	Poor (slight or restricted clinical impact)
4. Generalisability *(how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?)*		
Numerous types of noncardiac surgery included	A	Excellent (directly generalisable to target population)
	B	Good (directly generalisable to target population with some caveats)
	C	Satisfactory (not directly generalisable to the target population but could be sensibly applied)
	D	Poor (not directly generalisable to target population and hard to judge whether it is sensible to apply)
5. Applicability *(the extent to which the body of evidence is directly applicable to Australian healthcare context)*		
The study was conducted in Austria	A	Excellent (directly applicable to Australian healthcare context)
	B	Good (applicable to Australian healthcare context with few caveats)

	C	**Satisfactory** (probably applicable to Australian healthcare context with some caveats)
	D	**Poor** (not applicable to Australian healthcare context)

6. **Other factors** (*Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation)*

EVIDENCE STATEMENT *Please summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account. Please indicate any dissenting opinions*

In patients undergoing noncardiac surgery, postoperative anaemia is associated with an increased likelihood of transfusion (Grade C)

Component	Rating	Description
Evidence base	C	Good
Consistency	N/A	Not applicable
Clinical impact	C	Satisfactory
Generalisability	C	Satisfactory
Applicability	C	Satisfactory

Indicate any dissenting opinions

RECOMMENDATION *What recommendation (s) does the guideline development group draw from this evidence?*	GRADE OF RECOMMENDATION *(A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B)*	NA

No recommendation was made because this was a risk question. It did not examine the effect of an intervention.

UNRESOLVED ISSUES *If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up*

IMPLEMENTATION OF RECOMMENDATION *Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline*

Will this recommendation result in changes in usual care?	Yes	No
Are there any resource implications associated with the implementing this recommendation?	Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized?	Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation?	Yes	No

D5 Evidence matrix, Question 5

What is the effect of red blood cell transfusion on patient outcomes?

Key question What is the effect of red blood cell transfusion on mortality in patients undergoing cardiac surgery? (GN2.1a)	Evidence table ref: Surgenor et al (2009)[104]; Scott et al (2008)[107]; Ranucci et al (2008a)[108]; Murphy et al (2007)[109]; Koch et al (2006a)[111]; Koch et al (2006b)[112]; Kuduvalli et al (2005)[118]; Engoren et al (2002)[122]; Leal-Noval et al (2001)[123]	
1. Evidence base *(quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)*		
Nine Level III studies with a moderate risk of bias[104,107–109,111,112,118,122,123]	A	Excellent (One or more Level I studies with a low risk of bias or several Level II studies with a low risk of bias)
	B	Good (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	Satisfactory (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	Poor (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. Consistency *(the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)*		
All but one study showed that RBC transfusion was associated with a risk of mortality. Two studies reported a dose-dependent relationship between RBC transfusion and mortality	A	Excellent (all studies consistent)
	B	Good (most studies consistent and inconsistency can be explained)
	C	Satisfactory (some inconsistency, reflecting genuine uncertainty around question)
	D	Poor (evidence is inconsistent)
	NA	Not applicable (one study only)
3. Clinical impact *(the potential impact of recommendation ie. Size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)*		
Overall sample size was quite large with significant effects on mortality. Proving a direct effect of RBC transfusion on mortality is, however, difficult	A	Excellent (very large clinical impact)
	B	Good (substantial clinical impact)
	C	Satisfactory (moderate clinical impact)
	D	Poor (slight or restricted clinical impact)
4. Generalisability *(how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?)*		
All studies involved patients undergoing cardiac surgery; however, there was no control over who received a RBC transfusion and who did not	A	Excellent (directly generalisable to target population)
	B	Good (directly generalisable to target population with some caveats)
	C	Satisfactory (not directly generalisable to the target population but could be sensibly applied)
	D	Poor (not directly generalisable to target population and hard to judge whether it is sensible to apply)

5. Applicability *(the extent to which the body of evidence is directly applicable to Australian healthcare context)*		
Of the nine studies, four were performed in the USA, three in the UK, and one each in Italy and Spain. Although the UK and Australian healthcare systems are similar, the USA healthcare system is different from Australia's	A	**Excellent** (directly applicable to Australian healthcare context)
	B	**Good** (applicable to Australian healthcare context with few caveats)
	C	**Satisfactory** (probably applicable to Australian healthcare context with some caveats)
	D	**Poor** (not applicable to Australian healthcare context)

6. Other factors (*Indicate here any other factors that you took into account when assessing the evidence base, eg. Issues that might cause the group to downgrade or upgrade the recommendation)*

EVIDENCE STATEMENT *Please summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account. Please indicate any dissenting opinions*

In patients undergoing cardiac surgery, red blood cell transfusion is independently associated with increased morbidity (Grade B)[105–112,117,119–121,123] and mortality (Grade C)[104,107–109,111,112,118,122,123]. These relationships are dose-dependent (morbidity [Grade B][105–112,117,119–121,123] and mortality [Grade C][108,111])
Note: Combined for evidence statements GN2.1a and GN2.1b

Component	Rating	Description
Evidence base	C	Satisfactory
Consistency	B	Good
Clinical impact	C	Satisfactory
Generalisability	B	Good
Applicability	B	Good

Indicate any dissenting opinions

RECOMMENDATION *What recommendation (s) does the guideline development group draw from this evidence?*	GRADE OF RECOMMENDATION *(A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B)*	Mortality C

In patients undergoing cardiac surgery, preoperative anaemia should be identified, evaluated and managed to minimise RBC transfusion, which may be associated with an increased risk of morbidity, mortality, ICU length of stay and hospital length of stay (Grade C).
Note: This recommendation is derived from a combination of evidence statements GN2.1a, GN2.1b and GN2.2

UNRESOLVED ISSUES *If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up*

IMPLEMENTATION OF RECOMMENDATION *Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline*

Will this recommendation result in changes in usual care? This care is best delivered by a multi-disciplinary, multimodal patient blood management program	Yes	No
Are there any resource implications associated with the implementing this recommendation? Cost and resource associated with implementation of programs; initial cost outlays but savings associated with improved patient outcomes (hospital LOS, morbidity)	Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized? Reorganisation of perioperative care	Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation? Clinician and administration uptake; funding	Yes	No

Key question What is the effect of red blood cell transfusion on morbidity in patients undergoing cardiac surgery? (GN2.1b)	Evidence table ref: Hortal et al (2009)[105]; Cislaghi et al (2009)[106]; Scott et al (2008)[107]; Ranucci et al (2008a)[108]; Murphy et al (2007)[109]; Rogers et al (2007b)[110]; Koch et al (2006a)[111]; Surgenor et al (2006)[69]; Koch et al (2006b)[112]; Banbury et al (2006)[117]; Olsen et al (2003)[119]; Bucerius et al (2003)[120]; Chelemer et al (2002)[121]; Leal-Noval et al (2001)[123]	
1. Evidence base *(quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)*		
14 Level III studies with a moderate risk of bias[105–112,117,119–121,123]	A	Excellent (One or more Level I studies with a low risk of bias or several Level II studies with a low risk of bias)
	B	Good (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	Satisfactory (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	Poor (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. Consistency *(the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)*		
All studies demonstrated that red blood cell transfusion was a significant predictor of morbidity outcomes, and that the relationship between red blood cell transfusion and morbidity was dose-dependent	A	Excellent (all studies consistent)
	B	Good (most studies consistent and inconsistency can be explained)
	C	Satisfactory (some inconsistency, reflecting genuine uncertainty around question)
	D	Poor (evidence is inconsistent)
	NA	Not applicable (one study only)
3. Clinical impact (*the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)*		
Overall sample size was very large, with significant effects on morbidity, especially the morbidity outcome of infection. Proving a direct effect of RBC transfusion and morbidity, however, is difficult	A	Excellent (very large clinical impact)
	B	Good (substantial clinical impact)
	C	Satisfactory (moderate clinical impact)
	D	Poor (slight or restricted clinical impact)
4. Generalisability *(how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?)*		
All studies involved patients undergoing cardiac surgery. There was no control over who received red blood cell transfusion and who did not	A	Excellent (directly generalisable to target population)
	B	Good (directly generalisable to target population with some caveats)
	C	Satisfactory (not directly generalisable to the target population but could be sensibly applied)
	D	Poor (not directly generalisable to target population and hard to judge whether it is sensible to apply)
5. Applicability *(the extent to which the body of evidence is directly applicable to Australian healthcare context)*		
Of the 14 studies, eight were performed in the USA, two in Italy, and one each in Germany, Spain and the UK; the remaining study was conducted in a number of European countries. The healthcare system in the USA is quite different from	A	Excellent (directly applicable to Australian healthcare context)
	B	Good (applicable to Australian healthcare context with few caveats)
	C	Satisfactory (probably applicable to Australian healthcare context with some caveats)

that in Australia	D	Poor (not applicable to Australian healthcare context)

6. Other factors (*Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation)*

EVIDENCE STATEMENT *Please summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account. Please indicate any dissenting opinions*

In patients undergoing cardiac surgery, red blood cell transfusion is independently associated with increased morbidity (Grade B)[105–112,117,119–121,123] and mortality (Grade C)[104,107–109,111,112,118,122,123].
These relationships are dose-dependent (morbidity [Grade B][105–112,117,119–121,123] and mortality [Grade C][108,111])
Note: Combined for evidence statements GN2.1a and GN2.1b

Component	Rating	Description
Evidence base	C	Satisfactory
Consistency	A	Excellent
Clinical impact	B	Good
Generalisability	B	Good
Applicability	C	Satisfactory

Indicate any dissenting opinions

RECOMMENDATION *What recommendation (s) does the guideline development group draw from this evidence?*	GRADE OF RECOMMENDATION *(A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B)*	Morbidity: C

In patients undergoing cardiac surgery, preoperative anaemia should be identified, evaluated and managed to minimise RBC transfusion, which may be associated with an increased risk of morbidity, mortality, ICU length of stay and hospital length of stay (Grade C).
Note: This recommendation is derived from a combination of evidence statements GN2.1a, GN2.1b and GN2.2

UNRESOLVED ISSUES *If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up*

IMPLEMENTATION OF RECOMMENDATION *Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline*

Will this recommendation result in changes in usual care? This care is best delivered by a multi-disciplinary, multimodal patient blood management program	Yes	No
Are there any resource implications associated with the implementing this recommendation? Cost and resource associated with implementation of programs; initial cost outlays but savings associated with improved patient outcomes (hospital LOS, morbidity)	Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized? Reorganisation of perioperative care	Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation? Clinician and administration uptake; funding	Yes	No

Key question What is the effect of red blood cell transfusion on hospital and ICU length of stay in patients undergoing cardiac surgery? (GN2.2)		Evidence table ref: Scott et al (2008)[107]; Murphy et al (2007)[109]; Leal-Noval et al (2001)[123]
1. Evidence base *(quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)*		
Three Level III studies with a moderate risk of bias[107,109,123]	A	Excellent (One or more Level I studies with a low risk of bias or several Level II studies with a low risk of bias)
	B	Good (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	Satisfactory (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	Poor (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. Consistency *(the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)*		
All studies demonstrated that red blood cell transfusion was a significant predictor for increased hospital or ICU length of stay	A	Excellent (all studies consistent)
	B	Good (most studies consistent and inconsistency can be explained)
	C	Satisfactory (some inconsistency, reflecting genuine uncertainty around question)
	D	Poor (evidence is inconsistent)
	NA	Not applicable (one study only)
3. Clinical impact *(the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)*		
The studies reported a moderate clinical impact	A	Excellent (very large clinical impact)
	B	Good (substantial clinical impact)
	C	Satisfactory (moderate clinical impact)
	D	Poor (slight or restricted clinical impact)
4. Generalisability *(how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?)*		
All studies were performed in a perioperative patient population undergoing cardiac surgery	A	Excellent (directly generalisable to target population)
	B	Good (directly generalisable to target population with some caveats)
	C	Satisfactory (not directly generalisable to the target population but could be sensibly applied)
	D	Poor (not directly generalisable to target population and hard to judge whether it is sensible to apply)
5. Applicability *(the extent to which the body of evidence is directly applicable to Australian healthcare context)*		
Reduced applicability. One study was carried out in the USA, one in the UK and one in Spain. The healthcare system in the USA is quite different from Australia's	A	Excellent (directly applicable to Australian healthcare context)
	B	Good (applicable to Australian healthcare context with few caveats)
	C	Satisfactory (probably applicable to Australian healthcare context with some caveats)
	D	Poor (not applicable to Australian healthcare context)

6. Other factors (*Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation)*		
EVIDENCE STATEMENT *Please summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account. Please indicate any dissenting opinion*		
In patients undergoing cardiac surgery, RBC transfusion is independently associated with an increased intensive care unit LOS and hospital LOS (Grade C) [107,109,123]		
Component	Rating	Description
Evidence base	C	Satisfactory
Consistency	A	Excellent
Clinical impact	C	Satisfactory
Generalisability	A	Excellent
Applicability	C	Satisfactory
Indicate any dissenting opinions		

RECOMMENDATION *What recommendation (s) does the guideline development group draw from this evidence?*	GRADE OF RECOMMENDATION *(A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B)*	Length of stay (hospital and ICU) C
In patients undergoing cardiac surgery, preoperative anaemia should be identified, evaluated and managed to minimise RBC transfusion, which may be associated with an increased risk of morbidity, mortality, ICU length of stay and hospital length of stay (Grade C). Note: This recommendation is derived from a combination of evidence statements GN2.1a, GN2.1b and GN2.2		
UNRESOLVED ISSUES *If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up*		
IMPLEMENTATION OF RECOMMENDATION *Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline*		

Will this recommendation result in changes in usual care? This care is best delivered by a multi-disciplinary, multimodal patient blood management program	Yes	No
Are there any resource implications associated with the implementing this recommendation? Cost and resource associated with implementation of programs; initial cost outlays but savings associated with improved patient outcomes (hospital LOS, morbidity)	Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized? Reorganisation of perioperative care	Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation? Clinician and administration uptake; funding	Yes	No

Key question What is the effect of red blood cell transfusion on quality of life in patients undergoing cardiac surgery?(GN2.3)	Evidence table ref: Koch et al (2006d)[114]	
1. Evidence base *(quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)*		
One Level III study with a moderate risk of bias[114]	A	Excellent (One or more Level I studies with a low risk of bias or several Level II studies with a low risk of bias)
	B	Good (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	Satisfactory (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	Poor (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. Consistency *(the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)*		
Not applicable, one study provided the evidence	A	Excellent (all studies consistent)
	B	Good (most studies consistent and inconsistency can be explained)
	C	Satisfactory (some inconsistency, reflecting genuine uncertainty around question)
	D	Poor (evidence is inconsistent)
	NA	Not applicable (one study only)
3. Clinical impact *(the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)*		
Although the sample size in this study was quite large, the clinical impact of this outcome is not clear	A	Excellent (very large clinical impact)
	B	Good (substantial clinical impact)
	C	Satisfactory (moderate clinical impact)
	D	Poor (slight or restricted clinical impact)
4. Generalisability *(how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?)*		
The study was performed in a cardiac surgery population. There was no control over who received red blood cell transfusion and who did not	A	Excellent (directly generalisable to target population)
	B	Good (directly generalisable to target population with some caveats)
	C	Satisfactory (not directly generalisable to the target population but could be sensibly applied)
	D	Poor (not directly generalisable to target population and hard to judge whether it is sensible to apply)
5. Applicability *(the extent to which the body of evidence is directly applicable to Australian healthcare context)*		
The study was performed in the USA, where the healthcare system is quite different to that of Australia	A	Excellent (directly applicable to Australian healthcare context)
	B	Good (applicable to Australian healthcare context with few caveats)
	C	Satisfactory (probably applicable to Australian healthcare context with some caveats)
	D	Poor (not applicable to Australian healthcare context)

6. Other factors (*Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation)*		
EVIDENCE STATEMENT *Please summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account. Please indicate any dissenting opinions.*		
In patients undergoing cardiac surgery, there is insufficient evidence to determine the effect of RBC transfusion on quality of life (Grade D)[114]		
Component	Rating	Description
Evidence base	D	Poor
Consistency	NA	Not applicable
Clinical impact	C	Satisfactory
Generalisability	C	Satisfactory
Applicability	C	Satisfactory
Indicate any dissenting opinions		

RECOMMENDATION *What recommendation (s) does the guideline development group draw from this evidence?*	GRADE OF RECOMMENDATION *(A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B)*	NA
No recommendation was made		
UNRESOLVED ISSUES *If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up*		
IMPLEMENTATION OF RECOMMENDATION *Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline*		
Will this recommendation result in changes in usual care?	Yes	No
Are there any resource implications associated with the implementing this recommendation?	Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized?	Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation?	Yes	No

Key question What is the effect of red blood cell transfusion on mortality in patients undergoing noncardiac surgery?(GN2.4a)	Evidence table ref: Bursi et al (2009)[127]; Bernard et al (2009)[128]; Silva et al (2009)[129]; Johnson et al (2008)[130]; Engoren et al (2008)[131]; Ruttinger et al (2007)[132]; Halm et al (2003)[135]; Dunne et al (2002)[136]; Carson et al (1998a)[138]	
1. Evidence base *(quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)*		
Nine Level III studies with a moderate risk of bias[127–131,132,135,136,138]	A	Excellent (One or more Level I studies with a low risk of bias or several Level II studies with a low risk of bias)
	B	Good (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	Satisfactory (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	Poor (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. Consistency *(the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)*		
Most studies demonstrated that red blood cell transfusion was associated with a risk of mortality. Two studies reported a dose-dependent relationship between mortality and red blood cell transfusions in noncardiac surgery patients	A	Excellent (all studies consistent)
	B	Good (most studies consistent and inconsistency can be explained)
	C	Satisfactory (some inconsistency, reflecting genuine uncertainty around question)
	D	Poor (evidence is inconsistent)
	NA	Not applicable (one study only)
3. Clinical impact *(the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)*		
Overall sample size was quite large, and significant effects on mortality were reported. Proving a direct effect of red blood cell transfusion and mortality was, however, difficult	A	Excellent (very large clinical impact)
	B	Good (substantial clinical impact)
	C	Satisfactory (moderate clinical impact)
	D	Poor (slight or restricted clinical impact)
4. Generalisability *(how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?)*		
All studies included patients undergoing non cardiac surgery and a variety of surgeries were performed. However, there was no control over who received red blood cell transfusion and who did not	A	Excellent (directly generalisable to target population)
	B	Good (directly generalisable to target population with some caveats)
	C	Satisfactory (not directly generalisable to the target population but could be sensibly applied)
	D	Poor (not directly generalisable to target population and hard to judge whether it is sensible to apply)
5. Applicability *(the extent to which the body of evidence is directly applicable to Australian healthcare context)*		
Of the nine studies, six were performed in the USA, and one each in the UK, Germany and Brazil	A	Excellent (directly applicable to Australian healthcare context)
	B	Good (applicable to Australian healthcare context with few caveats)
	C	Satisfactory (probably applicable to Australian healthcare context with some caveats)
	D	Poor (not applicable to Australian healthcare context)

6. Other factors (*Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation)*

EVIDENCE STATEMENT *Please summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account. Please indicate any dissenting opinions*

In patients undergoing noncardiac surgery, red blood cell transfusion is independently associated with increased morbidity (Grade C)[124–126,128,130,100,134,136,137] and mortality (Grade C)[127–131,132,135,136,138].

These relationships are dose-dependent (Grade C)[128,129].
Note: This evidence statement is a combination of evidence statement GN2.4a and GN2.4b.

Component	Rating	Description
Evidence base	C	Satisfactory
Consistency	C	Satisfactory
Clinical impact	C	Satisfactory
Generalisability	B	Good
Applicability	C	Satisfactory

Indicate any dissenting opinions

RECOMMENDATION *What recommendation (s) does the guideline development group draw from this evidence?*	GRADE OF RECOMMENDATION *(A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B)*	Mortality: C

In patients undergoing noncardiac surgery, preoperative anaemia should be identified, evaluated and managed to minimise RBC transfusion, which may be associated with an increased risk of morbidity, mortality, ICU length of stay and hospital length of stay (Grade C).
Note: This recommendation is derived from a combination of evidence statements GN2.4a, GN2.4b and GN2.5

UNRESOLVED ISSUES *If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up*

IMPLEMENTATION OF RECOMMENDATION *Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline*

Will this recommendation result in changes in usual care? This care is best delivered by a multi-disciplinary, multimodal patient blood management program	Yes	No
Are there any resource implications associated with the implementing this recommendation? Cost and resource associated with implementation of programs; initial cost outlays but savings associated with improved patient outcomes (hospital LOS, morbidity)	Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized? Reorganisation of perioperative care	Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation? Clinician and administration uptake; funding	Yes	No

Key question What is the effect of red blood cell transfusion on morbidity in patients undergoing noncardiac surgery? (GN2.4b)	Evidence table ref: Soleimani et al (2009)[124]; Garcia-Alvarez et al (2009)[125]; Fuks et al (2009)[126]; Bernard et al (2009)[128]; Johnson et al (2008)[130]; Rogers et al (2007b)[100]; Weber et al (2005a)[134]; Dunne et al (2002)[136]; Chang et al (2000)[137]	
1. Evidence base *(quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)*		
Nine Level III studies with a moderate risk of bias[124–126,128,130,100,134,136,137]	A	**Excellent** (One or more Level I studies with a low risk of bias or several Level II studies with a low risk of bias)
	B	**Good** (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	**Satisfactory** (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	**Poor** (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. Consistency *(the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)*		
The majority of studies demonstrated that red blood cell transfusion was a significant predictor of morbidity outcomes. In those studies that did not report a significant effect, morbidity outcomes were obscure and related specifically to the condition for which the surgery was performed	A	**Excellent** (all studies consistent)
	B	**Good** (most studies consistent and inconsistency can be explained)
	C	**Satisfactory** (some inconsistency, reflecting genuine uncertainty around question)
	D	**Poor** (evidence is inconsistent)
	NA	**Not applicable** (one study only)
3. Clinical impact *(the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)*		
Overall sample size was very large with significant effects on morbidity reported, especially for infection. Proving a direct effect of red blood cell transfusion on morbidity was, however, difficult	A	**Excellent** (very large clinical impact)
	B	**Good** (substantial clinical impact)
	C	**Satisfactory** (moderate clinical impact)
	D	**Poor** (slight or restricted clinical impact)
4. Generalisability *(how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?)*		
All studies included patients undergoing non cardiac surgery and a variety of surgeries were performed. There was no control over who underwent red blood cell transfusion and who did not	A	**Excellent** (directly generalisable to target population)
	B	**Good** (directly generalisable to target population with some caveats)
	C	**Satisfactory** (not directly generalisable to the target population but could be sensibly applied)
	D	**Poor** (not directly generalisable to target population and hard to judge whether it is sensible to apply)
5. Applicability *(the extent to which the body of evidence is directly applicable to Australian healthcare context)*		
Reduced applicability. Of the nine studies, four were performed in the US, and one each in Iran, Spain, France, the Netherlands and Canada.	A	**Excellent** (directly applicable to Australian healthcare context)
	B	**Good** (applicable to Australian healthcare context with few caveats)
	C	**Satisfactory** (probably applicable to Australian healthcare context with some caveats)
	D	**Poor** (not applicable to Australian healthcare context)

6. Other factors (*Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation)*

EVIDENCE STATEMENT *Please summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account. Please indicate any dissenting opinions*

In patients undergoing noncardiac surgery, red blood cell transfusion is independently associated with increased morbidity (Grade C)[124–126,128,130,100,134,136,137] and mortality (Grade C)[127–131,132,135,136,138].

These relationships are dose-dependent (Grade C)[128,129].
Note: This evidence statement is a combination of evidence statement GN2.4a and GN2.4b.

Component	Rating	Description
Evidence base	C	Satisfactory
Consistency	B	Good
Clinical impact	B	Good
Generalisability	B	Good
Applicability	C	Satisfactory

Indicate any dissenting opinions

RECOMMENDATION *What recommendation (s) does the guideline development group draw from this evidence?*	GRADE OF RECOMMENDATION *(A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B)*	Morbidity: C

In patients undergoing noncardiac surgery, preoperative anaemia should be identified, evaluated and managed to minimise RBC transfusion, which may be associated with an increased risk of morbidity, mortality, ICU length of stay and hospital length of stay (Grade C)
Note: This recommendation is derived from a combination of evidence statements GN2.4a, GN2.4b and GN2.5

UNRESOLVED ISSUES *If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up*

IMPLEMENTATION OF RECOMMENDATION *Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline*

Will this recommendation result in changes in usual care? This care is best delivered by a multi-disciplinary, multimodal patient blood management program	Yes	No
Are there any resource implications associated with the implementing this recommendation? Cost and resource associated with implementation of programs; initial cost outlays but savings associated with improved patient outcomes (hospital LOS, morbidity)	Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized? Reorganisation of perioperative care	Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation? Clinician and administration uptake; funding	Yes	No

Key question What is the effect of red blood cell transfusion on hospital and intensive care unit LOS in patients undergoing noncardiac surgery? (GN2.5)	Evidence table ref: Ruttinger et al (2007)[132]; BuSaba et al (2007)[133]; Weber et al (2005a)[134]; Dunne et al (2002)[136]	
1. Evidence base *(quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)*		
4 Level III studies with a moderate risk of bias	A	Excellent (One or more Level I studies with a low risk of bias or several Level II studies with a low risk of bias)
	B	Good (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	Satisfactory (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	Poor (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. Consistency *(the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)*		
All studies demonstrated that red blood cell transfusion was a significant predictor for increased hospital or ICU lengths of stay	A	Excellent (all studies consistent)
	B	Good (most studies consistent and inconsistency can be explained)
	C	Satisfactory (some inconsistency, reflecting genuine uncertainty around question)
	D	Poor (evidence is inconsistent)
	NA	Not applicable (one study only)
3. Clinical impact *(the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)*		
The studies reported a moderate clinical impact	A	Excellent (very large clinical impact)
	B	Good (substantial clinical impact)
	C	Satisfactory (moderate clinical impact)
	D	Poor (slight or restricted clinical impact)
4. Generalisability *(how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?)*		
All studies were performed in perioperative patient populations with a good mix of patients	A	Excellent (directly generalisable to target population)
	B	Good (directly generalisable to target population with some caveats)
	C	Satisfactory (not directly generalisable to the target population but could be sensibly applied)
	D	Poor (not directly generalisable to target population and hard to judge whether it is sensible to apply)
5. Applicability *(the extent to which the body of evidence is directly applicable to Australian healthcare context)*		
Two studies were conducted in the USA, and one each in Germany and the Netherlands	A	Excellent (directly applicable to Australian healthcare context)
	B	Good (applicable to Australian healthcare context with few caveats)
	C	Satisfactory (probably applicable to Australian healthcare context with some caveats)
	D	Poor (not applicable to Australian healthcare context)

6. Other factors (*Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation)*		
EVIDENCE STATEMENT *Please summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account. Please indicate any dissenting opinions*		
In patients undergoing noncardiac surgery, red blood cell transfusion is independently associated with increased intensive care unit LOS (Grade C),[132,] and hospital LOS (Grade B)[132-134,136]		
Component	Rating	Description
Evidence base	C	Satisfactory
Consistency	A	Excellent
Clinical impact	C	Satisfactory
Generalisability	B	Good
Applicability	C	Satisfactory
Indicate any dissenting opinions		

RECOMMENDATION *What recommendation (s) does the guideline development group draw from this evidence?*	GRADE OF RECOMMENDATION *(A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B)*	Hos C ICU C
In patients undergoing noncardiac surgery, preoperative anaemia should be identified, evaluated and managed to minimise RBC transfusion, which may be associated with an increased risk of morbidity, mortality, ICU length of stay and hospital length of stay (Grade C) Note: This recommendation is derived from a combination of evidence statements GN2.4a, GN2.4b and GN2.5		
UNRESOLVED ISSUES *If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up*		
IMPLEMENTATION OF RECOMMENDATION *Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline*		
Will this recommendation result in changes in usual care? This care is best delivered by a multi-disciplinary, multimodal patient blood management program	Yes	No
Are there any resource implications associated with the implementing this recommendation? Cost and resource associated with implementation of programs; initial cost outlays but savings associated with improved patient outcomes (hospital LOS, morbidity)	Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized? Reorganisation of perioperative care	Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation? Clinician and administration uptake; funding	Yes	No

What is the effect of a liberal versus restrictive transfusion strategy on patient outcomes?

Key question What is the effect of a restrictive transfusion strategy on mortality, morbidity or hospital length of stay in patients undergoing cardiac surgery? (GN2.6)	Evidence table ref: Bracey et al (1999)[141]	
1. Evidence base *(quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)*		
One fair quality Level II study[141]	A	Excellent (One or more Level I studies with a low risk of bias or several Level II studies with a low risk of bias)
	B	Good (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	Satisfactory (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	Poor (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. Consistency *(the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)*		
Only one study	A	Excellent (all studies consistent)
	B	Good (most studies consistent and inconsistency can be explained)
	C	Satisfactory (some inconsistency, reflecting genuine uncertainty around question)
	D	Poor (evidence is inconsistent)
	NA	Not applicable (one study only)
3. Clinical impact *the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)*		
There was a moderate clinical impact	A	Excellent (very large clinical impact)
	B	Good (substantial clinical impact)
	C	Satisfactory (moderate clinical impact)
	D	Poor (slight or restricted clinical impact)
4. Generalisability *(how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?)*		
The results of the study are directly generalisable to a perioperative cardiac surgery population	A	Excellent (directly generalisable to target population)
	B	Good (directly generalisable to target population with some caveats)
	C	Satisfactory (not directly generalisable to the target population but could be sensibly applied)
	D	Poor (not directly generalisable to target population and hard to judge whether it is sensible to apply)

5. Applicability *(the extent to which the body of evidence is directly applicable to Australian healthcare context)*		
Reduced applicability—the study was conducted in the USA	A	**Excellent** (directly applicable to Australian healthcare context)
	B	**Good** (applicable to Australian healthcare context with few caveats)
	C	**Satisfactory** (probably applicable to Australian healthcare context with some caveats)
	D	**Poor** (not applicable to Australian healthcare context)

6. Other factors (*Indicate here any other factors that you took into account when assessing the evidence base, eg. Issues that might cause the group to downgrade or upgrade the recommendation)*

EVIDENCE STATEMENT *Please summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account. Please indicate any dissenting opinions*

In patients undergoing cardiac surgery, use of a restrictive transfusion strategy is not associated with increased mortality, morbidity or hospital length of stay (Grade C)[141]

Component	Rating	Description
Evidence base	C	Satisfactory
Consistency	N/A	Not applicable
Clinical impact	C	Satisfactory
Generalisability	A	Excellent
Applicability	C	Satisfactory

Indicate any dissenting opinions

RECOMMENDATION *What recommendation (s) does the guideline development group draw from this evidence?*	GRADE OF RECOMMENDATION *(A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B)*	NA
No recommendation was made		

UNRESOLVED ISSUES *If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up*

IMPLEMENTATION OF RECOMMENDATION *Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline*

Will this recommendation result in changes in usual care?	Yes	No
Are there any resource implications associated with the implementing this recommendation?	Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized?	Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation?	Yes	No

Key question What is the effect of a restrictive transfusion strategy on mortality and morbidity in patients undergoing noncardiac surgery? (GN2.7a)		Evidence table ref: Bush et al (1997)[142]; Grover et al (2006)[143]; Carson et al (1998b)[144]; Foss et al (2009)[145]
1. Evidence base *(quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)*		
Two good quality Level II studies[142,145] and two fair quality Level II studies[143,144]	A	Excellent (One or more Level I studies with a low risk of bias or several Level II studies with a low risk of bias)
	B	Good (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	Satisfactory (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	Poor (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. Consistency *(the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)*		
One study presented conflicting results. Foss et al (2009) showed an increase in mortality; however,there was an imbalance between study groups in severity of illness at baseline and mortality was not a primary outcome.	A	Excellent (all studies consistent)
	B	Good (most studies consistent and inconsistency can be explained)
	C	Satisfactory (some inconsistency, reflecting genuine uncertainty around question)
	D	Poor (evidence is inconsistent)
	NA	Not applicable (one study only)
3. Clinical impact *(the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)*		
There was a moderate clinical impact	A	Excellent (very large clinical impact)
	B	Good (substantial clinical impact)
	C	Satisfactory (moderate clinical impact)
	D	Poor (slight or restricted clinical impact)
4. Generalisability *(how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?)*		
The studies included patients undergoing orthopaedic[143-145] or vascular[142] surgery. The population undergoing orthopaedic surgery typically includes a large proportion of elderly patients, making it difficult to determine whether these results are generalisable to the wider noncardiac surgical perioperative patient population. Intervention not considered to be sufficiently restrictive.	A	Excellent (directly generalisable to target population)
	B	Good (directly generalisable to target population with some caveats)
	C	Satisfactory (not directly generalisable to the target population but could be sensibly applied)
	D	Poor (not directly generalisable to target population and hard to judge whether it is sensible to apply)
5. Applicability *(the extent to which the body of evidence is directly applicable to Australian healthcare context)*		
The studies were conduced in the USA, Denmark and the UK	A	Excellent (directly applicable to Australian healthcare context)
	B	Good (applicable to Australian healthcare context with few caveats)
	C	Satisfactory (probably applicable to Australian healthcare context with some caveats)
	D	Poor (not applicable to Australian healthcare context)

6. Other factors (*Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation)*		
EVIDENCE STATEMENT *Please summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account. Please indicate any dissenting opinions*		
In patients undergoing noncardiac surgery, the effect of a restrictive transfusion strategy on mortality and morbidity is uncertain(Grade C)[142–145]. In patients undergoing orthopaedic or vascular surgery, the use of a restrictive transfusion strategy is not associated with increased hospital length of stay (Grade B)[142–145] Note: This evidence statement is a combination of evidence statements 2.7a and 2.7b		
Component	Rating	Description
Evidence base	B	Good
Consistency	C	Satisfactory
Clinical impact	C	Satisfactory
Generalisability	D	Poor
Applicability	C	Satisfactory
Indicate any dissenting opinions		

RECOMMENDATION *What recommendation (s) does the guideline development group draw from this evidence?*	GRADE OF RECOMMENDATION *(A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B)*	NA
No recommendation was made		
UNRESOLVED ISSUES *If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up*		
IMPLEMENTATION OF RECOMMENDATION *Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline*		
Will this recommendation result in changes in usual care?	Yes	No
Are there any resource implications associated with the implementing this recommendation?	Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized?	Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation?	Yes	No

Key question What is the effect of a restrictive transfusion strategy on hospital LOS in a population undergoing noncardiac surgery? (GN2.7b)	Evidence table ref: Bush et al (1997)[142]; Grover et al (2006)[143]; Carson et al (1998b)[144]; Foss et al (2009)[145]	
1. Evidence base *(quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)*		
Two good quality Level II studies[142,145] and two fair quality Level II studies[143,144]	A	Excellent (One or more Level I studies with a low risk of bias or several Level II studies with a low risk of bias)
	B	Good (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	Satisfactory (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	Poor (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. Consistency *(the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)*		
The results of the studies are consistent in showing no effect on hospital LOS.	A	Excellent (all studies consistent)
	B	Good (most studies consistent and inconsistency can be explained)
	C	Satisfactory (some inconsistency, reflecting genuine uncertainty around question)
	D	Poor (evidence is inconsistent)
	NA	Not applicable (one study only)
3. Clinical impact *(the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)*		
There is moderate clinical impact	A	Excellent (very large clinical impact)
	B	Good (substantial clinical impact)
	C	Satisfactory (moderate clinical impact)
	D	Poor (slight or restricted clinical impact)
4. Generalisability *(how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?)*		
All studies included patients undergoing orthopaedic[143–145] or vascular[142] noncardiac surgery	A	Excellent (directly generalisable to target population)
	B	Good (directly generalisable to target population with some caveats)
	C	Satisfactory (not directly generalisable to the target population but could be sensibly applied)
	D	Poor (not directly generalisable to target population and hard to judge whether it is sensible to apply)
5. Applicability *(the extent to which the body of evidence is directly applicable to Australian healthcare context)*		
The studies were conducted in the USA (two studies), Denmark and the UK	A	Excellent (directly applicable to Australian healthcare context)
	B	Good (applicable to Australian healthcare context with few caveats)
	C	Satisfactory (probably applicable to Australian healthcare context with some caveats)
	D	Poor (not applicable to Australian healthcare context)

6. Other factors (*Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation)*				
EVIDENCE STATEMENT *Please summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account. Please indicate any dissenting opinions.*				
In patients undergoing noncardiac surgery, the effect of a restrictive transfusion strategy on mortality and morbidity is uncertain(Grade C)[142–145]. In orthopaedic or vascular surgery, the use of a restrictive transfusion strategy is not associated with an increased hospital length of stay (Grade B)[142–145] Note: This evidence statement is a combination of evidence statements 2.7a and 2.7b				
Component	Rating	Description		
Evidence base	B	Good		
Consistency	A	Excellent		
Clinical impact	C	Satisfactory		
Generalisability	C	Satisfactory		
Applicability	C	Satisfactory		
Indicate any dissenting opinions				
RECOMMENDATION *What recommendation (s) does the guideline development group draw from this evidence?*			GRADE OF RECOMMENDATION *(A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B)*	NA
No recommendation was made				
UNRESOLVED ISSUES *If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up*				
IMPLEMENTATION OF RECOMMENDATION *Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline*				
Will this recommendation result in changes in usual care?			Yes	No
Are there any resource implications associated with the implementing this recommendation?			Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized?			Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation?			Yes	No

D6 Evidence matrix, Question 6

What is the effect of interventions to increase haemoglobin concentration on morbidity, mortality and need for red blood cell transfusion?

Key question What is the effect of postoperative oral iron on haematological parameters in anaemic patients undergoing cardiac surgery? (GN3.1)	Evidence table ref: Aufricht et al (1994)[146]; Crosby et al (1994)[147]; Del Campo et al (1982)[148]	
1. Evidence base *(quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)*		
The evidence consists of two fair quality Level II studies[146,147] and one poor quality Level II study[148]	A	Excellent (One or more Level I studies with a low risk of bias or several Level II studies with a low risk of bias)
	B	Good (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	Satisfactory (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	Poor (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. Consistency *(the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)*		
All studies consistent	A	Excellent (all studies consistent)
	B	Good (most studies consistent and inconsistency can be explained)
	C	Satisfactory (some inconsistency, reflecting genuine uncertainty around question)
	D	Poor (evidence is inconsistent)
	NA	Not applicable (one study only)
3. Clinical impact *(the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)*		
Slight or restricted—no impact on haemoglobin, although iron stores improved	A	Excellent (very large clinical impact)
	B	Good (substantial clinical impact)
	C	Satisfactory (moderate clinical impact)
	D	Poor (slight or restricted clinical impact)
4. Generalisability *(how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?)*		
One study was performed in paediatric patients undergoing cardiac surgery while the other two studies were performed in adult patients undergoing cardiac surgery	A	Excellent (directly generalisable to target population)
	B	Good (directly generalisable to target population with some caveats)
	C	Satisfactory (not directly generalisable to the target population but could be sensibly applied)
	D	Poor (not directly generalisable to target population and hard to judge whether it is sensible to apply)
5. Applicability *(the extent to which the body of evidence is directly applicable to Australian healthcare context)*		

One study was conducted in Austria, one in Canada and the other in the USA	A	**Excellent** (directly applicable to Australian healthcare context)
	B	**Good** (applicable to Australian healthcare context with few caveats)
	C	**Satisfactory** (probably applicable to Australian healthcare context with some caveats)
	D	**Poor** (not applicable to Australian healthcare context)

6. **Other factors** (*Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation)*

EVIDENCE STATEMENT *Please summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account. Please indicate any dissenting opinions*

In paediatric and adult cardiac surgery patients with postoperative anaemia, postoperative oral iron had no effect on haemoglobin (Grade C)

Component	Rating	Description
Evidence base	C	Satisfactory
Consistency	A	Excellent
Clinical impact	D	Poor
Generalisability	C	Satisfactory
Applicability	C	Satisfactory

Indicate any dissenting opinions

RECOMMENDATION *What recommendation (s) does the guideline development group draw from this evidence?*	GRADE OF RECOMMENDATION *(A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B)*	NA

No recommendation was made

UNRESOLVED ISSUES *If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up*

IMPLEMENTATION OF RECOMMENDATION *Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline*

Will this recommendation result in changes in usual care?	Yes	No
Are there any resource implications associated with the implementing this recommendation?	Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized?	Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation?	Yes	No

Key question What is the effect of preoperative oral iron on haemoglobin levels in patients with preoperative anaemia undergoing noncardiac surgery? (GN3.2a)	Evidence table ref:; Lidder et al (2007)[150] ; Okuyama et al (2005)[154]	
1. Evidence base *(quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)*		
The evidence consists of one good quality Level II study[150], one fair quality Level III study[154]	A	**Excellent** (One or more Level I studies with a low risk of bias or several Level II studies with a low risk of bias)
	B	**Good** (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	**Satisfactory** (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	**Poor** (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. Consistency *(the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)*		
Most studies consistent and inconsistency can be explained by the patient population	A	**Excellent** (all studies consistent)
	B	**Good** (most studies consistent and inconsistency can be explained)
	C	**Satisfactory** (some inconsistency, reflecting genuine uncertainty around question)
	D	**Poor** (evidence is inconsistent)
	NA	**Not applicable** (one study only)
3. Clinical impact *(the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)*		
There is moderate clinical impact—approximately 1.0 g/dL as a consequence of preoperative iron supplementation	A	**Excellent** (very large clinical impact)
	B	**Good** (substantial clinical impact)
	C	**Satisfactory** (moderate clinical impact)
	D	**Poor** (slight or restricted clinical impact)
4. Generalisability *(how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?)*		
Studies included patients undergoing orthopaedic or cancer surgery, and the results are probably generalisable to a wider perioperative noncardiac surgical population	A	**Excellent** (directly generalisable to target population)
	B	**Good** (directly generalisable to target population with some caveats)
	C	**Satisfactory** (not directly generalisable to the target population but could be sensibly applied)
	D	**Poor** (not directly generalisable to target population and hard to judge whether it is sensible to apply)
5. Applicability *(the extent to which the body of evidence is directly applicable to Australian healthcare context)*		
The studies were conducted in Japan and the UK	A	**Excellent** (directly applicable to Australian healthcare context)
	B	**Good** (applicable to Australian healthcare context with few caveats)
	C	**Satisfactory** (probably applicable to Australian healthcare context with some caveats)
	D	**Poor** (not applicable to Australian healthcare context)

6. Other factors (*Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation)*
The highest quality study that had the most weight in the evidence base (Lidder et al, 2007) was in a population of colorectal cancer patients likely to have iron-deficiency anaemia.
Cuenca et al (2007) did not report preoperative change in haemoglobin and so was excluded for this outcome.

EVIDENCE STATEMENT *Please summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account. Please indicate any dissenting opinions*

GN3.2a In patients with preoperative anaemia undergoing noncardiac surgery, preoperative oral iron increases haemoglobin levels (Grade B) [150,154]

GN 3.2 In patients with preoperative anaemia undergoing noncardiac surgery, preoperative oral iron increases haemoglobin levels (Grade B) [150,154] and reduces the incidence of transfusion requirements[150153,154]
Note: Evidence Statement GN3.2 combines GN3.2a and GN3.2b

Component	Rating	Description
Evidence base	B	Good
Consistency	B	Good
Clinical impact	C	Satisfactory
Generalisability	B	Good
Applicability	B	Good

Indicate any dissenting opinions

RECOMMENDATION *What recommendation (s) does the guideline development group draw from this evidence?*	GRADE OF RECOMMENDATION *(A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B)*	B

In surgical patients with, or at risk of, iron-deficiency anaemia, preoperative oral iron therapy is recommended (Grade B)
(Refer to the preoperative anaemia management algorithm template [Appendix F of the perioperative guidelines] for further information on the optimal dosing strategy.)

UNRESOLVED ISSUES *If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up*

IMPLEMENTATION OF RECOMMENDATION *Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline*

Will this recommendation result in changes in usual care?	Yes	No
Are there any resource implications associated with the implementing this recommendation?	Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized?	Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation?	Yes	No

Key question What is the effect of preoperative oral iron on transfusion requirements in patients undergoing noncardiac surgery? (GN3.2b)	**Evidence table ref:** Lidder et al (2007)[150]; Cuenca et al (2007)[153]; Okuyama et al (2005)[154]	
1. **Evidence base** *(quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)*		
The evidence consists of one good quality Level II study[150], and two fair quality Level III studies[153,154]	A	**Excellent** (One or more Level I studies with a low risk of bias or several Level II studies with a low risk of bias)
	B	**Good** (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	**Satisfactory** (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	**Poor** (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. **Consistency** *(the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)*		
All studies reported similar results, despite slightly different dosing, the good quality Level II study and one of the fair quality studies [153] likely including patients who were non-anaemic.	A	**Excellent** (all studies consistent)
	B	**Good** (most studies consistent and inconsistency can be explained)
	C	**Satisfactory** (some inconsistency, reflecting genuine uncertainty around question)
	D	**Poor** (evidence is inconsistent)
	NA	**Not applicable** (one study only)
3. **Clinical impact** *(the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)*		
There is substantial clinical impact	A	**Excellent** (very large clinical impact)
	B	**Good** (substantial clinical impact)
	C	**Satisfactory** (moderate clinical impact)
	D	**Poor** (slight or restricted clinical impact)
4. **Generalisability** *(how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?)*		
Studies include patients from orthopaedics and colorectal surgery suggesting that the results should be generalisable to the wider noncardiac perioperative population	A	**Excellent** (directly generalisable to target population)
	B	**Good** (directly generalisable to target population with some caveats)
	C	**Satisfactory** (not directly generalisable to the target population but could be sensibly applied)
	D	**Poor** (not directly generalisable to target population and hard to judge whether it is sensible to apply)
5. **Applicability** *(the extent to which the body of evidence is directly applicable to Australian healthcare context)*		
The studies were conducted in Japan, Spain and the UK respectively	A	**Excellent** (directly applicable to Australian healthcare context)
	B	**Good** (applicable to Australian healthcare context with few caveats)
	C	**Satisfactory** (probably applicable to Australian healthcare context with some caveats)
	D	**Poor** (not applicable to Australian healthcare context)
6. **Other factors** (*Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation)*		

The highest quality study that had the most weight in the evidence base (Lidder et al, 2007) was in a population of colorectal cancer patients likely to have iron-deficiency anaemia.

EVIDENCE STATEMENT *Please summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account. Please indicate any dissenting opinions*

GN3.2b In patients with preoperative anaemia undergoing noncardiac surgery, preoperative oral iron reduces transfusion requirements (Grade B)

GN3.2 In patients with preoperative anaemia undergoing noncardiac surgery, preoperative oral iron increases haemoglobin levels (Grade B) [150,154] and reduces the incidence of transfusion requirements [150,153,154]

Note Evidence Statement GN3.2 combines GN3.2a and GN3.2b

Component	Rating	Description
Evidence base	B	Good
Consistency	A	Excellent
Clinical impact	B	Good
Generalisability	B	Good
Applicability	C	Satisfactory

Indicate any dissenting opinions

RECOMMENDATION *What recommendation (s) does the guideline development group draw from this evidence?*	GRADE OF RECOMMENDATION *(A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B).*	B

In surgical patients with, or at risk of, iron-deficiency anaemia, preoperative oral iron therapy is recommended (Grade B).
(Refer to the preoperative anaemia management algorithm template [Appendix F of the perioperative guidelines] for further information on the optimal dosing strategy.)

UNRESOLVED ISSUES *If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up*

IMPLEMENTATION OF RECOMMENDATION *Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline.*

Will this recommendation result in changes in usual care?	Yes	No
Are there any resource implications associated with the implementing this recommendation?	Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized?	Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation?	Yes	No

Key question What is the effect of preoperative oral iron on transfusion requirements in a noncardiac surgical population without preoperative anaemia? (GN3.3)		Evidence table ref: Cuenca et al (2007)[153]
1. Evidence base *(quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)*		
The evidence consists of one fair quality Level III study[153]	A	Excellent (One or more Level I studies with a low risk of bias or several Level II studies with a low risk of bias)
	B	Good (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	Satisfactory (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	Poor (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. Consistency *(the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)*		
NA – only one study	A	Excellent (all studies consistent)
	B	Good (most studies consistent and inconsistency can be explained)
	C	Satisfactory (some inconsistency, reflecting genuine uncertainty around question)
	D	Poor (evidence is inconsistent)
	NA	Not applicable (one study only)
3. Clinical impact *(the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)*		
There is moderate clinical impact	A	Excellent (very large clinical impact)
	B	Good (substantial clinical impact)
	C	Satisfactory (moderate clinical impact)
	D	Poor (slight or restricted clinical impact)
4. Generalisability *(how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?)*		
Study was performed in patients undergoing orthopaedic surgery and may not be generalisable to a wider perioperative noncardiac surgical patient population	A	Excellent (directly generalisable to target population)
	B	Good (directly generalisable to target population with some caveats)
	C	Satisfactory (not directly generalisable to the target population but could be sensibly applied)
	D	Poor (not directly generalisable to target population and hard to judge whether it is sensible to apply)
5. Applicability *(the extent to which the body of evidence is directly applicable to Australian healthcare context)*		
The studies were conducted in Spain	A	Excellent (directly applicable to Australian healthcare context)
	B	Good (applicable to Australian healthcare context with few caveats)
	C	Satisfactory (probably applicable to Australian healthcare context with some caveats)
	D	Poor (not applicable to Australian healthcare context)
6. Other factors (*Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation)*		

EVIDENCE STATEMENT *Please summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account. Please indicate any dissenting opinions*				
In noncardiac surgery patients without preoperative anaemia, there is insufficient evidence to determine whether oral iron treatment before surgery affects the incidence of transfusion (Grade D) [153]				
Component	Rating	Description		
Evidence base	C	Satisfactory		
Consistency	NA	Not Applicable - Only one study		
Clinical impact	C	Satisfactory		
Generalisability	C	Satisfactory		
Applicability	C	Satisfactory		
Indicate any dissenting opinions				
RECOMMENDATION *What recommendation (s) does the guideline development group draw from this evidence?*			GRADE OF RECOMMENDATION *(A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B)*	NA
No recommendation was made due to evidence statement being graded D.				
UNRESOLVED ISSUES *If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up*				
IMPLEMENTATION OF RECOMMENDATION *Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline*				
Will this recommendation result in changes in usual care?			Yes	No
Are there any resource implications associated with the implementing this recommendation?			Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized?			Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation?			Yes	No

Key question What is the effect of postoperative oral iron on haemoglobin levels in an anaemic noncardiac surgical population? (GN3.4)		Evidence table ref: Mundy et al (2005)[151] Weatherall et al (2004)[152]
1. Evidence base *(quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)*		
The evidence consists of one good quality Level II study[151] and one fair quality Level II study[152]	A	Excellent (One or more Level I studies with a low risk of bias or several Level II studies with a low risk of bias)
	B	Good (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	Satisfactory (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	Poor (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. Consistency *(the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)*		
Both studies report minimal effect.	A	Excellent (all studies consistent)
	B	Good (most studies consistent and inconsistency can be explained)
	C	Satisfactory (some inconsistency, reflecting genuine uncertainty around question)
	D	Poor (evidence is inconsistent)
	NA	Not applicable (one study only)
3. Clinical impact *(the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)*		
There is slight or restricted clinical impact	A	Excellent (very large clinical impact)
	B	Good (substantial clinical impact)
	C	Satisfactory (moderate clinical impact)
	D	Poor (slight or restricted clinical impact)
4. Generalisability *(how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?)*		
Both included studies were performed in orthopaedic patients and may not be generalisable to a wider perioperative noncardiac surgical patient population	A	Excellent (directly generalisable to target population)
	B	Good (directly generalisable to target population with some caveats)
	C	Satisfactory (not directly generalisable to the target population but could be sensibly applied)
	D	Poor (not directly generalisable to target population and hard to judge whether it is sensible to apply)
5. Applicability *(the extent to which the body of evidence is directly applicable to Australian healthcare context)*		
The studies were performed in the UK and New Zealand and therefore have good applicability to the Australian healthcare context	A	Excellent (directly applicable to Australian healthcare context)
	B	Good (applicable to Australian healthcare context with few caveats)
	C	Satisfactory (probably applicable to Australian healthcare context with some caveats)
	D	Poor (not applicable to Australian healthcare context)
6. Other factors (*Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation)*		

EVIDENCE STATEMENT *Please summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account. Please indicate any dissenting opinions*				
In noncardiac surgery patients with postoperative anaemia, postoperative oral iron is not clinically effective (Grade C)				
Component	Rating	Description		
Evidence base	B	Good		
Consistency	B	Good		
Clinical impact	D	Poor		
Generalisability	C	Satisfactory		
Applicability	B	Good		
Indicate any dissenting opinions				
RECOMMENDATION *What recommendation (s) does the guideline development group draw from this evidence?*			GRADE OF RECOMMENDATION *(A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B)*	B
In patients with postoperative anaemia, early oral iron therapy is not clinically effective; its routine use in this setting is not recommended (Grade B).				
UNRESOLVED ISSUES *If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up*				
IMPLEMENTATION OF RECOMMENDATION *Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline*				
Will this recommendation result in changes in usual care?			Yes	No
Are there any resource implications associated with the implementing this recommendation?			Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized?			Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation?			Yes	No

Key question What is the effect of preoperative or postoperative intravenous iron on transfusion requirements in an anaemic noncardiac surgical population? (GN3.5)		Evidence table ref: Cuenca et al (2004)[155]; Cuenca et al (2005)[156]; Munoz et al (2006)[157]
1. Evidence base *(quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)*		
The evidence consists of three fair quality Level III studies[155-157]	A	**Excellent** (One or more Level I studies with a low risk of bias or several Level II studies with a low risk of bias)
	B	**Good** (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	**Satisfactory** (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	**Poor** (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. Consistency *(the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)*		
All studies trended in the same direction; however, not all the results reached statistical significance. Study numbers were small	A	**Excellent** (all studies consistent)
	B	**Good** (most studies consistent and inconsistency can be explained)
	C	**Satisfactory** (some inconsistency, reflecting genuine uncertainty around question)
	D	**Poor** (evidence is inconsistent)
	NA	**Not applicable** (one study only)
3. Clinical impact *(the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)*		
There is slight or restricted clinical impact	A	**Excellent** (very large clinical impact)
	B	**Good** (substantial clinical impact)
	C	**Satisfactory** (moderate clinical impact)
	D	**Poor** (slight or restricted clinical impact)
4. Generalisability *(how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?)*		
All the studies were performed in an orthopaedic population and may not be directly generalisable to a wider perioperative noncardiac surgical patient population	A	**Excellent** (directly generalisable to target population)
	B	**Good** (directly generalisable to target population with some caveats)
	C	**Satisfactory** (not directly generalisable to the target population but could be sensibly applied)
	D	**Poor** (not directly generalisable to target population and hard to judge whether it is sensible to apply)
5. Applicability *(the extent to which the body of evidence is directly applicable to Australian healthcare context)*		
The studies were performed in Spain	A	**Excellent** (directly applicable to Australian healthcare context)
	B	**Good** (applicable to Australian healthcare context with few caveats)
	C	**Satisfactory** (probably applicable to Australian healthcare context with some caveats)
	D	**Poor** (not applicable to Australian healthcare context)
6. Other factors (*Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation)*		

EVIDENCE STATEMENT *Please summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account. Please indicate any dissenting opinions.*				
In noncardiac surgery patients, preoperative and postoperative intravenous iron may reduce mortality and hospital length of stay, risk of infection and incidence of transfusion (Grade D).				
Component	Rating	Description		
Evidence base	D	Poor		
Consistency	C	Satisfactory		
Clinical impact	D	Poor		
Generalisability	C	Satisfactory		
Applicability	C	Satisfactory		
Indicate any dissenting opinions				
RECOMMENDATION *What recommendation (s) does the guideline development group draw from this evidence?*			GRADE OF RECOMMENDATION *(A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B)*	NA
No recommendation was made due to evidence statement being graded D.				
UNRESOLVED ISSUES *If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up*				
IMPLEMENTATION OF RECOMMENDATION *Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline*				
Will this recommendation result in changes in usual care?			Yes	No
Are there any resource implications associated with the implementing this recommendation?			Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized?			Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation?			Yes	No

Key question What is the effect of postoperative intravenous iron and oral iron compared with postoperative oral iron alone on the incidence of transfusion, postoperative haemoglobin levels and ferritin levels in a cardiac and noncardiac surgical population? (GN3.6)		Evidence table ref: Karkouti et al (2006a)[159]
1. Evidence base *(quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)*		
The evidence consists of one fair quality Level II study[159]	A	Excellent (One or more Level I studies with a low risk of bias or several Level II studies with a low risk of bias)
	B	Good (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	Satisfactory (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	Poor (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. Consistency *(the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)*		
Only one study	A	Excellent (all studies consistent)
	B	Good (most studies consistent and inconsistency can be explained)
	C	Satisfactory (some inconsistency, reflecting genuine uncertainty around question)
	D	Poor (evidence is inconsistent)
	NA	Not applicable (one study only)
3. Clinical impact *(the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)*		
There is a slight or restricted clinical impact	A	Excellent (very large clinical impact)
	B	Good (substantial clinical impact)
	C	Satisfactory (moderate clinical impact)
	D	Poor (slight or restricted clinical impact)
4. Generalisability *(how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?)*		
The study was in patients undergoing cardiac surgery or orthopaedic surgery. The results may be generalisable to a wider perioperative patient population	A	Excellent (directly generalisable to target population)
	B	Good (directly generalisable to target population with some caveats)
	C	Satisfactory (not directly generalisable to the target population but could be sensibly applied)
	D	Poor (not directly generalisable to target population and hard to judge whether it is sensible to apply)
5. Applicability *(the extent to which the body of evidence is directly applicable to Australian healthcare context)*		
The study was conducted in Canada	A	Excellent (directly applicable to Australian healthcare context)
	B	Good (applicable to Australian healthcare context with few caveats)
	C	Satisfactory (probably applicable to Australian healthcare context with some caveats)
	D	Poor (not applicable to Australian healthcare context)
6. Other factors (*Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation)*		

EVIDENCE STATEMENT *Please summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account. Please indicate any dissenting opinions*		
In cardiac and orthopaedic surgery patients, the effectiveness of postoperative intravenous iron plus oral iron compared with postoperative oral iron alone on the incidence of transfusion and postoperative haemoglobin levels and ferritin levels is uncertain (Grade D)		
Component	Rating	Description
Evidence base	C	Satisfactory
Consistency	NA	Not applicable
Clinical impact	D	Slight or restricted
Generalisability	C	Satisfactory
Applicability	B	Good
Indicate any dissenting opinions		

RECOMMENDATION *What recommendation (s) does the guideline development group draw from this evidence?*	GRADE OF RECOMMENDATION *(A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B)*	NA
No recommendation was made due to evidence statement being graded D.		
UNRESOLVED ISSUES *If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up*		
IMPLEMENTATION OF RECOMMENDATION *Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline.*		
Will this recommendation result in changes in usual care?	Yes	No
Are there any resource implications associated with the implementing this recommendation?	Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized?	Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation?	Yes	No

Key question What is the effect of preoperative intravenous iron compared with preoperative oral iron at increasing haemoglobin and ferritin levels in a noncardiac surgical population? (GN3.7)		Evidence table ref: Kim et al (2009)[160]
1. Evidence base *(quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)*		
The evidence consists of one poor quality Level II study[160]	A	Excellent (One or more Level I studies with a low risk of bias or several Level II studies with a low risk of bias)
	B	Good (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	Satisfactory (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	Poor (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. Consistency *(the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)*		
Only one study	A	Excellent (all studies consistent)
	B	Good (most studies consistent and inconsistency can be explained)
	C	Satisfactory (some inconsistency, reflecting genuine uncertainty around question)
	D	Poor (evidence is inconsistent)
	NA	Not applicable (one study only)
3. Clinical impact *(the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)*		
There is slight or restricted clinical impact	A	Excellent (very large clinical impact)
	B	Good (substantial clinical impact)
	C	Satisfactory (moderate clinical impact)
	D	Poor (slight or restricted clinical impact)
4. Generalisability *(how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?)*		
The study was performed in women with anaemia due to menorrhagia undergoing surgery for this condition and therefore may not be directly generalisable to a wider perioperative noncardiac surgical population	A	Excellent (directly generalisable to target population)
	B	Good (directly generalisable to target population with some caveats)
	C	Satisfactory (not directly generalisable to the target population but could be sensibly applied)
	D	Poor (not directly generalisable to target population and hard to judge whether it is sensible to apply)
5. Applicability *(the extent to which the body of evidence is directly applicable to Australian healthcare context)*		
The study was performed in Korea and may not be applicable to the Australian healthcare context	A	Excellent (directly applicable to Australian healthcare context)
	B	Good (applicable to Australian healthcare context with few caveats)
	C	Satisfactory (probably applicable to Australian healthcare context with some caveats)
	D	Poor (not applicable to Australian healthcare context)
6. Other factors (*Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation)*		

EVIDENCE STATEMENT *Please summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account. Please indicate any dissenting opinions.*		
In gynaecological surgical patients with iron deficiency anaemia, preoperative intravenous iron is more effective than preoperative oral iron at increasing postoperative haemoglobin and ferritin levels (Grade D) [160]		
Component	Rating	Description
Evidence base	D	Poor
Consistency	NA	Not applicable
Clinical impact	D	Poor
Generalisability	C	Satisfactory
Applicability	C	Satisfactory
Indicate any dissenting opinions		

RECOMMENDATION *What recommendation (s) does the guideline development group draw from this evidence?*	GRADE OF RECOMMENDATION *(A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B)*	NA
No recommendation was made due to evidence statement being graded D		
UNRESOLVED ISSUES *If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up*		
IMPLEMENTATION OF RECOMMENDATION *Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline*		

Will this recommendation result in changes in usual care?	Yes	No
Are there any resource implications associated with the implementing this recommendation?	Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized?	Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation?	Yes	No

Key question What is the effect of preoperative ESAs in addition to iron on morbidity in in a noncardiac surgical population? (GN3.8)		Evidence table ref: COPES (1993)[166]; Faris et al (1996)[169]; Larson et al (2001)[175]
1. Evidence base *(quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)*		
The evidence consists of two good quality Level II studies[166,169,] and one fair quality Level II study[175]	A	Excellent (One or more Level I studies with a low risk of bias or several Level II studies with a low risk of bias)
	B	Good (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	Satisfactory (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	Poor (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. Consistency *(the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)*		
Studies were underpowered to detect a difference in this outcome	A	Excellent (all studies consistent)
	B	Good (most studies consistent and inconsistency can be explained)
	C	Satisfactory (some inconsistency, reflecting genuine uncertainty around question)
	D	Poor (evidence is inconsistent)
	NA	Not applicable (one study only)
3. Clinical impact (*the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)*		
There is moderate clinical impact	A	Excellent (very large clinical impact)
	B	Good (substantial clinical impact)
	C	Satisfactory (moderate clinical impact)
	D	Poor (slight or restricted clinical impact)
4. Generalisability *(how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?)*		
Two studies were performed in orthopaedic surgery and one in patients undergoing hysterectomy. The results a probably generalisable to a wider perioperative noncardiac surgical population	A	Excellent (directly generalisable to target population)
	B	Good (directly generalisable to target population with some caveats)
	C	Satisfactory (not directly generalisable to the target population but could be sensibly applied)
	D	Poor (not directly generalisable to target population and hard to judge whether it is sensible to apply)
5. Applicability *(the extent to which the body of evidence is directly applicable to Australian healthcare context)*		
One of the studies was conducted in Canada, and one each in Sweden and the USA	A	Excellent (directly applicable to Australian healthcare context)
	B	Good (applicable to Australian healthcare context with few caveats)
	C	Satisfactory (probably applicable to Australian healthcare context with some caveats)
	D	Poor (not applicable to Australian healthcare context)

6. Other factors (*Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation)*		
EVIDENCE STATEMENT *Please summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account. Please indicate any dissenting opinions*		
In noncardiac surgery patients, there is insufficient evidence to determine the effect on morbidity of preoperative treatment with an erythropoiesis-stimulating agent in combination with oral iron (Grade C) [166,169 ,175]		
Component	Rating	Description
Evidence base	A	Excellent
Consistency	C	Satisfactory
Clinical impact	C	Satisfactory
Generalisability	B	Good
Applicability	B	Good
Indicate any dissenting opinions		

RECOMMENDATION *What recommendation (s) does the guideline development group draw from this evidence?*	GRADE OF RECOMMENDATION *(A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B)*	NA
No recommendation was made		
UNRESOLVED ISSUES *If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up*		
IMPLEMENTATION OF RECOMMENDATION *Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline*		

Will this recommendation result in changes in usual care?	Yes	No
Are there any resource implications associated with the implementing this recommendation?	Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized?	Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation?	Yes	No

Key question What is the effect of perioperative ESAs in addition to iron on transfusion requirements in an anaemic orthopaedic surgical population? (GN3.9)	Evidence table ref: Faris et al (1996)[169]; Weber et al (2005b)[179]	
1. Evidence base *(quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)*		
The evidence consists of one good quality Level II studies[169], and one fair quality Level II[179]	A	Excellent (One or more Level I studies with a low risk of bias or several Level II studies with a low risk of bias)
	B	Good (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	Satisfactory (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	Poor (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. Consistency *(the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)*		
Both studies reported consistent results	A	Excellent (all studies consistent)
	B	Good (most studies consistent and inconsistency can be explained)
	C	Satisfactory (some inconsistency, reflecting genuine uncertainty around question)
	D	Poor (evidence is inconsistent)
	NA	Not applicable (one study only)
3. Clinical impact *(the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)*		
There is substantial clinical impact	A	Excellent (very large clinical impact)
	B	Good (substantial clinical impact)
	C	Satisfactory (moderate clinical impact)
	D	Poor (slight or restricted clinical impact)
4. Generalisability *(how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?)*		
Both studies were performed in patients undergoing orthopaedic surgery and are therefore directly generalisable to an orthopaedic surgical population. The results may not be generalisable to a wider perioperative population	A	Excellent (directly generalisable to target population)
	B	Good (directly generalisable to target population with some caveats)
	C	Satisfactory (not directly generalisable to the target population but could be sensibly applied)
	D	Poor (not directly generalisable to target population and hard to judge whether it is sensible to apply)
5. Applicability *(the extent to which the body of evidence is directly applicable to Australian healthcare context)*		
One study was conducted in the USA; one was a multicentre trial (Netherlands, France, Germany, Sweden, Belgium, Australia); and one was conducted in an unknown location	A	Excellent (directly applicable to Australian healthcare context)
	B	Good (applicable to Australian healthcare context with few caveats)
	C	Satisfactory (probably applicable to Australian healthcare context with some caveats)
	D	Poor (not applicable to Australian healthcare context)
6. Other factors (*Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation)*		

EVIDENCE STATEMENT *Please summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account. Please indicate any dissenting opinions*				
In orthopaedic surgery patients, preoperative treatment of anaemia with an erythropoiesis stimulating agent in combination with oral iron reduces the incidence of transfusion (Grade A) [169,179]				
Component	Rating	Description		
Evidence base	A	Excellent		
Consistency	A	Excellent		
Clinical impact	B	Good		
Generalisability	A	Excellent		
Applicability	B	Good		
Indicate any dissenting opinions				
RECOMMENDATION *What recommendation (s) does the guideline development group draw from this evidence?*			GRADE OF RECOMMENDATION *(A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B)*	A
In patients with preoperative anaemia, where an erythropoiesis-stimulating agent is indicated, it must be combined with iron therapy (Grade A). Note: This recommendation is developed from evidence statements GN3.9, GN3.10, GN3.11, GN3.12, and GN3.13				
UNRESOLVED ISSUES *If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up*				
IMPLEMENTATION OF RECOMMENDATION *Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline*				
Will this recommendation result in changes in usual care? Increase the co-administration of iron therapy			Yes	No
Are there any resource implications associated with the implementing this recommendation?			Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized?			Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation?			Yes	No

Key question What is the effect of preoperative ESAs in addition to iron on incidence of transfusion in a colorectal surgical population? (GN3.10)	**Evidence table ref:** Christodoulakis et al (2005)[167]; Heiss et al (1996)[172]; Kettelhack et al (1998)[173]; Qvist et al (1999)[176]	
1. **Evidence base** *(quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)*		
The evidence consists of one good quality Level II study[176] and three fair quality Level II studies[167,172,173]	A	**Excellent** (One or more Level I studies with a low risk of bias or several Level II studies with a low risk of bias)
	B	**Good** (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	**Satisfactory** (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	**Poor** (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. **Consistency** *(the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)*		
Only one study demonstrates an effect of ESAs on the outcome	A	**Excellent** (all studies consistent)
	B	**Good** (most studies consistent and inconsistency can be explained)
	C	**Satisfactory** (some inconsistency, reflecting genuine uncertainty around question)
	D	**Poor** (evidence is inconsistent)
	NA	**Not applicable** (one study only)
3. **Clinical impact** (*the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)*		
There is moderate clinical impact	A	**Excellent** (very large clinical impact)
	B	**Good** (substantial clinical impact)
	C	**Satisfactory** (moderate clinical impact)
	D	**Poor** (slight or restricted clinical impact)
4. **Generalisability** *(how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?)*		
Because all studies were performed in patients undergoing surgery for colorectal cancer, the results are directly transferable to this patient population. Results may not be generaliasable to a wider perioperative population	A	**Excellent** (directly generalisable to target population)
	B	**Good** (directly generalisable to target population with some caveats)
	C	**Satisfactory** (not directly generalisable to the target population but could be sensibly applied)
	D	**Poor** (not directly generalisable to target population and hard to judge whether it is sensible to apply)
5. **Applicability** *(the extent to which the body of evidence is directly applicable to Australian healthcare context)*		
Two studies were conducted in Germany and one each in Denmark and Greece	A	**Excellent** (directly applicable to Australian healthcare context)
	B	**Good** (applicable to Australian healthcare context with few caveats)
	C	**Satisfactory** (probably applicable to Australian healthcare context with some caveats)
	D	**Poor** (not applicable to Australian healthcare context)
6. **Other factors** (*Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation)*		

EVIDENCE STATEMENT *Please summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account. Please indicate any dissenting opinions*		
In colorectal surgery patients, preoperative treatment of anaemia with an erythropoiesis-stimulating agent in combination with oral iron starting less than 10 days before surgery has an inconsistent effect on incidence of transfusion (Grade C) [166,172,173,176]		
Component	Rating	Description
Evidence base	B	Good
Consistency	C	Satisfactory
Clinical impact	C	Satisfactory
Generalisability	A	Excellent
Applicability	C	Satisfactory
Indicate any dissenting opinions		

RECOMMENDATION *What recommendation (s) does the guideline development group draw from this evidence?*	GRADE OF RECOMMENDATION *(A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B)*	A
In patients with preoperative anaemia, where an erythropoiesis-stimulating agent is indicated, it must be combined with iron therapy (Grade A). Note: This recommendation is developed from evidence statements GN3.9, GN3.10, GN3.11, GN3.12, and GN3.13		
UNRESOLVED ISSUES *If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up*		
IMPLEMENTATION OF RECOMMENDATION *Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline*		
Will this recommendation result in changes in usual care?	Yes	No
Are there any resource implications associated with the implementing this recommendation?	Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized?	Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation?	Yes	No

Key question What is the effect of preoperative treatment with ESAs in addition to iron on haemoglobin levels in a noncardiac surgical population? (GN3.11)		Evidence table ref: Heiss et al (1996)[172]; Kosmadakis et al (2003)[174]; Larson et al (2001)[175]; Qvist et al (1999)[176]; Tsuji et al (1995)[178]; Weber et al (2005b)[179]
1. Evidence base *(quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)*		
The evidence consists of two good quality Level II studies[174,176] and three fair quality[172,175,179] and one poor quality[178] Level II studies	A	**Excellent** (One or more Level I studies with a low risk of bias or several Level II studies with a low risk of bias)
	B	**Good** (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	**Satisfactory** (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	**Poor** (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. Consistency *(the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)*		
All studies gave consistent results	A	**Excellent** (all studies consistent)
	B	**Good** (most studies consistent and inconsistency can be explained)
	C	**Satisfactory** (some inconsistency, reflecting genuine uncertainty around question)
	D	**Poor** (evidence is inconsistent)
	NA	**Not applicable** (one study only)
3. Clinical impact *(the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)*		
There is substantial clinical impact	A	**Excellent** (very large clinical impact)
	B	**Good** (substantial clinical impact)
	C	**Satisfactory** (moderate clinical impact)
	D	**Poor** (slight or restricted clinical impact)
4. Generalisability *(how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?)*		
Studies were performed in a range of noncardiac surgeries, although the majority were performed in orthopaedic and cancer surgeries. The results are probably generalisable to a wider perioperative noncardiac surgical population	A	**Excellent** (directly generalisable to target population)
	B	**Good** (directly generalisable to target population with some caveats)
	C	**Satisfactory** (not directly generalisable to the target population but could be sensibly applied)
	D	**Poor** (not directly generalisable to target population and hard to judge whether it is sensible to apply)
5. Applicability *(the extent to which the body of evidence is directly applicable to Australian healthcare context)*		
The studies were conducted in Canada, Germany, Sweden, Denmark, Greece and Japan; one was a multicentre study conducted in the Netherlands, France, Germany, Sweden, Belgium and Australia	A	**Excellent** (directly applicable to Australian healthcare context)
	B	**Good** (applicable to Australian healthcare context with few caveats)
	C	**Satisfactory** (probably applicable to Australian healthcare context with some caveats)
	D	**Poor** (not applicable to Australian healthcare context)

6. Other factors (*Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation)*		
EVIDENCE STATEMENT *Please summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account. Please indicate any dissenting opinions*		
In noncardiac surgery patients, preoperative treatment of anaemia with an erythropoiesis-stimulating agent in combination with iron increases preoperative haemoglobin levels (Grade A) [172,174, 175,176,178,179].		
Component	Rating	Description
Evidence base	A	Excellent
Consistency	A	Excellent
Clinical impact	B	Good
Generalisability	B	Good
Applicability	B	Good
Indicate any dissenting opinions		

RECOMMENDATION *What recommendation (s) does the guideline development group draw from this evidence?*	GRADE OF RECOMMENDATION *(A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B)*	A
In patients with preoperative anaemia, where an erythropoiesis-stimulating agent is indicated, it must be combined with iron therapy (Grade A). Note: This recommendation is developed from evidence statements GN3.9, GN3.10, GN3.11, GN3.12, and GN3.13,		
UNRESOLVED ISSUES *If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up*		
IMPLEMENTATION OF RECOMMENDATION *Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline*		

Will this recommendation result in changes in usual care? Increase the co-administration of iron therapy	Yes	No
Are there any resource implications associated with the implementing this recommendation?	Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized?	Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation?	Yes	No

Key question What is the effect of preoperative ESAs, in addition to iron, on hospital length of stay in a noncardiac surgical population? (GN3.12)		Evidence table ref: Larson et al (2001)[175]; Qvist et al (1999)[176]; Weber et al (2005b)[179]
1. Evidence base *(quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)*		
The evidence consists of one good quality Level II study[176] and two fair quality Level II studies[175,179]	A	**Excellent** (One or more Level I studies with a low risk of bias or several Level II studies with a low risk of bias)
	B	**Good** (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	**Satisfactory** (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	**Poor** (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. Consistency *(the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)*		
Only one study showed an effect on this outcome	A	**Excellent** (all studies consistent)
	B	**Good** (most studies consistent and inconsistency can be explained)
	C	**Satisfactory** (some inconsistency, reflecting genuine uncertainty around question)
	D	**Poor** (evidence is inconsistent)
	NA	**Not applicable** (one study only)
3. Clinical impact *(the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)*		
There is moderate clinical impact	A	**Excellent** (very large clinical impact)
	B	**Good** (substantial clinical impact)
	C	**Satisfactory** (moderate clinical impact)
	D	**Poor** (slight or restricted clinical impact)
4. Generalisability *(how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?)*		
Studies were performed in a range of noncardiac surgeries, and the results are probably generalisable to a wider perioperative noncardiac surgical population	A	**Excellent** (directly generalisable to target population)
	B	**Good** (directly generalisable to target population with some caveats)
	C	**Satisfactory** (not directly generalisable to the target population but could be sensibly applied)
	D	**Poor** (not directly generalisable to target population and hard to judge whether it is sensible to apply)
5. Applicability *(the extent to which the body of evidence is directly applicable to Australian healthcare context)*		
Studies were conducted in Denmark and Greece; and one was a multicentre study conducted in the Netherlands, France, Germany, Sweden, Belgium and Australia	A	**Excellent** (directly applicable to Australian healthcare context)
	B	**Good** (applicable to Australian healthcare context with few caveats)
	C	**Satisfactory** (probably applicable to Australian healthcare context with some caveats)
	D	**Poor** (not applicable to Australian healthcare context)
6. Other factors (*Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation)*		

EVIDENCE STATEMENT *Please summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account. Please indicate any dissenting opinions*				
In noncardiac surgery patients, preoperative treatment of anaemia with an erythropoiesis stimulating agent in combination with oral iron does not affect hospital length of stay (Grade B) [175,176,179]				
Component	Rating	Description		
Evidence base	B	Good		
Consistency	B	Good		
Clinical impact	C	Satisfactory		
Generalisability	B	Good		
Applicability	B	Good		
Indicate any dissenting opinions				
RECOMMENDATION *What recommendation (s) does the guideline development group draw from this evidence?*			GRADE OF RECOMMENDATION *(A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B)*	A
In patients with preoperative anaemia, where an erythropoiesis-stimulating agent is indicated, it must be combined with iron therapy (Grade A). Note: This recommendation is developed from evidence statements GN3.9 GN 10, GN3.11, GN3.12, and GN3.13				
UNRESOLVED ISSUES *If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up*				
IMPLEMENTATION OF RECOMMENDATION *Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline*				
Will this recommendation result in changes in usual care?			Yes	No
Are there any resource implications associated with the implementing this recommendation?			Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized?			Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation?			Yes	No

Key question What is the effect of a weekly preoperative ESAs in addition to iron compared with preoperative daily erythropoietin in addition to iron on increasing haemoglobin levels in an orthopaedic surgical population? (GN3.13)		Evidence table ref: Goldberg et al (1996)[171]
1. Evidence base *(quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)*		
The evidence consists of one fair quality Level II study[171]	A	Excellent (One or more Level I studies with a low risk of bias or several Level II studies with a low risk of bias)
	B	Good (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	Satisfactory (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	Poor (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. Consistency *(the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)*		
Only one study	A	Excellent (all studies consistent)
	B	Good (most studies consistent and inconsistency can be explained)
	C	Satisfactory (some inconsistency, reflecting genuine uncertainty around question)
	D	Poor (evidence is inconsistent)
	NA	Not applicable (one study only)
3. Clinical impact *(the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)*		
There is moderate clinical impact	A	Excellent (very large clinical impact)
	B	Good (substantial clinical impact)
	C	Satisfactory (moderate clinical impact)
	D	Poor (slight or restricted clinical impact)
4. Generalisability *(how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?)*		
The study was performed in patients undergoing orthopaedic surgery and may be generalisable to a wider perioperative noncardiac surgical population	A	Excellent (directly generalisable to target population)
	B	Good (directly generalisable to target population with some caveats)
	C	Satisfactory (not directly generalisable to the target population but could be sensibly applied)
	D	Poor (not directly generalisable to target population and hard to judge whether it is sensible to apply)
5. Applicability *(the extent to which the body of evidence is directly applicable to Australian healthcare context)*		
Study was performed in the USA	A	Excellent (directly applicable to Australian healthcare context)
	B	Good (applicable to Australian healthcare context with few caveats)
	C	Satisfactory (probably applicable to Australian healthcare context with some caveats)
	D	Poor (not applicable to Australian healthcare context)
6. Other factors (*Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation)*		

EVIDENCE STATEMENT *Please summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account. Please indicate any dissenting opinions*		
In orthopaedic surgery patients with anaemia, preoperative administration of an erythropoiesis stimulating agent (epoetin alfa) weekly is no different to daily administration in combination with oral iron, at increasing preoperative haemoglobin levels (Grade C) [171]		
Component	Rating	Description
Evidence base	C	Satisfactory
Consistency	NA	Not applicable
Clinical impact	C	Satisfactory
Generalisability	B	Good
Applicability	C	Satisfactory
Indicate any dissenting opinions		

RECOMMENDATION *What recommendation (s) does the guideline development group draw from this evidence?*	GRADE OF RECOMMENDATION *(A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B)*	A
In patients with preoperative anaemia, where an erythropoiesis-stimulating agent is indicated, it must be combined with iron therapy (Grade A). Note: This recommendation is developed from evidence statements GN3.9, GN3.10, GN3.11, GN3.12, and GN3.13		
UNRESOLVED ISSUES *If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up*		
IMPLEMENTATION OF RECOMMENDATION *Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline*		
Will this recommendation result in changes in usual care?	Yes	No
Are there any resource implications associated with the implementing this recommendation?	Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized?	Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation?	Yes	No

Key question What is the effect of postoperative erythropoietin in addition to intravenous iron on the incidence of transfusion in a cardiac and orthopaedic surgical population? (GN3.14)		Evidence table ref: Karkouti et al (2006a)[159]
1. Evidence base *(quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)*		
The evidence consists of one fair quality Level II study[159]	A	Excellent (One or more Level I studies with a low risk of bias or several Level II studies with a low risk of bias)
	B	Good (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	Satisfactory (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	Poor (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. Consistency *(the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)*		
Only one study	A	Excellent (all studies consistent)
	B	Good (most studies consistent and inconsistency can be explained)
	C	Satisfactory (some inconsistency, reflecting genuine uncertainty around question)
	D	Poor (evidence is inconsistent)
	NA	Not applicable (one study only)
3. Clinical impact *(the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)*		
There is slight or restricted clinical impact	A	Excellent (very large clinical impact)
	B	Good (substantial clinical impact)
	C	Satisfactory (moderate clinical impact)
	D	Poor (slight or restricted clinical impact)
4. Generalisability *(how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?)*		
The study was performed in patients undergoing cardiac surgery or orthopaedic surgery. The results are probably generalisable to a wider perioperative patient population	A	Excellent (directly generalisable to target population)
	B	Good (directly generalisable to target population with some caveats)
	C	Satisfactory (not directly generalisable to the target population but could be sensibly applied)
	D	Poor (not directly generalisable to target population and hard to judge whether it is sensible to apply)
5. Applicability *(the extent to which the body of evidence is directly applicable to Australian healthcare context)*		
The study was conducted in Canada	A	Excellent (directly applicable to Australian healthcare context)
	B	Good (applicable to Australian healthcare context with few caveats)
	C	Satisfactory (probably applicable to Australian healthcare context with some caveats)
	D	Poor (not applicable to Australian healthcare context)
6. Other factors (*Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation)*		

EVIDENCE STATEMENT *Please summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account. Please indicate any dissenting opinions*				
In cardiac and orthopaedic surgery patients, treatment of postoperative anaemia with an erythropoiesis stimulating agent in combination with intravenous iron may not decrease the incidence of transfusion compared with intravenous iron plus oral iron, or oral iron alone (Grade D) [159]				
Component	Rating	Description		
Evidence base	C	Satisfactory		
Consistency	NA	Not applicable		
Clinical impact	D	Poor		
Generalisability	B	Good		
Applicability	B	Good		
Indicate any dissenting opinions				
RECOMMENDATION *What recommendation (s) does the guideline development group draw from this evidence?*			GRADE OF RECOMMENDATION *(A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B)*	NA
No recommendation was made due to evidence statement being graded D				
UNRESOLVED ISSUES *If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up*				
IMPLEMENTATION OF RECOMMENDATION *Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline*				
Will this recommendation result in changes in usual care?			Yes	No
Are there any resource implications associated with the implementing this recommendation?			Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized?			Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation?			Yes	No

Key question What is the effect of postoperative ESAs in addition to oral iron on haemoglobin levels in an orthopaedic surgical population? (GN3.15)		Evidence table ref: Green et al (1996)[180]
1. Evidence base *(quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)*		
The evidence consists of one good quality Level II study[180]	A	Excellent (One or more Level I studies with a low risk of bias or several Level II studies with a low risk of bias)
	B	Good (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	Satisfactory (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	Poor (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. Consistency *(the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)*		
Only one study	A	Excellent (all studies consistent)
	B	Good (most studies consistent and inconsistency can be explained)
	C	Satisfactory (some inconsistency, reflecting genuine uncertainty around question)
	D	Poor (evidence is inconsistent)
	NA	Not applicable (one study only)
3. Clinical impact *(the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)*		
There is slight or restricted clinical impact	A	Excellent (very large clinical impact)
	B	Good (substantial clinical impact)
	C	Satisfactory (moderate clinical impact)
	D	Poor (slight or restricted clinical impact)
4. Generalisability *(how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?)*		
The study was performed in patients undergoing orthopaedic surgery. The results may be generalisable to a wider perioperative patient population	A	Excellent (directly generalisable to target population)
	B	Good (directly generalisable to target population with some caveats)
	C	Satisfactory (not directly generalisable to the target population but could be sensibly applied)
	D	Poor (not directly generalisable to target population and hard to judge whether it is sensible to apply)
5. Applicability *(the extent to which the body of evidence is directly applicable to Australian healthcare context)*		
The study was conducted in the USA	A	Excellent (directly applicable to Australian healthcare context)
	B	Good (applicable to Australian healthcare context with few caveats)
	C	Satisfactory (probably applicable to Australian healthcare context with some caveats)
	D	Poor (not applicable to Australian healthcare context)
6. Other factors (*Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation)*		

EVIDENCE STATEMENT *Please summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account. Please indicate any dissenting opinions*				
In orthopaedic surgery patients with postoperative anaemia, treatment with an erythropoiesis stimulating agent in combination with oral iron increases haemoglobin levels (Grade D) [180]				
Component	Rating	Description		
Evidence base	B	Good		
Consistency	NA	Not applicable		
Clinical impact	D	Poor		
Generalisability	C	Satisfactory		
Applicability	C	Satisfactory		
Indicate any dissenting opinions				
RECOMMENDATION *What recommendation (s) does the guideline development group draw from this evidence?*			GRADE OF RECOMMENDATION *(A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B)*	NA
No recommendation was made due to evidence statement being graded D				
UNRESOLVED ISSUES *If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up*				
IMPLEMENTATION OF RECOMMENDATION *Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline*				
Will this recommendation result in changes in usual care?			Yes	No
Are there any resource implications associated with the implementing this recommendation?			Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized?			Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation?			Yes	No

D7 Evidence matrix, Question 7

What is the effect of rFVIIa (prophylaxis or treatment) on morbidity, mortality and transfusion rate?

Key question What is the effect of rFVIIa (prophylaxis or treatment) on morbidity, mortality and transfusion rate? (GN4.1) The body of evidence discussed below refers to the effect of prophylactic or therapeutic use of rFVIIa on mortality in surgery	Evidence table ref: Zangrillo et al (2009)[182]; Ranucci et al (2008b)[183]; Gill et al (2009)[185]; Johansson et al (2007)[188];; Pugliese et al (2007)[190]; and Sachs et al (2007)[191]	
1. Evidence base *(quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)*		
Six studies: two Level I studies, one with a low risk of bias[183] and one with a moderate risk of bias[182]; four Level II studies, three with a moderate risk of bias[185,188,191] and one with a high risk of bias[190]. Included studies were small and underpowered	A	Excellent (One or more Level I studies with a low risk of bias or several Level II studies with a low risk of bias)
	B	Good (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	Satisfactory (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	Poor (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. Consistency *(the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)*		
Generally similar direction of effect among included studies. Inconsistent results between studies of cardiac surgery[182,185], with mortality increased by rFVIIa use in one small primary study[185], but unaffected when results were pooled in a systematic review[182]. Some uncertainty about consistency because of the small sample size of included studies and variety of surgical procedures investigated	A	Excellent (all studies consistent)
	B	Good (most studies consistent and inconsistency can be explained)
	C	Satisfactory (some inconsistency, reflecting genuine uncertainty around question)
	D	Poor (evidence is inconsistent)
	NA	Not applicable (one study only)
3. Clinical impact *(the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)*		
May be some benefit in the use of rFVIIa for some surgical procedures, but there is uncertainty because of the limited evidence base, which comprises small studies	A	Excellent (very large clinical impact)
	B	Good (substantial clinical impact)
	C	Satisfactory (moderate clinical impact)
	D	Poor (slight or restricted clinical impact)
4. Generalisability *(how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?)*		
Study populations are the same as the target population	A	Excellent (directly generalisable to target population)
	B	Good (directly generalisable to target population with some caveats)
	C	Satisfactory (not directly generalisable to the target population but could be sensibly applied)
	D	Poor (not directly generalisable to target population and hard to judge whether it is sensible to apply)
5. Applicability *(the extent to which the body of evidence is directly applicable to Australian healthcare context)*		

Most included studies were from Europe. There are some differences in the healthcare system between Australia//New Zealand and included studies	A	**Excellent** (directly applicable to Australian healthcare context)
	B	**Good** (applicable to Australian healthcare context with few caveats)
	C	**Satisfactory** (probably applicable to Australian healthcare context with some caveats)
	D	**Poor** (not applicable to Australian healthcare context)

6. **Other factors** (*Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation)*

EVIDENCE STATEMENT *Please summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account. Please indicate any dissenting opinions.*

In surgical patients, there is insufficient evidence to determine the effect of prophylactic or therapeutic use of rFVIIa on mortality (Grade C)[182,183,185,188,191]

Component	Rating	Description
Evidence base	B	Good
Consistency	C	Satisfactory
Clinical impact	D	Poor
Generalisability	A	Excellent
Applicability	B	Good

Indicate any dissenting opinions

RECOMMENDATION *What recommendation (s) does the guideline development group draw from this evidence?*	GRADE OF RECOMMENDATION *(A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B)*	C

Recommendation GN4.1 The prophylactic or routine therapeutic use of rFVIIa is not recommended because the studies performed to date have been inadequately powered to detect the effect of rFVIIa on morbidity and mortality. Concern still exists about the safety profile of rFVIIa, particularly in relation to thrombotic adverse events (Grade C).

This recommendation is based on the body of evidence for mortality (Evidence Statement GN4.1) and morbidity (Evidence Statement GN4.2).

UNRESOLVED ISSUES *If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up*

IMPLEMENTATION OF RECOMMENDATION *Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline*

Will this recommendation result in changes in usual care?	Yes	No
Are there any resource implications associated with the implementing this recommendation?	Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized?	Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation?	Yes	No

Key question What is the effect of rFVIIa (prophylaxis or treatment) on morbidity, mortality and transfusion rate? (GN4.2) The body of evidence discussed below refers to the effect of prophylactic or therapeutic use of rFVIIa on morbidity in surgery		Evidence table ref: Zangrillo et al (2009)[182]; Ranucci et al (2008b)[183] Gill et al (2009)[185]; Johansson et al (2007)[188];; Pugliese et al (2007)[190]; and Sachs et al (2007)[191]
1. Evidence base *(quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)*		
Six studies: two Level I studies, one with a low risk of bias[183] and one with a moderate risk of bias[182]; four Level II studies, four with a moderate risk of bias[185,188, 191], and one with a high risk of bias[190]. Included studies were small and underpowered	A	Excellent (One or more Level I studies with a low risk of bias or several Level II studies with a low risk of bias)
	B	Good (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	Satisfactory (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	Poor (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. Consistency *(the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)*		
Some inconsistency, with rFVIIa use responsible for a trend towards reduced MI in cardiac surgery patients who received rFVIIa[182], but an increased risk of stroke in the same patients[182]. The prophylactic use of rFVIIa does not appear to increase adverse events during some surgical procedures[183,188,190], whereas thromboembolic complications occurred in some patients who received rFVIIa therapeutically[191]. Although the difference in direction of effects may be explained by the different application of rFVIIa (i.e prophylactic vs. therapeutic), there is uncertainty about consistency because of the small sample size of included studies and variety of surgical procedures investigated	A	Excellent (all studies consistent)
	B	Good (most studies consistent and inconsistency can be explained)
	C	Satisfactory (some inconsistency, reflecting genuine uncertainty around question)
	D	Poor (evidence is inconsistent)
	NA	Not applicable (one study only)
3. Clinical impact *(the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)*		
Impact of rFVIIa on adverse effects is uncertain—effect of rFVIIa on thromboembolic events in included studies was not statistically significant, with confidence intervals capturing values representing "no effect" and an absence of appropriate study powering because of the small sample sizes	A	Excellent (very large clinical impact)
	B	Good (substantial clinical impact)
	C	Satisfactory (moderate clinical impact)
	D	Poor (slight or restricted clinical impact)
4. Generalisability *(how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?)*		
Study populations are the same as the target population	A	Excellent (directly generalisable to target population)
	B	Good (directly generalisable to target population with some caveats)
	C	Satisfactory (not directly generalisable to the target population but could be sensibly applied)
	D	Poor (not directly generalisable to target population and hard to judge whether it is sensible to apply)
5. Applicability *(the extent to which the body of evidence is directly applicable to Australian healthcare context)*		

Most included studies were from Europe. There are some differences in the healthcare system between Australia//New Zealand and included studies	A	**Excellent** (directly applicable to Australian healthcare context)
	B	**Good** (applicable to Australian healthcare context with few caveats)
	C	**Satisfactory** (probably applicable to Australian healthcare context with some caveats)
	D	**Poor** (not applicable to Australian healthcare context)

6. **Other factors** (*Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation)*

EVIDENCE STATEMENT *Please summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account. Please indicate any dissenting opinions*

In surgical patients there is insufficient evidence to determine the effect of prophylactic or therapeutic use of rFVIIa on the risk of thrombotic adverse events (Grade C)[182,183,185,188,190,191]

Component	Rating	Description
Evidence base	B	Good
Consistency	C	Satisfactory
Clinical impact	D	Poor
Generalisability	A	Excellent
Applicability	B	Good

Indicate any dissenting opinions

RECOMMENDATION *What recommendation (s) does the guideline development group draw from this evidence?*	GRADE OF RECOMMENDATION *(A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B)* C

Recommendation GN4.1 The prophylactic or routine therapeutic use of rFVIIa is not recommended because the studies performed to date have been inadequately powered to detect the effect of rFVIIa on morbidity and mortality. Concern still exists about the safety profile of rFVIIa, particularly in relation to thrombotic adverse events (Grade C).

This recommendation is based on the body of evidence for mortality (Evidence Statement GN4.1) and morbidity (Evidence Statement GN4.2)

UNRESOLVED ISSUES *If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up*

IMPLEMENTATION OF RECOMMENDATION

Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline.

Will this recommendation result in changes in usual care?	Yes	No
Are there any resource implications associated with the implementing this recommendation?	Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized?	Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation?	Yes	No

Key question What is the effect of rFVIIa (prophylaxis or treatment) on morbidity, mortality and transfusion rate? (GN4.3a) The body of evidence discussed below refers to the effect of prophylactic or therapeutic use of rFVIIa on transfusion requirements	Evidence table ref: Warren et al (2007)[181]; Ranucci et al (2008b)[183]; Essam (2007)[184]; Gill et al (2009)[185]; Pugliese et al (2007)[190]; and Sachs et al (2007)[191]	
1. Evidence base *(quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)*		
Six studies: two Level I studies, one with a high risk of bias[181] and one with a low risk of bias[183]; four Level II studies, three with a moderate risk of bias[184,185,191] and one with a high risk of bias[190]. Included studies were small and underpowered	A	Excellent (One or more Level I studies with a low risk of bias or several Level II studies with a low risk of bias)
	B	Good (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	Satisfactory (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	Poor (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. Consistency *(the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)*		
Most studies consistent—in general use of rFVIIa decreased transfusion requirements. However, prophylactic use of rFVIIa reduced transfusion requirements in adults[181] but had no effect in infants aged less than 1 year[181]. These studies were small and therefore underpowered for this outcome. Although the reduction in transfusion requirements was statistically significant in one Level I study with a low risk of bias[183], the effect of rFVIIa appears to vary between different surgical populations—I^2 results suggest moderate heterogeneity for this outcome across studies included in this Level I study[183]	A	Excellent (all studies consistent)
	B	Good (most studies consistent and inconsistency can be explained)
	C	Satisfactory (some inconsistency, reflecting genuine uncertainty around question)
	D	Poor (evidence is inconsistent)
	NA	Not applicable (one study only)
3. Clinical impact *(the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)*		
Reduction in transfusion requirements was statistically significant in one Level I study with a low risk of bias[183], with a clinically important benefit for the range of plausible effect estimates (95% CI values). However, there was variation in the effect of rFVIIa on transfusion requirements across different surgical populations[183], and any reduction in transfusion in cardiac surgery was not statistically significant[181,184,185]. Reductions in transfusion requirements were statistically significant when rFVIIa was used in liver transplant[190] and spinal surgery[191]. Overall there is uncertainty about the potential benefit of rFVIIa to reduce transfusion	A	Excellent (very large clinical impact)
	B	Good (substantial clinical impact)
	C	Satisfactory (moderate clinical impact)
	D	Poor (slight or restricted clinical impact)
4. Generalisability *(how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?)*		
Study populations are the same as the target population	A	Excellent (directly generalisable to target population)
	B	Good (directly generalisable to target population with some caveats)
	C	Satisfactory (not directly generalisable to the target population but could be sensibly applied)
	D	Poor (not directly generalisable to target population and hard to judge whether it is sensible to apply)

5. Applicability *(the extent to which the body of evidence is directly applicable to Australian healthcare context)*		
Most included studies were from Europe. There are some differences in the healthcare system between Australia/New Zealand and included studies	A	**Excellent** (directly applicable to Australian healthcare context)
	B	**Good** (applicable to Australian healthcare context with few caveats)
	C	**Satisfactory** (probably applicable to Australian healthcare context with some caveats)
	D	**Poor** (not applicable to Australian healthcare context)

6. Other factors (*Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation)*

EVIDENCE STATEMENT*Please summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account. Please indicate any dissenting opinions*

Overall Evidence Statement GN4.3

In surgical patients, the prophylactic or therapeutic use of rFVIIa reduces blood loss (Grade C)[191] and may reduce the incidence of transfusion (Grade C)[181,185,190,191]. In cardiac surgery patients, the prophylactic or therapeutic use of rFVIIa may also reduce the likelihood of re-operation (Grade C)[182,185]

Note: Evidence statements for transfusion requirements (GN4.3a), re-operation (GN4.3b) and blood loss (GN4.3c) were combined into one overall evidence statement

Component	Rating	Description
Evidence base	B	Good
Consistency	B	Good
Clinical impact	C	Satisfactory
Generalisability	A	Excellent
Applicability	C	Satisfactory

Indicate any dissenting opinions

RECOMMENDATION *What recommendation (s) does the guideline development group draw from this evidence?*	GRADE OF RECOMMENDATION *(A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B)*	
The prophylactic or routine therapeutic use of rFVIIa is not recommended. because concerns remain about its safety profile, particularly in relation to thrombotic adverse events (Grade C)		C

UNRESOLVED ISSUES *If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up*

IMPLEMENTATION OF RECOMMENDATION *Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline*

Will this recommendation result in changes in usual care?	Yes	No
Are there any resource implications associated with the implementing this recommendation?	Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized?	Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation?	Yes	No

Key question What is the effect of rFVIIa (prophylaxis or treatment) on morbidity, mortality and transfusion rate? (GN4.3b) The body of evidence discussed below refers to the effect of prophylactic or therapeutic use of rFVIIa on re-operation rate	**Evidence table ref:** Zangrillo et al (2009)[182]; Gill et al (2009)[185]	
1. **Evidence base** *(quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)*		
One Level I study[182] and one Level II study[185], both with a moderate risk of bias. Included studies were small and underpowered.	A	**Excellent** (One or more Level I studies with a low risk of bias or several Level II studies with a low risk of bias)
	B	**Good** (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	**Satisfactory** (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	**Poor** (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. **Consistency** *(the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)*		
The two studies provided consistent results (same direction of effect). However, analysis of heterogeneity in the Level I study showed a high degree of variability for the effect of rFVIIa on re-operation rate across studies included in the meta-analysis[182]	A	**Excellent** (all studies consistent)
	B	**Good** (most studies consistent and inconsistency can be explained)
	C	**Satisfactory** (some inconsistency, reflecting genuine uncertainty around question)
	D	**Poor** (evidence is inconsistent)
	NA	**Not applicable** (one study only)
3. **Clinical impact** *the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)*		
Re-operation rate was reduced, but results were only statistically significant only for one rFVIIa (low dose) treatment group in one small, underpowered study[185]. Analysis of heterogeneity indicates a variable effect of rFVIIa on re-operation rates in different types of cardiac surgery. Therefore, it is unclear whether rFVIIa use reduces the re-operation rate in all types of cardiac surgery	A	**Excellent** (very large clinical impact)
	B	**Good** (substantial clinical impact)
	C	**Satisfactory** (moderate clinical impact)
	D	**Poor** (slight or restricted clinical impact)
4. **Generalisability** *(how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?)*		
Study populations are the same as the target population	A	**Excellent** (directly generalisable to target population)
	B	**Good** (directly generalisable to target population with some caveats)
	C	**Satisfactory** (not directly generalisable to the target population but could be sensibly applied)
	D	**Poor** (not directly generalisable to target population and hard to judge whether it is sensible to apply)
5. **Applicability** *(the extent to which the body of evidence is directly applicable to Australian healthcare context)*		
Most included studies were from Europe. There are some differences in the healthcare system between Australia/New Zealand and included studies	A	**Excellent** (directly applicable to Australian healthcare context)
	B	**Good** (applicable to Australian healthcare context with few caveats)
	C	**Satisfactory** (probably applicable to Australian healthcare context with some caveats)

	D	Poor (not applicable to Australian healthcare context)

6. Other factors (*Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation)*

EVIDENCE STATEMENT *Please summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account. Please indicate any dissenting opinions*

Overall Evidence Statement GN4.3

In surgical patients the prophylactic or therapeutic use of rFVIIa reduces blood loss (Grade C)[191] and may reduce the incidence of transfusion (Grade C)[181,183,185,190,191]. In cardiac surgery patients, the prophylactic or therapeutic use of rFVIIa may also reduce the likelihood of re-operation (Grade C)[182,185]

Note: Evidence statements for transfusion requirements (GN4.3a), re-operation (GN4.3b) and blood loss (GN4.3c) were combined into one overall evidence statement

Component	Rating	Description
Evidence base	C	Satisfactory
Consistency	B	Good
Clinical impact	C	Satisfactory
Generalisability	A	Excellent
Applicability	C	Satisfactory

Indicate any dissenting opinions

RECOMMENDATION *What recommendation (s) does the guideline development group draw from this evidence?* The prophylactic or routine therapeutic use of rFVIIa is not recommended. because concerns remain about its safety profile, particularly in relation to thrombotic adverse events (Grade C)	GRADE OF RECOMMENDATION *(A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B)*	C

UNRESOLVED ISSUES *If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up*

IMPLEMENTATION OF RECOMMENDATION *Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline*

Will this recommendation result in changes in usual care?	Yes	No
Are there any resource implications associated with the implementing this recommendation?	Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized?	Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation?	Yes	No

Key question What is the effect of rFVIIa (prophylaxis or treatment) on morbidity, mortality and transfusion rate? (GN4.3c) The body of evidence discussed below refers to the effect of prophylactic or therapeutic use of rFVIIa on blood loss	Evidence table ref: Pugliese et al (2007)[190]; and Sachs et al (2007)[191]	
1. Evidence base *(quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)*		
Two Level II studies, one with a moderate risk of bias[191] and one with a high risk of bias[190]. Included studies were small and underpowered	A	Excellent (One or more Level I studies with a low risk of bias or several Level II studies with a low risk of bias)
	B	Good (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	Satisfactory (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	Poor (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. Consistency *(the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)*		
Similar direction of effect in two studies, one on liver transplant patients[190] (prophylactic rFVIIa) and the other on spinal surgery patients [191] (therapeutic rFVIIa).	A	Excellent (all studies consistent)
	B	Good (most studies consistent and inconsistency can be explained)
	C	Satisfactory (some inconsistency, reflecting genuine uncertainty around question)
	D	Poor (evidence is inconsistent)
	NA	Not applicable (one study only)
3. Clinical impact *(the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)*		
Evidence from three small studies employing rFVIIa in different surgical procedures suggests that blood loss is reduced. Reductions in blood loss in two studies were statistically significant[190,191], with a clinically important benefit observed for the estimated range of effects (95% CI) in one study[191]. Further evidence is required to establish whether this benefit is observed when rFVIIa is used in other surgical procedures	A	Excellent (very large clinical impact)
	B	Good (substantial clinical impact)
	C	Satisfactory (moderate clinical impact)
	D	Poor (slight or restricted clinical impact)
4. Generalisability *(how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?)*		
Study populations are the same as the target population	A	Excellent (directly generalisable to target population)
	B	Good (directly generalisable to target population with some caveats)
	C	Satisfactory (not directly generalisable to the target population but could be sensibly applied)
	D	Poor (not directly generalisable to target population and hard to judge whether it is sensible to apply)

5. Applicability *(the extent to which the body of evidence is directly applicable to Australian healthcare context)*		
One study from Europe[190] and one from the USA[191]	A	**Excellent** (directly applicable to Australian healthcare context)
	B	**Good** (applicable to Australian healthcare context with few caveats)
	C	**Satisfactory** (probably applicable to Australian healthcare context with some caveats)
	D	**Poor** (not applicable to Australian healthcare context)

6. Other factors (*Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation)*

EVIDENCE STATEMENT *Please summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account. Please indicate any dissenting opinions.*

Overall Evidence Statement GN4.3

In surgical patients the prophylactic or therapeutic use of rFVIIa reduces blood loss (Grade C) [190,191] and may reduce the incidence of transfusion (Grade C)[181,183,185,190,191]. In cardiac surgery patients, the prophylactic or therapeutic use of rFVIIa may also reduce the likelihood of re-operation (Grade C)[182,185]

Note: Evidence statements for transfusion requirements (GN4.3a), re-operation (GN4.3b) and blood loss (GN4.3c) were combined into one overall evidence statement

Component	Rating	Description
Evidence base	C	Satisfactory
Consistency	B	Good
Clinical impact	C	Satisfactory
Generalisability	A	Excellent
Applicability	C	Satisfactory

Indicate any dissenting opinions

RECOMMENDATION *What recommendation (s) does the guideline development group draw from this evidence?*	GRADE OF RECOMMENDATION *(A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B)*	
The prophylactic or routine therapeutic use of rFVIIa is not recommended. because concerns remain about its safety profile, particularly in relation to thrombotic adverse events (Grade C)		C

UNRESOLVED ISSUES*If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up*

IMPLEMENTATION OF RECOMMENDATION *Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline*

Will this recommendation result in changes in usual care?	Yes	No
Are there any resource implications associated with the implementing this recommendation?	Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized?	Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation?	Yes	No

Key question What is the effect of rFVIIa (prophylaxis or treatment) on morbidity, mortality and transfusion rate? (GN4.4) The body of evidence discussed below refers to the effect of prophylactic or therapeutic use of rFVIIa on ICU and hospital length of stay		**Evidence table ref:** Johansson et al (2007)[188]; Pugliese et al (2007)[190]
1. **Evidence base** *(quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)*		
Two Level II studies, one with a moderate risk of bias[188] and one with a high risk of bias[190]	A	**Excellent** (One or more Level I studies with a low risk of bias or several Level II studies with a low risk of bias)
	B	**Good** (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	**Satisfactory** (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	**Poor** (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. **Consistency** *(the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)*		
Consistent results between studies—prophylactic rFVIIa use had no statistically significant effect on ICU or hospital LOS.	A	**Excellent** (all studies consistent)
	B	**Good** (most studies consistent and inconsistency can be explained)
	C	**Satisfactory** (some inconsistency, reflecting genuine uncertainty around question)
	D	**Poor** (evidence is inconsistent)
	NA	**Not applicable** (one study only)
3. **Clinical impact** *(the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)*		
Based on the findings of two small studies, prophylactic rFVIIa appears to have no benefit for this outcome. This evidence base is too small to make definitive conclusions regarding the effect of rFVIIa on ICU or hospital LOS.	A	**Excellent** (very large clinical impact)
	B	**Good** (substantial clinical impact)
	C	**Satisfactory** (moderate clinical impact)
	D	**Poor** (slight or restricted clinical impact)
4. **Generalisability** *(how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?)*		
Study populations are the same as the target population	A	**Excellent** (directly generalisable to target population)
	B	**Good** (directly generalisable to target population with some caveats)
	C	**Satisfactory** (not directly generalisable to the target population but could be sensibly applied)
	D	**Poor** (not directly generalisable to target population and hard to judge whether it is sensible to apply)
5. **Applicability** *(the extent to which the body of evidence is directly applicable to Australian healthcare context)*		
One study conducted in the USA[190], the other conducted in Denmark[188]. There are some differences in the healthcare system between Australia/New Zealand and included studies	A	**Excellent** (directly applicable to Australian healthcare context)
	B	**Good** (applicable to Australian healthcare context with few caveats)
	C	**Satisfactory** (probably applicable to Australian healthcare context with some caveats)
	D	**Poor** (not applicable to Australian healthcare context)
6. **Other factors** (*Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation)*		

EVIDENCE STATEMENT *Please summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account. Please indicate any dissenting opinions.*		
In surgical patients, there is insufficient evidence to determine the impact of prophylactic or therapeutic use of rFVIIa on hospital or ICU LOS (Grade D)[188,190]		
Component	Rating	Description
Evidence base	C	Satisfactory
Consistency	B	Good
Clinical impact	D	Poor
Generalisability	A	Excellent
Applicability	C	Satisfactory
Indicate any dissenting opinions		

RECOMMENDATION *What recommendation (s) does the guideline development group draw from this evidence?*	GRADE OF RECOMMENDATION *(A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B)*	
No recommendation was made because there was insufficient evidence and the overall rating of the evidence statement was D.		NA

UNRESOLVED ISSUES *If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up*		
IMPLEMENTATION OF RECOMMENDATION *Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline.*		
Will this recommendation result in changes in usual care?	Yes	No
Are there any resource implications associated with the implementing this recommendation?	Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized?	Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation?	Yes	No

D8 Evidence matrix, Question 8

What is the effect of fresh frozen plasma, cryoprecipitate, fibrinogen concentrate, and/or platelet transfusion on patient outcome?

Key question What is the effect of fresh frozen plasma (FFP) on morbidity outcomes in patients undergoing cardiac surgery? (GN5.1)		Evidence table ref: Casbard et al (2004)[192]
1. Evidence base *(quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)*		
One Level I study with a low risk of bias[192]. See table 1 in Casbard et al (2004)	A	Excellent (One or more Level I studies with a low risk of bias or several Level II studies with a low risk of bias)
	B	Good (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	Satisfactory (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	Poor (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. Consistency *(the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)*		
Although only one study was included in the evidence, this study was a systematic review of six studies. The included studies showed similar non-significant results	A	Excellent (all studies consistent)
	B	Good (most studies consistent and inconsistency can be explained)
	C	Satisfactory (some inconsistency, reflecting genuine uncertainty around question)
	D	Poor (evidence is inconsistent)
	NA	Not applicable (one study only)
3. Clinical impact *(the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)*		
The studies reported a small, not clinically relevant clinical impact.	A	Excellent (very large clinical impact)
	B	Good (substantial clinical impact)
	C	Satisfactory (moderate clinical impact)
	D	Poor (slight or restricted clinical impact)
4. Generalisability *(how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?)*		
All studies were performed in a perioperative patient population involving cardiac surgery	A	Excellent (directly generalisable to target population)
	B	Good (directly generalisable to target population with some caveats)
	C	Satisfactory (not directly generalisable to the target population but could be sensibly applied)
	D	Poor (not directly generalisable to target population and hard to judge whether it is sensible to apply)

5. Applicability *(the extent to which the body of evidence is directly applicable to Australian healthcare context)*		
Of the six studies included in the systematic review, three were conducted in Germany and one each in the USA, Israel and the Netherlands	A	Excellent (directly applicable to Australian healthcare context)
	B	Good (applicable to Australian healthcare context with few caveats)
	C	Satisfactory (probably applicable to Australian healthcare context with some caveats)
	D	Poor (not applicable to Australian healthcare context)

6. Other factors (*Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation)*		
EVIDENCE STATEMENT *Please summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account. Please indicate any dissenting opinions*		
The prophylactic administration of fresh frozen plasma following cardiopulmonary bypass does not reduce perioperative blood loss (Grade B)		
Component	Rating	Description
Evidence base	B	Good
Consistency	B	Good
Clinical impact	D	Poor
Generalisability	B	Good
Applicability	C	Satisfactory
Indicate any dissenting opinions		

RECOMMENDATION *What recommendation (s) does the guideline development group draw from this evidence?*	GRADE OF RECOMMENDATION *(A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B)*	B
Recommendation GN5.1 The prophylactic use of fresh frozen plasma in cardiac surgery is not recommended (Grade B) This recommendation is derived from a combination of evidence statements GN5.1 and GN5.2		
UNRESOLVED ISSUES *If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up*		
IMPLEMENTATION OF RECOMMENDATION *Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline*		
Will this recommendation result in changes in usual care? Reduce any prophylactic use of fresh frozen plasma in cardiac surgery	Yes	No
Are there any resource implications associated with the implementing this recommendation?	Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized?	Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation?	Yes	No

Key question What is the effect of fresh frozen plasma (FFP) on infection outcomes in patients undergoing surgery? (GN5.2)	Evidence table ref: Sarani et al (2008)[193]	
1. Evidence base *(quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)*		
One Level III study with a moderate risk of bias[193]	A	Excellent (One or more Level I studies with a low risk of bias or several Level II studies with a low risk of bias)
	B	Good (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	Satisfactory (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	Poor (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. Consistency *(the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)*		
Only one available study	A	Excellent (all studies consistent)
	B	Good (most studies consistent and inconsistency can be explained)
	C	Satisfactory (some inconsistency, reflecting genuine uncertainty around question)
	D	Poor (evidence is inconsistent)
	NA	Not applicable (one study only)
3. Clinical impact *(the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)*		
The study reported a moderate clinical impact	A	Excellent (very large clinical impact)
	B	Good (substantial clinical impact)
	C	Satisfactory (moderate clinical impact)
	D	Poor (slight or restricted clinical impact)
4. Generalisability *(how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?)*		
The single study was performed in any surgical patients (with the exception of trauma) who were admitted to the ICU. While this most likely covered a wide range of surgeries, it may bias towards a more severely ill ICU population	A	Excellent (directly generalisable to target population)
	B	Good (directly generalisable to target population with some caveats)
	C	Satisfactory (not directly generalisable to the target population but could be sensibly applied)
	D	Poor (not directly generalisable to target population and hard to judge whether it is sensible to apply)
5. Applicability *(the extent to which the body of evidence is directly applicable to Australian healthcare context)*		
Study performed in the USA	A	Excellent (directly applicable to Australian healthcare context)
	B	Good (applicable to Australian healthcare context with few caveats)
	C	Satisfactory (probably applicable to Australian healthcare context with some caveats)
	D	Poor (not applicable to Australian healthcare context)
6. Other factors (*Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation)*		

EVIDENCE STATEMENT *Please summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account. Please indicate any dissenting opinions*		
Administration of fresh frozen plasma to a post-surgical population in intensive care is associated with an increase in the rate of infection (Grade C)		
Component	Rating	Description
Evidence base	C	Satisfactory
Consistency	NA	Not applicable
Clinical impact	C	Satisfactory
Generalisability	C	Satisfactory
Applicability	C	Satisfactory
Indicate any dissenting opinions		

RECOMMENDATION *What recommendation (s) does the guideline development group draw from this evidence?*	GRADE OF RECOMMENDATION *(A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B)*	B
Recommendation GN5.1 The prophylactic use of fresh frozen plasma in cardiac surgery is not recommended (Grade B) This recommendation is derived from a combination of evidence statements GN5.1 and GN5.2		
UNRESOLVED ISSUES *If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up*		
IMPLEMENTATION OF RECOMMENDATION *Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline*		
Will this recommendation result in changes in usual care? Reduce any prophylactic use of fresh frozen plasma in cardiac surgery	Yes	No
Are there any resource implications associated with the implementing this recommendation?	Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized?	Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation?	Yes	No

Key question What is the effect of platelet transfusion on mortality in patients undergoing cardiac surgery? (GN5.3a)		Evidence table ref: Karkouti et al (2006b)[194]; McGrath et al (2008)[195]; Spiess et al (2004)[196]
1. Evidence base *(quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)*		
Three Level III studies with a low risk of bias[194–196]	A	**Excellent** (One or more Level I studies with a low risk of bias or several Level II studies with a low risk of bias)
	B	**Good** (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	**Satisfactory** (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	**Poor** (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. Consistency *(the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)*		
One of the three studies showed contrasting results[196]. This study was smaller than the other two[194,195], and a comparatively small number of patients received platelet transfusion	A	**Excellent** (all studies consistent)
	B	**Good** (most studies consistent and inconsistency can be explained)
	C	**Satisfactory** (some inconsistency, reflecting genuine uncertainty around question)
	D	**Poor** (evidence is inconsistent)
	NA	**Not applicable** (one study only)
3. Clinical impact *(the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)*		
The studies showed a substantial clinical impact	A	**Excellent** (very large clinical impact)
	B	**Good** (substantial clinical impact)
	C	**Satisfactory** (moderate clinical impact)
	D	**Poor** (slight or restricted clinical impact)
4. Generalisability *(how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?)*		
The studies were all performed in patients undergoing cardiac surgery	A	**Excellent** (directly generalisable to target population)
	B	**Good** (directly generalisable to target population with some caveats)
	C	**Satisfactory** (not directly generalisable to the target population but could be sensibly applied)
	D	**Poor** (not directly generalisable to target population and hard to judge whether it is sensible to apply)
5. Applicability *(the extent to which the body of evidence is directly applicable to Australian healthcare context)*		
One study was conducted in Canada, one in the USA, and the other was a multicentre study performed in 37 institutions: one in Denmark, two in Israel, and 34 in the USA	A	**Excellent** (directly applicable to Australian healthcare context)
	B	**Good** (applicable to Australian healthcare context with few caveats)
	C	**Satisfactory** (probably applicable to Australian healthcare context with some caveats)
	D	**Poor** (not applicable to Australian healthcare context)
6. Other factors (*Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation)*		

EVIDENCE STATEMENT *Please summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account. Please indicate any dissenting opinions*		
In patients undergoing cardiac surgery, platelet transfusion may be associated with an increase in mortality (Grade C) [194–196]		
Component	Rating	Description
Evidence base	B	Good
Consistency	C	Satisfactory
Clinical impact	B	Good
Generalisability	B	Good
Applicability	C	Satisfactory
Indicate any dissenting opinions		

RECOMMENDATION *What recommendation (s) does the guideline development group draw from this evidence?* No recommendation was made as the biological basis for an increase in death with platelet use is unclear given the lack of trend in the morbidity data (see GN5.3b).	GRADE OF RECOMMENDATION *(A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B)*	NA
UNRESOLVED ISSUES *If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up*		
IMPLEMENTATION OF RECOMMENDATION *Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline*		

Will this recommendation result in changes in usual care?	Yes	No
Are there any resource implications associated with the implementing this recommendation?	Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized?	Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation?	Yes	No

Key question What is the effect of platelet transfusion on morbidity in patients undergoing cardiac surgery? (GN5.3b)		Evidence table ref: Karkouti et al (2006b)[194]; McGrath et al (2008)[195]; Spiess et al (2004)[196]
1. Evidence base *(quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)*		
Three Level III studies with a low risk of bias[194–196]	A	**Excellent** (One or more Level I studies with a low risk of bias or several Level II studies with a low risk of bias)
	B	**Good** (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	**Satisfactory** (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	**Poor** (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. Consistency *(the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)*		
One study [194] reported no effect. One study reported a significant effect on return to OR for bleeding[195] and another study[196] reported a non-signficant effect on stroke.	A	**Excellent** (all studies consistent)
	B	**Good** (most studies consistent and inconsistency can be explained)
	C	**Satisfactory** (some inconsistency, reflecting genuine uncertainty around question)
	D	**Poor** (evidence is inconsistent)
	NA	**Not applicable** (one study only)
3. Clinical impact *(the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)*		
The studies showed a substantial clinical impact	A	**Excellent** (very large clinical impact)
	B	**Good** (substantial clinical impact)
	C	**Satisfactory** (moderate clinical impact)
	D	**Poor** (slight or restricted clinical impact)
4. Generalisability *(how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?)*		
The studies were all performed in patients undergoing cardiac surgery	A	**Excellent** (directly generalisable to target population)
	B	**Good** (directly generalisable to target population with some caveats)
	C	**Satisfactory** (not directly generalisable to the target population but could be sensibly applied)
	D	**Poor** (not directly generalisable to target population and hard to judge whether it is sensible to apply)
5. Applicability *(the extent to which the body of evidence is directly applicable to Australian healthcare context)*		
One study was conducted in Canada, one in the USA, and the other was a multicentre study performed in 37 institutions: one in Denmark, two in Israel, and 34 in the USA	A	**Excellent** (directly applicable to Australian healthcare context)
	B	**Good** (applicable to Australian healthcare context with few caveats)
	C	**Satisfactory** (probably applicable to Australian healthcare context with some caveats)
	D	**Poor** (not applicable to Australian healthcare context)
6. Other factors (*Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation)*		

EVIDENCE STATEMENT *Please summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account. Please indicate any dissenting opinions*			
In patients undergoing cardiac surgery, the effect of platelet transfusion on morbidity is uncertain (Grade C) [194–196]			
Component	Rating	Description	
Evidence base	B	Good	
Consistency	C	Satisfactory	
Clinical impact	B	Good	
Generalisability	B	Good	
Applicability	C	Satisfactory	
Indicate any dissenting opinions			
RECOMMENDATION *What recommendation (s) does the guideline development group draw from this evidence?* No recommendation was made due to inconsistency in the direction of results.		GRADE OF RECOMMENDATION *(A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B)*	NA
UNRESOLVED ISSUES *If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up*			
IMPLEMENTATION OF RECOMMENDATION *Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline*			
Will this recommendation result in changes in usual care?		Yes	No
Are there any resource implications associated with the implementing this recommendation?		Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized?		Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation?		Yes	No

D9 Evidence matrix, Question 9

At what INR (or PT/APTT) for fresh frozen plasma, fibrinogen level for cryoprecipitate, platelet count for platelet concentrates should patients be transfused to avoid risks of significant adverse events?

Key question What is the INR or platelet threshold in patients undergoing invasive procedures? (GN6.1)	Evidence table ref: Dillon et al (1994)[197]; McVay et al (1990)[198]; Misra et al (2008)[199]; Ray and Shenoy (1997)[200]; Fisher and Mutimer (1999)[201]; Weigand et al (2009)[202]; Foster et al (1992)[203]; Doerfler et al (1996)[204]; Martin et al (2000)[205]; Mainwaring et al (1998)[206]; Howard et al (2000)[207]; Vavricka et al (2003)[208]; Ruell et al (2007)[209]; Darcy et al (1996)[210]; Weiss et al (1993)[211]; Wolf et al (2007)[212]	
1. Evidence base *(quantity, level, methodological quality and relevance to patients of the body of evidence for this question, based on critical appraisal of each individual study according to Minimum Requirements)*		
The evidence base consists of two Level II studies with a low risk of bias[201,210]; four Level II studies with a moderate risk of bias[197,200,202,211]; two Level III studies with a low risk of bias[204,207]; and eight Level III studies with a moderate risk of bias[198,199,203,205,206,208,209,212].	A	**Excellent** (One or more Level I studies with a low risk of bias or several Level II studies with a low risk of bias)
	B	**Good** (One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias)
	C	**Satisfactory** (One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias)
	D	**Poor** (Level IV studies or Level I to III studies/SRs with a high risk of bias)
2. Consistency *(the degree of consistency demonstrated by the available evidence. Where there are conflicting results indicate how the group formed a judgement as to the overall direction of the evidence)*		
All studies were consistent	A	**Excellent** (all studies consistent)
	B	**Good** (most studies consistent and inconsistency can be explained)
	C	**Satisfactory** (some inconsistency, reflecting genuine uncertainty around question)
	D	**Poor** (evidence is inconsistent)
	NA	**Not applicable** (one study only)
3. Clinical impact *(the potential impact of recommendation ie. size of patient population, relevance of outcomes to the question, balance of risks and benefits, relative benefit over other management options, resource and organisational implications)*		
Slight clinical impact	A	**Excellent** (very large clinical impact)
	B	**Good** (substantial clinical impact)
	C	**Satisfactory** (moderate clinical impact)
	D	**Poor** (slight or restricted clinical impact)
4. Generalisability *(how reasonable is it to generalise from the results of the studies used as evidence to the target population for this guideline?)*		
The evidence consisted of studies performed in patients undergoing various types of invasive procedures and is probably generalisable to a wider population undergoing invasive procedures	A	**Excellent** (directly generalisable to target population)
	B	**Good** (directly generalisable to target population with some caveats)
	C	**Satisfactory** (not directly generalisable to the target population but could be sensibly applied)

	D	Poor (not directly generalisable to target population and hard to judge whether it is sensible to apply)
5. Applicability *(the extent to which the body of evidence is directly applicable to Australian healthcare context)*		
Ten studies were conducted in the USA, four in the UK, one in Germany and one in Switzerland	A	Excellent (directly applicable to Australian healthcare context)
	B	Good (applicable to Australian healthcare context with few caveats)
	C	Satisfactory (probably applicable to Australian healthcare context with some caveats)
	D	Poor (not applicable to Australian healthcare context)
6. Other factors (*Indicate here any other factors that you took into account when assessing the evidence base, eg. issues that might cause the group to downgrade or upgrade the recommendation)*		

EVIDENCE STATEMENT

Please summarise the development group's synthesis of the evidence relating to the key question, taking all the above factors into account. Please indicate any dissenting opinions.

In patients undergoing invasive procedures, including biopsies (visceral, endoscopic and laparoscopic), central venous cannulation, lumbar puncture, nephrostomy and femoral arteriography, there is insufficient evidence to define a threshold platelet count, fibrinogen level or INR that is associated with significant adverse events (Grade B)[197–212]. Worsening thrombocytopenia may be associated with an increase in minor bleeding complications (Grade B) [198,201,204,208,210]

Component	Rating	Description
Evidence base	B	Good
Consistency	A	Excellent
Clinical impact	D	Poor
Generalisability	B	Good
Applicability	B	Good

Indicate any dissenting opinions

RECOMMENDATION *What recommendation (s) does the guideline development group draw from this evidence?*	GRADE OF RECOMMENDATION *(A recommendation cannot be graded A or B unless the evidence base and consistency of evidence are both either A or B).*	NA

No recommendation was made because this was a prognostic question and no intervention was tested thus a course of action cannot be recommended. Further, clinical impact was minimal.

UNRESOLVED ISSUES

If needed, keep note of specific issues that arise when each recommendation is formulated and that require follow-up

IMPLEMENTATION OF RECOMMENDATION

Please indicate Yes or No to the following questions. Where the answer is Yes please provide explanatory information about this to assist in developing the implementation plan for the guideline.

Will this recommendation result in changes in usual care?	Yes	No
Are there any resource implications associated with the implementing this recommendation?	Yes	No
Will the implementation of this recommendation require changes in the way care is currently organized?	Yes	No
Is the guideline development group aware of any barriers to the implementation of this recommendation?	Yes	No

Appendix E: Quality analyses

E1 Quality analysis, Question 1

What is the effect of a multidisciplinary, multimodal, programmatic approach to perioperative patient blood management on patient outcomes?

Systematic review

Citation	Ferraris et al (2007)[27]
☒	A. Was a clinical question clearly defined?
☐	B. Was an adequate search strategy used?
☐	C. Were the inclusion criteria appropriate and applied in an unbiased way?
☒	D. Was a quality assessment of included studies undertaken?
☐	E. Were the characteristics and results if the individual studies appropriately summarised?
☐	Were the methods for pooling the data appropriate?
☐	Were the sources of heterogeneity explored?
Comments	The search strategy was not clearly described and the inclusions and results from individual studies included were not adequately reported
Overall assessment	Poor

Cohort studies

Citation	Brevig et al (2009)[31]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☐	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments:	Brevig et al (2009) was a pre-post study with complete follow up and no exclusions from analysis
Overall assessment	Poor

Citation	Bui et al (2002)[32]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☐	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	Bui et al (2002) was a pre-post study
Overall assessment	Poor

Citation	DeAnda et al (2006)[29]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☐	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	DeAnda et al (2006) was a pre-post study with complete follow-up and no exclusions from analysis
Overall assessment	Poor

Citation	Freedman et al (2005)[28]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☐	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	Freedman et al (2005) was a pre-post study. Follow-up was complete and there were no exclusions from analysis.
Overall assessment	Poor

Citation	Freedman et al (2008)[30]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☐	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	Freedman et al (2008) was a pre-post study with complete follow up and no exclusions from analysis
Overall assessment	Poor

Case reports

Citation	Bolan et al (2001)[33]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☐	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☐	F. Was follow-up complete and were there exclusions from analysis?
Comments	Bolan et al (2001) was a case study with no comparator
Overall assessment	Poor

E2 Quality analysis, Question 2

Cardiac surgery

In patients undergoing surgery or invasive procedures, what effect does the cessation and timing of cessation of medications that affect haemostasis have on morbidity, mortality and transfusion requirements?

Randomised controlled trial

Citation	Ghaffarinejad et al (2007)[35]
☐	A. Was the allocation to treatment groups concealed from those responsible for recruiting subjects?
☐	B. Was the study double-blinded?
☒	C. Were patient characteristics and demographics similar between treatment arms at baseline?
☒	D. Were all randomised patients included in the analysis?
☒	E. Were the statistical methods appropriate?
☐	F. Were any subgroup analyses carried out?
Comments	
Overall assessment	Fair

Cohort studies

Citation	Ascione et al (2005)[39]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☐	E. Was follow-up long enough for outcomes to occur?
☐	F. Was follow-up complete and were there exclusions from analysis?
Comments	No blinding reported; follow up time not reported
Overall assessment	Poor

Citation	Berger et al (2008)[40]
☐	A. How were subjects selected for the 'new' intervention?
☒	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐NA	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	Chu et al (2004)[41]
☒	A. How were subjects selected for the 'new' intervention?
☒	B. How were subjects selected for the comparison or control group?
☐	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	Gerrah et al (2005)[36]
☒	A. How were subjects selected for the 'new' intervention?
☒	B. How were subjects selected for the comparison or control group?
☐	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	Gulbins et al (2009)[37]
☒	A. How were subjects selected for the 'new' intervention?
☒	B. How were subjects selected for the comparison or control group?
☐	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	Kamran et al (2008)[38]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☐	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	No details on how patients were selected for different interventions.
Overall assessment	Poor

Citation	Kang et al (2007)[45]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☐	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	Not reported as to why clopidogrel stopped at different times for different patients
Overall assessment	Poor

Citation	Kapetanakis et al (2006)[42]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐NA	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	Retrospective database review—no blinding done. Reasons for different ACT regimens not reported
Overall assessment	Fair

Citation	Picker et al (2007)[46]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☐	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Poor

Citation	Shim et al (2007)[43]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☐	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	No details on how patients were selected for different interventions. Also, no follow-up beyond hospital discharge
Overall assessment	Poor

Citation	Song et al (2008)[44]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☐	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Poor

Citation	Weightman et al (2002)[47]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☐	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	Reasons for stopping aspirin at different time not reported
Overall assessment	Poor

Noncardiac surgery

In patients before noncardiac surgery or invasive procedures, what effect does the cessation and timing of cessation of medication that affect haemostasis have on morbidity, mortality, and red blood cell transfusion?

Systematic reviews

Citation	Burger et al (2005)[48]
☒	A. Was a clinical question clearly defined?
☒	B. Was an adequate search strategy used?
☒	C. Were the inclusion criteria appropriate and applied in an unbiased way?
☐	D. Was a quality assessment of included studies undertaken?
☐	E. Were the characteristics and results of the individual studies appropriately summarised?
☒	F. Were the methods for pooling the data appropriate?
☐	G. Were the sources of heterogeneity explored?
Overall assessment	Fair

Citation	Dunn et al (2003)[49]
☒	A. Was a clinical question clearly defined?
☒	B. Was an adequate search strategy used?
☒	C. Were the inclusion criteria appropriate and applied in an unbiased way?
☐	D. Was a quality assessment of included studies undertaken?
☐	E. Were the characteristics and results of the individual studies appropriately summarised?
☒	F. Were the methods for pooling the data appropriate?
☐	G. Were the sources of heterogeneity explored?
Overall assessment	Fair

Citation	Nematullah et al (2009)[50]
☒	A. Was a clinical question clearly defined?
☒	B. Was an adequate search strategy used?
☒	C. Were the inclusion criteria appropriate and applied in an unbiased way?
☒	D. Was a quality assessment of included studies undertaken?
☒	E. Were the characteristics and results of the individual studies appropriately summarised?
☒	F. Were the methods for pooling the data appropriate?
☐	G. Were the sources of heterogeneity explored?
Overall assessment	Good

Randomised controlled trials

Citation	Devani et al (1998)[56]
☐	A. Was the allocation to treatment groups concealed from those responsible for recruiting subjects?
☐	B. Was the study double-blinded?
☐	C. Were patient characteristics and demographics similar between treatment arms at baseline?
☒	D. Were all randomised patients included in the analysis?
☐	E. Were the statistical methods appropriate?
☐	F. Were any subgroup analyses carried out?
Overall assessment	Poor

Citation	Campbell et al (2000)[57]
☐	A. Was the allocation to treatment groups concealed from those responsible for recruiting subjects?
☐	B. Was the study double-blinded?
☐	C. Were patient characteristics and demographics similar between treatment arms at baseline?
☒	D. Were all randomised patients included in the analysis?
☒	E. Were the statistical methods appropriate?
☐	F. Were any subgroup analyses carried out?
Overall assessment	Poor

Citation	El-Jack et al (2006)[58]
☒	A. Was the allocation to treatment groups concealed from those responsible for recruiting subjects?
☐	B. Was the study double-blinded?
☒	C. Were patient characteristics and demographics similar between treatment arms at baseline?
☒	D. Were all randomised patients included in the analysis?
☒	E. Were the statistical methods appropriate?
☐	F. Were any subgroup analyses carried out?
Overall assessment	Fair

Citation	Slappendel et al (2002)[52]
☒	A. Was the allocation to treatment groups concealed from those responsible for recruiting subjects?
☒	B. Was the study double-blinded?
☒	C. Were patient characteristics and demographics similar between treatment arms at baseline?
☒	D. Were all randomised patients included in the analysis?
☒	E. Were the statistical methods appropriate?
☐	F. Were any subgroup analyses carried out?
Overall assessment	Good

Cohort studies

Citation	Krishnan et al (2008)[51]
☒	A. How were subjects selected for the 'new' intervention?
☒	B. How were subjects selected for the comparison or control group?
☐	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Overall assessment	Fair

Citation	Ozao-Choy et al (2008)[55]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☐	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comment	Groups not matched (67% of subjects had urgent surgery in the clopidogrel group vs 13% in the control group). There was no attempt to control for confounding.
Overall assessment	Poor

Citation	Wysokinski et al (2008)[59]
☒	A. How were subjects selected for the 'new' intervention?
☒	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☒	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☐	F. Was follow-up complete and were there exclusions from analysis?
Overall assessment	Good

Citation	McLemore et al (2006)[60]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☐	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☒	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Overall assessment	Fair

Citation	Robinson et al (1993)[53]
☒	A. How were subjects selected for the 'new' intervention?
☒	B. How were subjects selected for the comparison or control group?
☐	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Overall assessment	Fair

Citation	An et al (1991)[54]
☒	A. How were subjects selected for the 'new' intervention?
☒	B. How were subjects selected for the comparison or control group?
☐	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Overall assessment	Fair

E3 Quality analysis, Question 3

In patients undergoing surgery, what is the effect of perioperative strategies that minimise blood loss on morbidity, mortality, and blood transfusion?

The body of evidence found by the systematic literature review and associated appendixes for Perioperative Foreground Question 3 are presented in a separate report.

E4 Quality analysis, Question 4

Is anaemia an independent risk factor for adverse outcomes?

Systematic review

Citation	Shander et al (2004)[61]
☒	A. Was a clinical question clearly defined?
☒	B. Was an adequate search strategy used?
☒	C. Were the inclusion criteria appropriate and applied in an unbiased way?
☐	D. Was a quality assessment of included studies undertaken?
☒	E. Were the characteristics and results of the individual studies appropriately summarised?
☐	Were the methods for pooling the data appropriate?
☐	Were the sources of heterogeneity explored?
Comments	This was not a well performed syatematic review. No studies were assessed on quality
Overall assessment	Fair

Cohort studies

Citation	DeFoe et al (2001)[62]
☒	A. How were subjects selected for the 'new' intervention?
☒	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Good

Citation	Gombotz et al (2007)[63]
☒	A. How were subjects selected for the 'new' intervention?
☒	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☒	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☐	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Good

Citation	Koch et al (2003)[64]
☒	A. How were subjects selected for the 'new' intervention?
☒	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Good

Citation	Kulier et al (2007)[65]
☒	A. How were subjects selected for the 'new' intervention?
☒	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☒	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Good

Citation	Lee et al (2007)[66]
☒	A. How were subjects selected for the 'new' intervention?
☒	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☐	E. Was follow-up long enough for outcomes to occur?
☐	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	Parr et al (2003)[67]
☒	A. How were subjects selected for the 'new' intervention?
☒	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Good

Citation	Rady et al (1998)[68]
☒	A. How were subjects selected for the 'new' intervention?
☒	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☒	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Good

Citation	Surgenor et al (2006)[69]
☒	A. How were subjects selected for the 'new' intervention?
☒	B. How were subjects selected for the comparison or control group?
☐	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	Swenne et al (2004)[70]
☒	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☐	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☐	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Poor

Citation	Zindrou et al (2002)[71]
☒	A. How were subjects selected for the 'new' intervention?
☒	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Good

Citation	Conlon et al (2008)[72]
☒	A. How were subjects selected for the 'new' intervention?
☒	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Good

Citation	Foss et al (2008)[73]
☒	A. How were subjects selected for the 'new' intervention?
☒	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Good

Citation	Halm et al (2004)[74]
☒	A. How were subjects selected for the 'new' intervention?
☒	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Good

Citation	Meltomaa et al (2000)[75]
☒	A. How were subjects selected for the 'new' intervention?
☒	B. How were subjects selected for the comparison or control group?
☐	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☐	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	Myers et al (2004)[76]
☒	A. How were subjects selected for the 'new' intervention?
☒	B. How were subjects selected for the comparison or control group?
☐	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☐	E. Was follow-up long enough for outcomes to occur?
☐	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Poor

Citation	Wallis et al (2005)[77]
☒	A. How were subjects selected for the 'new' intervention?
☒	B. How were subjects selected for the comparison or control group?
☐	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☐	E. Was follow-up long enough for outcomes to occur?
☐	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Poor

Citation	Wolters et al (1997)[78]
☒	A. How were subjects selected for the 'new' intervention?
☒	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Good

Citation	Bell et al (2008)[79]
☒	A. How were subjects selected for the 'new' intervention?
☒	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Good

Citation	Cladellas et al (2006)[80]
☒	A. How were subjects selected for the 'new' intervention?
☒	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Good

Citation	Fang et al (1997)[81]
☒	A. How were subjects selected for the 'new' intervention?
☒	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Good

Citation	Ferraris et al (1996)[82]
☒	A. How were subjects selected for the 'new' intervention?
☒	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☐	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	Habib et al (2003)[83]
☒	A. How were subjects selected for the 'new' intervention?
☒	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☐	E. Was follow-up long enough for outcomes to occur?
☐	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	Habib et al (2005)[84]
☒	A. How were subjects selected for the 'new' intervention?
☒	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Good

Citation	Higgins et al (1992)[85]
☒	A. How were subjects selected for the 'new' intervention?
☒	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Good

Citation	Karkouti et al (2009)[86]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	Karkouti et al (2008a)[87]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	Karkouti et al (2008b)[88]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	Karkouti et al (2005)[89]
☒	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☐	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☒	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☐	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	Litmathe et al (2003)[90]
☒	A. How were subjects selected for the 'new' intervention?
☒	B. How were subjects selected for the comparison or control group?
☐	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☐	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	McKechnie et al (2004)[91]
☒	A. How were subjects selected for the 'new' intervention?
☒	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Good

Citation	Reinecke et al (2003)[92]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	Beattie et al (2009)[93]
☒	A. How were subjects selected for the 'new' intervention?
☒	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☒	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Good

Citation	Carson et al (2002)[94]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	Dunkelgrun et al (2008)[95]
☒	A. How were subjects selected for the 'new' intervention?
☒	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Good

Citation	Gruson et al (2002)[96]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	Lawrence et al (2003)[97]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☐	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Poor

Citation	Lunn and Elwood (1970)[98]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☐	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☐	E. Was follow-up long enough for outcomes to occur?
☐	F. Was follow-up complete and were there exclusions from analysis?
Comments	Methods were unclear with a lot of information missing
Overall assessment	Poor

Citation	Marcantonio et al (1998)[99]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☐	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Poor

Citation	Rogers et al (2007a)[100]
☒	A. How were subjects selected for the 'new' intervention?
☒	B. How were subjects selected for the comparison or control group?
☐	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☐	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	Stoller et al (1994)[101]
☒	A. How were subjects selected for the 'new' intervention?
☒	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☐	E. Was follow-up long enough for outcomes to occur?
☐	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	Saleh et al (2007)[102]
☒	A. How were subjects selected for the 'new' intervention?
☒	B. How were subjects selected for the comparison or control group?
☐	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☐	E. Was follow-up long enough for outcomes to occur?
☐	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Poor

Citation	Wu et al (2007)[103]
☒	A. How were subjects selected for the 'new' intervention?
☒	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Good

E5 Quality analysis, Question 5

Effect of red blood cell transfusion

What is the effect of red blood cell transfusion on patient outcomes?

Cardiac surgery: Cohort studies

Citation	Surgenor et al (2009)[104]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	Hortal et al (2009)[105]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	Cislaghi et al (2009)[106]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	Scott et al (2008)[107]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☒	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	Ranucci et al (2008)[108]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☒	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☐	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	Murphy et al (2007)[109]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☒	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	Rogers et al (2007b)[110]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☒	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	Koch et al (2006a)[111]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☒	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	Surgenor et al (2006)[69]
☒	A. How were subjects selected for the 'new' intervention?
☒	B. How were subjects selected for the comparison or control group?
☐	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	Koch et al (2006b)[112]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☒	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	Koch et al (2006c)[113]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☒	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	Koch et al (2006d)[114]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☒	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	El Solh et al (2006)[115]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☒	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	Augoustides et al (2006)[116]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☒	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments:	
Overall assessment	Fair

Citation	Banbury et al (2006)[117]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☒	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☐	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	Kuduvalli et al (2005)[118]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	Olsen et al (2003)[119]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	Bucerius et al (2003)[120]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☒	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	Chelemer et al (2002)[121]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	Engoren et al (2002)[122]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	Leal-Noval et al (2001)[123]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Noncardiac surgery: Cohort studies

Citation	Soleimani et al (2009)[124]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☐	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Poor

Citation	Garcia-Alvarez et al (2009)[125]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	Fuks et al (2009)[126]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	Bursi et al (2009)[127]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	Bernard et al (2009)[128]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☒	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	Silva et al (2008)[129]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	Johnson et al (2008)[130]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☒	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	Engoren et al (2008)[131]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☐	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Poor

Citation	Rogers et al (2007a)[100]
☒	A. How were subjects selected for the 'new' intervention?
☒	B. How were subjects selected for the comparison or control group?
☐	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☐	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	Ruttinger et al (2007)[132]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	BuSaba et al (2007)[133]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	Weber et al (2005a)[134]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	Halm et al (2003)[135]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	Dunne et al (2002)[136]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	Chang et al (2000)[137]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	Carson et al (1998a)[138]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☒	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups?)
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Liberal versus restrictive transfusion strategy

What is the effect of a liberal versus restrictive transfusion strategy on patient outcomes in a perioperative population?

Randomised controlled trials

Citation	Bracey et al (1999)[141]
☐	A. Was the allocation to treatment groups concealed from those responsible for recruiting subjects?
☐	B. Was the study double-blinded?
☒	C. Were patient characteristics and demographics similar between treatment arms at baseline?
☐	D. Were all randomised patients included in the analysis?
☒	E. Were the statistical methods appropriate?
☒	F. Were any subgroup analyses carried out?
Comments	
Overall assessment	Fair

Citation	Bush et al (1997)[142]
☒	A. Was the allocation to treatment groups concealed from those responsible for recruiting subjects?
☐	B. Was the study double-blinded?
☒	C. Were patient characteristics and demographics similar between treatment arms at baseline?
☒	D. Were all randomised patients included in the analysis?
☒	E. Were the statistical methods appropriate?
☒	F. Were any subgroup analyses carried out?
Comments	
Overall assessment	Good

Citation	Grover et al (2006)[143]
☒	A. Was the allocation to treatment groups concealed from those responsible for recruiting subjects?
☐	B. Was the study double-blinded?
☒	C. Were patient characteristics and demographics similar between treatment arms at baseline?
☐	D. Were all randomised patients included in the analysis?
☒	E. Were the statistical methods appropriate?
☐	F. Were any subgroup analyses carried out?
Comments	
Overall assessment	Fair

Citation	Carson et al (1998b)[144]
☒	A. Was the allocation to treatment groups concealed from those responsible for recruiting subjects?
☐	B. Was the study double-blinded?
☒	C. Were patient characteristics and demographics similar between treatment arms at baseline?
☒	D. Were all randomised patients included in the analysis?
☒	E. Were the statistical methods appropriate?
☐	F. Were any subgroup analyses carried out?
Comments	
Overall assessment	Fair

Citation	Foss et al (2009)[145]
☒	A. Was the allocation to treatment groups concealed from those responsible for recruiting subjects?
☐	B. Was the study double-blinded?
☒	C. Were patient characteristics and demographics similar between treatment arms at baseline?
☒	D. Were all randomised patients included in the analysis?
☒	E. Were the statistical methods appropriate?
☒	F. Were any subgroup analyses carried out?
Comments	
Overall assessment	Good

E6 Quality analysis, Question 6

What is the effect of interventions to increase haemoglobin concentration on morbidity, mortality and need for red blood cell transfusion?

Effect of oral iron

Randomised controlled trials

Citation	Aufricht et al (1994)[146]
☐	A. Was the allocation to treatment groups concealed from those responsible for recruiting subjects?
☐	B. Was the study double-blinded?
☒	C. Were patient characteristics and demographics similar between treatment arms at baseline?
☒	D. Were all randomised patients included in the analysis?
☒	E. Were the statistical methods appropriate?
☐	F. Were any subgroup analyses carried out?
Comments	
Overall assessment	Fair

Citation	Crosby et al (1994)[147]
☐	A. Was the allocation to treatment groups concealed from those responsible for recruiting subjects?
☒	B. Was the study double-blinded?
☒	C. Were patient characteristics and demographics similar between treatment arms at baseline?
☒	D. Were all randomised patients included in the analysis?
☒	E. Were the statistical methods appropriate?
☐	F. Were any subgroup analyses carried out?
Comments	
Overall assessment	Fair

Citation	Del Campo et al (1982)[148]
☐	A. Was the allocation to treatment groups concealed from those responsible for recruiting subjects?
☐	B. Was the study double-blinded?
☐	C. Were patient characteristics and demographics similar between treatment arms at baseline?
☐	D. Were all randomised patients included in the analysis?
☐	E. Were the statistical methods appropriate?
☐	F. Were any subgroup analyses carried out?
Comments	
Overall assessment	Poor

Citation	Andrews et al (1997)[149]
☐	A. Was the allocation to treatment groups concealed from those responsible for recruiting subjects?
☐	B. Was the study double-blinded?
☒	C. Were patient characteristics and demographics similar between treatment arms at baseline?
☒	D. Were all randomised patients included in the analysis?
☒	E. Were the statistical methods appropriate?
☐	F. Were any subgroup analyses carried out?
Comments	Late exclusion as was found not to be an RCT for oral iron.
Overall assessment	Fair

Citation	Lidder et al (2007)[150]
☒	A. Was the allocation to treatment groups concealed from those responsible for recruiting subjects?
☒	B. Was the study double-blinded?
☒	C. Were patient characteristics and demographics similar between treatment arms at baseline?
☐	D. Were all randomised patients included in the analysis?
☒	E. Were the statistical methods appropriate?
☒	F. Were any subgroup analyses carried out?
Comments	
Overall assessment	Good

Citation	Mundy et al (2005)[151]
☒	A. Was the allocation to treatment groups concealed from those responsible for recruiting subjects?
☒	B. Was the study double-blinded?
☒	C. Were patient characteristics and demographics similar between treatment arms at baseline?
☐	D. Were all randomised patients included in the analysis?
☒	E. Were the statistical methods appropriate?
☒	F. Were any subgroup analyses carried out?
Comments	
Overall assessment	Good

Citation	Weatherall et al (2004)[152]
☒	A. Was the allocation to treatment groups concealed from those responsible for r recruiting subjects?
☒	B. Was the study double-blinded?
☒	C. Were patient characteristics and demographics similar between treatment arms at baseline?
☐	D. Were all randomised patients included in the analysis?
☒	E. Were the statistical methods appropriate?
☐	F. Were any subgroup analyses carried out?
Comments	
Overall assessment	Fair

Cohort studies

Citation	Cuenca et al (2007)[153]
☒	A. How were subjects selected for the 'new' intervention?
☒	B. How were subjects selected for the comparison or control group?
☐	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups)?
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	Okuyama et al (2005)[154]
☒	A. How were subjects selected for the 'new' intervention?
☒	B. How were subjects selected for the comparison or control group?
☐	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups)?
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Effect of intravenous iron

Cohort studies

Citation	Cuenca et al (2004)[155]
☒	A. How were subjects selected for the 'new' intervention?
☒	B. How were subjects selected for the comparison or control group?
☐	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups)?
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	Cuenca et al (2005)[156]
☒	A. How were subjects selected for the 'new' intervention?
☒	B. How were subjects selected for the comparison or control group?
☐	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups)?
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	Munoz et al (2006)[157]
☒	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups)?
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Effect of intravenous iron versus oral iron

Randomised controlled trials

Citation	Madi-Jebara et al (2004)[158]
☒	A. Was the allocation to treatment groups concealed from those responsible for recruiting subjects?
☒	B. Was the study double-blinded?
☒	C. Were patient characteristics and demographics similar between treatment arms at baseline?
☒	D. Were all randomised patients included in the analysis?
☒	E. Were the statistical methods appropriate?
☐	F. Were any subgroup analyses carried out?
Comments	
Overall assessment	Good

Citation	Karkouti et al (2006a)[159]
☐	A. Was the allocation to treatment groups concealed from those responsible for recruiting subjects?
☒	B. Was the study double-blinded?
☒	C. Were patient characteristics and demographics similar between treatment arms at baseline?
☒	D. Were all randomised patients included in the analysis?
☒	E. Were the statistical methods appropriate?
☐	F. Were any subgroup analyses carried out?
Comments	
Overall assessment	Fair

Citation	Kim et al (2009)[160]
☐	A. Was the allocation to treatment groups concealed from those responsible for recruiting subjects?
☐	B. Was the study double-blinded?
☒	C. Were patient characteristics and demographics similar between treatment arms at baseline?
☐	D. Were all randomised patients included in the analysis?
☒	E. Were the statistical methods appropriate?
☐	F. Were any subgroup analyses carried out?
Comments	
Overall assessment	Poor

Effect of erythropoietin with or without iron

Systematic reviews

Citation	Devon et al (2009)[161]
☒	A. Was a clinical question clearly defined?
☒	B. Was an adequate search strategy used?
☒	C. Were the inclusion criteria appropriate and applied in an unbiased way?
☒	D. Was a quality assessment of included studies undertaken?
☒	E. Were the characteristics and results if the individual studies appropriately summarised?
☒	Were the methods for pooling the data appropriate?
☒	Were the sources of heterogeneity explored?
Comments	This systematic review was well executed. Its limitations are from data limitations of original studies used and the specific population that it investigates
Overall assessment	Good

Citation	Laupacis et al (1998)[162]
☒	A. Was a clinical question clearly defined?
☒	B. Was an adequate search strategy used?
☒	C. Were the inclusion criteria appropriate and applied in an unbiased way?
☐	D. Was a quality assessment of included studies undertaken?
☒	E. Were the characteristics and results if the individual studies appropriately summarised?
☒	Were the methods for pooling the data appropriate?
☐	Were the sources of heterogeneity explored?
Comments	
Overall assessment	Fair

Randomised controlled trials

Citation	D'Ambra (1997)[163]
☒	A. Was the allocation to treatment groups concealed from those responsible for recruiting subjects?
☒	B. Was the study double-blinded?
☒	C. Were patient characteristics and demographics similar between treatment arms at baseline?
☐	D. Were all randomised patients included in the analysis?
☒	E. Were the statistical methods appropriate?
☒	F. Were any subgroup analyses carried out?
Comments	Late exclusion – non-anaemic population
Overall assessment	Good

Citation	Podesta et al (2000)[164]
☒	A. Was the allocation to treatment groups concealed from those responsible for recruiting subjects?
☐	B. Was the study double-blinded?
☒	C. Were patient characteristics and demographics similar between treatment arms at baseline?
☐	D. Were all randomised patients included in the analysis?
☒	E. Were the statistical methods appropriate?
☐	F. Were any subgroup analyses carried out?
Comments	Late exclusion – non-anaemic population
Overall assessment	Fair

Citation	Sowade et al (1997)[165]
☐	A. Was the allocation to treatment groups concealed from those responsible for recruiting subjects?
☒	B. Was the study double-blinded?
☒	C. Were patient characteristics and demographics similar between treatment arms at baseline?
☐	D. Were all randomised patients included in the analysis?
☒	E. Were the statistical methods appropriate?
☒	F. Were any subgroup analyses carried out?
Comments	Late exclusion – non-anaemic population
Overall assessment	Fair

Citation	COPES (1993)[166]
☒	A. Was the allocation to treatment groups concealed from those responsible for recruiting subjects?
☒	B. Was the study double-blinded?
☒	C. Were patient characteristics and demographics similar between treatment arms at baseline?
☒	D. Were all randomised patients included in the analysis?
☒	E. Were the statistical methods appropriate?
☐	F. Were any subgroup analyses carried out?
Comments	
Overall assessment	Good

Citation	Christodoulakis et al (2005)[167]
☒	A. Was the allocation to treatment groups concealed from those responsible for recruiting subjects?
☐	B. Was the study double-blinded?
☒	C. Were patient characteristics and demographics similar between treatment arms at baseline?
☐	D. Were all randomised patients included in the analysis?
☒	E. Were the statistical methods appropriate?
☐	F. Were any subgroup analyses carried out?
Comments	
Overall assessment	Fair

Citation	Faris et al (1996)[169]
☒	A. Was the allocation to treatment groups concealed from those responsible for recruiting subjects?
☒	B. Was the study double-blinded?
☒	C. Were patient characteristics and demographics similar between treatment arms at baseline?
☐	D. Were all randomised patients included in the analysis?
☒	E. Were the statistical methods appropriate?
☒	F. Were any subgroup analyses carried out?
Comments	
Overall assessment	Good

Citation	Feagan et al (2000)[170]
☒	A. Was the allocation to treatment groups concealed from those responsible for recrtuing subjects?
☒	B. Was the study double-blinded?
☒	C. Were patient characteristics and demographics similar between treatment arms at baseline?
☒	D. Were all randomised patients included in the analysis?
☒	E. Were the statistical methods appropriate?
☐	F. Were any subgroup analyses carried out?
Comments	Late exclusion – non-anaemic population
Overall assessment	Good

Citation	Goldberg et al (1996)[171]
☒	A. Was the allocation to treatment groups concealed from those responsible for recruiting subjects?
☐	B. Was the study double-blinded?
☒	C. Were patient characteristics and demographics similar between treatment arms at baseline?
☐	D. Were all randomised patients included in the analysis?
☒	E. Were the statistical methods appropriate?
☐	F. Were any subgroup analyses carried out?
Comments	
Overall assessment	Fair

Citation	Heiss et al (1996)[172]
☐	A. Was the allocation to treatment groups concealed from those responsible for recruiting subjects?
☒	B. Was the study double-blinded?
☒	C. Were patient characteristics and demographics similar between treatment arms at baseline?
☐	D. Were all randomised patients included in the analysis?
☒	E. Were the statistical methods appropriate?
☐	F. Were any subgroup analyses carried out?
Comments	
Overall assessment	Fair

Citation	Kettelhack et al (1998)[173]
☒	A. Was the allocation to treatment groups concealed from those responsible for recruiting subjects?
☒	B. Was the study double-blinded?
☐	C. Were patient characteristics and demographics similar between treatment arms at baseline?
☐	D. Were all randomised patients included in the analysis?
☒	E. Were the statistical methods appropriate?
☐	F. Were any subgroup analyses carried out?
Comments	
Overall assessment	Fair

Citation	Kosmadakis et al (2003)[174]
☒	A. Was the allocation to treatment groups concealed from those responsible for recruiting subjects?
☒	B. Was the study double-blinded?
☒	C. Were patient characteristics and demographics similar between treatment arms at baseline?
☒	D. Were all randomised patients included in the analysis?
☒	E. Were the statistical methods appropriate?
☐	F. Were any subgroup analyses carried out?
Comments	
Overall assessment	Good

Citation	Larson et al (2001)[175]
☒	A. Was the allocation to treatment groups concealed from those responsible for recruiting subjects?
☐	B. Was the study double-blinded?
☒	C. Were patient characteristics and demographics similar between treatment arms at baseline?
☐	D. Were all randomised patients included in the analysis?
☒	E. Were the statistical methods appropriate?
☐	F. Were any subgroup analyses carried out?
Comments	
Overall assessment	Fair

Citation	Qvist et al (1999)[176]
☒	A. Was the allocation to treatment groups concealed from those responsible for recruiting subjects?
☒	B. Was the study double-blinded?
☒	C. Were patient characteristics and demographics similar between treatment arms at baseline?
☒	D. Were all randomised patients included in the analysis?
☒	E. Were the statistical methods appropriate?
☐	F. Were any subgroup analyses carried out?
Comments	
Overall assessment	Good

Citation	Rohling et al (2000)[177]
☐	A. Was the allocation to treatment groups concealed from those responsible for recruiting subjects?
☐	B. Was the study double-blinded?
☒	C. Were patient characteristics and demographics similar between treatment arms at baseline?
☒	D. Were all randomised patients included in the analysis?
☒	E. Were the statistical methods appropriate?
☐	F. Were any subgroup analyses carried out?
Comments	Late exclusion – non-anaemic population
Overall assessment	Fair

Citation	Tsuji et al (1995)[178]
☐	A. Was the allocation to treatment groups concealed from those responsible for recruiting subjects?
☐	B. Was the study double-blinded?
☒	C. Were patient characteristics and demographics similar between treatment arms at baseline?
☐	D. Were all randomised patients included in the analysis?
☒	E. Were the statistical methods appropriate?
☐	F. Were any subgroup analyses carried out?
Comments	Late exclusion – predominantly non-anaemic population
Overall assessment	Poor

Citation	Weber et al (2005b)[179]
☐	A. Was the allocation to treatment groups concealed from those responsible for recruiting subjects?
☐	B. Was the study double-blinded?
☒	C. Were patient characteristics and demographics similar between treatment arms at baseline?
☐	D. Were all randomised patients included in the analysis?
☒	E. Were the statistical methods appropriate?
☒	F. Were any subgroup analyses carried out?
Comments	
Overall assessment	Fair

Citation	Green et al (1996)[180]
☒	A. Was the allocation to treatment groups concealed from those responsible for recruiting subjects?
☒	B. Was the study double-blinded?
☒	C. Were patient characteristics and demographics similar between treatment arms at baseline?
☒	D. Were all randomised patients included in the analysis?
☒	E. Were the statistical methods appropriate?
☐	F. Were any subgroup analyses carried out?
Comments	
Overall assessment	Good

E7 Quality analysis, Question 7

What is the effect of rFVIIa (prophylaxis or treatment) on morbidity, mortality and transfusion rate?

Systematic reviews

Citation	Ranucci et al (2008b)[183]
☒	A. Was a clinical question clearly defined?
☒	B. Was an adequate search strategy used?
☒	C. Were the inclusion criteria appropriate and applied in an unbiased way?
☒	D. Was a quality assessment of included studies undertaken?
☒	E. Were the characteristics and results if the individual studies appropriately summarised?
☒	Were the methods for pooling the data appropriate?
☒	Were the sources of heterogeneity explored?
Comments	
Overall assessment	Good

Citation	Warren et al (2007)[181]
☒	A. Was a clinical question clearly defined?
☒	B. Was an adequate search strategy used?
☐	C. Were the inclusion criteria appropriate and applied in an unbiased way?
☐	D. Was a quality assessment of included studies undertaken?
☐	E. Were the characteristics and results if the individual studies appropriately summarised?
☐	Were the methods for pooling the data appropriate?
☐	Were the sources of heterogeneity explored?
Comments	Inclusion criteria not reported
Overall assessment	Poor

Citation	Zangrillo et al (2009)[182]
☒	A. Was a clinical question clearly defined?
☒	B. Was an adequate search strategy used?
☒	C. Were the inclusion criteria appropriate and applied in an unbiased way?
☐	D. Was a quality assessment of included studies undertaken?
☒	E. Were the characteristics and results if the individual studies appropriately summarised?
☐	Were the methods for pooling the data appropriate?
☒	Were the sources of heterogeneity explored?
Comments	
Overall assessment	Fair

Randomised controlled trials

Citation	Alavi et al (2008)[187]
☐	A. Was the allocation to treatment groups concealed from those responsible for recruiting subjects?
☐	B. Was the study double-blinded?
☐	C. Were patient characteristics and demographics similar between treatment arms at baseline?
☐	D. Were all randomised pateints included in the analysis?
☐	E. Were the statistical methods appropriate?
☐	F. Were any subgroup analyses carried out?
Comments	Results reported in a letter – no quality appraisal possible
Overall assessment	N/A

Citation	Essam (2007)[184]
☐	A. Was the allocation to treatment groups concealed from those responsible for recruiting subjects?
☐	B. Was the study double-blinded?
☒	C. Were patient characteristics and demographics similar between treatment arms at baseline?
☒	D. Were all randomised patients included in the analysis?
☒	E. Were the statistical methods appropriate?
☐	F. Were any subgroup analyses carried out?
Comments	
Overall assessment	Fair

Citation	Gill et al (2009)[185]
☒	A. Was the allocation to treatment groups concealed from those responsible for recruiting subjects?
☒	B. Was the study double-blinded?
☒	C. Were patient characteristics and demographics similar between treatment arms at baseline?
☐	D. Were all randomised patients included in the analysis?
☒	E. Were the statistical methods appropriate?
☐	F. Were any subgroup analyses carried out?
Comments	
Overall assessment	Fair

Citation	Johansson et al (2007)[188]
☐	A. Was the allocation to treatment groups concealed from those responsible for recruiting subjects?
☒	B. Was the study double-blinded?
☒	C. Were patient characteristics and demographics similar between treatment arms at baseline?
☒	D. Were all randomised pateints included in the analysis?
☒	E. Were the statistical methods appropriate?
☐	F. Were any subgroup analyses carried out?
Comments	Allocation concealment unknown; no subgroup analyses
Overall assessment	Fair

Citation	Ma et al (2006)[186]
☐	A. Was the allocation to treatment groups concealed from those responsible for recruiting subjects?
☒	B. Was the study double-blinded?
☐	C. Were patient characteristics and demographics similar between treatment arms at baseline?
☐	D. Were all randomised pateints included in the analysis?
☐	E. Were the statistical methods appropriate?
☐	F. Were any subgroup analyses carried out?
Comments	Results reported in a foreign language paper – no quality appraisal possible
Overall assessment	N/A

Citation	Pihusch et al (2005)[189]
☐	A. Was the allocation to treatment groups concealed from those responsible for recruiting subjects?
☒	B. Was the study double-blinded?
☒	C. Were patient characteristics and demographics similar between treatment arms at baseline?
☒	D. Were all randomised patients included in the analysis?
☒	E. Were the statistical methods appropriate?
☐	F. Were any subgroup analyses carried out?
Comments	Allocation concealment unknown; no subgroup analyses. Late exclusion due to incorrect populatin
Overall assessment	Fair

Citation	Pugliese et al (2007)[190]
☐	A. Was the allocation to treatment groups concealed from those responsible for recruiting subjects?
☒	B. Was the study double-blinded?
☐	C. Were patient characteristics and demographics similar between treatment arms at baseline?
☒	D. Were all randomised patients included in the analysis?
☐	E. Were the statistical methods appropriate?
☐	F. Were any subgroup analyses carried out?
Comments	Allocation concealment unknown; no subgroup analyses; statistical analysis used (T-test) assumes normal distribution
Overall assessment	Poor

Citation	Sachs et al (2007)[191]
☐	A. Was the allocation to treatment groups concealed from those responsible for recruiting subjects?
☒	B. Was the study double-blinded?
☒	C. Were patient characteristics and demographics similar between treatment arms at baseline?
☒	D. Were all randomised patients included in the analysis?
☒	E. Were the statistical methods appropriate?
☐	F. Were any subgroup analyses carried out?
Comments	Allocation concealment unknown; no subgroup analyses
Overall assessment	Fair

E8 Quality analysis, Question 8

What is the effect of fresh frozen plasma, cryoprecipitate, fibrinogen concentrate, and/or platelet transfusion on patient outcome?

Effect of fresh frozen plasma

Systematic review

Citation	Casbard et al (2004)[192]
☐	A. Was a clinical question clearly defined?
☒	B. Was an adequate search strategy used?
☒	C. Were the inclusion criteria appropriate and applied in an unbiased way?
☒	D. Was a quality assessment of included studies undertaken?
☒	E. Were the characteristics and results if the individual studies appropriately summarised?
☒	Were the methods for pooling the data appropriate?
☒	Were the sources of heterogeneity explored?
Comments	
Overall assessment	Good

Cohort study

Citation	Sarani et al (2008)[193]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups)?
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Effect of platelets

Cohort studies

Citation	Karkouti et al (2006)[194]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☒	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups)?
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	Although there appears to be selection bias in the study design, the authors have made a considerable effort to control for confounding
Overall assessment	Good

Citation	McGrath et al (2008)[195]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups)?
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	Although there appears to be selection bias in the study design, the authors have made a considerable effort to control for confounding
Overall assessment	Good

Citation	Spiess et al (2004)[196]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☒	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups)?
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	Although there appears to be selection bias in the study design, the authors have made a considerable effort to control for confounding
Overall assessment	Good

E9 Quality analysis, Question 9

At what INR (or PT/APTT) for fresh frozen plasma, fibrinogen level for cryoprecipitate, platelet count for platelet concentrates should patients be transfused to avoid risks of significant adverse events?

Cohort studies

Citation	Dillon et al (1994)[197]
☐	A. How were subjects selected for the 'new' intervention?
☐	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups)?
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	McVay et al (1990)[198]
☒	A. How were subjects selected for the 'new' intervention?
☒	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups)?
☒	E. Was follow-up long enough for outcomes to occur?
☐	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	Misra et al (2008)[199]
☒	A. How were subjects selected for the 'new' intervention?
☒	B. How were subjects selected for the comparison or control group?
☐	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups)?
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	Ray and Shenoy (1997)[200]
☒	A. How were subjects selected for the 'new' intervention?
☒	B. How were subjects selected for the comparison or control group?
☐	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups)?
☒	E. Was follow-up long enough for outcomes to occur?
☐	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	Fisher and Mutimer (1999)[201]
☒	A. How were subjects selected for the 'new' intervention?
☒	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups)?
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Good

Citation	Weigand et al (2009)[202]
☒	A. How were subjects selected for the 'new' intervention?
☒	B. How were subjects selected for the comparison or control group?
☐	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups)?
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	Foster et al (1992)[203]
☒	A. How were subjects selected for the 'new' intervention?
☒	B. How were subjects selected for the comparison or control group?
☐	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups)?
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	Doerfler et al (1996)[204]
☒	A. How were subjects selected for the 'new' intervention?
☒	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups)?
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Good

Citation	Martin et al (2000)[205]
☒	A. How were subjects selected for the 'new' intervention?
☒	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups)?
☐	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	Mainwaring et al (1998)[206]
☒	A. How were subjects selected for the 'new' intervention?
☒	B. How were subjects selected for the comparison or control group?
☐	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups)?
☒	E. Was follow-up long enough for outcomes to occur?
☐	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	Howard et al (2000)[207]
☒	A. How were subjects selected for the 'new' intervention?
☒	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups)?
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Good

Citation	Vavricka et al (2003)[208]
☒	A. How were subjects selected for the 'new' intervention?
☒	B. How were subjects selected for the comparison or control group?
☐	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups)?
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	Ruell et al (2007)[209]
☒	A. How were subjects selected for the 'new' intervention?
☒	B. How were subjects selected for the comparison or control group?
☐	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups)?
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	Darcy et al (1996)[210]
☒	A. How were subjects selected for the 'new' intervention?
☒	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups)?
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Good

Citation	Weiss et al (1993)[211]
☒	A. How were subjects selected for the 'new' intervention?
☒	B. How were subjects selected for the comparison or control group?
☐	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups)?
☒	E. Was follow-up long enough for outcomes to occur?
☒	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Citation	Wolf et al (2007)[212]
☒	A. How were subjects selected for the 'new' intervention?
☒	B. How were subjects selected for the comparison or control group?
☒	C. Does the study adequately control for demographic characteristics, clinical features and other potential confounding variables in the study design or analysis?
☐	D. Was the measurement of outcomes unbiased (ie, blinded to treatment group and comparable across groups)?
☒	E. Was follow-up long enough for outcomes to occur?
☐	F. Was follow-up complete and were there exclusions from analysis?
Comments	
Overall assessment	Fair

Appendix F: Evidence summaries

F1 Evidence summaries, Question 1

What is the effect of a multidisciplinary, multimodal, programmatic approach to perioperative patient blood management on patient outcomes?

Level I evidence

<table>
<tr><td colspan="5">STUDY DETAILS</td></tr>
<tr><td colspan="5">Reference Ferraris VA, Ferraris SP, Saha SP, Hessel II EA, Haan CK, Royston BD, et al. Perioperative blood transfusion and blood conservation in cardiac surgery: the Society of Thoracic Surgeons and the Society of Cardiovascular Anesthesiologists clinical practice guideline. Ann Thorac Surg. 2007;83(5 Suppl):S27–S86</td></tr>
<tr><td colspan="5">Affiliation/Source of funds
The Society of Thoracic Surgeons; The Society of Cardiovascular Anesthesiologists; AstraZeneca; Aventis; Bayer; Network for Advancement of Transfusion Alternatives (NATA); American Heart Association; BioMarin Pharma; Guilford; Medtronic; National Heart, Lung and Blood Institute; The Medicines Company; Azko Nobel; GSK; Johnson & Johnson Pharmaceuticals; Department of Health (UK); Fresenius; Inotherapeutics; National Blood Service (UK); Dyax; Inspire; Synthetic Blood International; NovoNordisk; Physician Services Inc (PSI); Canadian Institutes of Health Research (CIHR)
Funding source: Research Grants were obtained from the following sources: American Heart Association; Aventis; Bayer; Biomarin Pharma; Guilford; Medtronic; National Heart, Lung and Blood Institute; The Medicines Company; Department of Health (UK); Fresenius; Inotherapeutics; National Blood Service (UK); Synthetic Blood International, Bayer; Physicians Services Inc (PSI); Canadian Institutes of Health and Research (CIHR)</td></tr>
<tr><td colspan="2">Study design
Systematic review</td><td>Level of evidence
I</td><td colspan="2">Location/setting
NR</td></tr>
<tr><td colspan="5">Population characteristics
Studies were included if they involved patients undergoing cardiac surgery</td></tr>
<tr><td colspan="2">Length of follow-up
NR</td><td colspan="3">Outcome(s) measured
A multimodality approach involving multiple stakeholders, institutional support, enforceable transfusion algorithms supplemented with point-of-care testing, and all of the already mentioned efficacious blood conservation interventions will limit blood transfusion and provide optimal blood conservation for cardiac operations</td></tr>
<tr><td colspan="5">INTERNAL VALIDITY</td></tr>
<tr><td>Allocation</td><td>Comparison of study groups</td><td>Blinding</td><td>Treatment/measurement bias</td><td>Follow-up (ITT</td></tr>
<tr><td>NR</td><td>NR</td><td>NR</td><td>NR</td><td>NR</td></tr>
<tr><td colspan="5">Overall quality assessment (descriptive): Poor</td></tr>
</table>

<table>
<tr><td colspan="2">RESULTS
A multimodal approach to perioperative patient blood management, involving multiple stakeholders, institutional support and enforceable transfusion algorithms, supplemented with point-of-care testing and efficacious blood conservation interventions, reduces the need for, or limits, blood transfusions and provides optimal blood conservation for patients undergoing cardiac surgery.</td></tr>
<tr><td>Clinical importance (1–4)
Unable to assess</td><td>Relevance (1–5)
1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival</td></tr>
<tr><td colspan="2">Any other adverse effects
None reported</td></tr>
<tr><td colspan="2">EXTERNAL VALIDITY</td></tr>
<tr><td colspan="2">Generalisability
Studies were performed in patients undergoing cardiac surgery and is generalisable to a wider perioperative cardiac surgery population</td></tr>
<tr><td colspan="2">Applicability
The results of this study are applicable to the Australian healthcare setting</td></tr>
<tr><td colspan="2">Comments
While the Writing Group and Review Group Members unanimously agreed with this recommendation, the weight of the evidence which was used to support this statement is unsubstantiated</td></tr>
</table>

Level III evidence

<table>
<tr><td colspan="6">STUDY DETAILS</td></tr>
<tr><td colspan="6">Reference Bui LL, Smith AJ, Bercovici M, Szalai JP, Hanna SS. Minimising blood loss and transfusion requirements in hepatic resection. HPB. 2002;4(1):5–10</td></tr>
<tr><td colspan="6">Affiliation/Source of funds
Division of General Surgery, Sunnybrook and Women's College Health Sciences Centre, Toronto, Ontario, Canada
Funding Source: None reported</td></tr>
<tr><td colspan="2">Study design:
Retrospective cohort study
N=151</td><td colspan="2">Level of evidence:
III</td><td colspan="2">Location/setting:
Hospital, Canada</td></tr>
<tr><td colspan="3">Intervention
Minimal blood loss program
Sample Size N=102</td><td colspan="3">Comparator(s)
Standard Care
Sample Size N=49</td></tr>
<tr><td colspan="6">Population characteristics
Patients who underwent liver resection
Intervention group—Mean age 61, male 52.9%, major resection 61 (59.8%), minor resection 41 (40.2%), hepatoma 9 (8.8%), metastatic tumour 76 (74.5%), benign tumour 17 (16.7%)
Comparator groups(s)—Mean age 59, male 49%, major resection 32 (65.3%), minor resection 17 (34.7%), hepatoma 4 (8.2%), metastatic tumour 34 (69.4%), benign tumour 11 (22.4%)</td></tr>
<tr><td colspan="3">Length of follow-up
Not reported</td><td colspan="3">Outcome(s) measured
Blood loss, patients requiring transfusion, units of homologous blood transfusion, morbidity, mortality, complications</td></tr>
<tr><td colspan="6">INTERNAL VALIDITY</td></tr>
<tr><td>Allocation</td><td>Comparison of study groups</td><td>Blinding</td><td>Treatment/measurement bias</td><td colspan="2">Follow-up (ITT)</td></tr>
<tr><td>The intervention group was compared to a historical control group</td><td>There were no signififcant differences in the baseline demographics between the two groups</td><td>No blinding details were reported</td><td>Apart from the intervention, all patients were treated the same</td><td colspan="2">ITT analysis</td></tr>
<tr><td colspan="6">Overall quality assessment (descriptive): This was a poor quality retrospective cohort study</td></tr>
</table>

RESULTS				
Outcome	Intervention group	Control group	OR 95% CI	P-value
Mean total no. of units transfused	3.0 ± 0.4	13.7 ± 1.8	NR	<0.001
Patients receiving ≥1 units of homologous blood	25.5%	91.8%	NR	<0.001
Clinical importance (1–4) Unable to assess		Relevance (1–5) 2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention		
Haemorrhage	2.9%	8.2%	NR	0.159
Bile leak	11.8%	12.2%	NR	0.949
Sepsis	8.8%	23.6%	NR	<0.001
Overall morbidity	25.5%	57.1%	NR	<0.001
Mortality	4.9%	10.2%	NR	<0.0001
Clinical importance (1–4) Unable to assess		Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		
Any other adverse effects None reported				
EXTERNAL VALIDITY				
Generalisability The patient population is hepatic resection patients which is a subset of the overall surgical population addressed by the systematic review question				
Applicability The study is set in Canada which is of similar health setting to an Australian setting				
Comment Systematic implementation of strategies designed to control blood loss are effective and may reduce morbidity and mortality associated with hepatic resections				

STUDY DETAILS				
Reference Freedman J, Luke K, Monga N, Lincoln S, Koen R, Escobar M, et al. A provincial program of blood conservation: The Ontario Transfusion Coordinators (ONTraC). Transfus Apheresis Sci. 2005;33(3):343–349				
Affiliation/Source of funds St Michael's Hospital and the University of Toronto, Toronto, Canada Funding Source: The study was funded by the Ministry of Health and Long Term Care of Ontario				
Study design Pre/post case series	Level of evidence IV	Location/setting Ontario Hospitals, Canada		
Intervention Introduction of a blood conservation program N=7200 (n=1200 knee arthroplasty in 19 hospitals, n=300 abdominal aortic aneurysm (AAA) in 17 hospitals and n=300 elective coronary artery bypass graft (CABG) surgery in 4 hospitals at each time point. Time points were baseline, 12, 18 and 24 months	Comparator(s) Prior to the establishment of the blood conservation program N=1800 (n=1200 knee arthroplasty in 19 hospitals, n=300 AAA in 17 hospitals and n=300 elective CABG surgery in 4 hospitals			
Population characteristics Targeted procedures for these studies were knee arthroplasty, abdominal aortic aneurysm surgery and elective coronary artery bypass graft surgery				
Length of follow-up 24 months	Outcome(s) measured LOS, infection rates, mortality			
INTERNAL VALIDITY				
Allocation	Comparison of study groups	Blinding	Treatment/measurement bias	Follow-up (ITT)
Not reported	Baseline demographics not reported	No blinding details were reported	No details are reported	No details are reported
Overall quality assessment (descriptive): Poor				
RESULTS				

Outcome	Intervention group	Control group	Measure of effect/effect size (95% CI)	Benefits (NNT) (95% CI)
Informed consent of transfusion	90%	20%	NR	NR
Functioning Transfusion Review Committee	55%	100%	NR	NR
Hospital LOS	NR	NR	NR	p<0.0001
Reduction in blood use	Knee arthroplasty= –24% AAA=–14% CABG=–23%	Knee arthroplasty=0% AAA=0% CABG=0%	NR	NR

Clinical importance (1–4) Unable to assess			Relevance (1–5) 2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention	
Postoperative infection rates	NR	NR	NR	p<0.05
Clinical importance (1–4) Unable to assess			Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival	
Any other adverse effects None reported				
EXTERNAL VALIDITY				
Generalisability The patient population is AAA, CABG and knee arthroplasty surgery patient patients which is a subset of the overall surgical population addressed by the systematic review question				
Applicability The study is set in Canada which is of similar health setting to an Australian setting				
Comments The reduction in allogeneic transfusion associated with the implementation of the ONTraC program represents important savings in costs associated with blood components, hospital stay and work in transfusion laboratories and nursing units, as well as enhancing patient satisfaction and safety				

STUDY DETAILS				
Reference Freedman J, Luke K, Escobar M, Vernich L,Chiavetta JA. Experience of a network of transfusion coordinators for blood conservation (Ontario Transfusion Coordinators [ONTraC]). Transfusion. 2008; 48: 237–250				
Affiliation/Source of funds From the St Michael's Hospital, Toronto Platelet Immunobiology Group (TPIG), Department of Public Health Sciences, EPI-STAT Research, Inc., University of Toronto, Toronto, Ontario, Canada Funding source: Ministry of Health and Long-term Care, Province of Ontario				
Study design Pre/post case series	Level of evidence IV	Location/setting Ontario, Hospitals, Canada		
Intervention Introduction of a blood conservation program N=7200 (n=1200 knee arthroplasty in 19 hospitals, n=300 abdominal aortic aneurysm (AAA) in 17 hospitals and n=300 elective coronary artery bypass graft (CABG) surgery in 4 hospitals at each time point. Time points were baseline, 12, 18 and 24 months	Comparator(s) Prior to the establishment of the blood conservation program N=1800 (n=1200 knee arthroplasty in 19 hospitals, n=300 AAA in 17 hospitals and n=300 elective CABG surgery in 4 hospitals			
Population characteristics Patients admitted for three designated procedures: knee arthroplasty, abdominal aortic aneurysm (AAA), and coronary artery bypass graft (CABG) surgery				
Length of follow-up 24 months	Outcome(s) measured LOS, infection rates, mortality			
INTERNAL VALIDITY				
Allocation	Comparison of study groups	Blinding	Treatment/measurement bias	Follow-up (ITT)
Not reported	Baseline demographics not reported	No blinding details were reported	No details are reported	No details are reported
Overall quality assessment (descriptive): Poor				
RESULTS				

Outcome	Intervention group	Control group	OR (95% CI)	p-value
CABG Patients				
Proportion of patients receiving transfusion	60%	43%	NR	P<0.001
Units transfused	1.2	2.0	NR	P<0.001
Infection	5.82%	10.95%	NR	P=6.20
LOS, days (95% CI)	7.81 (6.83, 8.76)	10.78 (9.80, 11.76)	NR	P<0.001
Mortality	0.73%	2.19%	NR	P=0.1888

Knee arthroplasty				
Proportion of patients receiving transfusion	18%	25%	NR	P<0.0001
Units transfused	0.3	0.5	NR	P<0.001
Infection	2.04%	3.76%	NR	P=0.0730
LOS, days (95% CI)	6.25 (5.64, 6.86)	7.16 (6.54, 7.47)	NR	P=0.0888
Mortality	0.18%	0.09%	NR	P=0.2142
AAA				
Proportion of patients receiving transfusion	45%	50%	NR	P<0.05
Units transfused	1.8	2.1	NR	NS
Infection	11.64%	9.76%	NR	P=0.8797
LOS, days (95% CI)	8.07 (5.45, 10.69)	12.91 (10.56, 15.26)	NR	P=0.0576
Mortality	1.29%	2.44%	NR	P=0.1640
Any other adverse effects None reported				
EXTERNAL VALIDITY				
Generalisability The patient population is AAA, CABG and knee arthroplasty surgery patients which is a subset of the overall surgical population addressed by the systematic review question				
Applicability The study is set in Canada which is of similar health setting to an Australian setting				
Comment The implementation of a provincial network of transfusion coordinators was feasible and allogeneic transfusion rates declined over the period the program has been in place				

STUDY DETAILS				
Reference Brevig J, McDonald J, Zelinka ES, Gallagher T, Jin R, Grunkemeier GL. Blood transfusion reduction in cardiac surgery: multidisciplinary approach at a community hospital. Ann Thorac Surg. 2009;87:532–539				
Affiliation/Source of funds Providence Regional Medical Center Everett, Washington; Advanced Perfusion Care, Inc, Pinehurst, North Carolina; Everett Cardiovascular and Thoracic Surgical Associates, Washington; Medical Data Research Center, Providence Health & Services, Portland, Oregon Funding source: None reported				
Study design Comparative with historic control	Level of evidence III	Location/setting Hospitals, USA		
Intervention A data driven, multidisciplinary effort to decrease allogeneic red blood cell transfusion was instituted in a community hospital. Numerous innovations in treatment protocols were implemented and evaluated Sample Size N=479 in 5th year of the program	Comparator(s) Baseline values prior to intervention Sample Size N=530			
Population characteristics Patients undergoing cardiac surgery				
Length of follow-up 5 years	Outcome(s) measured Blood utilisation, mortality			
INTERNAL VALIDITY				
Allocation	Comparison of study groups	Blinding	Treatment/measurement bias	Follow-up (ITT)
Not applicable	Not applicable	Not applicable	Not applicable	Not applicable
Overall quality assessment (descriptive): Poor				
RESULTS				

Outcome	Intervention group (in 5th year of followup)	Control group (at baseline)	Measure of effect/effect size 95% CI	Benefits (NNT) 95% CI
Incidence of RBC transfusion				
Observed	18%	43.2%		NR
Predicted	52.9%	53.9%		NR
Odds ratio	0.1	0.6%		NR
95% CI of OR	(0.4, 0.7)	(0.1, 0.2)		NR
Units of RBC transfused				
Mean per recipient	3.0	3.3		NR
Mean per patient population	0.5	1.4		

Units of other blood products (mean per patient population – isolated CABG only) Platelets Fresh frozen plasma Cryoprecipitate Discharge haematocrit Mortality	 0 0.007 0 28.8 ± 3.8 2.5%	 0 0 0 n/a 0.8%		 NR NR NR NR 0.452†
	Clinical importance (1–4) 2 The point estimate of effect is clinically important but the confidence interval includes clinically unimportant effects		Relevance (1–5) 2: Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention	
Any other adverse effects: NR				
EXTERNAL VALIDITY				
Generalisability: The patient population is cardiac surgery patients which is a subset of the overall surgical population addressed by the systematic review question				
Applicability: The study was reported in a US setting which has a considerably different health setting to the Australian health system				
COMMENTS: Cardiac surgery in a community hospital can be performed safely with low utilisation of allogeneic RBC transfusions. A multidisciplinary approach to blood conservation can result in lower transfusion rates and equivalent patient outcomes.				

<table>
<tr><td colspan="5">STUDY DETAILS</td></tr>
<tr><td colspan="5">Reference: DeAnda A Jr, Baker KM, Roseff SD, Green JA, Mccarthy H, Aron T, Spiess BD. Developing a blood conservation program in cardiac surgery. Am J Med Quality 2006;21(4):230–237</td></tr>
<tr><td colspan="5">Affiliation/Source of funds: Department of Cardiothoracic Surgery, Department of Nursing, Department of Pathology, Department of Anesthesiology, Montefiore Medical Center, Bronx, New York; Perfusion Services, Virginia Commonwealth University/Medical College of Virginia, Richmond, Virginia; Virginia Commonwealth University Reanimation Engineering Shock Center (VCURES)</td></tr>
<tr><td colspan="2">Study design: Pre/post case series</td><td colspan="2">Level of evidence: IV</td><td>Location/setting: Hospital</td></tr>
<tr><td colspan="2">Intervention
Sample Size
Introduction of a blood conservation program
N=477</td><td colspan="3">Comparator(s)
Sample Size
Standard care prior to intervention
N=521</td></tr>
<tr><td colspan="5">Population characteristics
Intervention—Cardiothoracic surgery patients
Comparator—Cardiothoracic surgery patients</td></tr>
<tr><td colspan="2">Length of follow-up
4 years</td><td colspan="3">Outcome(s) measured:
All patients transfused
RBC transfused
Preoperative Hg (g/dL)
ICU entry Hg (g/dL)
Discharge Hg (g/dL)
Any adverse outcome
Myocardial Infarction
Respiratory failure
Infection
Death
Balloon pump required
2 or more catecholamines
Renal failure
Re-operation for bleeding</td></tr>
<tr><td colspan="5">INTERNAL VALIDITY</td></tr>
<tr><td>Allocation: NR</td><td>Comparison of study groups: NR</td><td>Blinding: NR</td><td>Treatment/measurement bias: NR</td><td>Follow-up (ITT): NR</td></tr>
<tr><td colspan="5">Overall quality assessment (descriptive): Poor</td></tr>
</table>

RESULTS				
Outcome	Intervention group	Control group	Measure of effect/effect size 95% CI	Benefits (NNT) 95% CI
All patients transfused	39%	79%	NR	<0.05
RBC transfused	16%	35%	NR	<0.05
Preoperative Hg(g/dL)	12.2	12.2	NR	NS
ICU entry Hb (g/dL)	9.2	10.810.8	NR	<0.05
Discharge Hb (g/dL)	9.2	51.8%	NR	<0.05
Any adverse outcome	33.5%	0.5%	NR	<0.05
MI	0.4%	9.7%	NR	NS
Respiratory failure	8.3%	5.9%	NR	NS
Infection	5.4%	7.7%	NR	NS
Death	7.3%	15%	NR	NS
Balloon pump required	6.1%	43.1 %	NR	<0.05
≥2 catecholamines	23.3%	5.1% 4.8%	NR	<0.05
Renal failure	2.8%		NR	<0.05
Re-operation for bleeding	1.4%		NR	<0.05
	Clinical importance (1–4) 2: The point estimate of effect is clinically important but the confidence interval includes clinically unimportant effects		Relevance (1–5) 2: Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention	
Any other adverse effects: NR				
EXTERNAL VALIDITY				
Generalisability: The patient population was cardiac surgery patients which is a subset of the overall surgical population addressed by the systematic review question				
Applicability: The study was reported in a US setting which has a considerably different health setting to the Australian health system				
COMMENTS: This program has resulted in a decrease in cost while maintaining patient outcomes. The success of the program is believed to be a result of the multidisciplinary approach taken, with a commitment from all members of the blood reduction team being the key component of this success				

Level IV evidence

STUDY DETAILS				
Reference Bolan CD, Rick ME, Polly DW Jr. Transfusion medicine management for reconstructive spinal repair in a patient with von Willebrand's disease and a history of heavy surgical bleeding. Spine. 2001;26(23): E552–E556				
Affiliation/Source of funds Department of Transfusion Medicine, Warren Grant Magnuson Clinical Center, National Institutes of Health, Bethesda; Headquarters Company, Walter Reed Army Institute of Research, Silver Spring; Department of Laboratory Medicine, Grant Magnuson Clinical Center, and the Department of Orthopedic Surgery and Rehabilitation, Walter Reed Army Medical Centre, WA DC; and the Department of Surgery, Uniformed Services University of the Health Sciences, Bethesda, USA Funding source: None reported				
Study design Case report	Level of evidence IV	Location/setting Hospital, USA		
Intervention Multidisciplinary approach	Comparator(s) None			
Population characteristics Patient with von Willebrand disease and a history of heavy surgical bleeding				
Length of follow-up Not reported	Outcome(s) measured Blood loss			
INTERNAL VALIDITY				
Allocation	Comparison of study groups	Blinding	Treatment/measurement bias	Follow-up (ITT)
Not applicable	Not applicable	Not applicable	Not applicable	Not applicable
Overall quality assessment (descriptive): Poor				
RESULTS				

Outcome	Intervention group	Control group	Measure of effect/effect size 95% CI	Benefits (NNT) 95% CI
Estimated blood loss	5 L	NA	NA	NA
Replacement autologous RBC	9 units	NA	NA	NA
Replacement autologous plasma	6 units	NA	NA	NA
Replacement autologous plateletpheresis product	2 units	NA	NA	NA
Humate P administered	17,000 units	NA	NA	NA
Any other adverse effects				

None reported
EXTERNAL VALIDITY
Generalisability The population was one patient with von Willebrand disease and a history of heavy surgical bleeding which is a subset of the overall surgical population addressed by the systematic review question
Applicability Minimal: the study was conducted in a US setting and was a case study
COMMENTS Using a careful multidisciplinary approach, excellent haemostasis can be achieved with minimal exposure to untreated allogeneic blood products during aggressive spinal surgery in a patient with a clinically significant congenital coagulopathy

F2 Evidence summaries, Question 2

In patients undergoing surgery or invasive procedures, what effect does the cessation and timing of cessation of medications that affect haemostasis have on morbidity, mortality, and red blood cell transfusion?

Cardiac studies: Level II and III evidence

STUDY DETAILS				
Reference Ascione R, Ghosh A, Rogers CA, Cohen A, Monk C, Angelini GD. In-hospital patients exposed to clopidogrel before coronary artery bypass graft surgery: A word of caution. Ann Thorac Surg. 2005;79(4):1210–1216				
Affiliation/Source of funds				
None reported				
Study design	Level of evidence		Location/setting	
Prospective cohort	III-2		UK, Hospital	
Intervention		Comparator		
Clopidogrel stopped 2 to 5 days prior to surgery N=22		Clopidogrel stopped <2 days prior to surgery N=66		
Population characteristics				
In-hospital referral patients undergoing first time CABG (On/off pump CABG proportions NR for patients whose clopidogrel regimen was stopped for durations reported here) Emergency patients excluded Clopidogrel regimen: loading dose of 300 mg orally then 75 mg daily				
Length of follow-up		Outcomes measured		
Duration unclear		Mortality, transfusion requirements		
INTERNAL VALIDITY				
Allocation	Results	Blinding analysis	Treatment/measurement bias	Follow-up (ITT)
NA—*post-hoc* analysis reported	NR	NA—post-hoc analysis reported	None	NA—*post-hoc* analysis reported
Overall quality assessment (descriptive) Poor				

RESULTS			
Outcome	Intervention group	Comparator group	Statistical significance
Mortality (in hospital, OR, 95% CI)	2.52 (0.34,18.8)	21.7 (2.93, 160)	p<0.0001
	Clinical importance 2		Clinical relevance 1
Any other adverse effects NR			
EXTERNAL VALIDITY			
Generalisability			
Study population considered similar to target population			
Applicability			
Potentially reduced: timing of clopidogrel cessation may vary between this study and Australian/NZ clinical practice			
Comments			
Results reported here are for a *post-hoc* subgroup analysis, therefore unlikely if the study was powered to measure clinical difference in these subgroups. Reasons for variation of timing of clopidogrel cessation NR			

Abbreviations: CABG, coronary artery bypass graft surgery; NA, not applicable; NR, not reported; OR, odds ratio

STUDY DETAILS		
Reference Berger JS, Frye CB, Harshaw Q, Edwards FH, Steinhubl SR, Becker RC. Impact of clopidogrel in patients with acute coronary syndromes requiring coronary artery bypass surgery: A multicenter analysis. J Am Coll Cardiol. 2008; 52(21):1693–1701		
Affiliation/Source of funds		
Three authors receive research support from Aztrazeneca. Two authors from an independent economics research group contracted by Aztrazeneca. Study funded by Aztrazeneca		
Study design	Level of evidence	Location/setting
Retrospective, multicentre cohort	III-3	USA, 14 hospitals
Intervention	Comparator	
Clopidogrel-naïve or stopped >5 days prior to surgery (proportion in each group NR) Cases: urgent=emergency=7.0%; urgent=65.1%; elective=27.9% On pump CABG=72.5% N=298	Clopidogrel stopped ≤ 5 days prior to surgery Cases: urgent=emergency=12.1%; urgent=68.8%; elective=19.1% On pump CABG=72.1% N=298	
Population characteristics		
Patients with admitting diagnosis of ACS undergoing CABG during index hospitalization On and off-pump CABG used Mixed group of urgent, elective and emergency patients Clopidogrel regimen included 75 mg daily maintenance dose ± 300 mg loading dose Antifibrinolytics used (intervention 55.7% patients; comparator 66.1%)		
Length of follow-up	Outcomes measured	
30 days after CABG	Mortality, morbidity, blood loss, transfusion requirements, re-operation for bleeding, hospital and ICU LOS	

INTERNAL VALIDITY	
Allocation	Results
NA—retrospective study	Comparator groups patients had greater prevalence of: • prior cerebrovascular accident, comparator vs. intervention group=11.7% vs 6.87%, p=0.034 • prior MI, comparator vs. intervention group=28.5% vs. 19.1%, p=0.007 • prior PCI, comparator vs. intervention group=32.9% vs. 15.4%, p<0.001 During surgery antifibrinolytic drug use was greater in comparator vs. intervention group=66.1% vs. 55.7%, p=0.009. Other differences included: • number of vessels grafted: comparator vs. intervention group=3.38 ± 1.13 vs 3.73 ± 1.20 p<0.001 • postponed surgery due to antiplatelet therapy, comparator vs. intervention group=76.1% vs 31.3% p<0.001 • postponed surgery due to recent MI, comparator vs. intervention group=8.7% vs 31.3%, p=0.011

Blinding analysis	Treatment/measurement bias	Follow-up (ITT)
NA, retrospective study	None	NA, retrospective study
Overall quality assessment (descriptive) Fair		
RESULTS		

Outcome	Intervention group	Comparator group	Statistical significance	Effect measure (95% CI)
Mortality, in-hospital (proportion)	0.3%	1.3%	p=0.373	RR=0.25 (0.02,3.98) p=0.326

Clinical importance	Clinical relevance
2	1

Mortality, postoperative (proportion)	0%	1.0%	p=0.249	NA

Clinical importance	Clinical relevance
Unknown, results suggest clinical benefit, but not statistically significant. RR and CI can not be calculated	1

Morbidity (proportion)	AF=18.8% Infection=5.7% Ischemic CVA=1.0% Haemorrhagic CVA=0% Haemodynamic instability=8.4% Inotropes needed=24.5% Mediastinitis=0% Cardiac arrest=0.7%	AF=23.5% Infection=7.4% Ischemic CVA=1.7% Haemorrhagic CVA=0% Haemodynamic instability=12.4% Inotropes needed=34.2% Mediastinitis=0.7% Cardiac arrest=1.3%	AF, p=0.160 Infection, p=0.408 Ischemic CVA, p=0.725 Haemorrhagic CVA, NA Haemodynamic instability, p=0.107 Inotropes needed, p=0.009 Mediastinitis,p=0.157 Cardiac arrest, p=0.686

Relative risk: Intervention vs. comparator
AF: RR=0.80 (0.57,1.12), p= 0.190
Infection: RR=0.77 (0.40, 1.48), p=0.439
Ischemic CVA: RR=0.60 (0.12, 2.95), p=0.529
Haemodynamic instability: RR=0.68 (0.40,1.15), p=0.148
Inotropes needed: RR=0.72 (0.54, 0.95), p=0.02
Mediastinitis: RR not determined
Cardiac arrest: RR=0.50 (0.07,3.53) p=0.487

Clinical importance	Clinical relevance
1 for inotropes needed 2 for all other morbidity outcomes	1

Blood loss (mL, mean ± SD)	557.2 ± 339.01	668.3 ± 515.50	p=0.026

Clinical importance 3		Clinical relevance 1		
Transfusion requirements[a] (Intraoperative and postoperative combined, units, mean ± SD)	2.03 ± 3.75	4.90 ± 7.90	p<0.001	
Clinical importance 3		Clinical relevance 1		
Transfusion requirements[a], Preoperative(proportion)	1.3%	1.7%	p=0.751	RR=0.80 (0.20,3.17) p=0.751
Clinical importance Unknown, results suggest clinical benefit, but not statistically significant.		Clinical relevance 1		
Transfusion requirements[a], Intraoperative (proportion)	32.2%	43%	p=0.007	RR=0.75 (0.59,0.95) p=0.015
Clinical importance 1		Clinical relevance 1		
Transfusion requirements[a], Postoperative (proportion)	35.6%	50%	p<0.001	RR=0.71 (0.57,0.88) p=0.002
Clinical importance 1		Clinical relevance 1		
Re-operation for bleeding (proportion)	1.3%	4.7%	p=0.017	RR=0.29 (0.07,1.13) p=0.074
Clinical importance .2		Clinical relevance 1		
Hospital LOS (days, mean ± SD)	6.3 ± 3.87	7.2 ± 5.53	p=0.054	
Clinical importance 3		Clinical relevance 1		
ICU LOS (days, mean ± SD)	2.4 ± 2.52	2.7 ± 3.17	p=0.059	
Clinical importance 3		Clinical relevance 1		
Hospital readmission (proportion)	8.1%	9.1%	p=0.670	RR=0.89 (0.52,1.53) p=0.670

Clinical importance 2	Clinical relevance 1
Any other adverse effects NR	
EXTERNAL VALIDITY	
Generalisability	
Patients considered similar to guideline target population	
Applicability	
Reduced—study performed in the USA, which has some differences to Australia/NZ health system.	
Comments	
Univariate analysis demonstrated that exposure to clopidogrel within 5 days of surgery was associated with an increased risk of re-operation, bleeding and increased LOS. Transfusion requirements were also increased	

Abbreviations: ACS, acute coronary syndrome; AF, atrial fibrillation; CABG, coronary artery bypass graft surgery; CI, confidence interval; ICU, intensive care unit; LOS, length of stay; MI, myocardial infarction; NA, not applicable; NR, not reported; PCI, percutaneous coronary intervention; RR, relative risk; SD, standard deviation

[a] Includes platelets, RBC, FFP and cryoprecipitate

STUDY DETAILS		
Reference Chu MWA, Wilson SR, Novick RJ, Stitt LW, Quantz MA. Does clopidogrel increase blood loss following coronary artery bypass surgery? Ann Thorac Surg. 2004;78(5):1536–1541		
Affiliation/Source of funds		
NR		
Study design	Level of evidence	Location/setting
Prospective cohort	III-2	Canada, tertiary care centre

Intervention	Comparator
1. Clopidogrel stopped 5 to 8 days before operation N=39 OPCAB=33% 2. Clopidogrel discontinued > 8 days before operation N=232 OPCAB =17%	Clopidogrel stopped within 4 days of operation N=41 OPCAB=22%
Population characteristics	
Consecutive urgent or emergent CABG patients[a] (elective cases excluded)	
Length of follow-up	Outcomes measured
30 days from discharge in intervention group #1 and comparator group; unclear for intervention group #2	Mortality, morbidity, blood loss, transfusion requirements, re-operation for bleeding, hospital and ICU LOS, hospital readmission

INTERNAL VALIDITY	
Allocation	Results
NR	No clinical or statistically significant differences in patient baseline characteristics or in terms of preoperative medications that could contribute to postoperative bleeding. There was a significant difference in expected hospital mortality and hospital LOS scores: Expected LOS: Comparator group=7.8±1.6 Intervention group 1=6.9±1.0 Intervention group 2=7.2±1.4 Expected % risk mortality Comparator group=5.7±4.8 Intervention group 1=2.9±2.7 Intervention group 2=3.8±6.1 Intraoperative aprotinin use varied: Comparator group: 81% patients, dose 4.1±2.6 x 10^6 units (p=0.034 for dose) Intervention group 1: 72% patients, dose 2.7 ± 2.4 x 10^6 units Intervention group 2: 81% patients, dose 3.3 ± 2.4 x 10^6 units

Blinding analysis	Treatment/measurement bias	Follow-up (ITT)
None	None	All included patients
Overall quality assessment (descriptive) Fair		

<table>
<tr><td colspan="5">RESULTS</td></tr>
<tr><td>Outcome</td><td>Intervention group</td><td>Comparator group</td><td>Statistical significance</td><td>Effect measure (95% CI)</td></tr>
<tr><td>Mortality (proportion)</td><td>1. 0%
2. 4.5%</td><td>2.4%</td><td>p=0.63</td><td>2 vs comparator:
RR=1.77 (0.82,3.79) p=0.143</td></tr>
<tr><td colspan="2">Clinical importance
4. Intervention #2 increases risk of adverse event; confidence interval range compatible with no effect and beneficial effect</td><td colspan="3">Clinical relevance
1</td></tr>
<tr><td>Morbidity (proportion)</td><td>Mediastinitis
1. 0%
2. 2.1%
MI
1. 0%
2. 3.9%
Respiratory failure
1. 0%
2. 9.5%
Renal failure requiring dialysis
1. 0%
2. 0.4%
Wound infection
1. 7.7%
2. 6.9%
Stroke
1. 5.1%
2. 3.0%</td><td>Mediastinitis=0%
MI=4.9%
Respiratory failure=12.2%
Renal failure requiring dialysis=2.4%
Wound infection=4.9%
Stroke=9.8%</td><td colspan="2">Mediastinitis, p=0.89
MI, p=0.43
Respiratory failure, p=0.07
Renal failure requiring, dialysis, p=0.35
Wound infection, p=0.84
Stroke, p=0.09</td></tr>
<tr><td colspan="5">Relative risk: Intervention vs comparator
MI:
• 2 vs. comparator: RR=0.80 (0.35,1.80), p=0.582
Respiratory failure:
• 2 vs. comparator: RR=0.78 (0.52,1.16), p=0.220
Renal failure requiring dialysis:
• 2 vs. comparator: RR=0.18 (0.01, 2.73), p=0.215
Wound infection:
• 1 vs. comparator: RR=1.58 (0.34, 7.36), p=0.562
• 2 vs. comparator: RR=1.41(0.82, 2.43), p=0.210
Stroke:
• 1 vs. comparator: RR=0.53 (0.08, 3.56), p=0.510
• 2 vs. comparator: RR=0.31 (0.12,0.80), p=0.016</td></tr>
</table>

Clinical importance Stroke: 2 vs. comparator=1 Wound infection=4 Remaining morbidity outcomes=2		Clinical relevance 1	
Transfusion requirements (proportion)	1. 35.9% 2. 42.2%	75.6%	p<0.0001
Effect measure (95% CI): 1 vs. comparator: RR=0.47 (0.26,0.87), p=0.015 2 vs. comparator: OR=0.24 (0.11,0.50), p<0.001			
Clinical importance 1 vs. comparator=1 2 vs. comparator=1		Clinical relevance 1	
Transfusion requirements, total[b] (units, mean ± SD)	1. 1.2 ± 2.0 2. 2.6 ± 5.7	12.2 ± 2.0	p<0.001
Clinical importance 3		Clinical relevance 1	
Re-operation for bleeding	1. 2.6% 2. 1.7%	14.6%	p=0.002
Relative risk: 1 vs. comparator: RR=0.18 (0.01,2.71), p=0.212 2 vs. comparator: RR=0.12 (0.03,0.44), p=0.001			
Clinical importance 2 vs. comparator=1 1 vs. comparator=2		Clinical relevance 1	
Hospital LOS (days, median)	1. 7 2. 7	9	p=0.018
Clinical importance 1		Clinical relevance 1	
Hospital readmission, within 30 days (proportion)	1. 9.8% 2. 10.8%	7.7%	p=0.89
Relative risk: 1 vs. comparator: RR=1.40 (0.38,5.23), p=0.615 2 vs. comparator: RR=0.24 (0.06, 0.88), p=0.031			
Clinical importance 1 vs. comparator=4 2 vs. comparator=1		Clinical relevance 1	
EXTERNAL VALIDITY			
Generalisability			
Study population considered similar to guideline target population			
Applicability			
Reduced – study performed in Canada, which has some differences to Australia/NZ health system			

Comments
Use of clopidogrel within 4 days of CABG surgery is associated with an increased blood loss, transfusion requirements and re-operation for bleeding. There were also trends towards increased risk of stroke and respiratory failure in this patient group

Abbreviations: CABG, coronary artery bypass graft surgery; CI, confidence interval; LOS, length of stay; NA, not applicable; NR, not reported; OPCAB, off-pump coronary artery bypass; OR, odds ratio; RR, relative risk; SD, standard deviation

[a] Urgent patients were defined as those requiring revascularisation during the same hospital admission and emergent pateints were defined as ICU or coronary care unit patients with intractable angina requiring imminent operative intervention

[b] Includes platelets, RBC, FFP and cryoprecipitate

STUDY DETAILS				
Reference Gerrah R, Elami A, Stamler A, Smirnov A, Stoeger Z. Preoperative aspirin administration improves oxygenation in patients undergoing coronary artery bypass grafting. Chest. 2005;127(5):1622–1626				
Affiliation/Source of funds NR				
Study design	Level of evidence	Location/setting		
Prospective cohort	III-2	Israel, hospital		
Intervention	Comparator			
ASA therapy (100mg daily) stopped at least 7 days prior to surgery N=18 (4 urgent cases)	ASA given daily until surgery N=14 (2 urgent cases)			
Population characteristics				
Patients undergoing first time CABG, with CPB. Mixed population of elective and urgent[a] cases				
Length of follow-up	Outcomes measured			
Unclear—most likely to be until discharge	Mortality, transfusion requirements, change in Hb, hospital and ICU LOS			
INTERNAL VALIDITY				
Allocation	Results	Blinding analysis	Treatment/measurement bias	Follow-up (ITT)
NR	Preoperative data and baseline characteristics similar between study and control groups	None	None	All included patients
Overall quality assessment (descriptive) Fair				
RESULTS				
Outcome	Intervention group	Comparator group	Statistical significance	
Mortality (proportion)	0%	0%	NA	
Clinical importance NA—no difference between study groups		Clinical relevance 1		
Transfusion requirements (postoperative, units, mean ± SD)	Plasma=1.0 ± 1.5 RBC=1.9 ± 1.4	Plasma=0.8 ± 1.2 RBC=1.5 ± 1.22	p=0.7 p=0.5	
Clinical importance 4		Clinical relevance 1		
Haemoglobin (Preoperative, g/dL, mean ± SD)	13.3 ± 1.4	12.8 ± 1.3	p=0.4	
Clinical importance 4		Clinical relevance 1		

Haemoglobin (At hospital discharge, g/dL, mean ± SD)	11.3 ± 1.4	11.2 ± 1.5	p=0.8
Clinical importance 4		Clinical relevance 1	
Hospital LOS (days, mean ± SD,)	7.6 ± 2.3	7.2 ± 2	p=0.6
Clinical importance 4		Clinical relevance 1	
ICU LOS (days, mean ± SD)	2.5 ± 0.9	1.85 ± 0.7	p=0.04
Clinical importance 4		Clinical relevance 1	
EXTERNAL VALIDITY			
Generalisability			
Included patients considered similar to guideline target population			
Applicability			
Reduced—study performed in Israel—differences with Australian/NZ healthcare systems			
Comments			
With exception of ICU LOS, there were no statistically significant differences in outcomes between intervention and comparator groups. However, because of the small sample size, this study is not likely to be powered to show clinically meaningful differences in outcomes			

Abbreviations: ASA, aspirin; CPB, cardiopulmonary bypass; Hb, haemoglobin; ICU, intensive care unit; LOS, length of stay; NA, not applicable; NR, not reported

[a] Urgent operation defined by study investigators as one performed within 48 hr from the time of admission or from catheterisation in patients with refractory angina

STUDY DETAILS				
Reference Ghaffarinejad MH, Fazelifar AF, Shirvani SM, Asdaghpoor E, Fazeli F, Bonakdar HR, et al. The effect of preoperative aspirin use on postoperative bleeding and perioperative myocardial infarction in patients undergoing coronary artery bypass surgery. Cardiol J. 2007;14(5):453–457				
Affiliation/Source of funds NR				
Study design	Level of evidence	Location/setting		
RCT	II	Iran, hospital		
Intervention	Comparator			
ASA therapy (regimen NR) stopped at least 7 days prior to surgery. N=100	ASA until (regimen NR) surgery N=100			
Population characteristics				
Patients undergoing first time elective CABG (NR whether OPCAB or with CPB)				
Length of follow-up	Outcomes measured			
NR	Mortality, morbidity, blood loss, transfusion requirements			
INTERNAL VALIDITY				
Allocation	Results	Blinding analysis	Treatment/measurement bias	Follow-up (ITT)
NR	No differences in baseline patient characteristics	Single-blinded, NR whether patients or clinicians blinded	None	All included patients
Overall quality assessment (descriptive) Fair				
RESULTS				

Outcome	Intervention group	Comparator group	Statistical significance	Effect measure (95% CI)
Mortality (in-hospital, proportion)	0%	0%	NA	
Clinical importance No difference between intervention and comparator groups		Clinical relevance 1		
Morbidity[a,b] (proportion)	Definite MI=3% Probable MI=8%	Definite MI=0% Probable MI=5%	p=0.24 p=0.56	Probable MI RR=1.60 (0.63,4.10) p=0.327
Clinical importance Probable MI - 4		Clinical relevance 1		
Blood loss (postoperative, mL, mean ± SD)	483 ± 251.5	608 ± 359.7	p=0.005	

Clinical importance 2		Clinical relevance 1	
Transfusion requirements (postoperative, units, mean ± SD)	Platelet transfusion=0.28 ± 0.84 FFP=1.46 ± 1.64 RBC=0.94 ± 1.02	Platelet transfusion=0.45 ± 1.32 FFP=2 ± 1.84 RBC=1.32 ± 0.97	p=0.25 p=0.03 p=0.008
Clinical importance 2		Clinical relevance 1	
EXTERNAL VALIDITY			
Generalisability			
Patients considered similar to guideline target population			
Applicability			
Reduced, study performed in Iran where the healthcare system is different from Australia/NZ.			
Comments			
Results suggest that timing of cessation of aspirin monotherapy has no effect on patient outcomes. However, wide SD values indicate that the data is skewed – therefore no definitive conclusions can be made.			

Abbreviations: ASA, aspirin; CABG, coronary artery bypass graft surgery; FFP, fresh frozen plasma; MI, myocardial infarction; NA, not applicable; NR, not reported; OPCAB, off-pump coronary artery bypass; RBC, red blood cells; RCT, randomised controlled trial

[a] Definite MI=a new QS on ECG and a new RWMA on echo with or without CK-MB > 30 IU/L) (RWMA=regional wall motion abnormality; CK-MB=cardiac enzyme marker)

[b] Probable MI=defined as CK-MB > 30 IU/L, with a new QS on ECG or a new RWMA on echo

STUDY DETAILS				
Reference Gulbins H, Malkoc A, Ennker IC, Ennker J. Preoperative platelet inhibition with ASA does not influence postoperative blood loss following coronary artery bypass grafting. Thorac Cardiovasc Surg. 2009;57(1):18–21				
Affiliation/Source of funds				
NR				
Study design	Level of evidence		Location/setting	
Retrospective cohort	III-3		Germany, hospital	
Intervention		Comparator		
ASA therapy (regimen NR) stopped at least 5 days prior to surgery N=9504 (Emergencies=8.7% of all cases) CABG with ECC=84.6% OPCAB= 10.5% Redo=4.9%		ASA until (regimen NR) day of surgery N=2519 (Emergencies=8.8% of all cases) CABG with ECC=89.4 OPCAB= 5.8% Redo=4.8%		
Population characteristics				
Patients undergoing elective and emergency CABG Patients underwent conservative CABG with ECC (on-pump CABG); revascularisation with OPCAB or redo bypass grafting				
Length of follow-up		Outcomes measured		
NR		Mortality, morbidity, transfusion requirements, re-operation for bleeding, ICU		
INTERNAL VALIDITY				
Allocation	Results	Blinding analysis	Treatment/measurement bias	Follow-up (ITT)
NA—retrospective study	No significant differences in baseline demographic or clinical characteristics	NA – retrospective study	None	NA—retrospective study
Overall quality assessment (descriptive): Fair				
RESULTS				
Outcome	Intervention group	Comparator group	Statistical significance	
Mortality (In hospital, proportion for each type of CABG0)	On-pump CABG (ACB with ECC)=1.9%; OPCAB=1.8%; Redo=3.6%	On-pump CABG (ACB with ECC)=1.7%; OPCAB=2.1%; Redo=4.1%	p values for intervention vs comparator NR	

<table>
<tr><td colspan="4">Effect measure (95% CI)</td></tr>
<tr><td colspan="4">Relative risk: Intervention vs. comparator:
CABG with ECC: RR=1.04 (0.84,1.28), p=0.742
OPCAB: RR=0.87 (0.47,1.60), p=0.657
Redo: RR=0.88 (0.46,1.67), p=0.693</td></tr>
<tr><td colspan="2">Clinical importance
CABG with ECC=4
OPCAB=2
Redo=2</td><td colspan="2">Clinical relevance
1</td></tr>
<tr><td>Morbidity (proportion)</td><td>Perioperative infarction
ACB with ECC=1.8%; OPCAB=2%; Redo=3.6%
Pericardial effusion
All CABG patients: 1.8%</td><td>Perioperative infarction
ACB with ECC=2%; OPCAB=0.7% ; Redo=6.6%
Pericardial effusion
All CABG patients: 1.8%</td><td>p values for intervention vs comparator NR</td></tr>
<tr><td colspan="4">Effect measure (95% CI)</td></tr>
<tr><td colspan="4">Relative risk: Intervention vs. comparator:
Perioperative infarction
• CABG with ECC: RR=0.81 (0.65,1.01), p=0.065
• OPCAB: RR=2.89 (1.63, 5.15), p<0.001
• Redo: RR=4.39 (2.30, 8.37), p<0.001
Pericardial effusion:
• All CABG patients: RR=1.03 (0.86,1.25), p=0.727</td></tr>
<tr><td colspan="2">Clinical importance
Perioperative infarction:
CABG with ECC=2
OPCAB=4
Redo=4
Pericardial effusion=4</td><td colspan="2">Clinical relevance
1</td></tr>
<tr><td>Blood loss (chest drainage, postoperative) (mL, mean ± SD)</td><td>ACB with ECC=856 ± 717;
OPCAB=851 ± 696;
Redo=1005 ± 1198
All CABG patients=902 ± 811</td><td>ACB with ECC=781 ± 776;
OPCAB=774 ± 694 ;
Redo=970 ± 1021
All CABG patients=834 ± 781</td><td>p<0.05 (All CABG patients)</td></tr>
</table>

Clinical importance All CABG patients=4		Clinical relevance 1		
Transfusion requirements (RBC packages, mean ± SD)	Intraoperative ACB with ECC=0.3 ± 1; OPCAB=0.3 ± 1.4; Redo=0.6 ± 1.3 All CABG patients=0.3 ± 1.1 Postoperative ACB with ECC=0.8 ± 2.7; OPCAB=0.7 ± 2.6; Redo=2 ± 3.9 All CABG patients=0.88 ± 2.7	Intraoperative ACB with ECC=0.2 ± 1.0; OPCAB=0.14 ± 0.6 ; Redo=0.74 ± 2.2 All CABG patients=0.23 ± 1 Postoperative ACB with ECC=0.9 ± 2.8; OPCAB=0.7 ± 2.5 ; Redo=2.4 ± 5.6 All CABG patients=1.01 ± 2.9	Intraoperative p<0.05 (All CABG patients) Postoperative p<0.05 (All CABG patients)	
Clinical importance All CABG patients, intraoperative=4 All CABG patients, postoperative=4		Clinical relevance 1		
Re-operation for bleeding (proportion)	2.2%	2.1%	p value NR	RR=1.08 (0.89,1.29) p=0.438
Clinical importance All CABG patients=4		Clinical relevance 1		
ICU LOS (days, mean ± SD)	ACB with ECC=3.8 ± 6; OPCAB=3.9 ± 5.3; Redo=5.7 ± 8	ACB with ECC=3.4 ± 4.7; OPCAB=2.7 ± 2.5; Redo=5.9 ± 9.3	p value NR	
Clinical importance For each CABG surgery subset=4		Clinical relevance 1		
EXTERNAL VALIDITY				
Generalisability				
Patients considered similar to guideline target population				
Applicability				
Applicable – European study – healthcare system similar to Australia/NZ				
Comments				
Continuing aspirin therapy until the day of surgery does not result in increased perioperative blood loss or transfusion requirements. Ceasing aspirin 5 days or more prior to operation vs continuing until day of surgery does not result in differences in in-hospital mortality or morbidity. However, the wide overlapping SD values for several outcomes indicate that the data sets are skewed, therefore no definitive conclusions can be made from this study's findings				

Abbreviations: ACB with ECC, isolated coronary bypass grafting with extracorporeal circulation; ASA, aspirin; CABG, coronary artery bypass graft surgery; ECC, extracorporeal circulation; ICU, intensive care unit; LOS, length of stay; NA, not applicable; NR, not reported; OPCAB, off-pump coronary artery bypass; RBC, red blood cells; SD, standard deviation

STUDY DETAILS				
Reference Kamran M, Ahmed A, Dar MI, Khan AB. Effect of aspirin on postoperative bleeding in coronary artery bypass grafting. Ann Thorac Cardiovasc Surg. 2008;14(4):224–229				
Affiliation/Source of funds				
NR				
Study design	Level of evidence	Location/setting		
Prospective cohort	III-2	Pakistan, hospital		
Intervention	Comparator			
ASA therapy (regimen NR) stopped at least 5 days prior to surgery N=15	ASA until (regimen NR) day of surgery N=15			
Population characteristics				
Patients undergoing primary isolated off-pump CABG				
Length of follow-up	Outcomes measured			
To 76 hr postoperative	Blood loss, transfusion requirements, hospital and ICU LOS			
INTERNAL VALIDITY				
Allocation	Results	Blinding analysis	Treatment/measurement bias	Follow-up (ITT)
NR	No significant differences in baseline demographic or clinical characteristics	NR	None	All included patients
Overall quality assessment (descriptive): Poor				
RESULTS				
Outcome	Intervention group	Comparator group	Statistical significance	
Blood loss (Postoperative, mL, mean ± SD)	1st hr=125 ± 128 2nd hr=60.3 ± 60.1 3rd hr=48.0 ± 43.2 Next 24hr=619.3 ± 392.0 28 to 76 hr=102.8 ± 106.8	1st hr=88 ± 63 2nd hr=45 ± 23.3 3rd hr=47.0 ± 35.0 Next 24hr=392.3 ± 333.5 28 to 76 hr=32.0 ± 68.68	1st hr, p=0.074 2nd hr; p=0.004 3rd hr, p=0.48 Next 24hr, p=0.23 28 to 76 hrs, p=0.043	
Clinical importance 4		Clinical relevance 1		
Transfusion requirements (Intraoperative, pints, mean ± SD)	RBC =1.7 ± 1.7 FFP=0.4 ± 0.5 Platelets=0.13 ± 0.35	RBC=1.1 ± 1.2 FFP=0.13 ± 0.35; Platelets=0.06 ± 0.25	P values NR	
Clinical importance 4		Clinical relevance 1		
Hospital LOS (ward days, mean ± SD)	3.3 ± 0.48	3.3 ± 0.48	NS	

Clinical importance 4		Clinical relevance 1	
ICU LOS (days, mean ± SD)	2.4 ± 0.63	2.2 ± 0.88	NS
Clinical importance 4		Clinical relevance 1	
EXTERNAL VALIDITY			
Generalisability			
Patients considered similar to guideline target population			
Applicability			
Reduced applicability – study performed in Pakistan, where healthcare system is not similar to Australia/NZ			
Comments			
Results from this small study suggest that continuing aspirin therapy until the day of surgery is not associated with increased risks of bleeding or transfusion requirements. However, no data was reported on morbidity outcomes. Furthermore, the study population is small and is therefore not adequately powered to demonstrate clinical differences. The wide SD values reported for several outcomes indicate that the data set is skewed – therefore definitive conclusions cannot be made from this study's findings			

Abbreviations: ASA, aspirin; CABG, coronary artery bypass graft surgery; FFP, fresh frozen plasma; ICU, intensive care unit; LOS, length of stay; NA, not applicable; NR, not reported; RBC, red blood cells; SD, standard deviation

STUDY DETAILS				
Reference Kang W, Theman TE, Reed III JF, Stoltzfus J, Weger N. The effect of preoperative clopidogrel on bleeding after coronary artery bypass surgery. J Surg Educ. 2007;64(2):88–92				
Affiliation/Source of funds				
NR				
Study design	Level of evidence		Location/setting	
Retrospective cohort	III-3		USA, hospital	
Intervention		Comparator		
Clopidogrel not received within 7 days prior to surgery N=255		1 Clopidogrel continued to within 3 days of surgery N=25 2. Clopidogrel continued to 4 to 7 days before surgery N=40		
Population characteristics				
Patients undergoing isolated on-pump CABG Unclear if mixed population of emergency/elective Regimen: Clopidogrel loading dose of 300 mg, followed by a daily intake of 75 mg All patients were dosed with ASA—either 325 mg or 81 mg. Unclear if/when ASA stopped preoperatively				
Length of follow-up		Outcomes measured		
Unclear		Mortality, blood loss, transfusion requirements, re-operation for bleeding, ICU LOS		

INTERNAL VALIDITY				
Allocation	Results	Blinding analysis	Treatment/measurement bias	Follow-up (ITT)
NA—retrospective study	No significant differences in baseline demographic or clinical characteristics	NA—retrospective study	None	NA—retrospective study

Overall quality assessment (descriptive): Poor

RESULTS				
Outcome	Intervention group	Comparator group	Statistical significance	Effect measure (95% CI)
Mortality (operative, proportion)	3.1%	1. 8% 2. 0%	p=0.193 [intervention vs. comparator 1]	RR=0.39 (0.17,0.88) p=0.023

Clinical importance Intervention vs comparator #1=1		Clinical relevance 1	
Blood loss (chest tube output, mL, mean ± SD)	1720 ± 1258	1. 1811 ± 1223 2. 1596 ± 1238	p=0.775 [comparator 1 vs. intervention]
Clinical importance 4		Clinical relevance 1	
Blood transfusion requirements (units, mean ± SD)	3.4 ± 4.1	1. 5.8 ± 9.4 2. 2.8 ± 3.5	p=0.027 [comparator 1 vs. intervention]
Clinical importance 4		Clinical relevance 1	
Re-operation for bleeding (proportion)	4.3%	1. 8.0% 2. 5.0%	p=0.41 [comparator 1 vs. intervention]
Effect measure (95% CI)			
Intervention vs. comparator #1: RR=0.54 (0.29,1.01), p=0.053 Intervention vs. comparator #2: RR=0.86 (0.42,1.76), p=0.684			
Clinical importance 2		Clinical relevance 1	
ICU LOS (hrs, mean ± SD)	52.1 ± 77.9	1. 49.5 ± 63.5 2. 43.6 ± 39.3	p=0.786 [comparator (1) vs intervention]
Clinical importance 4		Clinical relevance 1	
EXTERNAL VALIDITY			
Generalisability			
Study population considered similar to target population			
Applicability			
Reduced applicability—study performed in USA—some differences with Australia/NZ healthcare systems			
Comments			
Stopping clopidogrel closer to surgery did not result in statistically significant increases in blood loss, or ICU LOS. However, the wide, overlapping SD values indicate that the data set is skewed; therefore no definitive conclusions can be made based on these results. When clopidogrel was stopped within 3 days of surgery operative mortality and re-operation rate were increased, although these increases were not statistically significant. Considering the small sample size in the comparator groups, and likely inadequate powering, the clinical significance of this effect on operative mortality and re-operation rate is unclear			

Abbreviations: ASA, aspirin; CABG, coronary artery bypass graft surgery; ICU, intensive care unit; LOS, length of stay; NA, not applicable; NR, not reported; RBC, red blood cells; SD, standard deviation

STUDY DETAILS				
Reference Kapetanakis EI, Medlam DA, Petro KR, Haile E, Hill PC, Dullum MK, et al. Effect of clopidogrel premedication in off-pump cardiac surgery: Are we forfeiting the benefits of reduced hemorrhagic sequelae? Circulation. 2006;113(13):1667–1674				
Affiliation/Source of funds				
NR				
Study design	Level of evidence		Location/setting	
Retrospective cohort	III-3		USA, hospital	
Intervention		Comparator		
Clopidogrel naïve or stopped ≥ 7 days prior to surgery (proportion in each group NR) N=1291 (18.7% urgent cases)		Clopidogrel regimen of 75 mg daily within 7 days of surgery or patients received a 300 mg oral loading dose before PCI N=281 (31.7% urgent cases)		
Population characteristics				
Patients undergoing isolated off-pump CABG (emergent cases not included) ASA given prior to surgery (regimen NR). Intraoperative anticoagulation: initial dose at 400 u/kg porcine heparin, with additional dosing during procedure to maintain target activated clotting time >480s. (Details of heparin reversal NR)				
Length of follow-up		Outcomes measured		
Unclear—likely until discharge		Mortality, morbidity, blood loss, transfusion requirements, re-operation for bleeding, hospital and ICU LOS		
INTERNAL VALIDITY				
Allocation	Results			
NA—retrospective study	Baseline preoperative characteristics and demographics for study groups were similar with key exceptions: History of MI: Intervention vs comparator=33.9% vs. 43.8%, p<0.01 Urgent case: Intervention vs comparator=18.7% vs. 31.7%, p<0.01			
Blinding analysis	Treatment/measurement bias		Follow-up (ITT)	
NA – retrospective study	None		NA – retrospective study	
Overall quality assessment (descriptive): Fair				
RESULTS				
Outcome	Intervention group	Comparator group	Statistical significance	Effect measure (95% CI)
Mortality, operative (proportion)	1.4%	1.4%	p=1.00	RR=0.98 (0.52,1.84) p=0.949
Clinical importance 2		Clinical relevance 1		
Morbidity, postoperative stroke (proportion)	1.6%	2.1%	p=0.44	RR=0.73 (0.40,1.32) p=0.292

Clinical importance 2		Clinical relevance 1		
Morbidity, postoperative MI (proportion)	0.6%	1.4%	p=0.25	RR=0.44 (0.17,1.14) p=0.092
Clinical importance 2		Clinical relevance 1		
Transfusion requirements				
Outcome	Intervention group	Comparator group	Statistical significance	Effect measure (95% CI)
Intraoperative, platelets (proportion)	1.0%	3.2%	p<0.01	RR=0.31 (0.15,0.67) p=0.003
Clinical importance 1		Clinical relevance 1		
Intraoperative, platelets, amount (mL, median, min to max)	300 (200–300)	300 (270–600)	p=0.13	
Clinical importance 4		Clinical relevance 1		
Intraoperative, FFP (proportion)	1.0%	1.8%	p=0.21	RR=0.44 (0.18,1.03) p=0.058
Clinical importance 2		Clinical relevance 1		
Intraoperative, FFP, amount (mL, median, min to max)	400 (350–750)	400 (100–3400)	p=0.15	
Clinical importance 4		Clinical relevance 1		
Intraoperative, RBC (proportion)	16.0%	22.1%	p<0.01	RR=0.72 (0.65,0.80) p<0.001
Clinical importance 1		Clinical relevance 1		
Intraoperative, RBC, amount (mL, median, min to max)	500 (250–1500)	500 (250–1250)	p=0.56	
Clinical importance 4		Clinical relevance 1		
Postoperative, platelets (proportion)	9.1%	19.6%,	p<0.01	RR=0.47 (0.38,0.57) p<0.001

Clinical importance 1		Clinical relevance 1		
Postoperative, FFP (proportion)	7.5%	12.1%	p <0.01	RR=0.62 (0.49,0.78) p<0.001
Clinical importance 1		Clinical relevance 1		
Postoperative, RBC (proportion)	34.4%	55.9%	p<0.01	OR=0.41 (0.32,0.54) p<0.001
Clinical importance 1		Clinical relevance 1		
Postoperative, RBC, amount (ml, median, min to max)	500 (250–2500)	500 (250–3250)	p<0.01	
Clinical importance 4		Clinical relevance 1		
Re-operation for bleeding (proportion)	1.4%	6.4%	p<0.01	RR=0.22 (0.12,0.41) p<0.001
Clinical importance 1		Clinical relevance 1		
Hospital LOS (days, median, min to max)	4 (1–79)	5 (1–62)	p=0.03	
Clinical importance 4		Clinical relevance 1		
ICU LOS (days, median, min to max)	1 (0–30)	1 (1–28)	p=0.30	
Clinical importance 4		Clinical relevance 1		
	Propensity matched pair analysis (278 pairs, n=556): Clopidogrel regimen of 75 mg daily within 7 days of surgery or patients received a 300 mg oral loading dose before PCI vs. clopidogrel naïve or stopped ≥7 days prior to surgery			
Outcome	Measure of effect		Statistical significance	
Mortality, operative (OR, 95% CI)	0.9 (0.24, 3.62)		p=0.92	
Clinical importance 2 – for comparator		Clinical relevance 1		
Transfusion requirements, received platelets (OR, 95% CI)	2.3 (1.48, 3.71)		p<0.01	

Clinical importance 3 – for comparator	Clinical relevance 1	
Transfusion requirements, received blood transfusion (OR, 95% CI)	2.7 (1.86, 3.92)	p<0.01
Clinical importance 3 – for comparator	Clinical relevance 1	
Transfusion requirements, received multiple units of blood (OR, 95% CI)	1.5 (0.91, 2.52)	p=0.11
Clinical importance 4 – for comparator	Clinical relevance 1	
Re-operation for bleeding (OR, 95% CI)	3.9 (1.42, 10.46)	p<0.01
Clinical importance 3 – for comparator	Clinical relevance 1	
	Logistic regression analysis Clopidogrel regimen of 75 mg daily within 7 days of surgery or patients received a 300 mg oral loading dose before PCI vs. clopidogrel naïve or stopped ≥7 days prior to surgery.	
Outcome	Measure of effect	Statistical significance
Mortality, operative (OR, 95% CI)	1.0 (0.31, 3.28)	p<0.01
Clinical importance 4 – for comparator	Clinical relevance 1	
Transfusion requirements, received platelets (OR, 95% CI)	2.5 (1.77, 3.66)	p<0.01
Clinical importance 3 – for comparator	Clinical relevance 1	
Transfusion requirements, received blood transfusion (OR, 95% CI)	2.6 (1.94, 3.6)	p<0.01
Clinical importance 3 – for comparator	Clinical relevance 1	
Transfusion requirements, received multiple units of blood (OR, 95% CI)	1.6 (1.07, 2.48)	p=0.02

Clinical importance 3 – for comparator		Clinical relevance 1	
Re-operation for bleeding (OR, 95% CI)	5.1 (2.47, 10.47)	p<0.01	Re-operation for bleeding (OR, 95% CI)
Clinical importance 3—for comparator		Clinical relevance 1	
EXTERNAL VALIDITY			
Generalisability			
Study population similar to guideline target population, but heparin dosing regime is different to the practice applied in Australia.			
Applicability			
Reduced—study performed in the USA—some differences with healthcare systems in Australia/NZ			
Comments			
Unadjusted analysis shows that clopidogrel administered within 7 days of off-pump CABG surgery increases the need for both intra and post operative RBC and platelets. In addition, clopidogrel within 7 days of surgery resulted in more patients requiring postoperative FFP. Mortality, morbidity, ICU and hospital LOS were not significantly different between study groups. When preoperative variables were accounted for by propensity score matched analysis, use of clopidogrel within 7 days of surgery increased the likelihood of re-exploration for bleeding, and increased requirements for RBC, and multiple unit and platelet transfusions. Similar results were found in the logistic regression analysis			

Abbreviations: ASA, aspirin; CABG, coronary artery bypass graft surgery; CI, confidence interval; FFP, fresh frozen plasma; ICU, intensive care unit; LOS, length of stay; MI, myocardial infarction; NA, not applicable; NR, not reported; OR, odds ratio; RBC, red blood cells; RR, relative risk; SD, standard deviation

STUDY DETAILS			
Reference Picker SM, Kaleta T, Hekmat K, Kampe S, Gathof BS. Antiplatelet therapy preceding coronary artery surgery: Implications for bleeding, transfusion requirements and outcome. Eur J Anaesthesiol. 2007;24(4):332–339			
Affiliation/Source of funds			
NR			
Study design	Level of evidence	Location/setting	
Retrospective cohort	III-3	Germany, hospital	
Intervention	Comparator		
No APT/ACT during the last 8 days prior to surgery N=40 APT/ACT regimen prior to surgery NR	APT/ACT continued until 1–7 days prior to surgery N=40 Various APT/ACT strategies: 11/40 ASA only (100mg daily); 28/40 ASA and ticlopidine (250 mg daily) or clopidogrel (75 mg daily); 1/40 clopidogrel only		
Population characteristics			
Patients who underwent first time elective CABG on CPB			
Length of follow-up	Outcomes measured		
Until hospital discharge	Mortality, morbidity, blood loss, transfusion requirements, change in Hb, re-operation for bleeding, hospital and ICU LOS		
INTERNAL VALIDITY			
Allocation	Results		
NR—retrospective analysis	Baseline demographic and clinical characteristics were similar for both groups, with the exception of CK-MB, which was higher in the intervention group, but remained within the normal range (data not shown)		
Blinding analysis	Treatment/measurement bias	Follow-up (ITT)	
NR—retrospective analysis	None	NR—retrospective analysis	
Overall quality assessment (descriptive): Poor			
RESULTS			
Outcome	Intervention group	Comparator group	Statistical significance
Mortality (30 day, proportion)	0	2.5%	NR
Clinical importance Unknown, CI could not be determined		Clinical relevance 1	
Morbidity (proportion)	Pneumonia=0% MI=7.5%	Pneumonia=2.5% MI=0%	NR
Clinical importance Unknown, CI could not be determined		Clinical relevance 1	
Blood loss (chest tube, at 12hr postoperative, mL, mean ± SD)	412 ± 590	940 ± 861	NR

Clinical importance 2		Clinical relevance 1	
Transfusion requirements, FFP (units, mean ± SD)	1.3 ± 2.5	4.9 ± 6.4	NR
Clinical importance 2		Clinical relevance 1	
Transfusion requirements, platelets (units, mean ± SD)	0.1 ± 0.2	1.5 ± 1.3	NR
Clinical importance 2		Clinical relevance	
Transfusion requirements, RBC (units, mean ± SD)	1.5 ± 2.9	4.5 ± 4.9	NR
Clinical importance 2		Clinical relevance	
Haemoglobin, baseline (g/dL, mean ± SD)	13.5 ± 1.5	14.0 ± 1.7	NR
Clinical importance 3		Clinical relevance 1	
Haemoglobin, discharge (g/dL, mean ± SD)	12.2 ± 1.5	11.9 ± 1.6	NR
Clinical importance 3		Clinical relevance 1	
Re-operation for bleeding (proportion)	7.5%	20%	p=0.190, NS
Relative risk (95% CI): intervention vs. comparator RR=0.38 (0.08,1.75), p=0.212			
Clinical importance 2		Clinical relevance 1	
Hospital LOS (days, mean ± SD)	10.4 ± 2.3	11.6 ± 3.9	NR
Clinical importance 4		Clinical relevance 1	
ICU LOS (days, mean ± SD)	1.7 ± 1.4	1.7 ± 1.3	NR
Clinical importance 4		Clinical relevance 1	
EXTERNAL VALIDITY			
Generalisability			
Study population similar to guideline target population			
Applicability			
Applicable: European study – health care system similar to Australia/NZ			

Comments
In elective CABG patients, ceasing combined APT/ACT closer to surgery appears to increase blood loss and transfusion requirements. However, the wide SD values for these outcomes indicate that the data set is skewed, therefore no definitive conclusions can be made. Cessation of combined APT/ACT closer to surgery also increased mortality and the rate of re-operation for bleeding

Abbreviations: ACT; anti-coagulant therapy; APT, anti-platelet therapy; ASA, aspirin; CABG, coronary artery bypass graft surgery; CI, confidence interval; CK-MB, creatine kinase isozyme MB); FFP, fresh frozen plasma; Hb, haemoglobin; ICU, intensive care unit; LOS, length of stay; MI, myocardial infarction; NA, not applicable; NR, not reported; SD, standard deviation

STUDY DETAILS				
Reference Shim JK, Choi YS, Oh YJ, Bang SO, Yoo KJ, Kwak YL. Effects of preoperative aspirin and clopidogrel therapy on perioperative blood loss and blood transfusion requirements in patients undergoing off-pump coronary artery bypass graft surgery. J Thorac Cardiovasc Surg. 2007;134(1):59–64				
Affiliation/Source of funds				
NR				
Study design	Level of evidence	Location/setting		
Prospective cohort	III-2	Korea, hospital		
Intervention	Comparator			
Aspirin and clopidogrel discontinued >6 days prior to surgery N=33 (100 mg aspirin and 75 mg clopidogrel, both oral, daily)	1. Aspirin and clopidogrel continued until 3 to 5 days before surgery N=50 2. Aspirin and clopidogrel continued within 3 days of surgery N=20 (100 mg aspirin and 75 mg clopidogrel, both oral, daily)			
Population characteristics				
Patients who underwent elective, off-pump CABG				
Length of follow-up	Outcomes measured			
76 hours postoperatively	Blood loss, transfusion requirements, change in haematocrit, ICU LOS			
INTERNAL VALIDITY				
Allocation	Results	Blinding analysis	Treatment/measurement bias	Follow-up (ITT)
NA	No significant differences in demographic and baseline clinical data	None	None	All patients followed up
Overall quality assessment (descriptive): Poor				
RESULTS				
Outcome	Intervention group	Control group	Statistical significance	
Blood loss, intraoperative (mL, mean ± SD)	265 ± 146	1. 330 ± 191 2. 323 ± 187	p=0.174 (comparison across all patient groups)	
Clinical importance 4		Clinical relevance 1		
Blood loss, during first 24 hours in ICU (mL, mean ± SD)	756 ± 408	1. 729 ± 485 2. 627 ± 257	p=0.425 (comparison across all patient groups)	

Clinical importance 4		Clinical relevance	
Transfusion requirements, intraoperative (proportion)	39%	1. 48% 2. 26%	p=0.255 (comparison among all patient groups)
Relative risk(95% CI): intervention vs. comparator: Intervention vs. comparator #1: RR=0.82 (0.42,1.59), p=0.558 Intervention vs. comparator #2: RR=1.58 (1.00,2.48), p=0.050			
Clinical importance Intervention vs. comparator #1=2 Intervention vs. comparator #2=3		Clinical relevance 1	
Transfusion requirements, during first 24 hours in ICU (proportion)	42%	1. 42% 2. 25%	p=0.368 (comparison among all patient groups)
Relative risk (95% CI): intervention vs. comparator: Intervention vs. comparator #1: RR=1.01 (0.54,1.89), p=0.975 Intervention vs. comparator #2: RR=1.70 (1.13, 2.55), p=0.011			
Clinical importance Intervention vs. comparator #1=4 Intervention vs. comparator #2=3		Clinical relevance 1	
Transfusion requirements, RBC, intraoperative (units, mean ± SD)	0.4 ± 0.5	1. 0.5 ± 0.5 2. 0.3 ± 0.4	p=0.260 (comparison among all patient groups)
Clinical importance 4		Clinical relevance 1	
Transfusion requirements, during first 24 hours in ICU (units, mean ± SD)	0.4 ± 0.7	1. 0.7 ± 1.0 2. 0.6 ± 1.0	p=0.512 (comparison among all patient groups)
Clinical importance 4		Clinical relevance 1	
Transfusion requirements, FFP/platelets, intraoperative	0	1. 0 2. 0	NA
Clinical importance Not assigned		Clinical relevance 1	
Transfusion requirements, FFP, postoperative	10 units in 4 patients	1. 13 units in 4 patients 2. 2 units in one patients	NR
Clinical importance Not assigned		Clinical relevance 1	
Transfusion requirements, platelets, postoperative	None	1. 8 units in 1 patient 2. 8 units in 1 patient	NR

Clinical importance Not assigned		Clinical relevance 1	
Haematocrit, preoperative (%, mean ± SD)	35.9 ± 5.7	1. 37.3 ± 5.3 2. 39.4 ± 4.5	p=0.063 (intergroup comparison)
Clinical importance 4		Clinical relevance 1	
Haematocrit, postoperative (%, mean ± SD)	25.9 ± 2.5	1. 24.8 ± 3.3 2. 24.1 ± 2.7	p=0.092 (intergroup comparison)
Clinical importance 4		Clinical relevance 1	
Hospital LOS, postoperative (days, mean ± SD)	12.9 ± 7.0	1. 11.0 ± 4.1 2. 10.1 ± 2.2	p=0.174 (intergroup comparison)
Clinical importance 4		Clinical relevance 1	
ICU LOS (days, mean ± SD)	2.9 ± 0.7	1. 2.8 ± 0.6 2. 2.7 ± 0.7	p=0.595 (intergroup comparison)
Clinical importance 4		Clinical relevance 1	
EXTERNAL VALIDITY			
Generalisability			
Study population considered similar to guideline target population			
Applicability			
Reduced applicability—study performed in Korea—which has a different healthcare system to Australia/NZ			
Comments			
In elective off pump CABG, timing of cessation of clopidogrel and aspirin does not appear to impact on blood loss, transfusion requirements, haematocrit values and hospital or ICU LOS. This study did not report the effect of timing cessation on morbidity outcomes. The study sample size is small; therefore, the study powering is likely to be too low to demonstrate any clinically meaningful differences. Therefore, no definitive conclusions can be made regarding the effects of varying the timing of cessation of combination antiplatelet therapy, In addition, it is unclear whether the results of this study are transferable to the guideline target population			

Abbreviations: ACT; anti-coagulant therapy; APT, anti-platelet therapy; ASA, aspirin; CABG, coronary artery bypass graft surgery; CI, confidence interval; FFP, fresh frozen plasma; Hb, haemoglobin; ICU, intensive care unit; LOS, length of stay; MI, myocardial infarction; NA, not applicable; NR, not reported; RR, relative risk; SD, standard deviation

STUDY DETAILS				
Reference Song SW, Youn YN, Yi G, Lee S, Yoo KJ. Effects of continuous administration of clopidogrel before off-pump coronary artery bypass grafting in patients with acute coronary syndrome. Circ J. 2008;72(4):626–632				
Affiliation/Source of funds				
NR				
Study design	Level of evidence		Location/setting	
Retrospective cohort	III-3		Korea, hospital	
Intervention		Comparator		
Surgery postponed ≥ 3 days prior to cessation of clopidogrel (75 mg daily) (period of cessation: mean=4.3 ± 1.2, range 3–7 days) N=102		Clopidogrel (75 mg daily) continued until immediately prior to surgery N=70		
Population characteristics				
Patients who underwent off-pump CABG (NR proportions of elective, emergent or urgent cases)				
Length of follow-up		Outcomes measured		
Unclear		Mortality, morbidity, transfusion requirements, change in Hb re-operation for bleeding, ICU LOS		
INTERNAL VALIDITY				
Allocation	Results	Blinding analysis	Treatment/measurement bias	Follow-up (ITT)
NR—retrospective analysis	Propensity matched score analysis used—no significant difference in baseline characteristics between patients in each study group	NR—retrospective analysis	None	NR—retrospective analysis
Overall quality assessment (descriptive): Poor				
RESULTS				
Outcome	Intervention group	Control group	Statistical significance	
Mortality, operative (proportion)	0%	1.4%	p=0.41	

Clinical importance Not assigned, RR and CI not determined		Clinical relevance 1	
Morbidity (proportion)	Perioperative MI=1.4% Coronary spasm=0% Respiratory failure=0% Pnemonia=1.0% Renal failure=1.0% Hepatic failure=1.0% Mediastinitis=0%	Perioperative MI=1.4% Coronary spasm=0% Respiratory failure=1.4% Pnemonia=0% Renal failures=0% Hepatic failure=0% Mediastinitis=1.4%	p=1.0 for perioperative MI; p=0.41 for all other morbidity outcomes
Clinical importance Not assigned, RR and CI not determined		Clinical relevance 1	
Blood loss, intraoperative (mL, mean ± SD)	273.8 ± 138.6	303.3 ± 149.5	p=0.842
Clinical importance 4		Clinical relevance 1	
Blood loss, postoperative (mL, mean ± SD)	673.2 ± 452.4	601.4 ± 312.6	p=0.616
Clinical importance 4		Clinical relevance 1	
Transfusion requirements, platelets, perioperative (proportion)	7.1%	2.9%	p=0.441
Outcome measure (95% CI) Intervention vs. comparator: RR=2.50 (0.76, 8.25), p=0.133			
Clinical importance 4		Clinical relevance 1	
Transfusion requirements, RBC, perioperative (proportion)	34.3%	33.3%	p=1.000
Outcome measure (95% CI) Intervention vs. comparator: RR=1.04 (0.66,1.65), p=0.856			
Clinical importance 4		Clinical relevance 1	
Transfusion requirements, RBC (units, mean ± SD)	0.5 ± 0.4	0.4 ± 0.3	p=0.624
Clinical importance 4		Clinical relevance 1	
Haemoglobin level, preoperative (g/dL, mean ± SD)	12.7 ± 1.8	12.7 ± 1.8	NA

Clinical importance 4		Clinical relevance 1	
Haemoglobin level, first day post-surgery (g/dL, mean ± SD)	9.1 ± 1.2	8.8 ± 1.2	p=0.046
Clinical importance 4		Clinical relevance 1	
Re-operation for bleeding (proportion)	1.4%	1.4%	p=1.00
Outcome measure (95% CI) Intervention vs. comparator: RR=1.0 [0.06,15.67], p=1.000			
Clinical importance 4		Clinical relevance 1	
ICU LOS (hrs, mean ± SD)	52.8 ± 19.6	53.0 ± 52.8	p=0.955
Clinical importance 4		Clinical relevance 1	
EXTERNAL VALIDITY			
Generalisability			
Study population considered similar to guideline target population			
Applicability			
Reduced applicability—study performed in Korea—which has a different healthcare system to Australia/NZ			
Comments			
Results suggest that continuous use of combined antiplatelet therapy until surgery does not increase transfusion requirements or risk of adverse events in comparison to patients whose combination antiplatelet therapy was stopped at least 3 days prior to surgery. However, the study population is not large and reported SD values indicate that the data set is skewed, therefore it is uncertain if similar results would be observed in the guideline target population			

Abbreviations: ACT; anti-coagulant therapy; APT, anti-platelet therapy; ASA, aspirin; CABG, coronary artery bypass graft surgery; CI, confidence interval; FFP, fresh frozen plasma; Hb, haemoglobin; ICU, intensive care unit; LOS, length of stay; MI, myocardial infarction; NA, not applicable; NR, not reported; RR, relative risk; SD, standard deviation

STUDY DETAILS			
Reference Weightman WM, Gibbs NM, Weidmann CR, Newman MAJ, Grey DE, Sheminant MR, et al. The effect of preoperative aspirin-free interval on red blood cell transfusion requirements in cardiac surgical patients. J Cardiothorac Vasc Anesth. 2002;16(1):54–58			
Affiliation/Source of funds			
NR			
Study design	Level of evidence	Location/setting	
Retrospective cohort	III-3	Australia, hospital	
Intervention	Comparator		
1. ASA discontinued 3 to 5 days prior to surgery N=255 2. ASA discontinued 6 to 7 days prior to surgery N=215 3. ASA discontinued >7 days prior to surgery N=187 (ASA regimen NR)	ASA continued until ≤ 2 days prior to surgery N=140 (ASA regimen NR)		
Population characteristics			
Patients who underwent first time CABG with CPB (Emergent cases not included)			
Length of follow-up	Outcomes measured		
Unclear	Mortality, transfusion requirements, change in haemoglobin re-operation for bleeding, hospital LOS		
INTERNAL VALIDITY			
Allocation	Blinding analysis	Treatment/measurement bias	Follow-up (ITT)
NR—retrospective analysis	NR—retrospective analysis	None	NR—retrospective analysis
RESULTS			
Intervention and comparator groups were similar with regards to demographics, and baseline surgical and risk factor variables, with exceptions: In intervention group #1, 67% of patients had preoperative nitrate therapy vs 61% in the comparator group; 52% in intervention group #2;,and 58% in intervention group #3 , p<0.05 for comparison with intervention group #2 For the proportion of patients with MI within 6 wks before surgery, the comparator group and intervention group #2 had 20% and 12% respectively vs 10% in intervention group #1 and 5% in intervention group #3, p<0.0.05 for comparison with intervention group #3			
Overall quality assessment (descriptive): Poor			
RESULTS			
Outcome	Intervention group	Control group	Statistical significance
Mortality	1. 1.6% 2. 2.8% 3. 1.6%	2.1%	NS

Relative risk (95% CI): Intervention vs. comparator Intervention #1 vs. comparator: RR=0.73 (0.19,2.87), p=0.654 Intervention #2 vs. comparator: RR=1.30 (0.43,3.94), p=0.640 Intervention #3 vs. comparator: RR=0.75 (0.15,3.65), p=0.720			
Clinical importance Intervention #1 vs. comparator=2 Intervention #2 vs. comparator=4 Intervention #3 vs. comparator=2		Clinical relevance 1	
Transfusion requirements, platelets (units, mean ± SD)	1. 1.6 ± 4.0 2. 1.5 ± 3.4 3. 0.9 ± 2.4	2.7 ± 6.0	p<0.05 (comparator vs group 3)
Clinical importance 4		Clinical relevance 1	
Transfusion requirements, RBC (units, mean ± SD)	1. 1.5 ± 2.0 2. 1.6 ± 2.8 3. 1.3 ± 1.9	2.2 ± 3.8	p<0.05 (comparator vs group 3)
Clinical importance 4		Clinical relevance 1	
Transfusion requirements, FFP (units, mean ± SD)	1. 0.8 ± 2.1 2. 0.9 ± 3.1 3. 0.6 ± 1.5	1.4 ± 3.1	p<0.05 (comparator vs group 3)
Clinical importance 4		Clinical relevance 1	
Haemoglobin, day 0 (g/dL, mean ± SD)	1. 14.3 ± 1.4 2. 14.3 ± 1.2 3. 14.2 ± 1.3	14.2 ± 1.4	NS
Clinical importance 4		Clinical relevance 1	
Haemoglobin, admission to ICU (g/dL, mean ± SD)	1. 10.1 ± 1.5 2. 10.1 ± 1.4 3. 10.1 ± 1.4	10.0 ± 1.4	NS
Clinical importance 4		Clinical relevance 1	
Haemoglobin, postoperative day 3 (g/dL, mean ± SD)	1. 11.0 ± 1.4 2. 11.0 ± 1.3 3. 11.0 ± 1.4	10.8 ± 1.4	NS
Clinical importance 4		Clinical relevance 1	
Re-operation for bleeding (proportion)	1. 3.1% 2. 5.5% 3. 2.7%	4.3 %	NS

Relative risk (95% CI): Intervention vs. comparator Intervention #1 vs. comparator: RR=0.73 (0.28,1.90), p=0.521 Intervention #2 vs. comparator: RR=1.30 (0.61,2.80), p=0.499 Intervention #3 vs. comparator: RR=0.62 (0.18,2.11), p=0.447			
Clinical importance Intervention #1 vs. comparator=2 Intervention #2 vs. comparator=4 Intervention #3 vs. comparator=2		Clinical relevance 1	
Hospital LOS (days, mean ± SD)	1. 8.2 ± 8 2. 7.6 ± 3 3. 8.3 ± 6	7.8 ± 4	NS
Clinical importance 4		Clinical relevance 1	
EXTERNAL VALIDITY			
Generalisability			
Study population considered similar to guideline target population			
Applicability			
Likely to be reduced, although this is an Australian study, it is retrospective and somewhat. It is possible that patient outcomes may be different now because of other differences in transfusion practice			
Comments			
Results show that patients who stop aspirin 2 days or less prior to surgery have increase transfusion requirements in comparison to those who stop more than 7 days preoperatively - there were no difference between groups in terms of re-operation, postoperative length of stay or mortality. No morbidity outcomes were reported. No significant differences in transfusion requirements were reported between patients who stopped aspirin 2 days or less preoperatively or who stop between 3 and 7 days preoperatively			

Abbreviations: ACT; anti-coagulant therapy; APT, anti-platelet therapy; ASA, aspirin; CABG, coronary artery bypass graft surgery; CI, confidence interval; FFP, fresh frozen plasma; Hb, haemoglobin; ICU, intensive care unit; LOS, length of stay; MI, myocardial infarction; NA, not applicable; NR, not reported; RR, relative risk; SD, standard deviation

Noncardiac studies: Level I evidence

<table>
<tr><td colspan="5">STUDY DETAILS</td></tr>
<tr><td colspan="5">Reference Burger W, Chemnitius JM, Kneissl GD, Rücker G. Low-dose aspirin for secondary cardiovascular prevention – cardiovascular risks after its perioperative withdrawal versus bleeding risks with its continuation — review and meta-analysis. J Intern Med. 2005;257:399–414.</td></tr>
<tr><td colspan="5">Affiliation/Source of funds:
Department of Interventional Cardiology, St Georg Hospital, Leipsig; Cardiologic Practice, Wolfenbuttel; Department of Rehabilitative and Preventative Sports Medicine, Medical Clinic, University of Freiburg, Germany.
Funding source: None reported. No conflict of Interest was declared</td></tr>
<tr><td colspan="2">Study design: Systematic Review
N = 41 studies</td><td colspan="2">Level of evidence: I</td><td>Location/setting: NA</td></tr>
<tr><td colspan="5">Population characteristics: Studies included patients undergoing noncardiac surgeries and invasive procedures. These included: spinal and epidural anaesthesia; oral surgical procedures; pancreas transplant biopsy; transbronchial biopsy; core needle breast biopsy; insertion, removal or replacement of peritoneal dialysis catheter; gastroenterologic endoscopy; ophthalmology; orthopaedic surgery; tonsillectomy; urology; vascular surgery.</td></tr>
<tr><td colspan="2">Length of follow-up: NA</td><td colspan="3">Outcome(s) measured: Bleeding complications</td></tr>
<tr><td colspan="5">INTERNAL VALIDITY</td></tr>
<tr><td>Allocation

NA</td><td>Comparison of study groups
Studies were compared by meta-analysis</td><td>Blinding

NA</td><td>Treatment/measurement bias
Studies reporting on similar or identical procedures and bleeding sequels were pooled for a meta-analsysis using Mantel-Haenszel statistics for nominal data. This was done even if randomised and observationa studies were mixed.</td><td>Follow-up (ITT)

ITT analysis.</td></tr>
<tr><td colspan="5">Overall quality assessment (descriptive):
This study was a fair quality systematic review.</td></tr>
<tr><td colspan="5">RESULTS</td></tr>
<tr><td>Outcome</td><td>Risk Measure</td><td colspan="2">OR</td><td>Statistical significance</td></tr>
<tr><td>Bleeding rate</td><td>Odds Ratio</td><td colspan="2">1.5</td><td>NR</td></tr>
<tr><td colspan="3">Clinical importance (1–4)
Unable to determine</td><td colspan="2">Relevance (1–5)
1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival.</td></tr>
<tr><td colspan="5">Any other adverse effects
None reported</td></tr>
<tr><td colspan="5">EXTERNAL VALIDITY</td></tr>
<tr><td colspan="5">Generalisability</td></tr>
</table>

The studies were performed in patients undergoing noncardiac surgeries and invasive procedures and is generalisable to this patient population
Applicability The study is most likely applicable to the Australian healthcare setting.
Comments The authors conclude that only if low-dose aspirin may cause bleeding risks with increased mortality or sequels comparable with the observed cardiovascular risks after aspirin withdrawal, it should not be discontinued prior to an intended operation or procedure.

STUDY DETAILS

Reference Nematullah A, Alabousi A, Blanas N, Douketis JD, Sutherland SE. Dental surgery for patients on anticoagulant therapy with warfarin: A systematic review and meta-analysis. J Can Dent Assoc. 2009;75(1):41-41i.

Affiliation/Source of funds:

Faculty of Dentistry, University of Toronto, Toronto, Ontario, Canada; Department of Dentistry, Sunnybrook Health Sciences Centre, Toronto, Ontorio; St Josephs Health Care, Ontario Hamilton; Department of Medicine McMaster University, Hamilton, Ontario, Canada.

Funding source: The authors have declared no financial interests.

Study design: Systematic Review N = 5 studies	Level of evidence: I	Location/setting: NA

Population characteristics: Studies were included if it was a randomised controlled trial assessing anticoagulant management for patients on warfarin therapy who required an elective dental procedure.

Length of follow-up: NA	Outcome(s) measured: thromboembolsim, postoperative bleeding

INTERNAL VALIDITY

Allocation	Comparison of study groups	Blinding	Treatment/measurement bias	Follow-up (ITT)
NA	Studies were compared by meta-analysis	NA	Not reported	ITT analysis.

Overall quality assessment (descriptive):

This study was a good quality systematic review. However, there is the potential for a type II error (false negative) in the interpretation of the results, as most included studies were underpowered to detect an increased risk of major bleeding with a continued warfarin strategy. There potential weaknesses of the review. Firstly, only literature in the English language was searched. Secondly, 4 of the 5 trials were of poor methodological quality.

RESULTS

Outcome	Risk Measure	RR (95% CI)	Statistical significance
Nonmajor bleeding	Relative risk (warfarin continuation vs warfarin interruption)	0.71 (0.39, 1.28)	p=0.65
Minor bleeding		1.19 (0.90, 1.58)	p=0.22

Clinical importance (1–4)	Relevance (1–5)
3 The confidence interval does not include any clinically important effects	1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival.

Any other adverse effects

None reported

EXTERNAL VALIDITY

Generalisability

The studies were performed in patients undergoing elective dental surgery and may not be generalisable to other types of surgeries or invasive procedures

Applicability

The study is most likely applicable to the Australian healthcare setting.

Comments

The authors conclude that continuing the regular dose of warfarin therapy does not seem to confer an increased risk of bleeding compared with discontinuing or modifying the warfarin dose for patients undergoing minor dental procedures.

Noncardiac studies: Level II and III evidence

STUDY DETAILS				
Reference An HS, Mikhail WE, Jackson WT, Tolin B, Dodd GA. Effects of hypotensive anesthesia, nonsteroidal antiinflammatory drugs, and polymethylmethacrylate on bleeding in total hip arthroplasty patients. J Arthroplasty. 1991;6:245–250.				
Affiliation/Source of funds: The Department of Orthopaedic Surgery, The Medical College of Wisconsin, Milwaukee, Wisconsin; Department of Orthopaedics, St Vincent Medical Centre, Toledo, Ohio; Department of Orthopaedics, The Medical College of Ohio, Toledo, Ohio; University of Pennsylvania, Philadelphia, Pennsylvania; and Medical College of Ohio, Toledo, Ohio, USA Funding source: No funding source reported				
Study design: Retrospective cohort study N = 140		Level of evidence: III		Location/setting: teaching hospitals affiliated with the Medical College of Ohio, Toledo, USA
Intervention No aspirin or NSAID therapy or discontinuation at least 2 weeks prior to surgery Sample size: n = 90		Comparator(s) Aspirin or NSAIDs until surgery Sample size: n = 55		
Population characteristics: Patients who underwent total hip arthroplasty				
Length of follow-up: NR		Outcome(s) measured: Intraoperative blood loss (determined by the volume of blood in suction apparatus and the weight of the sponges with blood), postoperative blood loss (determined by the amount of suction or drainage for 48 hours after the operation), haemoglobin drop		
INTERNAL VALIDITY				
Allocation Allocation was based on the patients prior exposure to NSAIDs	Comparison of study groups No baseline characteristics were presented	Blinding No blinding details were reported	Treatment/ measurement bias All patients were treated the same	Follow-up (ITT) ITT analysis performed
Overall quality assessment (descriptive): This was a fair quality retrospective cohort study				

RESULTS			
Outcome	No aspirin/ NSAIDs or therapy ceased at least 2 weeks before surgery	Aspirin/ NSAIDs continued until surgery	Statistical significance
Blood loss during surgery (cm^3)	481	499	NS
Blood loss 24 h after surgery (cm^3)	600	772	P=0.005
Clinical importance (1–4) Unable to determine		Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival.	
Mean fall in Hb (g/dL)	3.36	3.46	NS

Blood transfusion (cm^3)	644	532	NS
Clinical importance (1–4) Unable to determine		Relevance (1–5) 2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention	
Any other adverse effects None reported			
EXTERNAL VALIDITY			
Generalisability The study was performed in patients undergoing orthopaedic surgery and may not be generalisable to other types of surgeries or invasive procedures			
Applicability The study was performed in the USA and may be applicable to the Australian healthcare setting			
Comments The authors conclude that patients who had been on aspirin or NSAIDs prior to surgery had increased intraoperative and postoperative blood loss compared to the patients who did not take such medications			

STUDY DETAILS				
Reference Campbell JH, Alvarado F, Murray RA. Anticoagulation and minor oral surgery: should the anticoagulant regimen be altered? J Oral Maxillofac Surg. 2000;58:131–135.				
Affiliation/Source of funds: Department of Oral Surgery, Medicine, and Pathology, Indiana University School of Dentistry, Indianapolis; University of Michigan School of Dentistry, Ann Arbor; Oral and Maxillofacial Surgery, University of Michigan, Ann Arbor, USA. Funding source: Supported in part by a student research fellowship from American Association of Dental Research.				
Study design: Randomised controlled trial N = 25	Level of evidence: II	Location/setting: Teaching hospital, USA		
Intervention Warfarin stopped 72-96 hours prior Sample size: n = 13	Comparator(s) Warfarin continued Sample size: n = 12			
Population characteristics: Warfarinised patients requiring dental extractions.				
Length of follow-up: 1 day	Outcome(s) measured: Bleeding.			
INTERNAL VALIDITY				
Allocation Details of allocation are not reported.	Comparison of study groups There were no differences between groups at baseline.	Blinding No blinding details are reported	Treatment/measurement bias It is assumed all patients were treated the same.	Follow-up (ITT) Unclear
Overall quality assessment (descriptive): This study was a poor quality randomised controlled trial with a very small sample size.				
RESULTS				
Outcome	Intervention	Comparator	Statistical significance	
Serious postoperative bleeding	0%	0%	NA	
Blood loss (mL/unit of surgery)	1.4	2.2	P=0.15	
Clinical importance (1–4) Unable to determine		Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival.		
Any other adverse effects None reported				
EXTERNAL VALIDITY				
Generalisability The patient population included patients requiring dental extractions and may not be generalisable to other procedures.				
Applicability The study is most likely applicable to the Australian healthcare setting.				

Comments

The authors conclude that many patients can safely undergo routine outpatient oral surgical procedures without alteration of their regular therapeutic anticoagulation regimens and without additional medical intervention.

STUDY DETAILS		
Reference Devani P, Lavery KM, Howell CJT. Dental extractions in patients on warfarin: is alteration of anticoagulant regime necessary? Br J Oral Maxillofac Surg. 1998;36:107–111.		
Affiliation/Source of funds: Department of Oral and Maxillofacial Surgery, Queen Victoria Hospital, East Grinstead, Department of Oral and Maxillofacial Surgery, West Hill Hospital, Dartford, UK. Funding source: None reported.		
Study design: Randomised controlled trial N = 65	Level of evidence: II	Location/setting: Medical Centre, USA
Intervention Warfarin stopped 2-3 days prior Sample size: n = 32	Comparator(s) Warfarin continued Sample size: n = 33	
Population characteristics: Warfarinised patients requiring dental extractions.		
Length of follow-up: NR	Outcome(s) measured: Bleeding.	

INTERNAL VALIDITY				
Allocation Patients were allocated to warfarin interruption or continuation on an alternating basis.	Comparison of study groups There were no differences between groups at baseline.	Blinding No blinding details are reported	Treatment/measurement bias Antibiotic prophylaxis was used in patients at increased risk of bacterial endocarditis.	Follow-up (ITT) ITT
Overall quality assessment (descriptive): This study was a poor quality randomised controlled trial.				

RESULTS			
Outcome	Intervention	Comparator	Statistical significance
Bleeding (30 min after surgery)	0%	0%	NA
Bleeding (24 hrs after surgery)	0%	0%	NA
Oozing	1/32 (3.2%)	1/33 (3.0%)	NS
Clinical importance (1–4) Unable to determine		Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival.	
Any other adverse effects None reported			
EXTERNAL VALIDITY			
Generalisability The patient population included patients requiring dental extractions and may not be generalisable to other procedures.			

Applicability
The study is most likely applicable to the Australian healthcare setting.
Comments
The authors conclude that, provided the INR is within the therapeutic range (2.0-4.0) and local measures are used to control postoperative bleeding, there is no justification in altering warfarin treatment prior to dental extractions in these patients, and therby exposing them to the risk of thromboembolism.

STUDY DETAILS				
Reference Dunn AS, Turpie AGG. Perioperative management of patients receiving oral anticoagulants. Arch Intern Med. 2003;163:901–908.				
Affiliation/Source of funds: Department of Interventional Cardiology, St Georg Hospital, Leipsig; Cardiologic Practice, Wolfenbuttel; Department of Rehabilitative and Preventative Sports Medicine, Medical Clinic, University of Freiburg, Germany. Funding source: None reported. No conflict of Interest was declared				
Study design: Systematic Review N = 41 studies	Level of evidence: I	Location/setting: NA		
Population characteristics: Studies included patients undergoing noncardiac surgeries and invasive procedures. These included: spinal and epidural anaesthesia; oral surgical procedures; pancreas transplant biopsy; transbronchial biopsy; core needle breast biopsy; insertion, removal or replacement of peritoneal dialysis catheter; gastroenterologic endoscopy; ophthalmology; orthopaedic surgery; tonsillectomy; urology; vascular surgery.				
Length of follow-up: NA	Outcome(s) measured: Bleeding complications			
INTERNAL VALIDITY				
Allocation NA	Comparison of study groups Studies were compared by meta-analysis	Blinding NA	Treatment/measurement bias Studies reporting on similar or identical procedures and bleeding sequels were pooled for a meta-analysis using Mantel-Haenszel statistics for nominal data. This was done even if randomised and observationa studies were mixed.	Follow-up (ITT) ITT analysis.
Overall quality assessment (descriptive): This study was a fair quality systematic review.				
RESULTS				
Outcome	Risk Measure	OR	Statistical significance	
Bleeding rate	Odds Ratio	1.5	NR	
Clinical importance (1–4) Unable to determine		Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival.		
Any other adverse effects None reported				
EXTERNAL VALIDITY				
Generalisability The studies were performed in patients undergoing noncardiac surgeries and invasive procedures and is generalisable to this patient population				

Applicability
The study is most likely applicable to the Australian healthcare setting.
Comments
The authors conclude that only if low-dose aspirin may cause bleeding risks with increased mortality or sequels comparable with the observed cardiovascular risks after aspirin withdrawal, it should not be discontinued prior to an intended operation or procedure.

STUDY DETAILS				
Reference El-Jack SS, Ruygrok PN, Webster MWI, Stewart JT, Bass NM, Armstrong GP, et al. Effectiveness of manual pressure hemostasis following transfemoral coronary angiography in patients on therapeutic warfarin anticoagulation. Am J Cardiol. 2006;97:485–488.				
Affiliation/Source of funds: The Green Lane Cardiovascular Service, Auckland City Hospital, Auckland, New Zealand. Funding source: None reported.				
Study design: Randomised controlled trial N = 61	Level of evidence: II	Location/setting: Hospital, NZ		
Intervention Warfarin stopped ≥48 hours prior Sample size: n = 31	Comparator(s) Warfarin continued Sample size: n = 30			
Population characteristics: Patients referred for elective or semiacute diagnostic cardiac catheterisation.				
Length of follow-up: NR	Outcome(s) measured: Primary study endpoint was the incidence of a vascular access site complication, which was defined as any groin haematoma, bleeding that caused a significant decrease in haemoglobin (>5g/dL) or required transfusion, or arteriovenous fistula or pseudoaneurysm formation. Haematomas were further classified as large (>5cm) or small. The secondary endpoint was prolonged hospital stay due to an access site complication.			
INTERNAL VALIDITY				
Allocation Allocation was through a pseudorandom number-generation program.	Comparison of study groups There were no differences between groups at baseline.	Blinding No blinding details are reported	Treatment/measurement bias All patients were treated the same.	Follow-up (ITT) ITT
Overall quality assessment (descriptive): This study was a fair quality randomised controlled trial. The major limitation of the study is the relatively small number of randomised patients. The study lacked statistical power to detect differences between treatment groups, particularly as event rates in the two groups were low.				
RESULTS				
Outcome	Intervention	Comparator	Statistical significance	
Haematoma formation	2/31 (6.5%)	3/30 (10%)	NS	
Clinical importance (1–4) Unable to determine		Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival.		
Any other adverse effects None reported				

EXTERNAL VALIDITY
Generalisability The patient population included patients undergoing catheterisation and the results may not be generalisable to other surgeries or invasive procedures.
Applicability The study is most likely applicable to the Australian healthcare setting.
Comments The authors conclude that transfemoral coronary angiography appears to be safe in patients on warfarin with an INR of 2.0-3.0.

STUDY DETAILS		
Reference Krishnan B, Shenoy NA, Alexander M. Exodontia and antiplatelet therapy. J Oral Maxillofac Surg. 2008;66:2063–2066.		
Affiliation/Source of funds: Department of Oral and Maxillofacial Surgery, Mahatma Gandhi Postgraduate Institute of Dental Sciences, Indira Nagar, Pondicherry, India. Funding source: None reported.		
Study design: Prospective cohort N = 82	Level of evidence: III	Location/setting: Dental Institute, India
Intervention Asprin interrupted Sample size: n = 25	Comparator(s) Continuing aspirin Sample size: n = 32	
Population characteristics:Patients requiring dental extractions.		
Length of follow-up: NR	Outcome(s) measured: Clinically significant bleeding defined as bleeding continuing beyond 12 hours of the operative procedure, bleeding which caused a patients to call or return to the dental office or emergency department, bleeding which resulted in a large haematoma within the soft tissues and bleeding requiring a blood transfusion.	

INTERNAL VALIDITY				
Allocation Patients on aspirin were divided into 2 groups: patients whose aspirin was stopped prior to extraction and those whose aspirin was continued. Allocation was based on patient choice.	Comparison of study groups Analysis of variance was used to evaluate results among the groups and determine statistical significance	Blinding No blinding details were recorded	Treatment/measurement bias It is assumed that all patients were treated the same.	Follow-up (ITT) Not clear.
Overall quality assessment (descriptive): This study was a fair quality prospective cohort study. One of the limitations of the study may include a failure to homogenise the duration of interruption of antiplatelet therapy which ranged from 1 to 10 days. There is also the possibility that by choosing their own treatment, patients may have introduced bias into the study.				

<table>
<tr><td colspan="4">RESULTS</td></tr>
<tr><td>Outcome</td><td>Intervention</td><td>Comparator</td><td>Statistical significance</td></tr>
<tr><td>Bleeding time (minutes)</td><td>3 ± 2.75</td><td>2.75 ± 1.63</td><td>NS</td></tr>
<tr><td>Clotting time (minutes)</td><td>5.07 ± 1.63</td><td>4.87 ± 1.07</td><td>NS</td></tr>
<tr><td colspan="2">Clinical importance (1–4)
Unable to determine</td><td colspan="2">Relevance (1–5)
2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention</td></tr>
<tr><td>Prolonged bleeding</td><td>0%</td><td>0%</td><td>NA</td></tr>
<tr><td colspan="2">Clinical importance (1–4)
Unable to determine</td><td colspan="2">Relevance (1–5)
1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival.</td></tr>
<tr><td colspan="4">Any other adverse effects
None reported</td></tr>
<tr><td colspan="4">EXTERNAL VALIDITY</td></tr>
<tr><td colspan="4">Generalisability
The studies were performed in patients undergoing dental extractions and may not be generalisable to patients undergoing other surgeries or invasive procedures.</td></tr>
<tr><td colspan="4">Applicability
The study is most likely applicable to the Australian healthcare setting.</td></tr>
<tr><td colspan="4">Comments
The authors conclude that routine dental extractions can be safely performed in patients on long-term antiplatelet medication with no interruption or alteration of their medication. Such patients do not have an increased risk of prolonged or excessive postoperative bleeding.</td></tr>
</table>

STUDY DETAILS		
Reference McLemore EC, Harold KL, Cha SS, Johnson DJ, Fowl RJ. The safety of open inguinal herniorraphy in patients on chronic warfarin therapy. Am J Surg 2006;192:860–864.		
Affiliation/Source of funds: Department of Surgery, Mayo Clinic Arizona, Scottsdale, Arizona, USA; Division of Biostatistics, Mayo Clinic Rochester, Rochester, USA. Funding source: None reported.		
Study design: Retrospective cohort study N = 88	Level of evidence: III	Location/setting: Tertiary referral medical centre, USA
Intervention Warfarin stopped Sample size: n = 54	Comparator(s) Warfarin continued Sample size: n = 19 Warfarin stopped and bridging therapy with heparin Sample size: n = 15	
Population characteristics: Patients who underwent inguinal hernia repair.		
Length of follow-up: NR	Outcome(s) measured: Length of stay and postoperative complications within 30 days of the operation.	

INTERNAL VALIDITY				
Allocation Allocation to therapy was not reported.	Comparison of study groups There may be some differences between groups.	Blinding No blinding details are reported	Treatment/measurement bias It is assumed that all patients were treated the same	Follow-up (ITT) ITT

Overall quality assessment (descriptive):

This study was a fair quality retrospective cohort study with several limitations. A weakness of this study is the relatively small sample size. The current study may lack statistical power to detect a statistically significant difference in the rate of surgical site haematoma.

RESULTS

Outcome	Intervention	Comparator	Statistical significance
LOS (days)	0.54 ± 1.1	0.72 ± 1.6 3.3 ± 3.3	P<0.0001
Surgical site haematoma	2%	11% 13%	NS
Surgical site infection	2%	0% 0%	NS
Seroma	2%	5% 0%	NS
Urinary retention	4%	5% 13%	NS
UTI	0%	5% 0%	NS

Arrhythmia	2%	5% 7%	NS
Pneumonia	0%	0% 0%	NS
Other	1%	11% 0%	NS
Clinical importance (1–4) Unable to determine		Relevance (1–5) 2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention	
Any other adverse effects None reported			
EXTERNAL VALIDITY			
Generalisability The patient population included patients undergoing hernia repair and may not be generalisable to a wider patient population.			
Applicability The study is most likely applicable to the Australian healthcare setting.			
Comments The authors conclude that the continuation of warfarin may be a safe alternative to discontinuation of warfarin therapy in select patients undergoing open inguinal herniorraphy.			

STUDY DETAILS				
Reference Ozao-Choy J, Tammaro Y, Fradis M, Weber K, Divino CM. Clopidogrel and bleeding after general surgery procedures. Am Surgeon. 2008;74:721–725.				
Affiliation/Source of funds: Department of Surgery, The Mount Sinai School of medicine, New York, New York, USA. Funding source: None reported.				
Study design: Retrospective Cohort N = 50	Level of evidence: III	Location/setting: Hospital, USA		
Intervention Clopidogrel interrupted Sample size: n = 22	Comparator(s) Continuing Clopidogrel Sample size: n = 28			
Population characteristics: All patients taking clopidogrel and undergoing general surgery. General surgery procedures included: laproscopic cholecystectomy; ventral hernia repair; low anterior resection; open cholecystectomy; Hartmen's procedure; end ileostomy; small bowel resection; open colon resection; laproscopi colon resection; reversal of Hartmann's; abdominoperineal resection; laproscopic ventral hernia repair; laproscopic inguinal hernia repair; laproscopic low anterior resection; laproscopic assisted ieocolic resection; laproscopic vagotomy with esophagogastrectomy; resection of retroperitoneal mass, vena cava resection; femoral hernia repair; liver resection left lateral lobe; duodenal mass excision.				
Length of follow-up: NR	Outcome(s) measured: Primary outcomes included blood loss in the first 24 hours and transfusion requirements. Secondary outcomes included deaths, myocardial infarction, stroke, respiratory failure, renal failure, wound infections, and ICU and hospital stay.			
INTERNAL VALIDITY				
Allocation Patients who took clopidogrel within 6 days of surgery vs patients who stopped clopidogrel for 7 days or more.	Comparison of study groups There were no differences between the groups. Groups were compared using Fisher's exact test and student t-test	Blinding No blinding details were recorded	Treatment/measurement bias It is assumed that all patients were treated the same.	Follow-up (ITT) Not clear.
Overall quality assessment (descriptive): This study was a fair quality retrospective cohort study. A significant limitation of the study was a small sample size.				

RESULTS			
Outcome	Intervention	Comparator	Statistical significance
Blood transfusion in OR	27.0%	10.7%	P=0.12
Platelet transfusion in OR	0.0%	4.0%	P=0.56
FFP transfusion in OR	9.0%	0.0%	P=0.18
ICU stay	19.0%	24.0%	P=0.41
Postoperative transfusion	18.0%	21.0%	P=0.53
Late complications	9.0%	14.2%	P=0.45
Reoperation	0.0%	0.0%	P=1.00
Hospital stay	14.18 ± 19.0	8.61 ± 6.8	P=0.09
Clinical importance (1–4) Unable to determine		Relevance (1–5) 2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention	
Mortality	9.0%	4.0%	P=0.42
Significant bleeding requiring transfusion within 1 week	9.5%	21.4%	NR
Clinical importance (1–4) Unable to determine		Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival.	
Any other adverse effects None reported			
EXTERNAL VALIDITY			
Generalisability The patient population included patients undergoing general surgery and invasive procedures and is generalisable to this patient population.			
Applicability The study is most likely applicable to the Australian healthcare setting.			
Comments The authors conclude that in the case of a nonelective general surgery procedure where outcomes depend on timely surgery, clopidogrel taken within 6 days before surgery should not be a reason to delay surgery. However, careful attention must be paid to meticulous haemostasis, and platelets must be readily available for transfusion in the operating room.			

STUDY DETAILS				
Reference Robinson CM, Christie J, Malcolm-Smith N. Nonsteroidal antiinflammatory drugs, perioperative blood loss, and transfusion requirements in elective hip arthroplasty. J Arthroplasty. 1993;8(6):607–610				
Affiliation/Source of funds: The Orthopaedic Unit, Proncess Margaret Rose Orthopaedic Hospital, Edinburgh, United Kingdom Funding source: No funding source reported				
Study design: Prospective cohort study N = 160		Level of evidence: III		Location/setting: hospital, UK
Intervention No NSAID therapy Sample size: n = 75 (52 general anaesthesia; 23 spinal anaesthesia)		Comparator(s) NSAID therapy (for at least 6 months) continued until surgery Sample size: n = 85 (55 general anaesthesia; 30 spinal anaesthesia)		
Population characteristics: Patients undergoing cemented primary total hip arthroplastys performed for osteoarthritis				
Length of follow-up: NR		Outcome(s) measured— Operative blood loss assessed by swab weighing and suction and theatre drape loss, and the subsequent 24-hour postoperative loss was assessed by the suction draionage over this period		
Internal Validity				
Allocation Allocation was based on the patients prior exposure to NSAIDs	Comparison of study groups Baseline characteristics were similar between the 2 groups	Blinding No blinding details were reported	Treatment/ measurement bias All patients were treated the same	Follow-up (ITT) ITT analysis performed
Overall quality assessment (descriptive): This was a fair quality prospective cohort study				
RESULTS				

Outcome	No NSAID therapy N	NSAID therapy until surgery	Statistical significance
Blood loss during surgery (mL)	372 ± 144	682 ± 148	P<0.01
Blood loss 24 h after surgery (mL)	428 ± 179	672 ± 185	P<0.01
Total blood loss (mL)	800	1,354	P<0.01
Clinical importance (1–4) Unable to determine		Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival.	

Mean fall in Hb (g/dL)	-1.2	-0.8	NS
Clinical importance (1–4) Unable to determine		Relevance (1–5) 2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention	
Any other adverse effects Wound dehiscence, wound hematoma, wound infection, deep venous thrombosis pulmonary embolus			
External Validity			
Generalisability The study was performed in patients undergoing orthopaedic surgery and may not be generalisable to other types of surgeries or invasive procedures			
Applicability The study was carried out in the UK and the results are generalisable to the Australian healthcare setting			
Comments The authors conclude that the results of the study suggest that NSAIDs are implicated in increasing the operative blood loss in orthopaedic patients. The range of increased blood loss varied from 1.57 to 2.08 times the blood loss in the control group, and this effect was seen when the operation was carried out under spinal as well as when under general anaesthesia.			

STUDY DETAILS				
Reference Slappendel R, Weber EWG, Benraad B, Dirksen R, Bugter ML. Does ibuprofen increase perioperative blood loss during hip arthroplasty? Eur J Anaesthesiol. 2002;19:829–831.				
Affiliation/Source of funds: St Maartenskliniek, Departments of Anaesthesiology and Pharmacy, Nijmegen, The Netherlands Funding source: No funding source reported				
Study design: Randomised controlled trial N = 36	Level of evidence: II	Location/setting: Hospital, the Netherlands		
Intervention Placebo for 2 weeks before surgery Sample size: n = 19	Comparator(s) Ibuprofen for 2 weeks before surgery Sample size: n = 17			
Population characteristics: Patients undergoing their first elective total hip replacement for coxarthrosis during spinal anaesthesia. Patients receiving NSAIDs before the study were excluded				
Length of follow-up: NR	Outcome(s) measured — total blood loss (determined by taking into account the amount in the suction bottles, the weight of the surgical sponges and the irrigation fluid used), blood loss during surgery, blood loss in the 24 hours after surgery			
INTERNAL VALIDITY				
Allocation Patients were randomised but reandomisation procedures were not reported	Comparison of study groups There were no significant differences in the baseline characteristics between the two treatment groups	Blinding The pharmacist preparing the medication was the only person aware of the type of treatment, all other participants were blinded	Treatment/ measurement bias All patients were treated the same	Follow-up (ITT) Eight patients in the ibuprofen group and six in the placebo group terminated their participatin in the trial because of adverse effects of severe pain. It is not clear if these patients were included in the analysis
Overall quality assessment (descriptive): This was a good quality randomised controlled trial				

RESULTS			
Outcome	Placebo for 2 weeks before surgery	Ibuprofen for 2 weeks before surgery	Statistical significance
Blood loss during surgery (mL)	416 ± 203	700 ± 367	P<0.01
Blood loss 24 h after surgery (mL)	380 ± 169	461 ± 312	NS
Total blood loss (mL)	796 ± 337	1,161 ± 472	P<0.05
Clinical importance (1–4) Unable to determine		Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival.	
Any other adverse effects Lack of efficacy (increased pain), gastric acid, nausea			
EXTERNAL VALIDITY			
Generalisability The study was performed in patients undergoing orthopaedic surgery and may not be generalisable to other types of surgeries or invasive procedures			
Applicability The study was carried out in The Netherlands and the results are probably generalisable to the Australian healthcare setting			
Comments The authors conclude that pretreatment with ibuprofen before elective hip surgery increases the perioperative blood loss significantly. Early discontinuation of non-selective non-steroidal anti-inflammatory drugs is advised.			

STUDY DETAILS				
Reference Wysokinski WE, McBane RD, Daniels PR, Litin SC, Hodge DO, Dowling NF, Heit JA. Periprocedural anticoagulation management of patients with nonvalvular atrial fibrillation. Mayo Clin Proc. 2008;83:639–645.				
Affiliation/Source of funds: Thrombophillia Center, Division of Cardiovascular Diseases, Division of General Internal Medicine, and Division of Biostatistics, Mayo Clinic, Rochester; and Division of Blood Disorders, National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention, Atlanta, USA. Funding source: Funded in part y grants from the Centers for Disease Control and Prevention (30-0850), US Public Health Service, and Mayo Clinic.				
Study design: Prospective cohort study N = 345		Level of evidence: III		Location/setting: Thrombophyllia Center, USA
Intervention Warfarin stopped Sample size: n = 164		Comparator(s) Warfarin stopped and bridging therapy with heparin Sample size: n = 181		
Population characteristics: Patients with atrial fibrillation undergoing surgery or invasive procedures. The procedures included orthopaedic, gastroenterologic, urologic, cardiovascular, ophthalmologic, dental, vascular, neurologic and gynaecologic procedures.				
Length of follow-up: 3 months		Outcome(s) measured: The primary efficacy end point was symptomatic arterial venous TE occurring from 5 days before to 90 days after the procedure or surgery. Arterial TE was defined as ischaemic stroke, TIA, amaurosis fugax, unstable angina, myocardial infarction, or other peripheral artery TE. The primary safety endpoint was mjor bleeding defined as overt bleeding plus a haemoglobin decrease of 2 g/dL or more after the procedure or transfusion of 2 units or more of PRBCs, or intracranial, intraspinal, intraocular, retroperitoneal, pericardial or fatal bleeding. Minor bleeding was defined as overt bleeding that did not meet the criteria for major bleeding.		
INTERNAL VALIDITY				
Allocation Allocation to bridging therapy was based on a patient's cardiovascular risk.	Comparison of study groups There may be some differences between groups.	Blinding No blinding details are reported	Treatment/measurement bias All patients were treated the same. However, they underwent different procedures	Follow-up (ITT) ITT
Overall quality assessment (descriptive): This study was a good quality prospective cohort study with several limitations. Firstly, the delivery of LMWH was not assigned randomly. This was not an ITT trial and patient preferences could have contributed both favourable and unfavourably to outcomes. Secondly, there may also be some referral bias.				

RESULTS			
Outcome	Intervention	Comparator	Statistical significance
TE events	2/182 (1.2%)	2/204 (1.0%)	NS
Major bleeding	4/182 (2.3%)	6/204 (3.0%)	NS
Minor bleeding	2/182 (1.1%)	9/204 (4.6%)	NS
Clinical importance (1–4) Unable to determine		Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival.	
Any other adverse effects None reported			
EXTERNAL VALIDITY			
Generalisability The patient population included patients undergoing general surgery and invasive procedures and is generalisable to this patient population.			
Applicability The study is most likely applicable to the Australian healthcare setting.			
Comments The authors conclude that the 3 month cumulative incidence of TE and bleeding among patients with AF in which anticoagulation was temporarily interrupted for an invasive procedure was low and was not significantly influenced by bridging therapy.			

F3 Evidence summaries, Question 3

In patients undergoing surgery, what is the effect of perioperative strategies that minimise blood loss on morbidity, mortality, and blood transfusion?

The body of evidence found by the systematic literature review and associated appendixes for Perioperative Foreground Question 3 are presented in a separate report.

F4 Evidence summaries, Question 4

Is anaemia an independent risk factor for adverse outcomes?

Level I evidence: Cardiac studies

<table>
<tr><td colspan="5">STUDY DETAILS</td></tr>
<tr><td colspan="5">Reference Shander A, Knight K, Thurer R, Adamson J, Spence R. Prevalence of the outcomes of anaemia in surgery: A systematic review. Am J Med, 2004;116(7 Suppl 1):58S–69S</td></tr>
<tr><td colspan="5">Affiliation/Source of funds
Englewood Hospital Medical Center, Englewood, NJ, USA; Zynx Health, Beverly Hills, CA, USA, Beth Israel Deaconess Medical Centre, Boston, MA, USA; the Blood Center of Southeastern Wisconsin, Medical College of Wisconsin, Milwaukee, USA; and Baptist Health Systems Inc, Birmingham, AL, USA
Funding source: This article was sponsored b the National Anaemia Council, Inc, and funded by an educational grant from Amgen, Inc</td></tr>
<tr><td colspan="2">Study design
Systematic review of 13 prevalence studies and 20 outcomes studies</td><td colspan="2">Level of evidence
I</td><td>Location/setting
Various/hospital</td></tr>
<tr><td colspan="3">Intervention
Anaemia
Sample size: n=NR</td><td colspan="2">Comparator
No anaemia
Sample size n=NR</td></tr>
<tr><td colspan="5">Population characteristics
Surgical patients with and without anaemia</td></tr>
<tr><td colspan="3">Length of follow-up
Not reported</td><td colspan="2">Outcomes measured
Perioperative mortality; risk of blood transfusion; thrombotic events</td></tr>
<tr><td colspan="5">INTERNAL VALIDITY</td></tr>
<tr><td>Allocation</td><td>Comparison of study groups</td><td>Blinding analysis</td><td>Treatment/measurement bias</td><td>Follow-up (ITT)</td></tr>
<tr><td>Patients with different Hb levels</td><td>There was variability in the populations and outcomes used in the different studies. No pooled analysis was performed, only descriptive results are presented</td><td>No blinding details were reported</td><td>Not detected</td><td>None reported</td></tr>
<tr><td colspan="5">Overall quality assessment (descriptive)
This was a fair quality systematic review. No quality assessment of the different studies was performed and results were not pooled, but presented descriptively</td></tr>
</table>

RESULTS	
Mortality: Nine studies investigated the effect of anaemia on mortality. There was some suggestion that lower Hb levels are associated with decreased survival rates, although this was not found universally Morbidity and functional outcomes: Five studies examined morbidity and five studies examined signs, symptoms and physiologic measures or functional outcomes. No conclusions could be drawn on the effect of anaemia on any of these outcomes due to the lack of data Risk of transfusion: A total of 20 studies addressed the impact of anaemia on risk for and volume of transfusions. Many of these studies found that haemoglobin or haematocrit level were predictors of risk of transfusion	
Clinical importance (1–4) 1 A clinically important benefit for the full range of plausible estimates	Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival
EXTERNAL VALIDITY	
Generalisability The study is most likely generalisable to a wider perioperative patient population	
Applicability The study was performed in the United States which has some similarities to the Australian healthcare setting	

Level II evidence: Cardiac studies

<table>
<tr><td colspan="5">STUDY DETAILS</td></tr>
<tr><td colspan="5">Reference DeFoe GR, Ross CS, Olmstead EM, Surgenor SD, Fillinger MP, Groom RC, et al. Lowest hematocrit on bypass and adverse outcomes associated with coronary artery bypass grafting. Ann Thorac Surg. 2001;71:769–776</td></tr>
<tr><td colspan="5">Affiliation/Source of funds:
Dartmouth-Hitchcock medical Centre, Lebanon, NH; Centre for the Evaluative Clinical Sciences, Dartnouth Medical School, Havover, NH; Maine Medical centre, Portland, ME; Catholic Medical Centre, Manchester, NH; Eastern Maine Medical Centre, Bangor, ME; Fletcher Allen Health Care, Burlington, VT; Beth Israel Deaconess, Medical Centre, Boston, MA
Funding source: None mentioned</td></tr>
<tr><td colspan="2">Study design
Prospective cohort study
N=6980</td><td>Level of evidence
II</td><td colspan="2">Location/setting
6 Medical Centres in Maine, New Hampshire, Vermont and Massachusetts, USA</td></tr>
<tr><td colspan="5">Population characteristics
Patients undergoing isolated CABG surgery</td></tr>
<tr><td colspan="2">Length of follow-up
Time in hospital</td><td colspan="3">Outcome(s) measured
Use of intraoperative or postoperative IABP, intra- or postoperative stroke, return to bypass, return to operating room for postoperative haemorrhage, in hospital death</td></tr>
<tr><td colspan="5">INTERNAL VALIDITY</td></tr>
<tr><td>Allocation</td><td>Comparison of study groups</td><td>Blinding</td><td>Treatment/measurement bias</td><td>Follow-up (ITT)</td></tr>
<tr><td>Patients with anaemia vs. patients without anaemia</td><td>There may be some differences between anaemic and non-anameic patients. Groups were compared by logistic regression</td><td>No blinding details were reported</td><td>There may be some difference in the treatment of patients with different Hb levels</td><td>ITT analysis</td></tr>
<tr><td colspan="5">Overall quality assessment (descriptive)
This is a good prospective cohort study including a large patient population with highly significant results. Data were obtained from a number of medical centres by employing identical data definitions. The results also persisted after multivariate adjustment and were consistent across medical centres. This suggests that the findings of the study are unlikely to be a consequence of chance, bias or confounding</td></tr>
</table>

RESULTS					
Outcome	Risk measure	Definition of anaemia	Time of Hb measurement	Risk	Statistical significance
In-hospital mortality	%	Hct <19%	Intraoperative	3.90%	p<0.001
		Hct 19–20%		3.30%	
		Hct 21–22%		2.80%	
		Hct 23–24%		1.50%	
		Hct ≥25%		1.60%	
Clinical importance (1–4) 1 A clinically important benefit for the full range of plausible estimates			Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		
Intra- or postoperative IABP	%	Hct < 19%	Intraoperative	6.10%	p<0.001
		Hct ≥ 25%		3.60%	
Clinical importance (1–4) 1 A clinically important benefit for the full range of plausible estimates			Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		
Return to bypass	%	Hct < 19%	Intraoperative	7.50%	p<0.001
		Hct ≥ 25%		3.80%	
Clinical importance (1–4) 1 A clinically important benefit for the full range of plausible estimates			Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		
Any other adverse effects None reported					
EXTERNAL VALIDITY					
Generalisability The study is most likely generalisable to a cardiac perioperative patient population					
Applicability The study was performed in the United States which has some similarities to the Australian healthcare setting					

STUDY DETAILS

Reference Gombotz H, Rehak PH, Shander A, Hofmann A. Blood use in elective surgery: The Austrian benchmark study. Transfusion. 2007;47(8):1468–1480

Affiliation/Source of funds

Department of Anesthesiology and Intensive Care, General Hospital Linz, Linz, Austria; the Department of Surgery, Medical University of Graz, Graz, Austria; the Mt Sinai School of Medicine, NY; the Englewood Hospital and Medical Center, Englewood, NJ; and the Medical Society for Blood Management, laxenburg, Austria

Funding source: The study was sponsored by the Austrian Federal Structural Fund (with the Austrian Federal Ministry of Health and Women acting as executive secretariat) including design and conducting of the study and collection, management, analysis and interpretation of the data

Study design	Level of evidence	Location/setting
Prospective, multicentre cohort study	II	18 hospitals in Austria

Intervention	Comparator(s)
Sample size: 3793	Sample size

Population characteristics

Patients undergoing total hip replacement (THR), total knee replacement (TKR), hemicolectomy, or CABG

Intervention group

Comparator groups(s)

Length of follow-up	Outcome(s) measured
5 days after surgery	Intra- and postoperative amounts of allogeneic and autologous blood components transfused, prevalence of preoperative anaemia, calculated perioperative RBC loss, lowest measured Hb

INTERNAL VALIDITY

Allocation	Comparison of study groups	Blinding	Treatment/measurement bias	Follow-up (ITT)
Patients with anaemia vs patients without anaemia	There may be some differences between anaemic and non-anameic patients. Groups were compared by logistic regression	No blinding details are reported	There may be some difference in the treatment of patients with different Hb levels	Patients who had incomplete records and were protocol violators were excluded from the analysis

Overall quality assessment (descriptive)

This was a good quality prospective cohort study with several limitations. As it is an observational study, it suffers from a lack of randomisation. The lack of any medical interventions makes it impossible to demonstrate any appreciable differences in patient outcomes

<table>
<tr><td colspan="6">RESULTS</td></tr>
<tr><td>Outcome</td><td>Risk measure</td><td>Definition of anaemia</td><td>Time of Hb measurement</td><td>Risk</td><td>Statistical significance</td></tr>
<tr><td rowspan="2">Risk of RBC transfusion in THR</td><td rowspan="2">OR (95% CI)</td><td rowspan="2">Hb ≤13 g/dL men
Hb ≤12 g/dL women</td><td>Preoperative</td><td>1.5 (1.38, 1.64)</td><td>S</td></tr>
<tr><td>Postoperative</td><td>1.5 (1.38, 1.64)</td><td>S</td></tr>
<tr><td colspan="3">Clinical importance (1–4)
2 The point estimate of effect is clinically important but the confidence interval includes clinically unimportant effects</td><td colspan="3">Relevance (1–5)
2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention</td></tr>
<tr><td rowspan="2">Risk of RBC transfusion in TKR</td><td rowspan="2">OR (95% CI)</td><td rowspan="2">Hb ≤13 g/dL men; HB ≤12 g/dL women</td><td>Preoperative</td><td>1.49 (1.35, 1.64)</td><td>S</td></tr>
<tr><td>Postoperative</td><td>1.49 (1.35, 1.64)</td><td>S</td></tr>
<tr><td colspan="3">Clinical importance (1–4)
2 The point estimate of effect is clinically important but the confidence interval includes clinically unimportant effects</td><td colspan="3">Relevance (1–5)
2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention</td></tr>
<tr><td colspan="6">Any other adverse effects
None reported</td></tr>
<tr><td colspan="6">EXTERNAL VALIDITY</td></tr>
<tr><td colspan="6">Generalisability
The study was performed in orthopaedic or cardiac patients which has some generalisablity to both a cardiac and noncardiac perioperative patient population</td></tr>
<tr><td colspan="6">Applicability
The study was performed in Austria which has similarities to the Australian healthcare setting</td></tr>
</table>

STUDY DETAILS				
Reference Koch CG, Weng YS, Zhou SX, Savino JS, Mathew JP, Hsu PH, et al. Prevalence of risk factors, and not gender per se, determines short- and long-term survival after coronary artery bypass surgery. J Cardiothorac Vasc Anesth. 2003;17(5):585–593				
Affiliation/source of funds Ischemia Research and Education Foundation, San Francisco, CA; the Multicentre Study of Perioperative Ischemia Research Group, San Francisco, CA; the Cleveland Clinic Foundation, Cleveland, OH; University of Pennsylvania Medical Centre, Philadelphia, PA; Duke University Medical Centre, Durham NC; and Stanford University Medical Centre, Stanford, CA Funding source: Supported by a grant from the Ischemia Research and Education Foundation, San Francisco, CA				
Study design Prospective cohort study		Level of evidence II		Location/setting 24 medical centres in the United States
Intervention Sample size: 2417		Comparator(s) Sample size		
Population characteristics Patients undergoing CABG				
Length of follow-up 5 years		Outcome(s) measured Postoperative survival time, and 30 day, 6 month and 5 year mortality		
INTERNAL VALIDITY				
Allocation	Comparison of study groups	Blinding	Treatment/measurement bias	Follow-up (ITT)
Patients with anaemia vs patients without anaemia	There may be some differences between anaemic and non-anameic patients. Groups were compared by logistic regression	No blinding details were reported	There may be some difference in the treatment of patients with different Hb levels	ITT analysis
Overall quality assessment (descriptive) This is a good prospective cohort study with several limitations. One of the limitations to this study is that although this investigation started with many preoperative variables, there may be important confounding variables left unevaluated. The unmeasured extent, duration and severity of the preoperative risk factors present may also impact study results. Also, this investigation focused on preoperative factors, with no attempt to address possible confounding issues of intraoperative care or non-fatal perioperative morbid events and complications				

RESULTS					
Outcome	Risk measure	Definition of anaemia	Time of Hb measurement	Risk	Statistical significance
1 month mortality	HR	NR	Preoperative	1.6	p=0.279
6 month mortality				1.9	p=0.050
Last follow-up mortality				1.5	p=0.01
Clinical importance (1–4) 2 The point estimate of effect is clinically important but the confidence interval includes clinically unimportant effects			Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		
Any other adverse effects None reported					
EXTERNAL VALIDITY					
Generalisability The study is generalisable to a perioperative cardiac surgery population					
Applicability The study was performed in the US which has some applicability to the Australian healthcare setting					

STUDY DETAILS				
Reference Kulier A, Levin J, Moser R, Rumpold-Seitlinger G, Tudor IC, Snyder-Ramos SA, et al. Impact of preoperative anemia on outcome in patients undergoing coronary artery bypass graft surgery. Circulation. 2007;116(5):471–479				
Affiliation/Source of funds Department of Anesthesiology and Intensive Care Medicine, Medical University of Graz, Austria; Multicentre Study of Perioperative Ischemia Research Group; Department of Laboratory Medicine, University of California School of Medicine, San Francisco; Ischemia Research and Education Foundation, San Bruno, CA; Department of Anesthesiology, University of Heidelberg, Heidelburg, Germany; and Department of Anesthesiology, Ludwig-Maximilians University, Munich, Germany Funding source: The study was supported by a nonrestricted grant from the Ischemia Research and Education Foundation, San Bruno, CA				
Study design Prospective, multicentre cohort study N=4804		Level of evidence II		Location/setting 72 institutions in 17 countries including USA, Austria, Canada, Colombia, France, Germany, Hungary, India, Israel, Italy, Mexico, The Netherlands, Poland, Romania, Thailand, UK
Intervention Sample size: Anaemia, n=1427		Comparator(s) Sample Size: No anaemia, n=3377		
Population characteristics Patients undergoing CABG surgery with cardiopulmonary bypass				
Length of follow-up Period of hospitalisation	Outcome(s) measured Fatal and non-fatal outcomes occurring after surgery and during the index hospitalisation were classified as cardiac events (MI, CHF, or death from cardiac causes) or noncardiac events: cerebral events (encephalopathy, stroke, or death from cerebral causes); renal events (renal dysfunction or failure, death from renal causes); gastrointestinal events (ischemia or infarction, death from gastrointestinal causes); or other (such as infectious, pulmonary). Composite outcome was defined as any of all adverse outcomes, cardiac and noncardiac, including in-hospital mortality			
INTERNAL VALIDITY				
Allocation	Comparison of study groups	Blinding	Treatment/measurement bias	Follow-up (ITT)
Patients with anaemia versus patients with anaemia defined by WHO standard	There may be some differences between anaemic and non-anameic patients. Groups were compared by logistic regression	Investigators were blinded to treatment group	There may be some difference in the treatment of patients with different Hb levels	ITT analysis
Overall quality assessment (descriptive) This is a good quality prospective cohort study with some limitations. It is a cohort study and is therefore not randomised; there is a possibility that not all important variables were accounted for in the analysis				

RESULTS					
Outcome	Risk measure	Definition of anaemia	Time of Hb measurement	Risk	Statistical significance
Cardiac outcomes	OR (95% CI)	Hb 13–14 g/dL	Preoperative	0.97 (0.91, 1.04)	NS
		Hb 12–13 g/dL		0.95 (0.84, 1.07)	NS
		Hb 11–12 g/dL		0.92 (0.77, 1.11)	NS
		Hb 10–11 g/dL		0.90 (0.70, 1.15)	NS
		Hb <10 g/dL		0.87 (0.64, 1.19)	NS
		Hb 13–14 g/dL		0.97 (0.91, 1.04)	NS
Clinical importance (1–4) 3 The confidence interval does not include any clinically important effects			Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		
Noncardiac outcomes	OR (95% CI)	Hb 13–14 g/dL	Preoperative	1.14 (1.06, 1.24)	S
		Hb 12–13 g/dL		1.31 (1.12, 1.53)	S
		Hb 11–12 g/dL		1.49 (1.18, 1.89)	S
		Hb 10–11 g/dL		1.71 (1.25, 2.34)	S
		Hb <10 g/dL		1.95 (1.32, 2.90)	S
		Hb 13–14 g/dL		1.14 (1.06, 1.24)	S
		Hb 12–13 g/dL		1.31 (1.12, 1.53)	S
Clinical importance (1–4) 2 The point estimate of effect is clinically important but the confidence interval includes clinically unimportant effects			Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		
Any other adverse effects None reported					
EXTERNAL VALIDITY					
Generalisability The results of this study are probably generalisable to a wider perioperative cardiac surgical patient population					
Applicability This was a multicentre study and while it did not include a centre from Australia, the results are most likely applicable to the Australian healthcare setting					

STUDY DETAILS				
Reference Lee RJ, Shih KN, Lee SH, Shyu KG, Chiu CZ, Lin SC, et al. Predictors of long-term outcomes in patients after elective stent implantation for unprotected left main coronary artery disease. Heart Vessels. 2007;22(2):99–103				
Affiliation/Source of funds Yuanpei Institute of Science and Technology, Fu Jen Catholic University and Shin Kong Wu Ho-Su Memorial Hospital, Taipei, Taiwan Funding source: The study was supported in part by grants from the National Science Council (NSC 94-2314-B-341-001), and Shin Kong Wu Ho-Su Memorial Hospital (SKH-FJU-94-17), Taipei, ROC				
Study design Prospective cohort study N=76		Level of evidence II		Location/setting Shin Kong Wu Ho-Su Memorial Hospital, Taipei, Taiwan
Intervention Anaemia Sample size: n=23		Comparator(s) No anaemia Sample size: n=53		
Population characteristics Patients with medically refractory angina receiving coronary stenting for unprotected left main coronary artery (LMCA) disease				
Length of follow-up 40 ± 26 months		Outcome(s) measured Repeated PCI and/or CABG, cardiovascular mortality, total mortality		
INTERNAL VALIDITY				
Allocation	Comparison of study groups	Blinding	Treatment/measurement bias	Follow-up (ITT)
Patients with anaemia versus patients with anaemia defined by WHO standard	There may be some differences between anaemic and non-anameic patients. Groups were compared by logistic regression	No blinding details were given	There may be some difference in the treatment of patients with different Hb levels	ITT analysis
Overall quality assessment (descriptive) This was a fair quality prospective cohort study where the number of patients and total number of deaths were small. The main objective of the study was not focused on anaemia. There may be some variables not accounted for in the analysis				

RESULTS					
Outcome	Risk measure	Definition of anaemia	Time of Hb measurement	Risk	Statistical significance
Repeated PCI and/or CABG	OR (95% CI)	Hb ≤13 g/dL men Hb ≤11 g/dL women	NR	NR	P=0.8
Cardiovascular mortality	OR (95% CI)			NR	P=0.27
Total mortality	OR (95% CI)			NR	P = 0.22
Clinical importance (1–4) 3 The confidence interval does not include any clinically important effects			Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		
Any other adverse effects None reported					
EXTERNAL VALIDITY					
Generalisability The results may not be generalisable to a wider perioperative cardiac surgical patient population					
Applicability The study was performed in Taiwan and may not be applicable to the Australian healthcare setting					

STUDY DETAILS		
Reference Parr GK, Patel MA, Dekker R, Levin R, Glynn R, Avorn J, et al. Multivariate predictors of blood product use in cardiac surgery. J Cardiothorac Vasc Anesth. 2003;17(2):176–181		
Affiliation/Source of funds Department of Anesthesia, Union Memorial Hospital, Baltimore MD; Department of Medicine, the Division of Cardiac Surgery and the Division of Pharmacoepidemiology and Pharmacoeconomics, Brigham and Women's Hospital, Harvard Medical School, Boston, MA; Devision of Pharamcoepidemiology and Pharmacoeconomics, Harvard Medical School, Boston, MA; North Shore Medical Centre-Salem Hospital, Salem, MA Funding source: None reported		
Study design Prospective cohort study N=600	Level of evidence II	Location/setting Union Memorial Hospital, Baltimore, USA
Population characteristics Patients undergoing cardiac surgery with cardiopulmonary bypass Intervention group Comparator groups(s)		
Length of follow-up None reported	Outcome(s) measured Risk of receiving >2 units of RBC	

INTERNAL VALIDITY				
Allocation	Comparison of study groups	Blinding	Treatment/measurement bias	Follow-up (ITT)
Patients with anaemia versus patients with out anaemia. Anaemia was not defined	There may be some differences between anaemic and non-anameic patients. Groups were compared by logistic regression	No blinding details were given	There may be some difference in the treatment of patients with different Hb levels. Transfusion occurred at a Hct <25% or for debilitated patients at a Hct <30%	ITT analysis

Overall quality assessment (descriptive)

This was a good quality prospective cohort study with some limitations. As an observational study, there is the possibility of selection bias and outcome differences not caused by treatment

RESULTS					
Outcome	Risk measure	Definition of anaemia	Time of Hb measurement	Risk	Statistical significance
Risk of <2 U RBC transfusion	OR (95% CI)	Increase Hct %	Preoperative	0.48 (0.38, 0.62)	S

Clinical importance (1–4)	Relevance (1–5)
1 A clinically important benefit for the null range of plausible estimates. The confidence limit closest to the measure of no effect rules out a clinically unimportant effect of the intervention	2. Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention.

Any other adverse effects None reported
EXTERNAL VALIDITY
Generalisability The results of this study are generalisable to a perioperative cardiac surgical patient population
Applicability The study was conducted in the USA and is probably applicable to the Australian healthcare setting

STUDY DETAILS					
Reference Rady MY, Ryan T, Starr NJ. Perioperative determinants of morbidity and mortality in elderly patients undergoing cardiac surgery. Crit Care Med. 1998;26:225–235					
Affiliation/Source of funds Division of Anesthesiology and Critical Care Medicine, Department of Cardiovascular Anaesthesia, Cleveland Clinic Foundation, Cleveland, OH Funding source: None reported					
Study design Prospective cohort study N=1157		Level of evidence II		Location/setting Department of Cardiothoracic Anaesthesia, Cleveland Clinic Foundation, Cleveland, USA	
Population characteristics Patients aged ≥75 yrs undergoing cardiac surgery					
Length of follow-up 30 days	Outcome(s) measured Morbidity—cardiac dysfunction (low cardiac output syndrome) or postoperative MI, postoperative cardiac arrhythmias, pulmonary dysfunction, protracted weaning from ventricular support if the duration of mechanical ventilation was >3 days, renal dysfunction, gastrointestinal dysfunction, hepatic dysfunction, coagulopathy, nosocomial infection, neurologic dysfunction. Mortality and ICU LOS				
INTERNAL VALIDITY					
Allocation	Comparison of study groups	Blinding	Treatment/measurement bias	Follow-up (ITT)	
Patients with anaemia versus patients with out anaemia. Anaemia was not defined	There may be some differences between anaemic and non-anameic patients. Groups were compared by logistic regression	No blinding details were given	There may be some difference in the treatment of patients with different Hb levels	ITT analysis	
Overall quality assessment (descriptive) This is a good quality prospective cohort study with some limitations. The study is not randomised and important variables may not have been included in the regression analsysis					
RESULTS					
Outcome	Risk measure	Definition of anaemia	Time of Hb measurement	Risk	Statistical significance
Mortality	OR (95% CI)	Hb <10 g/dL or Hct <30%	ICU	5.80 (3.25, 11.18)	p<0.001
Clinical importance (1–4) 2 The point estimate of effect is clinically important but the confidence interval includes clinically unimportant effects			Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		
Any other adverse effects None reported					

EXTERNAL VALIDITY
Generalisability The results of this study are generalisable to an elderly perioperative cardiac surgical patient population. The results may not be generalisbale to a younger patient population
Applicability The study was conducted in the USA and is probably applicable to the Australian healthcare setting

STUDY DETAILS				
Reference Surgenor SD, DeFoe GR, Fillinger MP, Likosky DS, Groom RC, Clark C, et al. Intraoperative red blood cell transfusion during coronary artery bypass graft surgery increases the risk of postoperative low-output heart failure. Circulation. 2006;114(Suppl I):I43–I48				
Affiliation/Source of funds Northern New England Cardiovascular Disease Study Group: Dartmouth-Hitchcock Medical Centre, Lebanon, NH; Fletcher Allen Health Care, Burlington, VT; Portsmouth Regional Hospital, Portsmouth, NH; Maine Medical Centre, Portland, ME; Eastern Maine Medical Centre, Bangor, ME; Catholoc Medical Centre, Manchester, NH; Concord Hospital, Concord, NH; Central Maine Medical Centre, Lewiston, Me; Dartmouth Medical School, Hanover, NH Funding source: None				
Study design Prospective cohort study N=8004	Level of evidence II		Location/setting 8 medical centres in Vermont, New Hampshire, and Maine in the USA.	
Intervention Anaemia Sample size: n=1315	Comparator(s) No anaemia Sample size: n=6689			
Population characteristics Patients undergoing isolated CABG procedures				
Length of follow-up NR	Outcome(s) measured Risk of LOF defined as needing intraoperative intra-aortic balloon pump (IABP), return to CPB after initial separation, or ≥ 2 inotropes at 48 hours postoperatively			
INTERNAL VALIDITY				
Allocation	Comparison of study groups	Blinding	Treatment/measurement bias	Follow-up (ITT)
Patients with anaemia versus patients with out anaemia. Anaemia was defined as Hct ≤20%	There may be some differences between anaemic and non-anameic patients. Groups were compared by logistic regression	No blinding details were given	There may be some difference in the treatment of patients with different Hb levels	ITT analysis
Overall quality assessment (descriptive) The study was a fair quality prospective cohort study. As the study is observational, it is subject to confounding. While the authors, through previous experience, captured all variables important to patient outcomes, it is possible that other confounding variables do exist that could be pertinent to this analysis				

<table>
<tr><td colspan="6">RESULTS</td></tr>
<tr><td>Outcome</td><td>Risk measure</td><td>Definition of anaemia</td><td>Time of Hb measurement</td><td>Risk</td><td>Statistical significance</td></tr>
<tr><td rowspan="3">Low-operative heart failure</td><td rowspan="3">OR (95% CI)</td><td>Hct < 35</td><td rowspan="3">Preoperative</td><td>1.05 (0.8, 1.36)</td><td>p=0.738</td></tr>
<tr><td>Hct 35–40</td><td>0.96 (0.78, 1.18)</td><td>p=0.701</td></tr>
<tr><td>Nadir Hct</td><td>0.90 (0.82, 0.98)</td><td>p=0.016</td></tr>
<tr><td colspan="3">Clinical importance (1–4)
2 The point estimate of effect is clinically important but the confidence interval includes clinically unimportant effects
3 The confidence interval does not include any clinically important effects</td><td colspan="3">Relevance (1–5)
1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival</td></tr>
<tr><td colspan="6">Any other adverse effects
None reported</td></tr>
<tr><td colspan="6">EXTERNAL VALIDITY</td></tr>
<tr><td colspan="6">Generalisability
Results are generalisable to a perioperative cardiac surgical patient population</td></tr>
<tr><td colspan="6">Applicability
The study was conducted in the USA and is probably applicable to the Australian healthcare setting</td></tr>
</table>

STUDY DETAILS					
Reference Swenne CL, Lindholm C, Borowiec J, Carlsson M. Surgical-site infections within 60 days of coronary artery by-pass graft surgery. J Hosp Infect. 2004;57(1):14–24					
Affiliation/Source of funds Department of Cardiothoracic Surgery, Uppsala University Hospital, Uppsala, Sweden; Department of Public Health and Care Sciences, Uppsala Science Park, Uppsala, Sweden; FoUU-board, Karolinska University Hospital, Stockholm, Sweden Funding source: This study was supported by the Vardal Foundation for Health Care Sciences and Allergy Research, the Swedish Diabetes Association and Uppsala University					
Study design Prospective cohort study N=396		Level of evidence II		Location/setting Department of Cardiothoracic Surgery, University Hospital of Uppsala, Sweden	
Population characteristics Patients undergoing CABG surgery with or without a preoperative diagnosis of diabetes mellitus					
Length of follow-up Not reported		Outcome(s) measured Risk of infection			
INTERNAL VALIDITY					
Allocation	Comparison of study groups	Blinding	Treatment/measurement bias	Follow-up (ITT)	
No definition of anaemia	There may be some differences between anaemic and non-anameic patients. Groups were compared by logistic regression	No blinding details were given	There may be some difference in the treatment of patients with different Hb levels	22 patients did not complete the study and were not included in the analysis	
Overall quality assessment (descriptive) This is a poor quality prospective cohort study whose main focus was on diabetes and not anaemia					
RESULTS					
Outcome	Risk measure	Definition of anaemia	Time of Hb measurement	Risk	Statistical significance
Any leg wound infection	OR (95% CI)	Hb <14 g/dL	Preoperative	1.36 (0.75, 2.46)	p=0.312
Late leg wound infection				2.91 (0.95, 8.89)	p=0.061
Clinical importance (1–4) 4 The range of estimates defined by the confidence interval includes clinically important effects but the range of estimates defined by the confidence interval is also compatible with no effect, or a harmful effect			Relevance (1–5) 2. Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention		
Superficial sternal wound				4.16 (1.80, 9.62)	p=0.001

Clinical importance (1–4)	Relevance (1–5)
2 The point estimate of effect is clinically important but the confidence interval includes clinically unimportant effects	2. Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention
Any other adverse effects None reported	
EXTERNAL VALIDITY	
Generalisability Results should be generalisable to a perioperative cardiac surgical patient population	
Applicability The study was carried out in Sweden and is probably applicable to the Australian healthcare setting	

STUDY DETAILS					
Reference Zindrou D, Taylor KM, Bagger JP. Preoperative haemoglobin concentration and mortality rate after coronary artery bypass surgery. Lancet. 2002;359:1748–1751					
Affiliation/Source of funds Faculty of Medicine, Imperial College School of Science, Technology and Medicine, Hammersmith Hospital, London, UK Funding source: None declared					
Study design Prospective cohort study N=2059		Level of evidence II		Location/setting Hammersmith Hospital, London, UK	
Population characteristics Patients undergoing isolated CABG					
Length of follow-up 28 days		Outcome(s) measured Mortality			
INTERNAL VALIDITY					
Allocation	Comparison of study groups	Blinding	Treatment/measurement bias	Follow-up (ITT)	
Patients with Hb >10 g/dL compared with Hb ≤10 g/dL	There may be some differences between anaemic and non-anameic patients. Groups were compared by logistic regression	No blinding details were given	There may be some difference in the treatment of patients with different Hb levels	ITT analysis	
Overall quality assessment (descriptive) This was a good quality prospective cohort study investigating the effect of anaemia on survival in patients undergoing cardiac surgery					
RESULTS					
Outcome	Risk measure	Definition of anaemia	Time of Hb measurement	Risk	Statistical significance
Operative mortality	OR (95% CI)	Hb ≤ 10 g/dL	Preoperative	3.17 (1.24, 8.08)	S
Clinical importance (1–4) 2 The point estimate of effect is clinically important but the confidence interval includes clinically unimportant effects			Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		
Any other adverse effects None reported					
EXTERNAL VALIDITY					
Generalisability The results of the study are generalisable to a perioperative cardiac surgical patient population					
Applicability The study was conducted in the UK and the results are most likely applicable to the Australian healthcare setting					

Level II evidence: Noncardiac studies

<table>
<tr><td colspan="6">STUDY DETAILS</td></tr>
<tr><td colspan="6">Reference Conlon NP, Bale EP, Herbison GP, McCarroll M. Postoperative anemia and quality of life after primary hip arthroplasty in patients over 65 years old. Anesth Analg. 2008;106(4):1056–1061</td></tr>
<tr><td colspan="6">Affiliation/Source of funds Department of Anesthesia, Cappagh National Orthopaedic Hospital, Finglas, Dublin, Ireland; the Department of Preventative and Social Medicine, Dunedin School of Medicine, Dunedin, New Zealand; funding source: NR</td></tr>
<tr><td colspan="2">Study design
Prospective cohort study, N=87</td><td colspan="2">Level of evidence
II</td><td colspan="2">Location/setting
An elective orthopaedic hospital: Cappagh National Orthopaedic Hospital Finglas, Dublin, Ireland</td></tr>
<tr><td colspan="6">Population characteristics Patients aged >65 years, scheduled for primary elective unilateral hip arthroplasty</td></tr>
<tr><td colspan="3">Length of follow-up 2 months</td><td colspan="3">Outcome(s) measured QoL via the SF-36 and FACT anaemia</td></tr>
<tr><td colspan="6">INTERNAL VALIDITY</td></tr>
<tr><td>Allocation</td><td>Comparison of study groups</td><td>Blinding</td><td colspan="2">Treatment/measurement bias</td><td>Follow-up (ITT)</td></tr>
<tr><td>Day 8 Hb levels</td><td>There may be some differences between anaemic and non-anameic patients. Groups were compared by correlation coefficients</td><td>No blinding details were given</td><td colspan="2">There may be some difference in the treatment of patients with different Hb levels</td><td>8 patients did not complete the study and are excluded from the analysis</td></tr>
<tr><td colspan="6">Overall quality assessment (descriptive) A good quality prospective cohort study investigating the association of postoperative Hb levels with quality of life. The study had several limitations, including the observational design. Hb levels were not determined at 2 months postoperatively when the questionnaires were completed</td></tr>
<tr><td colspan="6">RESULTS</td></tr>
<tr><td>Outcome</td><td>Risk measure</td><td>Definition of anaemia</td><td>Time of Hb measurement</td><td>Risk</td><td>Statistical significance</td></tr>
<tr><td>SF-36</td><td>Correlation</td><td>Increasing Hb level</td><td>Day 8 postoperatively</td><td>0.49</td><td>p<0.0005</td></tr>
<tr><td>FACT-anaemia</td><td></td><td></td><td></td><td>0.46</td><td>p<0.0005</td></tr>
<tr><td colspan="3">Clinical importance (1–4)
Unable to determine</td><td colspan="3">Relevance (1–5)
1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival</td></tr>
<tr><td colspan="6">Any other adverse effects NR</td></tr>
<tr><td colspan="6">EXTERNAL VALIDITY</td></tr>
<tr><td colspan="6">Generalisability The study only included patients having total hip arhtroplasty. This surgery usually had a positive impact on quality of life and so the results of this study may not be generalisable to other surgical procedures</td></tr>
<tr><td colspan="6">Applicability The study was performed in Ireland and is probably applicable to the Australian healthcare setting</td></tr>
</table>

STUDY DETAILS					
Reference Foss NB, Kristensen MT, Kehlet H. Anaemia impedes functional mobility after hip fracture surgery. Age Ageing. 2008;37(2):173–178					
Affiliation/Source of funds Departments of Anaesthesia, Orthopaedic Surgery and Pgysiotherapy, Hvidovre University Hospital, Hvidovre, Denmark; Department of Surgical Pathophysiology, Rigshopitalet, Copenhagen, Denmark; **Funding source:** None declared					
Study design Prospective cohort study; N=510	**Level of evidence** II	**Location/setting** Hvidovre university Hospital, Hvidovre, Denmark			
Population characteristics Patients undergoing hip fracture surgery					
Length of follow-up 30 days	**Outcome(s) measured** Complications, LOS and 30 day mortality. A complication was defined as being present in any patient who postoperatively developed any of the following: CVA, delirium, AMI or unstable angina, acute CHF, new onset arrhythmia, pneumonia, respiratory insufficiency, gastric or duodenal ulceration, renal dysfunction, septicaemia, PE, DVT or wound infection				
INTERNAL VALIDITY					
Allocation	**Comparison of study groups**	**Blinding**	**Treatment/measurement bias**	**Follow-up (ITT)**	
Anaemia versus no anaemia. Anameia defined as Hb <10 g/dL	There may be some differences between anaemic and non-anameic patients. Groups were compared by logistic regression	No blinding details were given	There may be some difference in the treatment of patients with different Hb levels. Transfusion threshold was Hb <9.8 g/dL at any point during admission	23 patients were excluded after postoperative day 1 and are not included in the analysis	
Overall quality assessment (descriptive) This is a good quality prospective cohort study					
RESULTS					
Outcome	**Risk measure**	**Definition of anaemia**	**Time of Hb measurement**	**Risk**	**Statistical significance**
Ability to walk on third postoperative day	OR (95% CI)	Hb <10 g/dL	Day 1 postoperatively	0.41 (0.23, 0.73)	p=0.002
Clinical importance (1–4) 2 The point estimate of effect is clinically important but the confidence interval includes clinically unimportant effects			**Relevance (1–5)** 4 Evidence of an effect on proven surrogate outcomes but for a different intervention and population		
Any other adverse effects None reorted					
EXTERNAL VALIDITY					
Generalisability This study was performed in hip fracture patients with the primary outcome being specific to this type of surgery. Therefore, it is unlikely that these results are generalisable to a wider perioperative patient population					
Applicability The results are probably applicable to the Australian healthcare setting					

<table>
<tr><td colspan="5">STUDY DETAILS</td></tr>
<tr><td colspan="5">Reference Halm EA, Wang JJ, Boockvar K, Penrod J, Silberzweig SB, Magaziner J, et al. The effect of perioperative anemia on clinical and functional outcomes in patients with hip fracture. J Orthop Trauma. 2004;18(6):369–374</td></tr>
<tr><td colspan="5">Affiliation/Source of funds
Departments of Medicine, Geriatrics and Adult Development, and Epidemiology and Preventative Medicine, University of Maryland School of Medicine, Baltimore, MD; and Department of Orthopaedics, Hospital for Joint Diseases, New York, NY
Funding source: None reported</td></tr>
<tr><td colspan="2">Study design
Prospective cohort study
N=550</td><td>Level of evidence
II</td><td colspan="2">Location/setting
3 university teaching hospitals and 1 community teaching hospital in the USA</td></tr>
<tr><td colspan="2">Intervention
Anaemia
Sample size: n=222</td><td colspan="3">Comparator(s)
No anaemia
Sample size: n=328</td></tr>
<tr><td colspan="5">Population characteristics: Patients undergoing surgery for hip fracture</td></tr>
<tr><td colspan="2">Length of follow-up
60 days after discharge</td><td colspan="3">Outcome(s) measured
Death, readmission, and functional mobility 60 days after hospital discharge (measured using the FIM)</td></tr>
<tr><td colspan="5">INTERNAL VALIDITY</td></tr>
<tr><td>Allocation</td><td>Comparison of study groups</td><td>Blinding</td><td>Treatment/measurement bias</td><td>Follow-up (ITT)</td></tr>
<tr><td>Anaemia versus no anaemia. Anameia defined as Hb <12 g/dL</td><td>There may be some differences between anaemic and non-anameic patients. Groups were compared by logistic regression</td><td>No blinding details were given</td><td>There may be some difference in the treatment of patients with different Hb levels</td><td>ITT population analysed</td></tr>
<tr><td colspan="5">Overall quality assessment (descriptive)
This study is a good quality prospective cohort study with some limitiations. Because it is an observational study, caution should be taken when inferring cause and effect relationships</td></tr>
</table>

RESULTS					
Outcome	Risk measure	Definition of anaemia	Time of Hb measurement	Risk	Statistical significance
Mortality	OR (95% CI)	Hb < 12 g/dL	Preoperative	0.65 (0.48, 0.89)	S
			Postoperative	1.29 (0.86, 1.94)	S
Clinical importance (1–4) 2 The point estimate of effect is clinically important but the confidence interval includes clinically unimportant effects			Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		
Readmission	OR (95% CI)	Hb < 12 g/dL	Preoperative	0.86 (0.74, 1.00)	S
			Postoperative	0.78 (0.64, 0.95)	S
Clinical importance (1–4) 2 The point estimate of effect is clinically important BUT the confidence interval includes clinically unimportant effects			Relevance (1–5) 2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention.		
Mobility score	β correlation	Hb < 12 g/dL	Preoperative	0.05 (–0.15, 0.24)	NS
			Postoperative	0.15 (–0.09, 0.38)	NS
Clinical importance (1–4) 3 The confidence interval does not include any clinically important effects			Relevance (1–5) 3 Evidence of an effect on proven surrogate outcomes but for a different intervention		
LOS	β correlation	Hb <12 g/dL	Preoperative	–0.76 (–1.04, –0.47)	S
			Postoperative	–0.76 (–1.68, 0.35)	NS
Clinical importance (1–4) 2 The point estimate of effect is clinically important but the confidence interval includes clinically unimportant effects			Relevance (1–5) 2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention		
Any other adverse effects None reported					
EXTERNAL VALIDITY					
Generalisability The study included elderly hip fracture population and may not be generalisable to a wider perioperative patient population					
Applicability The study was conducted in the USA and is probably applicable to the Australian healthcare setting					

STUDY DETAILS					
Reference Meltomaa SS, Makinen JI, Taalikka MO, Helenius HY. Incidence, risk factors and outcome of infection in a 1-year hysterectomy cohort: a prospective follow-up study. J Hosp Infect. 2000;45(3):211–217					
Affiliation/Source of funds Department of Obstetrics and Gynaecology and Department of Biostatistics, University of Turku, Turku, Finland. Funding source: None reported					
Study design Prospective cohort study N=687		Level of evidence II		Location/setting Turku University Hospital, Turku, Finland	
Population characteristics Patients undergoing hysterectomy for benign conditions					
Length of follow-up 1 year		Outcome(s) measured Incidences and risk factors for infections			
INTERNAL VALIDITY					
Allocation	Comparison of study groups	Blinding	Treatment/measurement bias	Follow-up (ITT)	
Anaemia versus no anaemia. Anameia was not defined	There may be some differences between anaemic and non-anameic patients. Groups were compared by logistic regression	No blinding details were given	There may be some difference in the treatment of patients with different Hb levels	ITT population was used for in hospital analysis; 142 patients were excluded from the 4-6 week postoperative analysis and 121 patients were excluded from the one year analysis	
Overall quality assessment (descriptive) This was a fair quality prospective cohort study					
RESULTS					
Outcome	Risk measure	Definition of anaemia	Time of Hb measurement	Risk	Statistical significance
Risk of infection	OR (95% CI)	NR	Postoperative	2.7 (1.5, 4.7)	p<0.001
Clinical importance (1–4) 1 A clinically important benefit for the null range of plausible estimates. The confidence limit closest to the measure of no effect rules out a clinically unimportant effect of the intervention			Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		
Any other adverse effects NR					
EXTERNAL VALIDITY					
Generalisability This study included women undergoing hysterectomy and may not be generalisable to a wider perioperative patient population					
Applicability The study was performed in Finland and is probably applicable to the Australian healthcare setting					

STUDY DETAILS					
Reference Myers E, Grady PO, Dolan AM. The influence of preclinical anaemia on outcome following total hip replacement. Arch Orthop Trauma Surg. 2004;124(10):699–701					
Affiliation/Source of funds Regional Orthopaedic Unit, Our Lady's Hospital, Navan, County Meath, Ireland. Funding source: None reported					
Study design Prospective cohort study N=225		Level of evidence II		Location/setting Regional Orthopaedic Unit, Our Lady's Hospital, Navan, Ireland	
Intervention Anaemia Sample size: n=35		Comparator(s) No anaemia Sample size: n=190			
Population characteristics Patients undergoing elective primary hip arthroplasties					
Length of follow-up NR	Outcome(s) measured Postoperative complications including blood transfusion, urinary tract infection, and respiratory tract infection and hospital LOS				
INTERNAL VALIDITY					
Allocation	Comparison of study groups	Blinding	Treatment/measurement bias	Follow-up (ITT)	
Anaemia versus no anaemia. Anameia was defined as Hb<12.5 g/dL for men, and Hb <11.5 g/dL for women	There may be some differences between anaemic and non-anameic patients. Groups were compared by chi squared analysis	No blinding details were given	There may be some difference in the treatment of patients with different Hb levels. Transfusion in the postoperative period was based on a transfusion protocol of Hct <30%	ITT population was used	
Overall quality assessment (descriptive) This was a poor quality study with a number of limitations. Firstly, the sample size is small with a very small anaemic group. Secondly, no regression analysis was peformed and therefore demographic differences have not been taken into account in the analysis of the results					
RESULTS					
Outcome	Risk measure	Definition of anaemia	Time of Hb measurement	Risk	Statistical significance
Blood transfusion	Rates anaemia vs. no anaemia	Hb<12.5 g/dL men, Hb <11.5 g/dL women	Preoperative	71% vs 10.5%	p<0.001
UTI				28% vs 14%	p=0.039
RTI				14% vs 12%	p=0.55
Hospital LOS	Days anaemia vs no anaemia			18 days vs 11 days	NR

Clinical importance (1–4)	Relevance (1–5)
NA	1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival
Any other adverse effects None reported	
EXTERNAL VALIDITY	
Generalisability The study included elderly hip fracture population and may not be generalisable to a wider perioperative patient population	
Applicability The study was performed in Ireland and the results are probably applicable to the Australian healthcare setting	

STUDY DETAILS					
Reference Wallis JP, Wells AW, Whitehead S, Brewster N. Recovery from postoperative anaemia. Transfus Med. 2005;15(5):413–418					
Affiliation/Source of funds Departments of Haematology andf Orthopaedic Surgery, Freeman Hospital, Newcastle upon Tyne, UK Funding source: None reported					
Study design Prospective cohort study N=30		Level of evidence II		Location/setting Freeman Hospital, Newcastle upon Tyne, UK	
Population characteristics Patients undergoing first time elective unilateral hip arthroplasty					
Length of follow-up 56 days		Outcome(s) measured QoL using the SF-36			
INTERNAL VALIDITY					
Allocation	Comparison of study groups	Blinding	Treatment/measurement bias	Follow-up (ITT)	
Different Hb levels	There may be some differences between anaemic and non-anameic patients. Groups were compared by logistic regression	No blinding details were given	There may be some difference in the treatment of patients with different Hb levels. Transfusion was based on the transfusion trigger of <9 g/dL	ITT population was used for week 8 analysis, 1 patient was excluded from week 4 analysis	
Overall quality assessment (descriptive) This study is a poor quality prospective cohort study with a very small samle size					
RESULTS					
Outcome	Risk measure	Definition of anaemia	Time of Hb measurement	Risk	Statistical significance
SF-36	Correlation	Increasing Hb level	Post- and preoperative	No correlation	NS
Clinical importance (1–4) NA			Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		
Any other adverse effects None reported					
EXTERNAL VALIDITY					
Generalisability This study was performed in elderly hip fracture patients and may not be generalisable to a wider perioperative patient population					
Applicability The study was performed in the UK and is applicable to the Australian healthcare setting					

STUDY DETAILS					
Reference Wolters U, Wolf T, Stutzer H, Schroder Y, Pichlmaier H. Risk factors, complications, and outcome in surgery: A multivariate analysis. Eur J Surg. 1997;163(8):563–568					
Affiliation/Source of funds Departments of General, Vascular and Thoracic Surgery, Anaesthesia and Intensive Care, and Medical Statistics and Biometrics, University of Cologne, Germany Funding source: None reported					
Study design Prospective cohort study N=6304	Level of evidence II	Location/setting Department of General and Vascular Surgery, University of Cologne, Cologne, Germany (Teaching Hosptial)			
Intervention Anaemia; sample size: n=893	Comparator No anaemia; sample size: n=5411				
Population characteristics Patients undergoing general surgery					
Length of follow-up Time in hospital	Outcome(s) measured Postoperative complications including pulmonary complications, cardiac complications, wound infection and UTI. Postoperative mortality included all deaths in hospital				
INTERNAL VALIDITY					
Allocation	Comparison of study groups	Blinding	Treatment/measurement bias	Follow-up (ITT)	
Patients with anaemia versus patients without anaemia. Anaemia was defined as Hb <10 g/dL	There may be some differences between anaemic and non-anameic patients. Groups were compared by logistic regression	No blinding details were given	There may be some difference in the treatment of patients with different Hb levels	ITT population was used	
Overall quality assessment (descriptive) This is a good quality large prospective cohort study					
RESULTS					
Outcome	Risk measure	Definition of anaemia	Time of Hb measurement	Risk	Statistical significance
Postoperative complications	OR (95% CI)	Hb <10 g/dL	Preoperative	1.23 (1.03, 1.48)	S
Clinical importance (1–4) 2 The point estimate of effect is clinically important but the confidence interval includes clinically unimportant effects	Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival				
Any other adverse effects None reported					
EXTERNAL VALIDITY					
Generalisability The study was perforemed in general surgery patients and is therefore generalisable to a perioperative noncardiac surgical population					
Applicability The study was performed in Germany and is propable applicable to the Australian healthcare setting					

Level III evidence: Cardiac studies

<table>
<tr><td colspan="5">STUDY DETAILS</td></tr>
<tr><td colspan="5">Reference Bell ML, Grunwald GK, Baltz JH, McDonald GO, Bell MR, Grover FL, et al. Does preoperative hemoglobin independently predict short-term outcomes after coronary artery bypass graft surgery? Ann Thorac Surg. 2008;86(5):1415–1423</td></tr>
<tr><td colspan="5">Affiliation/Source of funds:
Department of Preventative and Social Medicine, University of Otago, Dunedin, New Zealand; Division of Cardiac Research, Eastern Colorado Health Care System Department of Veterans Affairs Medical Centre, Departments of Biostatistics and Informatics, Surgery, and Medicine, University of Colorado Denver, CO; Department of Veterans' Affairs, Office of Patient Care Services, Washington, DC; and Department of Veterans' Affairs Medical Centre, Northport, NY
Funding source: Funding for this study was initially provided by the Department of Veterans' Affairs Health Services Research and Development Grant IHY 99214-1, with ongoing support from the Office of Patient Care Services, VA Central Office, Washington DC. This project was supported, in part, by the Offices of Research and Development Offices at the Northport and the Eastern Colorado Health Care System Denver Veterans' Affairs Medical Centres</td></tr>
<tr><td colspan="2">Study design
Retrospective cohort study
N=36,658</td><td>Level of evidence
III</td><td colspan="2">Location/setting
44 Veterans' Affairs cardiac surgical centres, USA</td></tr>
<tr><td colspan="2">Intervention
Anaemia
Sample size: n=6143</td><td colspan="3">Comparator
No anaemia
Sample size: n=30,196</td></tr>
<tr><td colspan="5">Population characteristics
Patients undergoing CABG-only procedures with cardiopulmonary bypass</td></tr>
<tr><td colspan="2">Length of follow-up
NA</td><td colspan="3">Outcome(s) measured
30 day operative mortality and 30 day operative morbidity (including endocarditis, renal failure requiring dialysis, mediastinitis, reoperation for bleeding, mechanical ventialtor used postoperatively >48 hrs, repeat cardiac surgery, stroke, coma >24 hours, cardiac arrest requiring cardiopulmonary resuscitation</td></tr>
<tr><td colspan="5">INTERNAL VALIDITY</td></tr>
<tr><td>Allocation</td><td>Comparison of study groups</td><td>Blinding</td><td>Treatment/measurement bias</td><td>Follow-up (ITT)</td></tr>
<tr><td>Patients with anaemia vs patients without anaemia. Anaemia defined as Hb <12 g/dL</td><td>There may be some differences between anaemic and non-anameic patients. Groups were compared by logistic regression</td><td>No blinding details were given</td><td>There may be some difference in the treatment of patients with different Hb levels</td><td>319 (0.9%) patients were missing Hb values</td></tr>
<tr><td colspan="5">Overall quality assessment (descriptive)
This was a good quality retrospective cohort study with some limitations. While the sample was large, patients were predominantly male (99%) exhibiting complex, multiple chronic comorbidities. After the start of the surgical procedure, data were not captured to assess intraoperative or perioperative Hb levels and monitor blood product use</td></tr>
</table>

RESULTS					
Outcome	Risk measure	Definition of anaemia	Time of Hb measurement	Risk	Statistical significance
30 day mortality	OR (95% CI)	Hb < 10 g/dL	Preoperative	1.29 (0.99, 1.68)	p=0.0641
30 day postoperative morbidity				1.20 (1.02, 1,43)	p=0.033
Clinical importance (1–4) 2 The point estimate of effect is clinically important but the confidence interval includes clinically unimportant effects			Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		
Any other adverse effects None reported					
EXTERNAL VALIDITY					
Generalisability The study was performed in an elderly, predominantly male population which may not be generalisable to a wider perioperative patient population					
Applicability The study was performed in the USA and may be applicable to the Australian healthcare setting					

STUDY DETAILS		
Reference Cladellas M, Bruguera J, Comin J, Vila J, De Jaime E, Marti J, et al. Is preoperative anaemia a risk marker for in-hospital mortality and morbidity after valve replacement? Eur Heart J. 2006;27(9):1093–1099		
Affiliation/Source of funds Department of Cardiology, Hospital del Mar, Barcelona, Spain; Institut Municipal d'Investigacio Medica; and Department of Geriatrics, Insitut Municipal d'Investigacio Mediica, Barcelona, Spain Funding source: No conflicts of interests were declared		
Study design Retrospective cohort study N=233 (201 patients analyses)	Level of evidence III	Location/setting Department of Cardiology, Hospital del Mar, Barcelona, Spain
Intervention Anaemia Sample size: n=42	Comparator No anaemia Sample size: n=159	
Population characteristics Patients undergoing elective valve replacement		
Length of follow-up Time in hospital	Outcome(s) measured 30 day mortality, 30 day MACE (major postoperative complications)	
INTERNAL VALIDITY		

Allocation	Comparison of study groups	Blinding	Treatment/measurement bias	Follow-up (ITT)
Patients with anaemia versus patients without anaemia. Anaemia was defined as Hb <12 g/dL	There may be some differences between anaemic and non-anameic patients. Groups were compared by logistic regression	No blinding details were given	There may be some difference in the treatment of patients with different Hb levels	32 patient records were excluded from the analysis

Overall quality assessment (descriptive)

This study was a good quality retrospective cohort study. As the study is retrospective, it is subject to limitations inherent in this type of clinical investigation

RESULTS

Outcome	Risk measure	Definition of anaemia	Time of Hb measurement	Risk	Statistical significance
Mortality	OR (95% CI)	Hb <12 g/dL	preoperative	3.23 (1.09, 9.55)	p=0.033
Clinical importance (1–4) 2 The point estimate of effect is clinically important but the confidence interval includes clinically unimportant effects			Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		
MACE				5.18 (2.18, 12.3)	p<0.001
MACE (after EUROscore adjustment)				4.67 (2.14, 10.36)	p<0.001
Clinical importance (1–4) 1 A clinically important benefit for the null range of plausible estimates. The confidence limit closest to the measure of no effect rules out a clinically unimportant effect of the intervention			Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		

Any other adverse effects

None reported

EXTERNAL VALIDITY

Generalisability

This study is probably generalisable to a wider perioperative cardiac surgery population

Applicability

The study was performed in Spain and is probably applicable to the Australian healthcare setting

STUDY DETAILS					
Reference Fang WC, Helm RE, Krieger KH, Rosengart TK, DuBois WJ, Sason C, et al. Impact of minimum hematocrit during cardiopulmonary bypass on mortality in patients undergoing coronary artery surgery. Circulation. 1997;96(9 Suppl):II194–II199					
Affiliation/Source of funds Department of Surgery, University of Massachusetts Medical Centre, Worcester, MA; the Department of Cardiothoracic Surgery, Cornell University Medical College, New York, NY; the Department of Research, Division of Biostatistics, North Shore University Hospital, Massachussetts; and the Department of Cardiothoracic Surgery, Albert Einstein College of Medicine, New York, NY **Funding source:** None reported					
Study design Retrospective cohort study; N=2738		**Level of evidence** III		**Location/setting** US tertiary academic medical centre	
Population characteristics Patients undergoing CABG surgery					
Length of follow-up Time in hospital		**Outcome(s) measured** Postoperative in hospital mortality			
INTERNAL VALIDITY					
Allocation	**Comparison of study groups**	**Blinding**	**Treatment/measurement bias**	**Follow-up (ITT)**	
Patients with different lowest Hct values	There may be some differences between anaemic and non-anameic patients. Groups were compared by logistic regression	No blinding details were given	There may be some difference in the treatment of patients with different Hb levels	ITT population analysed	
Overall quality assessment (descriptive) This study was a good quality retrospective cohort study. As the study is retrospective, it is subject to limitations inherent in this type of clinical investigation					
RESULTS					
Outcome	**Risk measure**	**Definition of anaemia**	**Time of Hb measurement**	**Risk**	**Statistical significance**
Mortality	OR (95% CI)	Lowest Hct	Intraoperative	3.987	p=0.0001
		Hct <15%		2.7	p<0.001
Clinical importance (1–4) Unable to determine			**Relevance (1–5)** 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		
Any other adverse effects NR					
EXTERNAL VALIDITY					
Generalisability The results of this study is generalisable to a perioperative cardiac surgery patient population					
Applicability The study was performed in the USA and is most likely applicable to the Australian healthcare setting					

STUDY DETAILS					
Reference Ferraris VA, Ferraris SP, Edwards FH, Guyton RA, Reitz BA. Risk factors for postoperative morbidity. J Thorac Cardiovasc Surg. 1996;111(4):731–741					
Affiliation/Source of funds Division of Cardiothoracic Surgery, Albany Medical College, Albany, NY Funding source: None reported					
Study design Retrospective cohort study N=938		Level of evidence III		Location/setting Albany Medical Centre Hospital, Albany, NY, USA	
Population characteristics Patients undergoing CABG surgery					
Length of follow-up Time in hospital	Outcome(s) measured Hospital mortality, hospital LOS, serious postoperative morbidity (defined as postoperative MI, stroke, pulmonary failure, renal failure necessitating dialysis, postoperative cardiogenic shock necessitating LVAD or IABP, sepsis, or mediastinitis)				
INTERNAL VALIDITY					
Allocation	Comparison of study groups	Blinding	Treatment/measurement bias	Follow-up (ITT)	
Different RBCVOL defined as patient's blood volume multiplied by the preoperative Hct value	There may be some differences between patients with differing Hct levels. Groups were compared by logistic regression	No blinding details were given	There may be some difference in the treatment of patients with different Hb levels	ITT population analysed	
Overall quality assessment (descriptive) This was a fair quality retrospective cohort study. Because all the results were obtained from one institution, it is not clear how generally applicable they will be to other smaller or larger facilities. A more serious shortcoming involves selction bias. Only surgical patients were included in the study					
RESULTS					
Outcome	Risk measure	Definition of anaemia	Time of Hb measurement	Risk	Statistical significance
Operative mortality	OR (95% CI)	Age/RBCVOL	Preoperative	NR	NS
Clinical importance (1–4) Unable to determine			Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		
Serious postoperative morbidity	OR (95% CI)	Age/RBCVOL	Preoperative	13.7 (6.7, 27.7)	S

<table>
<tr><td colspan="3">Clinical importance (1–4)
1 A clinically important benefit for the null range of plausible estimates. The confidence limit closest to the measure of no effect rules out a clinically unimportant effect of the intervention</td><td colspan="3">Relevance (1–5)
1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival</td></tr>
<tr><td>Hospital LOS ≥ 8.4 days</td><td>OR (95% CI)</td><td>Age/RBCVOL</td><td>Preoperative</td><td>2.6 (1.9, 3.4)</td><td>S</td></tr>
<tr><td colspan="3">Clinical importance (1–4)
1 A clinically important benefit for the null range of plausible estimates. The confidence limit closest to the measure of no effect rules out a clinically unimportant effect of the intervention</td><td colspan="3">Relevance (1–5)
2 Evidence of an effect on a surrogate outcome that has shown to be predictive of patient relevant outcomes for the same intervention</td></tr>
<tr><td colspan="6">Any other adverse effects
None reported</td></tr>
<tr><td colspan="6">EXTERNAL VALIDITY</td></tr>
<tr><td colspan="6">Generalisability
The study is probably generalisable to a perioperative cardiac surgery population</td></tr>
<tr><td colspan="6">Applicability
The study was performed in the USA and is most likely applicable to the Australian healthcare setting</td></tr>
</table>

STUDY DETAILS					
Reference Habib RH, Zacharias A, Schwann TA, Riordan CJ, Durham SJ, Shah A. Adverse effects of low hematocrit during cardiopulmonary bypass in the adult: Should current practice be changed? J Thorac Cardiovasc Surg. 2003;125:1438–1450					
Affiliation/Source of funds Cardiovascular Surgery, St Vincent Mercy Medical Center, Toledo, OH; Saint Luke's Hospital, Maumee, OH; Department of Surgery, Medical College of Ohio, Toledo, OH Funding source: None reported					
Study design Retrospective cohort study N=5000		Level of evidence III		Location/setting St Vincent Mercy Medical Centre, Toledo, OH, USA	
Population characteristics Patients undergoing cardiac operations with cardiopulmonary bypass					
Length of follow-up 8–93 months		Outcome(s) measured Complications, operative mortality, ICU and hospital LOS			
INTERNAL VALIDITY					
Allocation	Comparison of study groups	Blinding	Treatment/measurement bias	Follow-up (ITT)	
Different lowest Hct	There may be some differences between patients with differing Hct levels. Groups were compared by logistic regression	No blinding details were given	There may be some difference in the treatment of patients with different Hb levels	Identified cohort population followed up	
Overall quality assessment (descriptive) This was a fair quality retrospective cohort study					
RESULTS					
Outcome	Risk measure	Definition of anaemia	Time of Hb measurement	Risk	Statistical significance
Operative mortality	OR (95% CI)	Hct continuous	Intraoperative	0.86 (0.82, 0.92)	p<0.001
Clinical importance (1–4) 1 A clinically important benefit for the null range of plausible estimates. The confidence limit closest to the measure of no effect rules out a clinically unimportant effect of the intervention			Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		
CICU >2 days	OR (95% CI)	Hct continuous	Intraoperative	0.97 (0.96, 0.98)	p<0.001

Clinical importance (1–4) 1 A clinically important benefit for the null range of plausible estimates. The confidence limit closest to the measure of no effect rules out a clinically unimportant effect of the intervention			Relevance (1–5) 2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention		
Postoperative hospital stay >8 days	OR (95% CI)	Hct continuous	Intraoperative	0.95 (0.93, 0.98)	p<0.001
Clinical importance (1–4) 1 A clinically important benefit for the null range of plausible estimates. The confidence limit closest to the measure of no effect rules out a clinically unimportant effect of the intervention			Relevance (1–5) 2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention		
0–6 year mortality	RR (95% CI)	Hct continuous	Intraoperative	0.95 (0.92, 0.98)	p=0.001
Clinical importance (1–4) 1 A clinically important benefit for the null range of plausible estimates. The confidence limit closest to the measure of no effect rules out a clinically unimportant effect of the intervention			Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		
Any other adverse effects None reported					
EXTERNAL VALIDITY					
Generalisability The study is probably generalisable to a perioperative cardiac surgery population					
Applicability The study was performed in the USA and is most likely applicable to the Australian healthcare setting					

STUDY DETAILS

Reference Habib RH, Zacharias A, Schwann TA, Riordan CJ, Engoren M, Durham SJ, et al. Role of hemodilutional anemia and transfusion during cardiopulmonary bypass in renal injury after coronary revascularization: Implications on operative outcome. Crit Care Med. 2005;33(8):1749–1756

Affiliation/Source of funds

Department of Cardiovascular Surgery, St Vincent Mercy Medical Centre, Toledo, OH; Departments of Medicine and Surgery, Medical College of Ohio, Toledo, OH; and Saint Luke's Hospital, Maumee, OH

Funding source: None reported

Study design	Level of evidence	Location/setting
Retrospective cohort study N=1760	III	St Vincent Mercy Medical Centre, Toledo, OH, USA

Population characteristics

Adult CABG surgery patients with cardiopulmonary bypass but no preoperative renal failure

Length of follow-up	Outcome(s) measured
30 days after discharge	Post cardiopulmonary acute renal failure

INTERNAL VALIDITY

Allocation	Comparison of study groups	Blinding	Treatment/measurement bias	Follow-up (ITT)
Different lowest Hct	There may be some differences between patients with differing Hct levels. Groups were compared by logistic regression	No blinding details were given	There may be some difference in the treatment of patients with different Hb levels	ITT population analysed

Overall quality assessment (descriptive)

This study is a good quality observational retrospective analysis from a large clinical database. While this may represent a powerful tool to identify clinical associations, the reported results are not sufficient to prove a causal effect of low Hct on renal dysfunction. Also, despite the multivariate analyses, the potential for residual confounding due to incomplete covariate adjustment cannot be ruled out

RESULTS

Outcome	Risk measure	Definition of anaemia	Time of Hb measurement	Risk	Statistical significance
Acute renal failure	Coefficient	Lowest Hct	Intraoperative	0.93 (0.88, 0.98)	p=0.007
		Hct 20–24		1.80 (0.94, 3.44)	p=0.074
		Hct <20		2.46 (1.32, 4.56)	p=0.004

Clinical importance (1–4)	Relevance (1–5)
1 A clinically important benefit for the null range of plausible estimates. The confidence limit closest to the measure of no effect rules out a clinically unimportant effect of the intervention	1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival

Any other adverse effects None reported
EXTERNAL VALIDITY
Generalisability The study is probably generalisable to a perioperative cardiac surgery population
Applicability The study was performed in the USA and is most likely applicable to the Australian healthcare setting

STUDY DETAILS					
Reference Higgins TL, Estafanous FG, Loop FD, Beck GJ, Blum JM, Paranandi L. Stratification of morbidity and mortality outcome by preoperative risk factors in coronary artery bypass patients: a clinical severity score. JAMA. 1992;267:2344–2348					
Affiliation/Source of funds Departments of Cardiothoracic Anaesthesiology, Thoracic and Cardiovascular Surgery, and Biostatistics and Epidemiology, The Cleveland Clinic Foundation Funding source: Not reported					
Study design Retrospective cohort N=5051 (reference group) N=4169 (validation group)		Level of evidence III		Location/setting Hospital setting, USA	
Population characteristics Patients undergoing CABG surgery					
Length of follow-up Not reported		Outcome(s) measured Mortality, morbidity (cardiac complication, prolonged ventilation, central nervous system complication, oliguric or anuric renal failure, serious infection, death)			
INTERNAL VALIDITY					
Allocation	Comparison of study groups	Blinding	Treatment/measurement bias		Follow-up (ITT)
Anaemia versus no anaemia. Anameia defined as Hct ≤ 34	There may be some differences between anaemic and non-anameic patients. Groups were compared by logistic regression	No blinding details were given	There may be some difference in the treatment of patients with different Hb levels		ITT population analysed
Overall quality assessment (descriptive) This is a good quality retrospective cohort study					
RESULTS					
Outcome	Risk measure	Definition of anaemia	Time of Hb measurement	Risk	Statistical significance
Morbidity	OR (95% CI)	Hct ≤ 34	Preoperative	1.57 (1.20, 2.04)	p=0.001
Clinical importance (1–4) 1 A clinically important benefit for the null range of plausible estimates. The confidence limit closest to the measure of no effect rules out a clinically unimportant effect of the intervention			Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		
Mortality	OR (95% CI)	Hct ≤ 34	Preoperative	2.68 (1.71, 4.20)	p<0.0001

Clinical importance (1–4)	Relevance (1–5)
1 A clinically important benefit for the null range of plausible estimates. The confidence limit closest to the measure of no effect rules out a clinically unimportant effect of the intervention	1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival
Any other adverse effects None reported	
EXTERNAL VALIDITY	
Generalisability The study is probably generalisable to a perioperative cardiac surgery population	
Applicability The study was performed in the USA and is most likely applicable to the Australian healthcare setting	

STUDY DETAILS				
Reference Karkouti K, Wijeysundera DN, Yau TM, Callum JL, Cheng DC, Crowther M, et al. Acute kidney injury after cardiac surgery: focus on modifiable risk factors. Circulation. 2009;119(4):495–502				
Affiliation/Source of funds Department of Anesthesia, Toronto General Hospital, University Health Network, University of Toronto; Department of Health Policy, Management and Evaluation, University of Toronto; Department of Surgery, Division of Cardiac Surgery, Toronto General Hospital, University Health Network, University of Toronto; Department of Clinical Pathology, Sunnybrook Health Sciences Centre, University of Toronto, Toronto, Ontario, Canada; Department of Anaesthesia, University of Western Ontario, London, Ontario, Canada; Department of Medicine, Division of Haematology, McMaster University, Hamilton, Ontario, Canada; Department of Anaesthesia, University of Ottowa, Ottowa, Ontario, Canada; Department of Surgery, Division of Cardiac and Vascular Surgery, Sunnybrook Health Sciences Centre, University of Toronto, Toronto, Ontario, Canada; Department of Anesthesia, Dalhousie University, Halifax, Nova Scotia, Canada; Department of Anesthesia, Sunnybrook Health Sciences Centre, University of Toronto, Toronto, Ontario, Canada; Department of Surgery, Division of Cardiac Surgery, McMaster University, Hamilton, Ontario, Canada; Department of Surgery, Division of Cardiac Surgery, Dalhousie University, Halifax, Nova Scotia, Canada; Department of Anesthesia and Critical Care, Keenan Research Centre in the LI Ka Shing Knowledge Institute, St Michaels Hospital, University of Toronto, Toronto, Ontario, Canada; Department of Surgery, Division of Cardiac Surgery, University of Ottawa, Ontario, Canada; Department of Anaesthesia, McMaster University, Hamilton, Ontario, Canada Funding source: Funding for this project was provided by the Canadian Institutes of Health Research and Canadian Blood Services through an operating grant and by Novo Nordisk through an unrestricted research grant. There were no other disclosures declared				
Study design Retrospective cohort study N=3500		Level of evidence III		Location/setting 7 academic Canadian hospitals
Population characteristics Patients undergoing cardiac surgery from 7 hospitals				
Length of follow-up NR		Outcome(s) measured Development of acute kidney injury (AKI)		
INTERNAL VALIDITY				
Allocation	Comparison of study groups	Blinding	Treatment/measurement bias	Follow-up (ITT)
Different Hb levels	There may be some differences in the treatment of patients with different Hb levels. Groups were compared by logistic regression	No blinding details were given	There may be some difference in the treatment of patients with different Hb levels	40 patients were excluded from the cohort

Overall quality assessment (descriptive)

This was a fair quality retrospective cohort study. There are several limitations to be considered when interpreting the present study. First, postoperative renal fundtion was estimated with the Cockcroft-Gault equation, which uses serum creatinine and weight to estimate renal function after surgery. During the postoperative period, however, these estimates may not be accurate due to imbalances between creatinine production and elimination. Second, because only patients undergoing cardiac surgery with CPB were included in the study, results cannot be generalised to other populations. Third, because this is a retrospective observational study, causality could not be determined

RESULTS

Outcome	Risk measure	Definition of anaemia	Time of Hb measurement	Risk	Statistical significance
AKI, >25% decrease in GFR	OR (95% CI)	Hb 12–13.9 g/dL	Preoperative	1.23 (1.07, 1.49)	S
		Hb 10–11.9 g/dL		1.63 (1.25, 2.12)	S
		Hb < 10 g/dL		1.99 (1.29, 3.08)	S
AKI, >50% decrease in GFR	OR (95% CI)	Hb 12–13.9 g/dL	Preoperative	1.06 (0.73, 1.54)	NS
		Hb 10–11.9 g/dL		1.65 (1.07, 2.54)	S
		Hb < 10 g/dL		2.94 (1.66, 5.23)	S
AKI, >75% decrease in GFR	OR (95% CI)	Hb 12–13.9 g/dL	Preoperative	1.00 (0.58, 1.67)	NS
		Hb 10–11.9 g/dL		1.82 (1.04, 3.17)	S
		Hb < 10 g/dL		1.83 (0.84, 3.95)	NS

Clinical importance (1–4)

1 A clinically important benefit for the null range of plausible estimates. The confidence limit closest to the measure of no effect rules out a clinically unimportant effect of the intervention

Relevance (1–5)

1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival

Any other adverse effects

None reported

EXTERNAL VALIDITY

Generalisability

The study may not be generalisable to a perioperative cardiac surgery population

Applicability

The study was performed in Canada and is probably applicable to the Australian healthcare setting

STUDY DETAILS				
Reference Karkouti K, Wijeysundera DN, Beattie WS. Risk associated with preoperative anemia in cardiac surgery: a multicenter cohort study. Circulation. 2008a;117(4):478–484				
Affiliation/Source of funds Departments of Anesthesia; Health Policy, Management and Evaluation; and Surgery, University Health Network, University of Toronto, Toronto, Ontario, Canada Funding source: None reported				
Study design Retrospective cohort study N=10,179	Level of evidence III	Location/setting Toronto General Hospital, Toronto, Canada		
Population characteristics Patients undergoing cardiac surgery with cardiopulmonary bypass				
Length of follow-up Time in hospital	Outcome(s) measured Composite outcome of in-hospital mortality, stroke, or acute kidney failure			
INTERNAL VALIDITY				
Allocation	Comparison of study groups	Blinding	Treatment/measurement bias	Follow-up (ITT)
Lowest Hb level	There may be some differences in the treatment of patients with different Hb levels. Groups were compared by logistic regression and propensity score-based matching	No blinding details were given	There may be some difference in the treatment of patients with different Hb levels	ITT population used
Overall quality assessment (descriptive) This is a fair quality retrospective cohort study with several important limitations. First, because this study was retrospective, causality could not be determined. Second, because the last available preoperative Hb concentration was used as a surrogate for the patients' baseline Hb concentration, normal Hb levels may have been underestimated. Another important limitation is that the study's results are not generalisable. The study sample was limited to non-anaemic, non-erythrocytotic adult patients who underwent non-emergent, on-pump cardiac surgery				

<table>
<tr><td colspan="6">RESULTS</td></tr>
<tr><td>Outcome</td><td>Risk measure</td><td>Definition of anaemia</td><td>Time of Hb measurement</td><td>Risk</td><td>Statistical significance</td></tr>
<tr><td>Adverse outcome</td><td>OR (95% CI)</td><td>Hb <7 g/dL</td><td>Lowest intraoperative</td><td>1.15 (0.84, 1.56)</td><td>p=0.4</td></tr>
<tr><td colspan="3">Clinical importance (1–4)
1 A clinically important benefit for the null range of plausible estimates. The confidence limit closest to the measure of no effect rules out a clinically unimportant effect of the intervention</td><td colspan="3">Relevance (1–5)
1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival.</td></tr>
<tr><td>Adverse outcome</td><td>OR (95% CI)</td><td><50% decrease from baseline</td><td>Intraoperative</td><td>1.53 (1.12, 2.08)</td><td>p=0.007</td></tr>
<tr><td colspan="3">Clinical importance (1–4)
4 The range of estimates defined by the confidence interval includes clinically important effects BUT the range of estimates defined by the confidence interval is also compatible with no effect, or a harmful effect</td><td colspan="3">Relevance (1–5)
1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival</td></tr>
<tr><td colspan="6">Any other adverse effects
None reported</td></tr>
<tr><td colspan="6">EXTERNAL VALIDITY</td></tr>
<tr><td colspan="6">Generalisability
The study may not be generalisable to a perioperative cardiac surgery population</td></tr>
<tr><td colspan="6">Applicability
The study was performed in Canada and is probably applicable to the Australian healthcare setting</td></tr>
</table>

STUDY DETAILS				
Reference Karkouti K, Wijeysundera DN, Yau TM, McCluskey SA, Van Rensburg A, Beattie WS. The influence of baseline hemoglobin concentration on tolerance of anemia in cardiac surgery. Transfusion. 2008b;48(4):666–672				
Affiliation/Source of funds Departments of Anesthesia and Health Policy, Management, and Evaluation, University of Health Network, University of Toronto, Toronto, Ontario, Canada Funding source: The Canadian Institutes of Health Research provided funding for this project				
Study design Retrospective cohort study N=3500	Level of evidence III	Location/setting 7 university-affiliated Canadian hospitals		
Intervention Patients with anaemia Sample size: n=774	Comparator(s) Non-anaemic patients Sample size: n=2512			
Population characteristics Patients undergoing cardiac surgery from 7 hospitals				
Length of follow-up Time in hospital	Outcome(s) measured Composite outcome of in-hospital mortality, stroke, or acute kidney failure			
INTERNAL VALIDITY				
Allocation	Comparison of study groups	Blinding	Treatment/measurement bias	Follow-up (ITT)
Anaemia versus no anaemia. Anameia defined as Hb <12.5 g/dL	There may be some differences in the treatment of patients with different Hb levels. Groups were compared by logistic regression and propensity score-based matching	No blinding details were given	There may be some difference in the treatment of patients with different Hb levels	214 patients were excluded from the analysis
Overall quality assessment (descriptive) This was a fair quality retrospective cohort study with several limitations. First, because this was a retrospective observational study, causality could not be determined. Therefore, it is possible that preoperative anaemia was associated with adverse outcomes simply because it is a marker for severity of illness. Second, the effects of unknown or unmeasured confounders on the observed association cannot be ruled out. Third, neither the cause nor duration of preoperative anaemia, both of which have prognostic implications, were known				

RESULTS					
Outcome	Risk measure	Definition of anaemia	Time of Hb measurement	Risk	Statistical significance
Adverse outcome	OR (95% CI)	Hb < 12.5 g/dL	Preoperative	2.0 (1.4, 2.8)	p<0.0001
Clinical importance (1–4) 1 A clinically important benefit for the null range of plausible estimates. The confidence limit closest to the measure of no effect rules out a clinically unimportant effect of the intervention			Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		
Any other adverse effects None reported					
EXTERNAL VALIDITY					
Generalisability The study may be generalisable to a perioperative cardiac surgery population					
Applicability The study was performed in Canada and is probably applicable to the Australian healthcare setting					

STUDY DETAILS

Reference Karkouti K, Djaiani,G, Borger MA, Beattie WS, Fedorko L, Wijeysundera D, et al. Low hematocrit during cardiopulmonary bypass is associated with increased risk of perioperative stroke in cardiac surgery. Ann Thorac Surg. 2005;80(4):1381–1387

Affiliation/Source of funds

Department of Anesthesia and Division of Cardiovascular Surgery, University Health Network, and Department of Health Policy, Management, and Evaluation, University of Toronto, Toronto, Ontario, Canada

Funding source: Dr Karkouti was supported in part by the Canadian Institutes of Health Research and Canadian Blood Services. Dr Beattie is the F. Frasier Elliot Chair of Cardiac Anesthesia. No third-party funding was used for the study

Study design	Level of evidence	Location/setting
Retrospective cohort study N=10,949	III	Toronto General Hospital, Toronto, Canada—a quaternary care teaching hospital affiliated with the University of Toronto, Canada

Population characteristics Patients undergoing cardiac surgery with CPB

Length of follow-up	Outcome(s) measured
Time in hospital	Perioperative stroke

INTERNAL VALIDITY

Allocation	Comparison of study groups	Blinding	Treatment/measurement bias	Follow-up (ITT)
Nadir Hct	There may be some differences in the treatment of patients with different Hct levels. Groups were compared by logistic regression	No blinding details were given	There may be some difference in the treatment of patients with different Hb levels	Patients with missing values were excluded if a categorical variable or nadir haematocrti was missing

Overall quality assessment (descriptive)

This was a fair quality prospective cohort study with several limitations. It is an observational study, and therefore, causality cannot be inferred from the observational associations. In addition, the effects of unmeasured confounding variables or complex interactions between covariates on the observed association cannot be ruled out. Finally, the databases used were created before this study was conceived, and therefore, subtle errors in recording of perioperative variables are possible

RESULTS

Outcome	Risk measure	Definition of anaemia	Time of Hb measurement	Risk	Statistical significance
Perioperative stroke	OR (95% CI)	+1% decrease Hb ≤12 g/dL	Intraoperative	1.10 (1.04, 1.18) 45%	S

Clinical importance (1–4)	Relevance (1–5)
2 The point estimate of effect is clinically important but the confidence interval includes clinically unimportant effects	1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival

Any other adverse effects None reported
EXTERNAL VALIDITY
Generalisability The study may be generalisable to a perioperative cardiac surgery population
Applicability The study was performed in Canada and is probably applicable to the Australian healthcare setting

STUDY DETAILS					
Reference Litmathe J, Boeken U, Feindt P, Gams E. Predictors of homologous blood transfusion for patients undergoing open heart surgery. Thorac Cardiovasc Surg. 2003;51:17–21					
Affiliation/Source of funds Department of Thoracic and Cardiovascular Surgery, Heinrich-Heine-University, Dusseldorf, Germany Funding source: None reported					
Study design Retrospective cohort study N=400		Level of evidence III		Location/setting Department of Thoracic and Cardiovascular Surgery, Heinrich-Heine-University, Dusseldorf, Germany	
Population characteristics Patients undergoing CABG					
Length of follow-up Time in hospital		Outcome(s) measured Risk of transfusion			
INTERNAL VALIDITY					
Allocation	Comparison of study groups	Blinding	Treatment/measurement bias	Follow-up (ITT)	
Patients with or without anaemia. Anaemia defined as Hb <11.0 g/dL	There may be some differences in the treatment of patients with different Hb levels. Groups were compared by logistic regression	No blinding details were given	There may be some difference in the treatment of patients with different Hb levels. The decision to transfuse RBC was made when intraoperative Hb <7 g/dL and postoperative Hb <8 g/dL	ITT analysis used	
Overall quality assessment (descriptive) This was a fair quality retrospective cohort study with several limitations. As it is an observational study, causality cannot be established. There may also be other confounding factors not accounted for in the analysis. In addition, because this is a retrospective study, the databases were created before the study was conceived					
RESULTS					
Outcome	Risk measure	Definition of anaemia	Time of Hb measurement	Risk	Statistical significance
Risk of RBC transfusion	OR (95% CI)	Hb <11 g/dL	Preoperative	2.1 (1.6, 3.0)	p=0.0001
Clinical importance (1–4) 1 A clinically important benefit for the null range of plausible estimates. The confidence limit closest to the measure of no effect rules out a clinically unimportant effect of the intervention			Relevance (1–5) 2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient relevant outcomes for the same intervention		
Any other adverse effects None reportd					
EXTERNAL VALIDITY					
Generalisability The study is probably generalisable to a wider perioperative cardiac surgery population					
Applicability The study was performed in Germany and is most likely applicable to the Australian healthcare setting					

STUDY DETAILS				
Reference McKechnie RS, Smith D, Montoye C, Kline-Rogers J, O'Donnell MJ, DeFranco AC, et al. Prognostic implication of anemia on hospital outcomes after percutaneous coronary intervention. Circulation. 2004;110:271–277				
Affiliation/Source of funds Blue Cross Blue Shield of Michigan Cardiovascular Consortium Funding source: None reported				
Study design Retrospective cohort study N=48,851	Level of evidence III	Location/setting A consortium of 18 hospitals in the USA, including 3 academic centres, 4 tertiary referral centres and 11 community hospitals		
Intervention Anaemia Sample size: 11,130	Comparator(s) No anaemia Sample size: 34,035			
Population characteristics Patients undergoing percutaneous coronary intervention at 18 hospitals				
Length of follow-up Time in hospital	Outcome(s) measured In-hospital mortality, in-hospital cerebrovascular event, in-hospital postprocedural MI, and a combined end point of major cardiovascular events (MACEs) including all 3 endpoints			
INTERNAL VALIDITY				
Allocation	Comparison of study groups	Blinding	Treatment/measurement bias	Follow-up (ITT)
Patients with or without anaemia. Anaemia defined by WHO (<12.0 g/dL in women and <13.0 g/dL in men)	There may be some differences between patients with different Hb levels. Groups were compared by logistic regression	No blinding details were given	There may be some difference in the treatment of patients with different Hb levels	45,165 patients were included in the analysis
Overall quality assessment (descriptive) This was a good quality retrospective cohort study with some limitations. Although a rigorous analysis was performed to adjust for other confounders, one cannot rule out the possibility that the analysis was unable to adjust for other unknown confounders and that therefore anaemia is just an indirect marker of disease severity				

<table>
<tr><td colspan="6">RESULTS</td></tr>
<tr><td>Outcome</td><td>Risk measure</td><td>Definition of anaemia</td><td>Time of Hb measurement</td><td>Risk</td><td>Statistical significance</td></tr>
<tr><td>In-hospital mortality</td><td>OR (95% CI)</td><td>Hb ≤13 g/dL men
Hb ≤ 12 g/dL women</td><td>Preoperative</td><td>2.29 (1.79, 2.92)</td><td>p<0.0001</td></tr>
<tr><td colspan="3">Clinical importance (1–4)
1 A clinically important benefit for the null range of plausible estimates. The confidence limit closest to the measure of no effect rules out a clinically unimportant effect of the intervention</td><td colspan="3">Relevance (1–5)
1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival</td></tr>
<tr><td>MI</td><td>OR (95% CI)</td><td>Hb ≤ 13 g/dL men
Hb ≤ 12 g/dL women</td><td>Preoperative</td><td>1.34 (1.05, 1.72)</td><td>p=0.02</td></tr>
<tr><td colspan="3">Clinical importance (1–4)
2 The point estimate of effect is clinically important but the confidence interval includes clinically unimportant effects</td><td colspan="3">Relevance (1–5)
1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival</td></tr>
<tr><td>MACE</td><td>OR (95% CI)</td><td>Hb ≤ 13 g/dL men
Hb ≤ 12 g/dL women</td><td>Preoperative</td><td>1.2 (1.05, 1.34)</td><td>p<0.01</td></tr>
<tr><td colspan="3">Clinical importance (1–4)
2 The point estimate of effect is clinically important but the confidence interval includes clinically unimportant effects</td><td colspan="3">Relevance (1–5)
1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival</td></tr>
<tr><td colspan="6">Any other adverse effects
None reported</td></tr>
<tr><td colspan="6">EXTERNAL VALIDITY</td></tr>
<tr><td colspan="6">Generalisability
These results may not be generalisable to a wider perioperative cardiac surgery population</td></tr>
<tr><td colspan="6">Applicability
The study was performed in the USA and is probably generalisable to the Australian healthcare setting</td></tr>
</table>

<table>
<tr><td colspan="5">STUDY DETAILS</td></tr>
<tr><td colspan="5">Reference Reinecke H, Trey T, Wellmann J, Heidrich J, Fobker M, Wichter T, et al. Haemoglobin-related mortality in patients undergoing percutaneous coronary interventions. Eur Heart J. 2003;24:2142–2150</td></tr>
<tr><td colspan="5">Affiliation/Source of funds
Medizinische Klinik und Poliklinik C (Department of Cardiology and Angiology), Hospital of the University of Munster, Munster, Germany; Institut fur Epidemiologie und Sozialmedizin (Institute for Epidemiology und Social Medicine), Hospital of the University of Munster, Munster, Germany; Institut fur Klinische Chemie und Laboratoriumsmedizin (Institute of Clinical Chemistry and Laboratory Medicine), Hospital of the University of Munster, Munster, Germany; Medizinische Klinik und Poliklinik D (Department of Nephrology), Hospital of the University of Munster, Munster, Germany; Department of Biochemistry, Southwestern Medical Center, Dallas, USA
Funding source: None reported</td></tr>
<tr><td colspan="2">Study design
Retrospective cohort study
N=700</td><td colspan="2">Level of evidence
III</td><td>Location/setting
Hospital of the University of Munster, Munster, Germany</td></tr>
<tr><td colspan="2">Intervention
Anaemia
Sample size: n=144</td><td colspan="3">Comparator(s)
No anaemia
Sample size: n = 545</td></tr>
<tr><td colspan="5">Population characteristics
Male patients undergoing elective percutaneous coronary interventions</td></tr>
<tr><td colspan="2">Length of follow-up
Up to 1200 days</td><td colspan="3">Outcome(s) measured
In-hospital mortality, long term mortality</td></tr>
<tr><td colspan="5">INTERNAL VALIDITY</td></tr>
<tr><td>Allocation</td><td>Comparison of study groups</td><td>Blinding</td><td>Treatment/measurement bias</td><td>Follow-up (ITT)</td></tr>
<tr><td>Patients with or without anaemia. Anaemia defined by Hb ≤12.9 g/dL</td><td>There may be some differences between patients with different Hb levels. Groups were compared by logistic regression</td><td>No blinding details were given</td><td>There may be some difference in the treatment of patients with different Hb levels</td><td>11 patients had missing Hb values and were excluded from the analysis
Another 50 patients were lost to long term follow-up and were thus excluded from this analysis</td></tr>
<tr><td colspan="5">Overall quality assessment (descriptive)
This is a fair quality retrospective cohort study. Due to the retrospective data collection in this study, no firm conclusions on pathophysiologic background can be drawn</td></tr>
</table>

RESULTS					
Outcome	Risk measure	Definition of anaemia	Time of Hb measurement	Risk	Statistical significance
Mortality	OR (95% CI)	Hb ≤ 12.9 g/dL	Preoperative	4.09 (1.52, 11.05)	p=0.008 (compared to Hb 14.6-15.2)
Clinical importance (1–4) 1 A clinically important benefit for the null range of plausible estimates. The confidence limit closest to the measure of no effect rules out a clinically unimportant effect of the intervention			Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		
Any other adverse effects None reported					
EXTERNAL VALIDITY					
Generalisability The results of this study may not be generalisable to a wider perioperative cardiac surgery population					
Applicability This study was performed in Germany and is probably applicable to the Australian healthcare setting					

Level III evidence: Noncardiac studies

<table>
<tr><td colspan="5">STUDY DETAILS</td></tr>
<tr><td colspan="5">Reference Beattie WS, Karkouti K, Wijeysundera DN, Tait G. Risk associated with preoperative anemia in noncardiac surgery: a single-center cohort study. Anesthesiology. 2009;110(3):574–581</td></tr>
<tr><td colspan="5">Affiliation/Source of funds
Department of Anesthesia, University Health Network, Toronto General Hospital, Toronto, Ontario, Canada
Funding source: None reported</td></tr>
<tr><td colspan="2">Study design
Retrospective cohort study
N=7760</td><td>Level of evidence
III</td><td colspan="2">Location/setting
Toronto General Hospital, Toronto, Canada</td></tr>
<tr><td colspan="2">Intervention
Anaemia
Sample size: n=3047</td><td colspan="3">Comparator(s)
No anaemia
Sample size: n=4632</td></tr>
<tr><td colspan="5">Population characteristics
Noncardiac surgery patients including vascular and oncology surgery in head and neck, urology, and thoracic, hepatobiliary, general and gynaecologic procedures</td></tr>
<tr><td colspan="2">Length of follow-up 90 days</td><td colspan="3">Outcome(s) measured Mortality within 90 days of the index surgery</td></tr>
<tr><td colspan="5">INTERNAL VALIDITY</td></tr>
<tr><td>Allocation</td><td>Comparison of study groups</td><td>Blinding</td><td>Treatment/measurement bias</td><td>Follow-up (ITT)</td></tr>
<tr><td>Patients with or without anaemia. Anaemia defined by WHO (<12.0 g/dL in women and <13.0 g/dL in men)</td><td>There may be some differences between patients with different Hb levels. Groups were compared by logistic regression and propensity score-based matching</td><td>A blinded trained technician manually retrieved the details of blood products used within the first 7 days of the hospital stay from the blood bank database</td><td>There may be some difference in the treatment of patients with different Hb levels</td><td>81 patients were excluded from the analysis</td></tr>
<tr><td colspan="5">Overall quality assessment (descriptive)
This was a good quality retrospective cohort study with several limitations. First, as this was retrospective, causality could not be determined. It is possible that preoperative anaemia was associated with adverse outcomes simply because it is a marker for severity of illness. Second, the effects of unknown or unmeasured confounders on the observed association cannot be ruled out. Third, neither the cause nor the duration of preoperative anaemia, both of which have prognostic implications, was known</td></tr>
</table>

<table>
<tr><td colspan="6">RESULTS</td></tr>
<tr><td>Outcome</td><td>Risk measure</td><td>Definition of anaemia</td><td>Time of Hb measurement</td><td>Risk</td><td>Statistical significance</td></tr>
<tr><td>90 day mortality</td><td>OR (95% CI)</td><td>Hb ≤13 g/dL men; Hb ≤12 g/dL women</td><td>Preoperative</td><td>2.36 (1.57. 3.41)</td><td>p<0.0001</td></tr>
<tr><td colspan="3">Clinical importance (1–4)
1 A clinically important benefit for the null range of plausible estimates. The confidence limit closest to the measure of no effect rules out a clinically unimportant effect of the intervention</td><td colspan="3">Relevance (1–5)
1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival</td></tr>
<tr><td colspan="6">Any other adverse effects
None reported</td></tr>
<tr><td colspan="6">EXTERNAL VALIDITY</td></tr>
<tr><td colspan="6">Generalisability
As this study involved a mixed surgical population, the results are generalisable to a perioperative noncardiac surgery population</td></tr>
<tr><td colspan="6">Applicability
The study was performed in Canada and is most likely applicable to the Australian healthcare setting</td></tr>
</table>

STUDY DETAILS

Reference Carson JL, Noveck H, Berlin JA, Gould SA. Mortality and morbidity in patients with very low postoperative Hb levels who decline blood transfusion. Transfusion. 2002;42:812–818

Affiliation/Source of funds

Division of General Internal Medicine, Department of Medicine, University of Medicine and Dentistry of NJ, Robert Wood Johnson Medical School, New Brunswick, NJ; Center for Clinical Epidemiology and Biostatistics, Department of Biostatistics and Epidemiology, University of Pennsylvania School of Medicine, Philadelphia, PA; and Northfield Laboratories, Evanston, IL

Funding source: Supported in part by a grant from Northfield Laboratories, Evanston, IL, and by Grant R01HL41523 from the National Heart, Lung, and Blood Institute. One of the authors (SAG) owns stock in a company that produces a Hb-based oxygen carrier

Study design	Level of evidence	Location/setting
Retrospective cohort study N=2083	III	Cooper Hospital/Universty Medical Centre, Camden, NJ, USA and another 12 hospitals enrolled in a multi-institutional study in the USA

Intervention	Comparator(s)
Patients with Hb ≤8 g/dL Sample size: n=300	Patients with Hb >8 g/dL Sample size: n=1783

Population characteristics

Patients 18 years or older undergoing surgery who declined blood transfusion due to religious reasons

Length of follow-up	Outcome(s) measured
30 days or time in hospital	30 day mortality, composite outcome of 30 day mortality or in hospital 30 day morbidity (defined as myocardial infarction, arrhythmia, congestive heart failure, or infection)

INTERNAL VALIDITY

Allocation	Comparison of study groups	Blinding	Treatment/measurement bias	Follow-up (ITT)
Differing Hb levels	There may be some differences between patients with different Hb levels. Groups were compared by logistic regression	No blinding details were recorded	There may be some difference in the treatment of patients with different Hb levels	ITT analysis

Overall quality assessment (descriptive)

This is a fair quality retrospective cohort study with several limitations. First, it is possible that the analysis has not adequately controlled for differences between patients with different Hb levels despite adjusting for multiple factors including age, cardiovascular disease and APACHE II score. Second, 42.8% of patients in the original cohorts never had a postoperative Hb level recorded. Third, patients included in this analysis were hospitalised up to 20 years ago. It is likely that perioperative care has improved during this time period so that a similar patient cared for today might have a lower mortality. Fourth, despite starting with 300 patients, the numbers of patients and outcomes in each Hb level category in this study were relatively small, reducing the precision of the estimate of risk. Fifth, it would be preferable to use 30 day mortality instead of in hospital mortality up to 30 days. Sixth, data were not collected on delirium or stroke which may be associated with anaemia. Finally, it is possible that the underlying illness that led to the low Hb level may be responsible for the mortality or morbidity rather than the adverse effect of anaemia

RESULTS					
Outcome	Risk measure	Definition of anaemia	Time of Hb measurement	Risk	Statistical significance
Mortality	OR (95% CI)	+1 g/dL increase in Hb	Postoperative	2.1 (1.7, 2.6)	S
Mortality	Rates	Hb 1.1–2 g/dL	Postoperative	100%	p<0.01
		Hb 2.1–3 g/dL		54.20%	
		Hb 3.1–4 g/dL		25%	
		Hb 4.1–5 g/dL		34.40%	
		Hb 5.1–6 g/dL		9.30%	
		Hb 6.1–7 g/dL		8.90%	
		Hb 7.1–8 g/dL		0%	
Mortality or morbidity	Rates	Hb 1.1–2 g/dL	Postoperative	100%	p<0.01
		Hb 2.1–3 g/dL		91.70%	
		Hb 3.1–4 g/dL		52.60%	
		Hb 4.1–5 g/dL		57.70%	
		Hb 5.1–6 g/dL		28.60%	
		Hb 6.1–7 g/dL		22%	
		Hb 7.1–8 g/dL		9.40%	
Clinical importance (1–4) 1 A clinically important benefit for the null range of plausible estimates. The confidence limit closest to the measure of no effect rules out a clinically unimportant effect of the intervention			Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		
Any other adverse effects None reported					
EXTERNAL VALIDITY					
Generalisability The results of the study are generalisable to a perioperative noncardiac surgery population					
Applicability The study was performed in the USA and is probably applicable to the Australian healthcare setting					

STUDY DETAILS

Reference Dunkelgrun M, Hoeks SE, Welten GMJM, Vidakovic R, Winkel TA, Schouten O, et al. Anemia as an independent predictor of perioperative and long-term cardiovascular outcome in patients scheduled for elective vascular surgery. Am J Cardiol. 2008;101(8):1196–1200

Affiliation/Source of funds

Departments of Vascular Surgery, Clinical Epidemiology, Cardiology, and Anesthesiology, Erasmus Medical Centre, Rotterdam; Department of Cardilology, Leiden University Medical Centre, Leiden, The Netherlands; and Division of Renal Diseases and Hypertension, University of Colorado Health Sciences Center, Denver, CO

Funding source: Dr Dunkelgrun is supported by an unrestricted research grant (Grant 2003B143) from the Netherlands Heart Foundation, The Hague, The Netherlands. Dr Schouten is supported by an unrestricted research grant from the Netherlands Organisation of Health Research and Development (ZonMW), The Hague, The Netherlands. Dr Hoeks and Dr Vidakovic are supported by an unrestricted research grant from the Lijf & Level Foundation, Rotterdam, The Netherlands

Study design	Level of evidence	Location/setting
Retrospective cohort study N=1211	III	The Erasmus Medical Centre, Rotterdam, The Netherlands

Intervention	Comparator(s)
Anaemia Sample size: n=399	No anaemia Sample size: n=812

Population characteristics

Patients undergoing elective noncardiac open vascular surgery with known or suspected coronary artery disease

Length of follow-up	Outcome(s) measured
5 years	Cardiac death (AMI, cardiac arrhythmias, congestive heart failure) and composite outcome of major adverse cardiac event (MACE—defined as non-fatal MI and cardiac death). Both outcomes were measured at 30 days and 5 years

INTERNAL VALIDITY

Allocation	Comparison of study groups	Blinding	Treatment/measurement bias	Follow-up (ITT)
Differing Hb levels. Anaemia was defined by WHO: Hb <13 g/dL for men and Hb <12 g/dL for women	There may be some differences between patients with different Hb levels. Groups were compared by logistic regression	No blinding details were recorded	There may be some difference in the treatment of patients with different Hb levels	ITT analysis

Overall quality assessment (descriptive)

This was a good quality retrospective cohort study with limitations inherent to a retrospective analysis. The study population consisted of patients referred to a tertiary care centre and may not fully represent a general population scheduled for elective vascular surgery. Also due to the observational nature of the study, a causal relation could not be determined between preoperative anaemia and perioperative MACEs. Furthermore, the cause of the measured anaemia remains unknown, which could be important in determining possible preoperative treatments

RESULTS					
Outcome	Risk measure	Definition of anaemia	Time of Hb measurement	Risk	Statistical significance
30 day MACE	OR (95% CI)	Hb 12.2–13.0 g/dL men, 11.2–12.0 g/dL women	Preoperative	1.8 (0.8, 4.1)	NS
		11.0–12.1 g/dL men, 10.2–11.1 g/dL women		2.3 (1.1, 5.4)	S
		7.2–11.0 g/dL men, 7.5–10.1 g/dL women		4.7 (2.6, 10.9)	S
5 year MACE	OR (95% CI)	Hb 12.2–13.0 g/dL men, 11.2–12.0 g/dL women	Preoperative	2.4 (1.5, 4.2)	S
		11.0–12.1 g/dL men, 10.2–11.1 g/dL women		3.6 (2.4, 5.6)	S
		7.2–11.0 g/dL men, 7.5–10.1 g/dL women		6.1 (4.1, 9.1)	S
Clinical importance (1–4) 1 A clinically important benefit for the null range of plausible estimates. The confidence limit closest to the measure of no effect rules out a clinically unimportant effect of the intervention			Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		
Any other adverse effects None reported					
EXTERNAL VALIDITY					
Generalisability The study only included a noncardiac vascular population and may not be generalisable to a wider perioperative population					
Applicability The study was performed in The Netherlands which is most likely applicable to the Australian healthcare setting					

STUDY DETAILS		
Reference Gruson KI, Aharonoff GB, Egol KA. The relationship between admission haemoglobin level and outcome after hip fracture. J Orthop Trauma. 2002;16:39–44		
Affiliation/Source of funds Geriatric Hip Fracture Research Group, Department of Orthopedic Surgery, Hospital for Joint Diseases Orthopedic Institute, New York, New York, USA Funding source: No financial support for this project was received or will be received in the future		
Study design Retrospective cohort study N=395	Level of evidence III	Location/setting The Hospital for Joint Diseases, New York, USA
Intervention Anaemia Sample size: n=180	Comparator(s) No anaemia Sample size: n=215	
Population characteristics Patients who had sustained an operatively treated hip fracture		
Length of follow-up 12 months	Outcome(s) measured Postoperative medical complications, in-hospital mortality, hospital LOS, hospital discharge status, place of residence at one year, and mortality and recovery of ambulatory ability and activities of daily living status at 3, 6 and 12 months after surgery	

INTERNAL VALIDITY

Allocation	Comparison of study groups	Blinding	Treatment/measurement bias	Follow-up (ITT)
Differing Hb levels. Anaemia was defined by WHO: Hb <13 g/dL for men and Hb <12 g/dL for women	There may be some differences between patients with different Hb levels. Groups were compared by logistic regression	No blinding details were recorded	There may be some difference in the treatment of patients with different Hb levels	ITT analysis

Overall quality assessment (descriptive)

This was a fair quality retrospective cohosrt study with limitations inherent to this type of restrospective analysis. The follow-up data were obtained by telephone interview. This method may be less reliable than direct patient observation. Furthermore, it was not known whether patients were anaemic before their hip fracture

RESULTS

Outcome	Risk measure	Definition of anaemia	Time of Hb measurement	Risk	Statistical significance
3 month mortality	OR (95% CI)	Hb ≤13 g/dL men; Hb ≤12 g/dL women	Preoperative	1.4 (0.5, 4.2)	NS
6 month mortality				2.9 (1.2, 7.3)	p=0.02
12 month mortality				2.6 (1.2, 5.5)	p=0.01

Clinical importance (1–4) 1 A clinically important benefit for the null range of plausible estimates. The confidence limit closest to the measure of no effect rules out a clinically unimportant effect of the intervention			Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		
Increased hospital LOS	Correlation	Hb ≤ 13 g/dL men Hb ≤12 g/dL women	Preoperative	NR	p<0.01
Clinical importance (1–4) Unable to determine			Relevance (1–5) 2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention		
Any other adverse effects None reported					
EXTERNAL VALIDITY					
Generalisability The study was performed in an elderly hip fracture population and may not be generalisable to a wider perioperative patient population					
Applicability The study was performed in the USA and is probably applicable to the Australian healthcare setting					

STUDY DETAILS				
Reference Lawrence VA, Silverstein JH, Cornell JE. Higher Hb level is associated with better early functional recovery after hip fracture repair. Transfusion. 2003;43:1717–1722				
Affiliation/Source of funds Veterans' Evidence-Based Research and Dissemination and Implementation Center (VERDICT), a Veterans' Affairs Health Services Research and Development Centre of Excellence, South Texas Veterans' Health Care System, San Antonio, TX; Division of General Medicine, Department of Medicine, University of Texas Health Science Center at San Antonio, TX; Department of Anesthesiology, the Mount Sinai School of Medicine of New York University, NY; Division of General Internal Medicine, Department of Medicine, University of Medicine and Dentistry of New Jersey, Robert Wood Johnson Medical School, New Brunswick, NJ Funding source: Supported by the Agency for Healthcare Research and Quality (formerly Agency for Health Care Policy and Research) 1 RO1HSO7322 and the Veterans' Evidence-Based Research Dissemination and Implementation Center (VERDICT), a Veterans' Affairs Health Services Research and Development Center of Excellence				
Study design Retrospective cohort study N=5793	Level of evidence III	Location/setting 20 academic and community hospitals in the USA		
Intervention Hb <12 g/dL Sample size: n=5121	Comparator(s) Hb ≥12 g/dL Sample size: n=672			
Population characteristics Patients 60 years or older undergoing hip fracture repair at 20 academic and community hospitals				
Length of follow-up Time in hospital	Outcome(s) measured Distance walked at time of discharge			
INTERNAL VALIDITY				
Allocation	Comparison of study groups	Blinding	Treatment/measurement bias	Follow-up (ITT)
Differing Hb levels	There may be some differences between patients with different Hb levels. Groups were compared by regression	No blinding details were recorded	There may be some difference in the treatment of patients with different Hb levels	ITT analysis
Overall quality assessment (descriptive) This was a poor quality retrospective cohort study. The study had several limitations that should be considered in the interpretation of the findings. First, the distribution of the distance wlaked was highly skewed and there appeared to be digit preference with rounding to the nearest natural benchmark. Second, the study used retrospective data collection, which did not permit measurement of Hb concentrations and walking distance at standardised time periods. Third, this study was not a clinical trial and it is possible that differences in patient characteristics were not completely controlled for, despite adjusting for many comorbid illnesses in the regression analysis. Fourth, the authors were unaware of any direct evidence that distance walked at discharge is associated with long-term functional recovery. Fifth, the study includes relatively old data (1982–1993)				

RESULTS					
Outcome	Risk measure	Definition of anaemia	Time of Hb measurement	Risk	Statistical significance
Distance walked at time of discharge	feet (95% CI)	Hb 7 g/dL	Postoperative	56 (42, 70)	p<0.001
		Hb 8 g/dL		61 (54, 68)	p<0.001
		Hb 9 g/dL		67 (64, 70)	p<0.001
		Hb 10 g/dL		74 (72, 77)	p<0.001
		Hb 11 g/dL		83 (80, 85)	p<0.001
		Hb 12 g/dL		92 (87, 96)	p<0.001

Clinical importance (1–4)	Relevance (1–5)
1 A clinically important benefit for the null range of plausible estimates. The confidence limit closest to the measure of no effect rules out a clinically unimportant effect of the intervention	4 Evidence of an effect on proven surrogate outcomes but for a different intervention and population

Any other adverse effects

None reported

EXTERNAL VALIDITY

Generalisability

The study was done in an elderly orthopaedic population with an outcome specific for this population, therefore, the results are not generalisable to a wider perioperative population

Applicability

The study was performed in the USA and is probably applicable to the Australian healthcare setting

STUDY DETAILS					
Reference Lunn JN, Elwood PC. Anaemia and surgery. Br Med J. 1970;3(714):71–73					
Affiliation/Source of funds Senior Lecturer in Anaesthetics, Welsh National School of Medicine, Cardiff; Member of MRC Epidemiology Research Unit, Cardiff, Wales Funding source: Not reported					
Study design Retrospective cohort study N=2441		Level of evidence III		Location/setting Teaching hospitals in Wales, UK	
Population characteristics Patients undergoing surgery					
Length of follow-up Time in hospital		Outcome(s) measured Complications, postoperative hospital LOS, mortality			
INTERNAL VALIDITY					
Allocation	Comparison of study groups	Blinding	Treatment/measurement bias	Follow-up (ITT)	
Differing Hb levels	There may be some differences between patients with different Hb levels	No blinding details were recorded	There may be some difference in the treatment of patients with different Hb levels	857 (35%) patients were missing Hb values and were excluded from the analysis	
Overall quality assessment (descriptive) The study was a poor quality retrospective cohort study with some limitations. Firstly, Hb levels were missing for a large proportion of patients. In addition, the statistics were poorly performed with no regression analysis					
RESULTS					
Outcome	Risk measure	Definition of anaemia	Time of Hb measurement	Risk	Statistical significance
Postoperative complications (men)	Rates	Hb < 10 g/dL	Preoperative	15.90%	p<0.01
		Hb ≥ 10 g/dL		5.70%	
Postoperative complications (women)		Hb < 10 g/dL		5.90%	p>0.7
		Hb ≥ 10 g/dL		6.80%	
Clinical importance (1–4) Unable to determine			Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		
Mortality (men)	rates	Hb < 10 g/dL	preoperative	15.30%	p<0.01
		Hb ≥ 10 g/dL		2.90%	
Mortality (women)		Hb < 10 g/dL		19%	p<0.01
		Hb ≥ 10 g/dL		2.10%	

Clinical importance (1–4)	Relevance (1–5)
Unable to determine	1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival
Any other adverse effects None reported	
EXTERNAL VALIDITY	
Generalisability Although this study uses a general surgery population and should be generalsiable to a perioperative patient population, the study is quite old with data from 1969. Due to treatment differences and differing standards of care between the time of the study and currently, the results may not be generalisable to a current perioperative patient population	
Applicability The study was performed in the UK and is most likely applicable to the Australian healthcare setting	

STUDY DETAILS		
Reference Marcantonio ER, Goldman L, Orav EJ, Cook EF, Lee TH. The association of intraoperative factors with the development of postoperative delirium. Am J Med. 1998;105:380–384		
Affiliation/Source of funds Sections for Clinical Epidemiology and Gerontology, Division of General Medicine, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA; the Departments of Biostatistics and Epidemiology, Harvard School of Public Health, Boston, MA; and the Department of Medicine, University of California, San Francisco, CA Funding source: Supported in part by a grant from the Agency for Health Care Policy and Research (RO1-HS06573). Dr Marcantonio was supported by a National Research Service Award for Research in Primary care International Medicine (5T32PE110011-04)		
Study design Retrospective cohort study N=1341	Level of evidence III	Location/setting Brigham and Women's Hospital, Boston, MA, USA
Population characteristics Patients undergoing major elective noncardiac surgery		
Length of follow-up Up to 5 days	Outcome(s) measured Postoperative delirium	

INTERNAL VALIDITY				
Allocation	Comparison of study groups	Blinding	Treatment/measurement bias	Follow-up (ITT)
Differing Hct levels	There may be some differences between patients with different Hct levels. Groups were compared by logistic regression	No blinding details were recorded	There may be some difference in the treatment of patients with different Hct levels	ITT analysis

Overall quality assessment (descriptive)

This was a poor quality retrospective cohort study with several limitations. Most notable, the associations identified in the study may not be cause-effect. Lower postoperative Hct may be a marker for other unrecognised factors that increase the risk of delirium. Second, although an association between postoperative psychoactive medications and delirium have been previously found, medication information was not available in the current analysis. Third, delirium was not examined on postoperative day 1; therefore mild transient episodes of delirium may have been missed. Fourth, postoperative Hct values were drawn at the discretion of the treating physician rather than as part of the study. Finally, because this study was performed in elective surgery patients at a tertiary care institution, the results may not be generalisable to other populations, particularly high-risk elderly undergoing emergency surgery

RESULTS

Outcome	Risk measure	Definition of anaemia	Time of Hb measurement	Risk	Statistical significance
Development of delirium	OR (95% CI)	Hct <30%	Postoperative	1.7 (1.1, 2.7)	p=0.03

Clinical importance (1–4)	Relevance (1–5)
2 The point estimate of effect is clinically important but the confidence interval includes clinically unimportant effects	5 Evidence confined to unproven surrogate outcomes
Any other adverse effects None reported	
EXTERNAL VALIDITY	
Generalisability The study may not be generalisable to a wider perioperative patient population	
Applicability The study was performed in the USA and is probably applicable to the Australian healthcare setting	

STUDY DETAILS					
Reference Rogers J, Kilaru RK, Hosokawa P, Henderson WG, Zinner MJ, Khuri SF. Multivariable predictors of postoperative venous thromboembolic events after general and vascular surgery: Results from the patient safety in surgery study. J Am Coll Surg. 2007a;204(6):1211–1221					
Affiliation/Source of funds Department of Surgery and Center for Surgery and Public Health, Brigham and Women's Hospital, Boston, MA; Division of Cardiology, Danbury Hospital, Danbury, CT; National Surgical Quality Improvement Program, Office of Patient Care Services, Department of Veterans Affairs, Aurora, CO; University of Colorado Health Outcomes Program, Aurora, CO; VA Boston Healthcare System, West Roxbury, MA; Harvard Medical School and the Brigham and Women's Hospital, Boston, MA Funding source: None reported					
Study design Retrospective cohort study N=184,120		Level of evidence III		Location/setting 128 Veterans Affairs' Medical Centres and 14 private-sector hospitals in the USA	
Intervention Hct ≤0.38 Sample size: n=62,138		Comparator(s) Hct >0.38 Sample size: n=120,931			
Population characteristics Patients from 128 Veterans' Affairs medical centres and 14 private-sector hospitals who underwent major general or vascular procedures					
Length of follow-up 30 days		Outcome(s) measured Postoperative venous thromboembolic events			
INTERNAL VALIDITY					
Allocation	Comparison of study groups	Blinding	Treatment/measurement bias	Follow-up (ITT)	
Differing Hct levels	There may be some differences between patients with different Hct levels	No blinding details were recorded	There may be some difference in the treatment of patients with different Hct levels	1337 (0.7%) patients were were excluded from the analysis	
Overall quality assessment (descriptive) This was a fair quality retrospective cohort study with some limitations. Even though high mortality was noted in patients with VTE, it is difficult to predict accurately whether this was a result of the occurrence of VTE alone or the underlying severity of the illness, which could be the reason behind both the mortality and VTE. The models are also limited in part by variables which were not collected and might impact the rates of VTE. An additional limitation is that information about the process of VTE prophylaxis to link the process and the outcomes was absent in this patient cohort					
RESULTS					
Outcome	Risk measure	Definition of anaemia	Time of Hb measurement	Risk	Statistical significance
Venous thromboembolism	OR (95% CI)	Hct ≤ 38	Preoperative	1.32 (1.09, 1.60)	p=0.004

Clinical importance (1–4)	Relevance (1–5)
2 The point estimate of effect is clinically important but the confidence interval includes clinically unimportant effects	1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival
Any other adverse effects None reported	
EXTERNAL VALIDITY	
Generalisability The study was performed in patients undergoing general or vascular surgery and is generalisable to a wider perioperative noncardiac surgery population	
Applicability The study was performed in the USA and is probably applicable to the Australian healthcare setting	

STUDY DETAILS					
Reference Stoller ML, Wolf J, St.Lezin MA. Estimated blood loss and transfusion rates associated with percutaneous nephrolithotomy. J Urol. 1994;152(6 I):1977–1981					
Affiliation/Source of funds Department of Urology, University of California School of Medicine, San Francisco, CA Funding source: None reported					
Study design Retrospective cohort study N=96		Level of evidence III		Location/setting Not reported	
Population characteristics Patients undergoing percutaneous nephrolithotomy					
Length of follow-up Not reported		Outcome(s) measured Risk of transfusion			
INTERNAL VALIDITY					
Allocation	Comparison of study groups	Blinding	Treatment/measurement bias	Follow-up (ITT)	
Differing Hb levels	There may be some differences between patients with different Hb levels	No blinding details were recorded	There may be some difference in the treatment of patients with different Hb levels	ITT analysis	
Overall quality assessment (descriptive) This was a fair quality retrospective cohort study					
RESULTS					
Outcome	Risk measure	Definition of anaemia	Time of Hb measurement	Risk	Statistical significance
Transfusion	Rates	Hb >12 g/dL	Preoperative	14%	p<0.05
		Hb ≤ 12 g/dL		45%	
Clinical importance (1–4) Unable to determine			Relevance (1–5) 2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient relevant outcomes for the same intervention		
Any other adverse effects None reported					
EXTERNAL VALIDITY					
Generalisability The results of this study may not be generalisable to a wider perioperative patient population					
Applicability It is not clear where the study was carried out although it may be assumed that it was in the USA. If this is the case, then the results of the study are probably applicable to the Australian healthcare setting					

STUDY DETAILS					
Reference Saleh E, McClelland DBL, Hay A, Semple D, Walsh TS. Prevalence of anaemia before major joint arthroplasty and the potential impact of preoperative investigation and correction on perioperative blood transfusions. Br J Anaesth. 2007;99(6):801–808					
Affiliation/Source of funds Department of Anaesthesia, Intensive Care, and Pain Medicine, Edinburgh University, Edinburgh Royal Infirmary, Little France, Edinburgh, UK; Department of Anaesthesia, Intensive Care, and Pain Medicine, Faculty of Medicine, Menoufia University, Egypt; Scottish National Blood Transfusion Service, Liberton, Edinburgh, UK Funding source: This work was supported by the Clinical Effectiveness Group of the Scottish National Blood transfusion Service, the Transfusion Medicine Education and Research Foundation, and the Edinburgh Royal Infirmary Intensive Care Unit Research Fund. Dr Saleh received financial support through an unrestricted educational grant from Novo Nordisk					
Study design Retrospective cohort study N=1322		Level of evidence III		Location/setting The Princess Margaret Rose Hospital (PMR), Edinburgh, a specialised Scottish orthopaedic hospital	
Intervention Anaemia Sample size: n=224		Comparator(s) No anaemia Sample size: n=918			
Population characteristics Patients undergoing elective orthopaedic procedures					
Length of follow-up Not reported		Outcome(s) measured Risk of transfusion			
INTERNAL VALIDITY					
Allocation	Comparison of study groups	Blinding	Treatment/measurement bias	Follow-up (ITT)	
Anaemia versus no anaemia. Anaemia was defined as Hb <13 g/dL for men and <11.5 g/dL for women	There may be some differences between patients with different Hb levels. Groups were compared with logistic regression	No blinding details were recorded	There may be some difference in the treatment of patients with different Hb levels	180 (13.6%) patients had missing pre-admission Hb data and were excluded from the analysis	
Overall quality assessment (descriptive) This study was a poor quality retrospective cohort study with limitations inherent to this type of study					
RESULTS					
Outcome	Risk measure	Definition of anaemia	Time of Hb measurement	Risk	Statistical significance
Transfusion	OR (95% CI)	Hb 11.1–13.0 g/dL	Preoperative	2.42 (1.69, 3.48)	p<0.001
		Hb ≤ 11 g/dL		13.92 (7.77, 24.90)	p<0.001

Clinical importance (1–4)	Relevance (1–5)
1 A clinically important benefit for the null range of plausible estimates. The confidence limit closest to the measure of no effect rules out a clinically unimportant effect of the intervention	1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival
Any other adverse effects None reported	
EXTERNAL VALIDITY	
Generalisability The study was performed in an orthopaedic population and may not be applicable to a wider perioperative patient population	
Applicability The study was performed in Scotland in the UK and is most likely applicable to the Australian healthcare setting	

STUDY DETAILS				
Reference Wu WC, Schifftner TL, Henderson WG, Eaton CB, Poses RM, Uttley G, et al. Preoperative hematocrit levels and postoperative outcomes in older patients undergoing noncardiac surgery. JAMA. 2007;297(22):2481–2488				
Affiliation/Source of funds Target Research Enhancement Program, Providence Veterans Affairs Medical Center and Department of Community Health (Drs Wu and Friedmann), Department of Medicine (Drs Wu, Poses, Sharma, and Friedmann), Center for Primary Care and Prevention, Memorial Hospital of Rhode Island and Department of Family Medicine (Dr Eaton), and Surgical Service, Providence Veterans Affairs Medical Center and Department of Surgery (Ms Uttley and Dr Vezeridis), Brown Medical School, and Medical Service, Providence Veterans Affairs Medical Center (Drs Wu and Sharma), Providence, RI; National Surgical Quality Improvement Program Denver Data Analysis Center, Denver VA Medical Center, University of Colorado Health Outcomes Program, Denver (Ms Schifftner and Dr Henderson); and Surgical Service VA Boston Healthcare System and Department of Surgery, Harvard Medical School, Boston, MA (Dr Khuri) Funding source: This work was supported by the VA Merit Review Award in Health Services Research and Development Grant IIR 04-313				
Study design Retrospective cohort study N=310,311		Level of evidence III		Location/setting 132 Veterans' Affairs medical centres across the USA
Intervention Anaemia Sample size: n=132,970		Comparator(s) No anaemia Sample size: n=176,704		
Population characteristics Veterans aged 65 years or older undergoing major noncardiac surgery				
Length of follow-up 30 days	Outcome(s) measured 30 day postoperative mortality, combined outcome of 30 day mortality or cardiac events			
INTERNAL VALIDITY				
Allocation	Comparison of study groups	Blinding	Treatment/measurement bias	Follow-up (ITT)
Differing Hct levels. Anaemia was defined as Hct <0.39	There may be some differences between patients with different Hct levels. Groups were compared with logistic regression	No blinding details were recorded	There may be some difference in the treatment of patients with different Hct levels	ITT analysis used
Overall quality assessment (descriptive) This is a good quality retrospective cohort study with some limitations. Firstly, approximately 21% of preoperative Hct values were obtained more than 4 weeks prior to surgery and may not accurately reflect Hct levels at the time of surgery. Secondly, given the observational nature of the study, one cannot determine the causal relationship between low or high Hct values and risk of postoperative adverse events. Neither can one relate the aetiology and chronicity of the abnormal Hct value with outcomes				

RESULTS					
Outcome	Risk measure	Definition of anaemia	Time of Hb measurement	Risk	Statistical significance
30 day mortality and cardiac event rate	OR (95% CI)	Hct <18	Preoperative	2.41 (1.55, 3.73)	S
		Hct 18–20.9		1.52 (1.12, 2.07)	S
		Hct 21–23.9		1.11 (0.93, 1.34)	NS
		Hct 24–26.9		1.27 (1.13, 1.44)	S
		Hct 27–29.9		1.25 (1.13, 1.38)	S
		Hct 30–32.9		1.19 (1.08, 1.31)	S
		Hct 33–35.9		1.2 (1.09, 1.32)	S
		Hct 36–38.9		1.12 (1.03, 1.23)	S
		Hct 39–41.9		1.10 (1.01, 1.20)	S
		Hct 42–44.9		1.06 (0.97, 1.17)	NS
		+1% decrease		1.02 (1.01, 1.05)	S
Clinical importance (1–4) 1 A clinically important benefit for the null range of plausible estimates. The confidence limit closest to the measure of no effect rules out a clinically unimportant effect of the intervention			Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		
Any other adverse effects None reported					
EXTERNAL VALIDITY					
Generalisability The study was performed in general surgery and is generalisable to a wider perioperative noncardiac surgery population					
Applicability The study was performed in the USA and is probably applicable to the Australian healthcare setting					

F5 Evidence summaries, Question 5

Red blood cell transfusion

What is the effect of red blood cell transfusion on patient outcomes?

Level III evidence: Cardiac studies

<table>
<tr><td colspan="5">STUDY DETAILS</td></tr>
<tr><td colspan="5">Reference Surgenor SD, Kramer RS, Olmstead EM, Ross CS, Sellke FW, Likosky DS, et al. The association of perioperative red blood cell transfusions and decreased long-term survival after cardiac surgery. Anesth Analg. 2009;108(6):1741–1746</td></tr>
<tr><td colspan="5">Affiliation/Source of funds
Dartmouth-Hitchcock Medical Center, Lebanon, NH; Maine Medical Center, Portland, ME; Dartmouth Medical School, Hanover, NH; Beth Israel Deaconness Medical Center, Boston MA; Portsmouth Regional Hospital, Portsmouth, NH; Fletcher Allen Health Care, Burlington, VT; New England heart Institute, Catholic Medical Center, Manchester, NH; Eastern Maine Medical Center, Bangor, ME; Central Maine Medical Center, Lewiston, ME; Concord Hospital, Concord, NH; Dartmouth Institute for Health Policy and Clinical Practice, Dartmouth College, Dartmouth College, Lebanon, NH
Funding source: Not specified</td></tr>
<tr><td colspan="2">Study design
Retrospective cohort study
N=9079</td><td colspan="2">Level of evidence
III-2</td><td>Location/setting
8 centres in the northern New England region, USA</td></tr>
<tr><td colspan="3">Intervention
RBC transfusion
Sample size n=3254</td><td colspan="2">Comparator(s)
No RBC transfusion
Sample size n=5825</td></tr>
<tr><td colspan="5">Population characteristics
9079 consecutive cardiac surgery patients undergoing CABG, valve or CABG/valve surgeries at 8 centres in northern New England USA during 2001–2004</td></tr>
<tr><td colspan="3">Length of follow-up
None specified</td><td colspan="2">Outcome(s) measured
Morbidity and mortality</td></tr>
<tr><td colspan="5">INTERNAL VALIDITY</td></tr>
<tr><td>Allocation</td><td>Comparison of study groups</td><td>Blinding</td><td>Treatment/measurement bias</td><td>Follow-up (ITT)</td></tr>
<tr><td>Patients receiving RBC transfusion or not. The decision to transfuse was at the discretion of the patient care team</td><td>There were significant differences in baseline characteristics between patients receiving RBCs and those not</td><td>No blinding details are reported</td><td>It is not clear whether all patients were treated the same</td><td>ITT analysis used</td></tr>
</table>

<table>
<tr><td colspan="6">Overall quality assessment (descriptive)
This is a fair quality retrospective cohort study with limitations. The study did not evaluate cause and effect for the observed findings. Also, the study was not able to differentiate the use of leukoreduced transfusions. The study did not measure exposure to platelets, FFP or cryoprecipitate. Further these types of studies are subject to confounding.</td></tr>
<tr><td colspan="6">RESULTS</td></tr>
<tr><td>Outcome</td><td>Units RBC Transfused</td><td>Transfusion</td><td>No transfusion</td><td>HR (95% CI)</td><td>Statistical Significance</td></tr>
<tr><td>6 month mortality</td><td>Any</td><td>NR</td><td>NR</td><td>1.67 (1.21, 2.28)</td><td>P=0.002</td></tr>
<tr><td colspan="3">Clinical importance (1–4)
1 A clinically important benefit for the null range of plausible estimates. The confidence limit closest to the measure of no effect rules out a clinically unimportant effect of the intervention</td><td colspan="3">Relevance (1–5)
1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival</td></tr>
<tr><td>5 year mortality</td><td>Any</td><td>NR</td><td>NR</td><td>1.16 (1.01, 1.33)</td><td>P=0.035</td></tr>
<tr><td colspan="3">Clinical importance (1–4)
4 The range of estimates defined by the confidence interval includes clinically important effects BUT the range of estimates defined by the confidence interval is also compatible with no effect, or a harmful effect</td><td colspan="3">Relevance (1–5)
1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival</td></tr>
<tr><td colspan="6">Any other adverse effects
None reported</td></tr>
<tr><td colspan="6">EXTERNAL VALIDITY</td></tr>
<tr><td colspan="6">Generalisability
The study was performed in patients undergoing cardiac surgery and is generalisable to a wider cardiac surgery population</td></tr>
<tr><td colspan="6">Applicability
The study was performed in the USA and is probably generalisable to the Australian healthcare setting</td></tr>
<tr><td colspan="6">Comments
The authors conclude that exposure to 1-2 U of RBCs is associated with a 16% increased hazard of decreased survival after cardiac surgery</td></tr>
</table>

STUDY DETAILS					
Reference Hortal J, Munoz P, Cuerpo G, Litvan H, Rosseel PM, Bouza E, European Study Group on Nosocomial Infections, European Workgroup of Cardiothoracic Intensivists. Ventilator-associated pneumonia in patients undergoing major heart surgery: An incidence study in Europe. Crit Care. 2009;13(3):R80.					
Affiliation/Source of funds Departments of Anaesthesia, Clinical Microbiology and Infectious Diseases, Cardiac Surgery at the Hospital General Universitario Gregorio Maranon, Madrid, Spain; Anaesthesia Department, Hospital Sant Creu I sant Pau, Barcelona, Spain; Anaesthesia and Critical Care Department, Thoraxcenter Amphia, Breda, Holland; Centor de Investigacion Biomedica en Red de Enfermedades Respiratorias, Fundacion Caubert-Cimera, Bunyoia, Mallorca, Spain Funding not reported					
Study design Prospective cohort study N=986		Level of evidence III-2		Location/setting 25 hospitals in 8 European countries	
Intervention RBC transfusion Sample size NR			Comparator(s) No RBC transfusion Sample size NR		
Population characteristics Patients undergoing major heart surgery who developed suspicion of VAP					
Length of follow-up None reported			Outcome(s) measured Nosocomial infection, particularly VAP		
INTERNAL VALIDITY					
Allocation	Comparison of study groups	Blinding	Treatment/measurement bias	Follow-up (ITT)	
The study did not report on how patients were allocated	Not reported	Not reported	It is unclear if all patients were treated the same	15 patients were excluded due to a protocol violation and were therefore not included in the analysis	
Overall quality assessment (descriptive) This is a fair quality prospective cohort study with limitations inherent to this type of study. Further countries and institutions were not randomly selected among the whole continent and the relative weight of the European countries is not equilibrated.					
RESULTS					
Outcome	Units RBC Transfused	Transfusion	No transfusion	OR (95% CI)	Statistical Significance
VAP (risk per unit transfused)	Each unit	NR	NR	1.08 (1.04, 1.13)	P<0.001
Clinical importance (1–4) 2 The point estimate of effect is clinically important BUT the confidence interval includes clinically unimportant effects.			Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		

Any other adverse effects None reported
EXTERNAL VALIDITY
Generalisability The results of this study are probably generalisable to a wider cardiac surgery population
Applicability The study was performed in Europe and is probably applicable to the Australian healthcare setting
Comment The authors conclude that patients undergoing aortic surgery and those with complicated post-intervention courses, requiring multiple transfusions or re-intervention, constitute a high-risk group probably requiring more active preventive measures.

STUDY DETAILS					
Reference Cislaghi F, Condemi AM, Corona A. Predictors of prolonged mechanical ventilation in a cohort of 5123 cardiac surgical patients. Eur J Anaesthesiol. 2009;26(5):396–403					
Affiliation/Source of funds Cardiac Anaesthetic and ICU Departments, Azienda Ospedaliera Luigi Sacco, Polo Universitario, Milan, Italy; Centre for Intensive Care Medicine and Bloomsbury Institute of Intensive Care Medicine, University College, London, UK Funding not reported					
Study design Prospective cohort study N=5,123	Level of evidence III-2	Location/setting ICU centre in Italy			
Intervention RBC transfusion Sample size NR	Comparator(s) No RBC transfusion Sample size NR				
Population characteristics Cardiac surgery patients admitted to the ICU over a 6 year period					
Length of follow-up Not reported	Outcome(s) measured Prolonged mechanical ventilation				
INTERNAL VALIDITY					
Allocation	Comparison of study groups	Blinding	Treatment/measurement bias	Follow-up (ITT)	
The study did not report on how patients were allocated	Not reported	Not reported	It is unclear if all patients were treated the same	ITT analysis	
Overall quality assessment (descriptive) This was a fair quality prospective cohort study with limitations inherent to this type of study. The most critical methodological weakness of the study was the definition of PMV. Two other weaknesses are firstly, that it is observational in nature and does not give strong reproducible general conclusions. Secondly, the high number of investigators could affect the validation of data entry.					
RESULTS					
Outcome	Units RBC Transfused	Transfusion	No transfusion	OR (95% CI)	Statistical Significance
Prolonged mechanical ventilation	>4 units	NR	NR	5.43 (3.63, 8.07)	P<0.0001
Clinical importance (1–4) 1 A clinically important benefit for the null range of plausible estimates. The confidence limit closest to the measure of no effect rules out a clinically unimportant effect of the intervention			Relevance (1–5) 2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention		
Any other adverse effects None reported					

EXTERNAL VALIDITY
Generalisability The results of this study are generalisable to a cardiac surgery population
Applicability The study was performed in Italy and is probably applicable to the Australian healthcare setting

STUDY DETAILS					
Reference Scott BH, Seifert FC, Grimson R. Blood transfusion is associated with increased resource utilisation, morbidity and mortality in cardiac surgery. Ann Card Anaesth. 2008;11(1):15–19					
Affiliation/Source of funds Departments of Anesthesiology and Surgery, SUNY at Stony Brook, NY, USA Funding: nil					
Study design Retrospective cohort study N=1,746	Level of evidence III-2	Location/setting Teaching hospital, NY, USA			
Intervention RBC transfusion Sample size n=1,069	Comparator(s) No RBC transfusion Sample size n=677				
Population characteristics Patients undergoing on- and off-pump CABG					
Length of follow-up 30 days	Outcome(s) measured Resource utilisation, postoperative morbidity, mortality				
INTERNAL VALIDITY					
Allocation	Comparison of study groups	Blinding	Treatment/measurement bias	Follow-up (ITT)	
The study did not report on how patients were allocated	There are significant differences in the baseline characteristics of transfused and non transfused patients	No blinding details are reported	All patients undergoing each type of surgery were treated the same	ITT analysis used	
Overall quality assessment (descriptive) This was a fair quality retrospective cohort study with limitations inherent to this type of study.					
RESULTS					
Outcome	Units RBC Transfused	Transfusion	No transfusion	Correlation coefficient	Statistical Significance
Mortality	NR	33/1,069 (3.1%)	0/677 (0%)	0.383	P<0.001
Time to extubation (h)	NR	8.0 ± 7.5	4.3 ± 2.0	0.259	P<0.001
Prolonged LOS (days)	NR	7.2 ± 6.8	4.3 ± 2.0	0.434	P<0.001
ICU LOS (days)	Nr	1.6 ±1.6	1.2 ± 0.7	0.209	P<0.001
Clinical importance (1–4) 1 A clinically important benefit for the null range of plausible estimates. The confidence limit closest to the measure of no effect rules out a clinically unimportant effect of the intervention			Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		

Any other adverse effects None reported
EXTERNAL VALIDITY
Generalisability The results of this study are probably generalisable to a wider cardiac surgery population
Applicability The study was performed in the USA and is probably applicable to the Australian healthcare setting
Comments The authors concluded that patients who received transfusion had significantly longer time to extubation, ICU LOS and PLOS. They also had significantly higher incidence of 30 day mortality. PLOS increased with the number of PRBCs transfused.

<table>
<tr><td colspan="5">STUDY DETAILS</td></tr>
<tr><td colspan="5">Reference Ranucci M, Bozzetti G, Ditta A, Cotza M, Carboni G, Ballotta A. Surgical re-exploration after cardiac operations: why a worse outcome? Ann Thorac Surg. 2008a;86(5):1557–1562</td></tr>
<tr><td colspan="5">Affiliation/Source of funds
Department of Cardiothoracic-Vascular Anesthesia and Intensive Care, IRCCS Policlinico, Milan, Italy
Funding source not reported</td></tr>
<tr><td colspan="2">Study design
Retrospective case control study
N=464</td><td colspan="2">Level of evidence
III</td><td>Location/setting
Milan, Italy</td></tr>
<tr><td colspan="3">Intervention
RBC transfusion
Sample size NR</td><td colspan="2">Comparator(s)
No RBC transfusion
Sample size NR</td></tr>
<tr><td colspan="5">Population characteristics
Intervention—Patients who underwent surgical re-exploration relating to postsurgical bleeding following cardiac surgery
Comparator—Controlled, propensity-matched group</td></tr>
<tr><td colspan="3">Length of follow-up
Not applicable</td><td colspan="2">Outcome(s) measured
Morbidity, mortality</td></tr>
<tr><td colspan="5">INTERNAL VALIDITY</td></tr>
<tr><td>Allocation</td><td>Comparison of study groups</td><td>Blinding</td><td>Treatment/ measurement bias</td><td>Follow-up (ITT)</td></tr>
<tr><td>Study group comprised all the patients having undergone surgical reexploration because of bleeding. The control group of patients who had not undergone surgical reexploation was created using a propensity-score approach</td><td>There was no difference in baseline characteristics between the two groups</td><td>No details are reported</td><td>Patients were not treated the same</td><td>ITT analysis used</td></tr>
<tr><td colspan="5">Overall quality assessment (descriptive)
This was a fair quality retrospective case-control study.</td></tr>
</table>

RESULTS					
Outcome	Units RBC Transfused	Transfusion	No transfusion	OR (95% CI)	Statistical Significance
Low cardiac output	Increasing	NR	NR	1.14 (1.04,1.25)	P=0.003
Acute renal failure	Increasing	NR	NR	1.10 (1.02, 1.19)	P=0.012
Sepsis	Increasing	NR	NR	1.11 (1.03, 1.21)	P=0.008
Hospital mortality	Increasing	NR	NR	1.08 (1.01, 1.16)	P=0.031

Clinical importance (1–4)	Relevance (1–5)
2 The point estimate of effect is clinically important BUT the confidence interval includes clinically unimportant effects.	1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival

Any other adverse effects

None reported

EXTERNAL VALIDITY

Generalisability

The results of this study may not be generalisable to a wider cardiac surgery population

Applicability

The study was performed in Italy and is probably applicable to the Australian healthcare setting

Comment

The authors concluded that the main determinant of morbidity and mortality for patients requiring a surgical reexploration after cardiac operations is the amount of packed RBCs transfused.

STUDY DETAILS				
Reference Murphy GJ, Reeves BC, Rogers CA, Rizvi SIA, Culliford L, Angelini GD. Increased mortality, postoperative morbidity, and cost after red blood cell transfusion in patients having cardiac surgery. Circulation. 2007;116(22):2544–2552				
Affiliation/Source of funds Bristol Heart Institute, University of Bristol, Bristol, UK Funding: British Heart Foundation				
Study design Retrospective cohort study N=8,598	Level of evidence III	Location/setting Bristol, UK		
Intervention RBC transfusion Sample size N=3689	Comparator(s) No RBC transfusion Sample size N=4909			
Population characteristics All adult (≥16 years) cardiac surgery patients admitted to Bristol Heart Institute, from a database covering admissions from April 1996 to December 2003				
Length of follow-up Not reported	Outcome(s) measured Infection (respiratory, wound, or septicaemia) Ischaemia (MI, stroke, renal impairment, renal failure) Resource costs			
INTERNAL VALIDITY				
Allocation	Comparison of study groups	Blinding	Treatment/ measurement bias	Follow-up (ITT)
The study did not report on how patients were allocated	There are significant differences in the baseline characteristics of transfused and non transfused patients	No blinding details are reported	It is not clear whether all patients were treated the same	A total of 63 patients were excluded from the analysis
Overall quality assessment (descriptive) This was a fair quality retrospective cohort study with limitations. Transfused patients were sicker before their operations and may have had poorer outcomes. Some data were missing for patients. Exposures and outcomes may have been misclassified for some patients.				

RESULTS					
Outcome	Units RBC Transfused	Transfusion	No transfusion	OR (95% CI) or HR (95% CI)	Statistical Significance
30 day mortality (HR)	Any	NR	NR	6.69 (3.66, 15.1)	P<0.0001
Infection (OR)	Any	NR	NR	3.73 (2.32, 5.07)	S
Ischaemic outcome (OR)	Any	NR	NR	4.05 (2.63, 5.70)	S
Reative increase in cost (OR)	Any	NR	NR	1.42 (1.37, 1.46)	S
ICU discharge (HR)	Any	NR	NR	0.69 (0.65, 0.72)	P<0.0001
Hospital discharge (HR)	Any	NR	NR	0.63 (0.60, 0.67)	P<0.0001
Clinical importance (1–4) 1 A clinically important benefit for the null range of plausible estimates. The confidence limit closest to the measure of no effect rules out a clinically unimportant effect of the intervention			Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		
Any other adverse effects None reported					
EXTERNAL VALIDITY					
Generalisability The results of this study are generalisable to a cardiac surgery population					
Applicability The study was performed in the UK and is probably applicable to the Australian health care system					
Comment The authors conclude that red blood cell transfusion in patients having cardiac surgery is strongly associated with both infection and ischaemic postoperative morbidity, hospital stay, increased early and late mortality, and hospital costs.					

STUDY DETAILS					
Reference Rogers MAM, Blumberg N, Heal JM, Hicks J. Increased risk of infection and mortality in women after cardiac surgery related to allogeneic blood transfusion. J Womens Health. 2007b;16(10):1412–1420					
Affiliation/Source of funds Division of General Medicine, Department of Internal Medicine, University of Michigan, Ann Arbor, MI; VA Medical Center and University of Michigan Health System, Ann Arbor, MI, Department of Pathology and Laboratory Medicine, University of Rochester Medical Center, Rochester, NY; Department of Medicine and Cardiac Surgery Unit, Department of Surgery, University of Rochester, NY, USA Funding source not reported					
Study design Retrospective cohort study N=380	Level of evidence III	Location/setting University of Rochester Medical Center, NY, USA			
Intervention RBC transfusion Sample size N=326	Comparator(s) No RBC transfusion Sample size N=54				
Population characteristics Adult patients who underwent CABG surgery, valve replacement surgery, or both					
Length of follow-up Not reported	Outcome(s) measured Postoperative infection; pulmonary dysfunction; in-hospital mortality				
INTERNAL VALIDITY					
Allocation	Comparison of study groups	Blinding	Treatment/measurement bias	Follow-up (ITT)	
The study did not report on how patients were allocated	The study does not report baseline comparisons between the two groups	No blinding details are reported	It is not clear whether all patients were treated the same	ITT analysis	
Overall quality assessment (descriptive) This was a fair quality retrospective cohort study with some limitations. As the study was not an RCT, it was not possible to determine whether the relation between transfusion and infection was due to confounding by indication.					
RESULTS					
Outcome	Units RBC Transfused	Transfusion	No transfusion	OR (95% CI)	Statistical Significance
Infection	Any	NR	NR	4.4 (1.5, 13.2)	P=0.009
Clinical importance (1–4) 1 A clinically important benefit for the null range of plausible estimates. The confidence limit closest to the measure of no effect rules out a clinically unimportant effect of the intervention			Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		
Any other adverse effects None reported					

EXTERNAL VALIDITY
Generalisability The study is probably generalisable to a wider cardiac surgery population
Applicability The study was performed in the USA and is probably applicable to the Australian healthcare setting
Comment The authors conclude thattransfusion increased the risk of infection; infection then increased the likelihood of pulmonary dysfunction and mortality.

STUDY DETAILS					
Reference Koch CG, Li L, Duncan AI, Mihaljevic T, Loop FD, Starr NJ, et al. Transfusion in coronary artery bypass grafting is associated with reduced long-term survival. Ann Thorac Surg. 2006a;81(5):1650–1657					
Affiliation/Source of funds Departments of Cardiothoracic Anesthesia, Qualitative Health Sciences, and Cardiovascular Surgery, The Cleveland Clinic Foundation, Cleveland, OH, USA Funding source not reported					
Study design Retrospective cohort study N=10,289	Level of evidence III	Location/setting Cleveland, OH, USA			
Intervention RBC transfusion Sample size N=5,812	Comparator(s) No RBC transfusion Sample size N=5,056				
Population characteristics Assessment of survival status in a large population (N=10,289) of patients who underwent CABG between January 1995 and June 2002					
Length of follow-up 9 years	Outcome(s) measured All cause mortality during the follow-up period				
INTERNAL VALIDITY					
Allocation	Comparison of study groups	Blinding	Treatment/ measurement bias	Follow-up (ITT)	
The study did not report on how patients were allocated	There are significant differences in the baseline characteristics of transfused and non transfused patients	No blinding details are reported	It is not clear whether all patients were treated the same	ITT analysis	
Overall quality assessment (descriptive) This is a fair quality retrospective cohort study with limitations specific to nonrandomised study designs. These include whether transfusion was a marker for increased illness not captured in the database or is an independent predictor for reduced survival cannot be determined with certainty.					
RESULTS					
Outcome	Units RBC Transfused	Transfusion	No transfusion	HR (SE)	Statistical Significance
All cause mortality	Increasing	NR	NR	0.074 (0.016)	P<0.0001
Clinical importance (1–4) 1 A clinically important benefit for the null range of plausible estimates. The confidence limit closest to the measure of no effect rules out a clinically unimportant effect of the intervention			Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		
Any other adverse effects None reported					

EXTERNAL VALIDITY
Generalisability The study is probably generalisable to a wider cardiac surgery population
Applicability The study was performed in the USA and is probably applicable to the Australian healthcare setting
Comment The authors conclude that perioperative RBC transfusion is associated with adverse long-term sequela in isolated CABG.

STUDY DETAILS

Reference Surgenor SD, DeFoe GR, Fillinger MP, Likosky DS, Groom RC, Clark C, et al. Intraoperative red blood cell transfusion during coronary artery bypass graft surgery increases the risk of postoperative low-output heart failure. Circulation. 2006;114(Suppl I):I43–I48

Affiliation/Source of funds

Northern New England Cardiovascular Disease Study Group; Dartmouth-Hitchcock Medical Centre, Lebanon, NH; Fletcher Allen Heath Care, Burlington, VT; Portsmouth Regional Hospital, Portsmouth, NH; Maine Medical Center, Portland, MR; Eastern Maine Medical Center, Bangor, ME; Catholic Medical Center, Manchester, NH; Concord Hospital, Concord, NH; Central Maine Medical Centre, Lewiston, ME; Dartmouth Medical School, Hanover ME, USA

Funding source not reported

Study design	Level of evidence	Location/setting
Prospective cohort study N=8004	III	8 centres in northern New England, USA

Intervention	Comparator(s)
RBC transfusion Sample size N=1802	No RBC transfusion Sample size N=6208

Population characteristics

Patients undergoing isolated CABG over a 9 year period

Length of follow-up	Outcome(s) measured
Not reported	Low operative heart failure

INTERNAL VALIDITY

Allocation	Comparison of study groups	Blinding	Treatment/ measurement bias	Follow-up (ITT)
The study did not report on how patients were allocated	There are significant differences in the baseline characteristics of transfused and non transfused patients	No blinding details are reported	It is not clear whether all patients were treated the same	ITT analysis

Overall quality assessment (descriptive)

This was a fair quality prospective cohort study with limitations inherent to observational studies.

RESULTS

Outcome	Units RBC Transfused	Transfusion	No transfusion	OR (95% CI)	Statistical Significance
Low operative heart failure	1-2 units	223.1,802 (12.4)	422/6,208 (6.8)	1.27 (1.00, 1.61)	p=0.047

Clinical importance (1–4)	Relevance (1–5)
2 The point estimate of effect is clinically important BUT the confidence interval includes clinically unimportant effects.	1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival

Any other adverse effects

None reported

EXTERNAL VALIDITY
Generalisability The results of this study are probably generalisable to a wider cardiac surgery population
Applicability The study was performed in the USA and is probably applicable to the Australian healthcare setting

STUDY DETAILS				
Reference Koch CG, Li L, Duncan AI, Mihaljevic T, Cosgrove DM, Loop FD, Starr NJ, Blackstone EH. Morbidity and mortality risk associated with red blood cell and blood-component transfusion in isolated coronary artery bypass grafting. Crit Care Med. 2006b;34(6):1608–1616				
Affiliation/Source of funds Departments of Cardiothoracic Anesthesia, Qualitative Health Sciences, Thoracic and Cardiovascular Surgery, The Cleveland Clinical Foundation, Cleveland, OH, USA Funding source: There were no external sources of financial support associated with this project. All support was provided from within the institution. The authors have no financial interests associated with this project to report.				
Study design Retrospective cohort study N=11,963	Level of evidence III	Location/setting Large tertiary care referral centre, Cleveland, OH, USA		
Intervention RBC and blood component transfusion Sample size N=5812	Comparator(s) No transfusion Sample size N=6151			
Population characteristics Patients who underwent isolated CABG over a 7.5 year period				
Length of follow-up Not reported	Outcome(s) measured In hospital morbidity (renal failure, prolonged ventilatory support, serious infection, cardiac complications, neurologic events) and mortality			
INTERNAL VALIDITY				
Allocation	Comparison of study groups	Blinding	Treatment /measurement bias	Follow-up (ITT)
The study did not report on how patients were allocated	There are significant differences in the baseline characteristics of transfused and non transfused patients	No blinding details are reported	It is not clear whether all patients were treated the same	ITT analysis
Overall quality assessment (descriptive) This was a fair quality retrospective cohort study with limitations. Firstly it was a nonrandomised study in which unmeasured patient or procedure-related variables may have influenced the study results. Furthermore, this study was conducted at a large tertiary referral centre and may not be broadly representative of community practice.				

RESULTS					
Outcome	Units RBC Transfused	Transfusion	No transfusion	OR (95% CI)	Statistical Significance
In-hospital mortality	Any	178/5,812 (3.07)	3/6,151 (0.05)	1.77 (1.67, 1.87)	p<0.0001
Renal morbidity	Each unit	105/5,812 (1.81)	0/6.151 (0.0)	2.06 (1.87, 2.27)	p<0.0001
Prolonged ventilatory support	Each unit	531/5,812 (9.14)	27/6,151 (0.44)	1.79 (1.72, 1.86)	p<0.0001
Serious postoperative infection	Each unit	292/5,812 (5.03)	15/6,151 (0.24)	1.76 (1.68, 1.84)	p<0.0001
Cardiac morbidity	Each unit	176/5,812 (3.03)	3/6,151 (0.05)	1.55 (1.47, 1.63)	p<0.0001
Neurologic morbidity	Each unit	140/5,812 (2.41)	23/6,151 (0.37)	1.37 (1.30, 1.44)	p<0.0001
Overall morbidity	Each unit	717/5,812 (12.33)	59/6,151 (0.96)	1.73 (1.67, 1.80)	p<0.0001
Clinical importance (1–4) 1 A clinically important benefit for the null range of plausible estimates. The confidence limit closest to the measure of no effect rules out a clinically unimportant effect of the intervention			Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		
Any other adverse effects None reported					
EXTERNAL VALIDITY					
Generalisability The results of this study may not be generalisable to a wider cardiac surgery population					
Applicability The study was performed in the USA and is probably applicable to the Australian healthcare setting					
Comment The authors concluded that perioperative red blood cell transfusion is the single factor most reliably associated with increased risk of postoperative morbid events after isolated coronary artery bypass grafting. Each unit of red cells transfused is associated with incrementally increased risk for adverse outcome.					

STUDY DETAILS					
Reference Koch CG, Li L, Van Wagoner DR, Duncan AI, Gillinov AM, Blackstone EH. Red cell transfusion is associated with an increased risk for postoperative atrial fibrillation. Ann Thorac Surg. 2006c;82(5):1747–1756					
Affiliation/Source of funds Departments of Cardiothoracic Anesthesia, Qualitative Health Sciences, Cardiovascular Medicine, Thoracic and Cardiovascular Surgery, and Atrial Fibrillation Innovation Center, The Cleveland Clinical Foundation, Cleveland, OH, USA Funding source: This work was supported in part by a grant from the State of Ohio's Third Frontier Project; State of Ohio TECH 05-066, Atrial Fibrillation Innovation Centre					
Study design Prospective cohort study N=5,841		Level of evidence III		Location/setting Large tertiary care referral centre, Cleveland, OH, USA	
Intervention RBC transfusion in ICU Sample size N=1,360		Comparator(s) No RBC transfusion Sample size N=4,481			
Population characteristics Patients undergoing CABG over a 3 year period					
Length of follow-up Not reported		Outcome(s) measured Atrial fibrillation			
INTERNAL VALIDITY					
Allocation	Comparison of study groups	Blinding	Treatment/measurement bias	Follow-up (ITT)	
The study did not report on how patients were allocated	The study does not report baseline comparisons between the two groups	No blinding details are reported	It is not clear whether all patients were treated the same	ITT analysis	
Overall quality assessment (descriptive) This is a fair quality prospective cohort study with limitations. Although this was a prospective investigation, it was not a randomised trial with respect to transfusion, and therefore there may be biases with respect to unmeasured or uncontrolled variables.					
RESULTS					
Outcome	Units RBC Transfused	Transfusion	No transfusion	OR (95% CI)	Statistical Significance
Atrial fibrillation in on-pump population	Any	NR	NR	1.18 (1.14, 1.23)	p<0.0001
Atrial fibrillation in off-pump population	Any	NR	NR	1.25 (1.16, 1.34)	p<0.0001

Clinical importance (1–4)	Relevance (1–5)
2 The point estimate of effect is clinically important BUT the confidence interval includes clinically unimportant effects.	1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival
Any other adverse effects None reported	
EXTERNAL VALIDITY	
Generalisability The results of this study are probably generalisable to a wider cardiac surgery population	
Applicability The study was performed in the USA and is probably applicable to the Australian healthcare setting	
Comments The authors concluded that ICU RBC transfusion is associated with increased occurrence of postoperative AF after cardiac surgery.	

STUDY DETAILS					
Reference Koch CG, Khandwala F, Li L, Estafanous FG, Loop FD, Blackstone EH. Persistent effect of red cell transfusion on health-related quality of life after cardiac surgery. Ann Thorac Surg 2006d; 82:13-20					
Affiliation/Source of funds Departments of Cardiothoracic Anesthesia, Quantitative Health Sciences, Thoracic and Cardiovascular Surgery, and Division of Anaesthesia and Critical Care, The Cleveland Clinical Foundation, Cleveland, OH, USA Funding source not reported					
Study design Retrospective cohort study N=7321	Level of evidence III	Location/setting Clevelend Clinic Foundation, Ohio, USA			
Intervention RBC transfusion Sample size N=4195	Comparator(s) No RBC transfusion Sample size N=3126				
Population characteristics Of 12,536 patients who underwent CABG, valve repair or replacement, or a combination of CABG and valve procedures between May 1995 and January 1999, 7321 completed a self-administered DASI survey preoperatively					
Length of follow-up Follow-up DASI surveys at 6 and 12 month intervals postoperatively	Outcome(s) measured Health related QoL; postoperative morbidities				
INTERNAL VALIDITY					
Allocation	Comparison of study groups	Blinding	Treatment/ measurement bias	Follow-up (ITT)	
The study did not report on how patients were allocated	The study does not report baseline comparisons between the two groups	No blinding details are reported	It is not clear whether all patients were treated the same	ITT analysis used	
Overall quality assessment (descriptive) This was a fair quality retrospective cohort study with limitations. Firstly, this is an observational study in which patients were not randomised to perioperative RBC or component transfusion. Secondly, as in any observational study, unknown or unaccounted-for variables could have influenced the final results.					
RESULTS					
Outcome	Units RBC Transfused	Transfusion	No transfusion	OR (95% CI)	Statistical Significance
QoL using DASI	Any	NR	NR	0.89 (0.87, 0.92)	P<0.0001
Clinical importance (1–4) 2 The point estimate of effect is clinically important BUT the confidence interval includes clinically unimportant effects.			Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		
Any other adverse effects None reported					

EXTERNAL VALIDITY
Generalisability The results of this study are probably generalisable to a wider cardiovascular surgery population
Applicability The study was conducted in the USA and is probably applicable to the Australian healthcare setting
Comment The authors conclude that red blood cell and platelet transfusion have an unintended persistently negative risk-adjusted effect on health related quality of life after cardiac surgery that extends well beyond initial hospitalisation. Reductions in functional recovery paralleled increasing units of red blood cells transfused.

STUDY DETAILS					
Reference El Solh AA, Bhora M, Pineda L, Dhillon R. Nosocomial pneumonia in elderly patients following cardiac surgery. Respir Med. 2006;100(4):729–736					
Affiliation/Source of funds Division of Pulmonary, Critical Care and Sleep Medicine, Department of medicine, University at Buffalo School of Medicine and Biomedical sciences, Erie County Medical Center, Buffalo, NY, USA Funding source not reported					
Study design Case-control N=73 cases with matched controls	Level of evidence III	Location/setting Postoperative ICU, tertiary level hospital, NY, USA			
Intervention RBC transfusion Sample size NR	Comparator(s) No RBC transfusion Sample size NR				
Population characteristics Patients aged ≥65 years undergoing CABG, valve replacement, or both, in the period January 2000–December 2003, N=876					
Length of follow-up No follow-up	Outcome(s) measured Development of nosocomial pneumonia in the postoperative period				
INTERNAL VALIDITY					
Allocation	Comparison of study groups	Blinding	Treatment/measurement bias	Follow-up (ITT)	
The study did not report on how patients were allocated	The study does not report baseline comparisons between the two groups	No blinding details are reported	It is not clear whether all patients were treated the same	ITT analysis	
Overall quality assessment (descriptive) This was a fair quality case-control study					
RESULTS					
Outcome	Units RBC Transfused	Transfusion	No transfusion	OR (95% CI)	Statistical Significance
Risk of pneumonia	≥4 units	Nr	NR	2.8 (1.2, 6.3)	P=0.01
Clinical importance (1–4) 2 The point estimate of effect is clinically important BUT the confidence interval includes clinically unimportant effects.			Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		
Any other adverse effects None reported					

EXTERNAL VALIDITY
Generalisability This study is generalisable to an elderly cardiac surgery population
Applicability The study was conducted in the USA and is probably applicable to the Australian healthcare setting
Comments The authors conclude that although there are limited effective measures to lessen the burden of comorbidities, avoinding reintubation, finding a substitute to allogenic RBC transfusion, and improved assessment of pain management could reduce the rate of NP in the postoperative period of cardiac surgery in the elderly population

STUDY DETAILS					
Reference Augoustides JG, Pochettino A, McGarvey ML, Cowie D, Weiner J, Gambone AJ, et al. Clinical predictors for mortality in adults undergoing thoracic aortic surgery requiring deep hypothermic circulatory arrest. Ann Card Anaesth. 2006;9(2):114–119					
Affiliation/Source of funds Department of Anesthesiology and Critical Care, Cardiothoracic and Vascular Section, Department of Surgery, Division of Cardiothoraic Surgery, Department of Neurology, Perioperative Neuromonitoring Section and Department of Clinical Perfusion, Hospital of the University of Pennsylvania, Philadelphia PA Funding source not reported					
Study design Retrospective cohort study N=144		Level of evidence III		Location/setting Dulles Hospital of the University of Pennsylvania	
Intervention RBC transfusion Sample size N=NR			Comparator(s) No RBC transfusion Sample size N=NR		
Population characteristics All adults undergoing thoracic aortic surgery requiring deep hypothermic circulatory arrest					
Length of follow-up NR			Outcome(s) measured Mortality		
INTERNAL VALIDITY					
Allocation	Comparison of study groups	Blinding	Treatment/ measurement bias	Follow-up (ITT)	
The study did not report on how patients were allocated	The study does not report baseline comparisons between the two groups	No blinding details are reported	All patients were treated the same	ITT analysis	
Overall quality assessment (descriptive) This is a fair quality retrospective cohort study with limitations inherent to this study design					
RESULTS					
Outcome	Units RBC Transfused	Transfusion	No transfusion	OR (95% CI)	Statistical Significance
Mortality	Any	NR	NR	NR	NS
Clinical importance (1–4) Unable to determine			Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		
Any other adverse effects None reported					

EXTERNAL VALIDITY
Generalisability The results of this study may not be generalisable to a wider cardiac surgery population
Applicability This study was conducted in the USA and is probably applicable to the Australian healthcare setting

STUDY DETAILS					
Reference Banbury MK, Brizzio ME, Rajeswaran J, Lytle BW, Blackstone EH. Transfusion increases the risk of postoperative infection after cardiovascular surgery. J Am Coll Surg. 2006;202(1):131–138					
Affiliation/Source of funds Departments of Thoracic and Cardiovascular Surgery and Qualitative Health Sciences, Cleveland Clinic Foundation, Cleveland, OH, USA Funding source not reported The authors declared that there were no competing interests					
Study design Retrospective cohort N=15,592		Level of evidence III-2		Location/setting Cleveland Clinic Foundation	
Intervention RBC transfusion Sample size N=8,539			Comparator(s) No RBC transfusion Sample size N=7,053		
Population characteristics Patients undergoing cardiovascular surgery over a 5 year period					
Length of follow-up NR			Outcome(s) measured Septicaemia/bacteraemia (coefficient [SD]) Superficial sternal wound infection Deep sternal wound infection		
INTERNAL VALIDITY					
Allocation	Comparison of study groups	Blinding	Treatment/ measurement bias	Follow-up (ITT)	
The study did not report on how patients were allocated	The study does not report baseline comparisons between the two groups	No blinding details are reported	All patients were treated the same	ITT analysis	
Overall quality assessment (descriptive) This was a fair quality retrospective cohort study with limitations. This was a single institution study but included a large number of patients. Like all studies of transfusion, number of units administered cannot be randomised. In addition, the threshold for transfusion varied across time and among surgeons.					
RESULTS					
Outcome	Units RBC Transfused	Transfusion	No transfusion	coefficient (SD)	Statistical Significance
Septicaemia/bacteraemia	Increasing	NR	NR	0.23 (0.0210)	p<0.0001
Superficial sternal wound infection	Increasing	NR	NR	0.029 (0.0087)	p=0.0008
Deep sternal wound infection	Increasing	NR	NR	0.12 (0.023)	p<0.0001

Clinical importance (1–4)	Relevance (1–5)
Unable to determine	1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival
Any other adverse effects None reported	
EXTERNAL VALIDITY	
Generalisability The results of this study are generalisable to a cardiac surgery population	
Applicability The study was conducted in the USA and is probably applicable to the Australian healthcare setting	
Comments The authors concluded that blood products tended to be used in the sickest patients but after accounting for this, risk of infection increased incrementally with each unit of blood transfused. Although cause and effect cannot be established, results suggested that blood product transfusion is an independent risk factor for postoperative infection in cardiac surgical patients, blood products are more likely to be used in the sickest patients, and no amount of blood loss treated by transfusion is innocuous	

STUDY DETAILS					
Reference Kuduvalli M, Oo AY, Newall N, Grayson AD, Jackson M, Desmond MJ, et al. Effect of perioperative red blood cell transfusion on 30-day and 1-year mortality following coronary artery bypass surgery. Eur J Cardiothorac Surg. 2005;27(4):592–598					
Affiliation/Source of funds Departments of Cardiothoracic Surgery, Cardiology, Clinical Governance, Anaesthesiology, Cardiothoracic Centre–Liverpool, Liverpool, UK Funding source not reported					
Study design Retrospective cohort N=3024	Level of evidence III	Location/setting Liverpool, UK			
Intervention RBC transfusion Sample size N=940	Comparator(s) No RBC transfusion Sample size N=2084				
Population characteristics Patients who underwent isolated CABG over a 3 year period					
Length of follow-up Not reorted	Outcome(s) measured Mortality				
INTERNAL VALIDITY					
Allocation	Comparison of study groups	Blinding	Treatment/ measurement bias	Follow-up (ITT)	
The study did not report on how patients were allocated	There are significant differences in the baseline characteristics of transfused and non transfused patients	No blinding details are reported	It is not clear whether all patients were treated the same	ITT analysis	
Overall quality assessment (descriptive) This was a fair quality retrospective cohort study with limitations. Firstly, being a retrospective database study, by its nature, it is only capable of showing associations between variables and outcomes, and is unable to demonstrate cause and effect, Furthermore, the retrospective nature cannot account for uncollected or unknown variables affecting the outcome of transfusion bias that are not correlated strongly with the variables used in the risk adjustment. Another limitation is that there were no strict transfusion triggers and they were dependent on the treating physician.					
RESULTS					
Outcome	Units RBC Transfused	Transfusion	No transfusion	HR (95% CI)	Statistical Significance
30 day mortality	Any	NR	NR	1.88 (1.23, 3.00)	p<0.01
Clinical importance (1–4) 1 A clinically important benefit for the null range of plausible estimates. The confidence limit closest to the measure of no effect rules out a clinically unimportant effect of the intervention	Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival				
Any other adverse effects					

None reported
EXTERNAL VALIDITY
Generalisability The results of this study are probably generalisable to a wider cardiac surgery population
Applicability The study was conducted in the UK and is applicable to he Australian healthcare setting
Comments The authors concluded that perioperative RBC transfusion appears to be associated with an increased 30-day mortality in patients undergoing coronary artery bypass grafting

STUDY DETAILS

Reference Olsen MA, Sundt TM, Lawton JS, Damiano J, Hopkins-Broyles D, Lock-Buckley P, Fraser VJ. Risk factors for leg harvest surgical site infections after coronary artery bypass graft surgery. J Thorac Cardiovasc Surg. 2003;126(4):992–999

Affiliation/Source of funds

Division of Infectious Diseases, Department of Internal Medicine, Department of Surgery, Washington University School of Medicine, St Louis, MO; Department of Surgery, Mayo Clinic, Rochester, MI; Department of Infection Control, Barnes-Jewish Hospital, St Louis, MO, USA

Supported by the Centers of Disease Control Cooperative Prevention epicentres Agreement #UR/CCU715087-01

Study design	Level of evidence	Location/setting
Retrospective cohort N=1,980	III	St Louis, MO, USA

Intervention	Comparator(s)
RBC transfusion Intraopertaive Sample size N=691 Postoperative Sample size N=1,332	No RBC transfusion No intraoperative Sample size N=1,289 No postoperative Sample size N=648

Population characteristics

Patients undergoing CABG over a 3.5 year period

Length of follow-up	Outcome(s) measured
Not reported	Leg harvest site infection

INTERNAL VALIDITY

Allocation	Comparison of study groups	Blinding	Treatment/ measurement bias	Follow-up (ITT)
The study did not report on how patients were allocated	The study does not report baseline comparisons between the two groups	No blinding details are reported	It is not clear whether all patients were treated the same	ITT analysis

Overall quality assessment (descriptive)

This was a fair quality retrospective cohort study and is subject to limitations inherent to this study design

RESULTS

Outcome	Units RBC Transfused	Transfusion	No transfusion	OR (95% CI)	Statistical Significance
Total leg infections	≥5 units	18/135 (13.3)	58/1141 (5.1)	2.8 (1.5, 5.0)	p=0.001
Confirmed leg infections	≥5 units	NR	NR	3.1 (1.7, 5.7)	p<0.001

Clinical importance (1–4)	Relevance (1–5)
1 A clinically important benefit for the null range of plausible estimates. The confidence limit closest to the measure of no effect rules out a clinically unimportant effect of the intervention	1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival

Any other adverse effects

None reported

EXTERNAL VALIDITY

Generalisability
The results of this study are probably generalisable to a wider cardiac surgery population
Applicability
The study was conducted in the USA and is probably applicable to the Australian healthcare setting

STUDY DETAILS					
Reference Bucerius J, Gummert JF, Borger MA, Walther T, Doll N, Onnasch JF, et al. Stroke after cardiac surgery: A risk factor analysis of 16,184 consecutive adult patients. Ann Thorac Surg. 2003;75(2):472–478					
Affiliation/Source of funds Department of Cardiac Surgery, Heart Center, University of Leipzig, Leipzig, Germany Funding source not reported					
Study design Prospective cohort study N=16,184		Level of evidence III		Location/setting University Centre, Leipzig, Germany	
Intervention RBC transfusion Sample size N=NR		Comparator(s) No transfusion Sample size N=NR			
Population characteristics Patients undergoing cardiac surgery over a 5 year period					
Length of follow-up Mean 11.7 ± 9.5 days		Outcome(s) measured Perioperative stroke			
INTERNAL VALIDITY					
Allocation	Comparison of study groups	Blinding	Treatment/ measurement bias	Follow-up (ITT)	
The study did not report on how patients were allocated	The study does not report baseline comparisons between the two groups	No blinding details are reported	It is not clear whether all patients were treated the same	ITT analysis	
Overall quality assessment (descriptive) This was a fair quality prospective cohort study with limitations inherent to this type of study design					
RESULTS					
Outcome	Units RBC Transfused	Transfusion	No transfusion	OR (95% CI)	Statistical Significance
Perioperative stroke	High transfusion requirement	NR	NR	6.04 (5.05, 7.23)	p<0.0001
Clinical importance (1–4) 1 A clinically important benefit for the null range of plausible estimates. The confidence limit closest to the measure of no effect rules out a clinically unimportant effect of the intervention			Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		
Any other adverse effects None reported					

EXTERNAL VALIDITY
Generalisability The results of this study are generalisable to a cardiac surgery population
Applicability The study was conducted in Germany and is probably applicable to the Australian healthcare setting
Comments The authors concluded that high transfusion requirement was a strong risk factor for stroke in the analysis. However, this variable did not distinguish between intraoperative and postoperative transfusions and therefore may have simply been a marker for postoperative complications. The interpretation of this risk factor is therefore difficult

STUDY DETAILS					
Reference Chelemer SB, Prato BS, Cox J, O'Connor GT, Morton JR. Association of bacterial infection and red blood cell transfusion after coronary artery bypass surgery. Ann Thorac Surg. 2002;73(1):138–142					
Affiliation/Source of funds Departments of Medicine, Surgery and Critical Care Medicine, Maine Medical Center, Portland ME and Department of Medicine, Dartmouth-Hitchcock Medical Center, Lebanon, NH, USA Source of funding not reported					
Study design Prospective cohort study N=533	Level of evidence III	Location/setting Medical Centre, Maine, USA			
Intervention RBC transfusion Sample size N=271	Comparator(s) No RBC transfusion Sample size N=262				
Population characteristics Patients undergoing primary isolated CABG surgery over a 7 month period					
Length of follow-up Not reorted	Outcome(s) measured Bacterial infection				
INTERNAL VALIDITY					
Allocation	Comparison of study groups	Blinding	Treatment/ measurement bias	Follow-up (ITT)	
The study did not report on how patients were allocated	There are significant differences in the baseline characteristics of transfused and non transfused patients	No blinding details are reported	It is not clear whether all patients were treated the same	ITT analysis	
Overall quality assessment (descriptive) This was a fair quality prospective cohort study with limitations inherent to this study design					
RESULTS					
Outcome	Units RBC Transfused	Transfusion	No transfusion	OR (95% CI)	Statistical Significance
Bacterial infection	1–2 units	NR	NR	2.11 (0.97, 5.59)	p=0.06
	3–5 units	NR	NR	6.67 (2.60, 17.12)	p<0.001
	≥6 units	NR	NR	10.27 (2.66, 39.71)	p=0.001
Clinical importance (1–4) 1 A clinically important benefit for the null range of plausible estimates. The confidence limit closest to the measure of no effect rules out a clinically unimportant effect of the intervention	Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival				
Any other adverse effects None reported					
EXTERNAL VALIDITY					

Generalisability
The results of this study are probably generalisable to a wider cardiac surgery population
Applicability
The study was conducted in the USA and is probably applicable to the Australian healthcare setting
Comments
The authors concluded that RBC transfusions were independently associated with a higher incidence of post-CABG bacterial infections. The risk of infection increased in proportion to the number of units of RBC transfused.

STUDY DETAILS					
Reference Engoren M, Habib RH, Zacharias A, Schwann TA, Riordan CJ, Durham SJ. Effect of blood transfusion on long-term survival after cardiac operation. Ann Thorac Surg. 2002;74:1180–1186					
Affiliation/Source of funds Departments of Anesthesiology and Cardiovascular Surgery, St Vincent Mercy Medical Center, and Medical College of Ohio, Toledo, OH, USA Funding source: institutional and departmental funds					
Study design Retrospective cohort study N=1953	Level of evidence III	Location/setting Toledo, OH, USA			
Intervention RBC transfusion Sample size N=649	Comparator(s) No RBC transfusion Sample size N=1,266				
Population characteristics Patients who underwent first time isolated CABG with CPB over a 3.5 year period					
Length of follow-up 5 years	Outcome(s) measured Long-term survival; mortality				
INTERNAL VALIDITY					
Allocation	Comparison of study groups	Blinding	Treatment/ measurement bias	Follow-up (ITT)	
The study did not report on how patients were allocated	The study does not report baseline comparisons between the two groups	No blinding details are reported	It is not clear whether all patients were treated the same	53 patients died within 12 months and were removed from the analysis	
Overall quality assessment (descriptive) This was a fair quality retrospective cohort study. A limitation of the study was its retrospective nature, which can only find associations and not show causality. Because criterion for transfusion was not established a priori and patients were not randomised to different thresholds of transfusion, transfusion may merely be a marker for sicker, more symptomatic patients.					
RESULTS					
Outcome	Units RBC Transfused	Transfusion	No transfusion	RR (95% CI)	Statistical Significance
5 year mortality	Any	99/659 (15.0)	82/1,266 (6.5)	1.7 (1.4, 2.0)	p=0.001
	Intraoperative	20/164 (12.2)	82/1,266 (6.5)	1.2 (0.6, 1.7)	p=0.534
	Postoperative	33/303 (10.9)	82/1,266 (6.5)	1.6 (1.2, 2.0)	p=0.029
	Both	46/192 (24.0)	82/1,266 (6.5)	2.4 (2.0, 2.8)	p<0.001
Clinical importance (1–4) 1 A clinically important benefit for the null range of plausible estimates. The confidence limit closest to the measure of no effect rules out a clinically unimportant effect of the intervention	Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival				
Any other adverse effects					

None reported
EXTERNAL VALIDITY
Generalisability The results of this study are probably generalisable to a wider cardiac surgery population
Applicability The study was conducted in the USA and is probably applicable to the Australian healthcare setting
Comments The authors concluded that transfusing blood during or after cardiac operation is associated with an increased 5-year mortality

STUDY DETAILS				
Reference Leal-Noval SR, Rincon-Ferrari MD, Garcia-Curiel A, Hervuzo-Aviles A, Camacho-Larana P, Garnacho-Montero J, Amaya-Villar R. Transfusion of blood components and postoperative infection in patients undergoing cardiac surgery. Chest. 2009;119(5):1461–1468				
Affiliation/Source of funds Critical Care and Microbiology Divisions, Hospital Universitario Virgen del Rocio, Seville, Spain Source of funding not reported				
Study design Prospective cohort study N=738	Level of evidence III	Location/setting Hospital, Seville, Spain		
Intervention RBC transfusion Sample size N=592	Comparator(s) No RBC transfusion Sample size N=146			
Population characteristics Patients undergoing cardiac surgery				
Length of follow-up Not reported	Outcome(s) measured Infection, mortality, ICU LOS			
INTERNAL VALIDITY				
Allocation	Comparison of study groups	Blinding	Treatment/ measurement bias	Follow-up (ITT)
The criteria for transfusion were Hb≤8g/dL; Hb 8-10 g/dL in normovolemic patients, with clinical signs of myocardial, cerebral, or respiratory dysfunction; and severe haemorrhage	The study does not report baseline comparisons between the two groups	No blinding details are reported	All patients were treated the same	ITT analysis
Overall quality assessment (descriptive) This was a fair quality prospective cohort study with limitations. With an observational design, researchers can only control the effects of confounding factors that are known and are measureable. Other multiple factors related to the difficulty of surgery, personnel, equipment, manipulation, and length of stay may have been discarded involuntarily.				

RESULTS					
Outcome	Units RBC Transfused	Transfusion	No transfusion	OR (95% CI)	Statistical Significance
Severe postoperative infection	≥4 units	NR	NR	2.0 (1.0, 4.0)	p=0.042
Pneumonia	≥4 units	NR	NR	2.6 (1.1, 5.8)	p=0.016
Mortality	Any	79/592 (13.3)	13/146 (8.9)	NR	p<0.01
Clinical importance (1–4) 2 The point estimate of effect is clinically important BUT the confidence interval includes clinically unimportant effects.			Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		
ICU LOS (days)	Any	6.1 days	3.7 days	NR	p<0.01
Clinical importance (1–4) Unable to determine			Relevance (1–5) 2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention		
Any other adverse effects None reported					
EXTERNAL VALIDITY					
Generalisability The results of this study are generalisble to a cardiac surgery population					
Applicability The study was conducted in Spain and is probably applicable to the Australian healthcare setting					
Comments The authors conclude that the administration of blood derivatives, mainly RBCs, is associated in a dose-dependent manner with the development of serious postoperative infections, primarily nosocomial pneumonia.					

Level III evidence: Noncardiac studies

STUDY DETAILS					
Reference Garcia-Alvarez F, Al Ghanem R, Garcia-Alvarez I, Lopez-Baisson A, Bernal M. Risk factors for postoperative infections in patients with hip fracture treated by means of Thompson arthroplasty. Arch Gerontol Geriatr. 2010,50(1):51–55. Epub 2009 Feb 23					
Affiliation/Source of funds Faculty of Medicine, University of Zaragoza; Department of Medicine, Hospital Royo Villanova, Zaragoza, Spain Source of funding not reported The authors declared that there were no conflicts of interest					
Study design Prospective cohort study N=290	Level of evidence III-2	Location/setting Hospital, Zaragoza, Spain			
Intervention RBC transfusion Sample size N=120	Comparator(s) No RBC transfusion Sample size N=170				
Population characteristics Patients with displaced sub-capital hip fracture who underwent Thompson hip hemi-arthroplasty					
Length of follow-up Until death, or 2 years postoperative	Outcome(s) measured Postoperative infection, mortality				
INTERNAL VALIDITY					
Allocation	Comparison of study groups	Blinding	Treatment/ measurement bias	Follow-up (ITT)	
The study did not report on how patients were allocated	The study does not report baseline comparisons between the two groups	No blinding details are reported	It is not clear whether all patients were treated the same	ITT	
Overall quality assessment (descriptive) This was a fair quality prospective cohort study with limitations inherent to this type of study					
RESULTS					
Outcome	Units RBC Transfused	Transfusion	No transfusion	OR (95% CI)	Statistical Significance
Superficial wound infection	Any	NR	NR	1.96 (1.05, 3.62)	p<0.05
UTI	Any	NR	NR	1.76 (1.08, 2.89)	p<0.05
Pneumonia	Any	NR	NR	2.85 (1.21, 6.69)	p<0.05
Clinical importance (1–4) 2 The point estimate of effect is clinically important BUT the confidence interval includes clinically unimportant effects.	Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival				
Any other adverse effects None reported					

EXTERNAL VALIDITY
Generalisability This study was performed in patients undergoing orthopaedic surgery and may not be generalisable to a wider noncardiac surgery population
Applicability The study was conducted in Spain and is probably applicable to the Australian healthcare setting
Comments The authors concluded that transfusion and longer waiting time for surgery have been associated with the septic complications in elderly patients treated surgically for hip fracture.

STUDY DETAILS					
Reference Fuks D, Piessen G, Huet E, Tavernier M, Zerbib P, Michot F, et al. Life-threatening postoperative pancreatic fistula (grade C) after pancreaticoduodenectomy: incidence, prognosis, and risk factors. Am J Surg. 2009;197(6):702–709					
Affiliation/Source of funds Federation of Digestive Disease, Amiens North Hospital, University of Picardy Medical Centre, Amiens; Department of Digestive and Oncological Surgery, Huriez Hospital, Lille University Medical Centre, Lille; Department of Digestive Surgery, Charle-Nicolle Hospital, Rouen University Medical Centre, Rouen; Hepatobiliary Surgical Department, Cote de Nacre Hospital, Caen University Medical Centre, Caen; Transplantation and Hepatobiliary Surgery, Huriez Hospital, Lille University Medical Centre, Lille, France Source of funding not reported					
Study design Prospective cohort study N=680		Level of evidence III-2		Location/setting Digestive surgery departments in Lille, Amiens, Rouen and Caen, France	
Intervention RBC transfusion Sample size N=NR			Comparator(s) No RBC transfusion Sample size N=NR		
Population characteristics Patients who underwent pancreatico-duodenectomy at 5 centres in France over 6 years					
Length of follow-up Not reported			Outcome(s) measured Postoperative pancreatic fistula		
INTERNAL VALIDITY					
Allocation	Comparison of study groups	Blinding	Treatment/ measurement bias	Follow-up (ITT)	
The study did not report on how patients were allocated	The study does not report baseline comparisons between the two groups	No blinding details are reported	All patients were treated the same	ITT analysis	
Overall quality assessment (descriptive) This was a fair quality prospective cohort study with limitation inherent to this type of study					
RESULTS					
Outcome	Units RBC Transfused	Transfusion	No transfusion	OR (95% CI)	Statistical Significance
Grade C pancreatic fistula	Any	NR	NR	1.72 (0.10, 28.75)	p=0.70
	>2 units	NR	NR	1.98 (0.09, 4.79)	p=0.65
Clinical importance (1–4) 4 The range of estimates defined by the confidence interval includes clinically important effects BUT the range of estimates defined by the confidence interval is also compatible with no effect, or a harmful effect.			Relevance (1–5) 2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention		

Any other adverse effects None reported
EXTERNAL VALIDITY
Generalisability The results of this study are not generalisbale to other types of noncardiac surgery populations
Applicability The study was conducted in France and is probably applicable to the Australian healthcare setting

STUDY DETAILS				
Reference Bursi F, Barbieri A, Politi L, Di Girolamo A, Malagoli A, Grimaldi T, et al. Perioperative red blood cell transfusion and outcome in stable patients after elective major vascular surgery. Eur J Vasc Endovasc Surg. 2009;37(3):311–318				
Affiliation/Source of funds Institute of Cardiology, Institute of Vascular Surgery, Division of Anaesthesiology, Policlinico University Hospital, Modena and Reggio Emilia University, Modena, Italy; Cardiology and Laboratory Medicine, Mayo Clinic, Rochester, MN, USA Funding: Partly supported by a grant from the Ministero Dell'Universita e della Ricerca Scientifico e Technologica				
Study design Retrospective cohort study N=359	Level of evidence III-2	Location/setting University hospital, Modena, Italy		
Intervention Perioperative RBC transfusion Sample size N=95	Comparator(s) No perioperative RBC transfusion Sample size N=264			
Population characteristics Patients undergoing elective major vascular surgery				
Length of follow-up Not reported	Outcome(s) measured 30 day mortality; 30 day MI; Combined outcomes of 30 mortality and 30 day MI			
INTERNAL VALIDITY				
Allocation	Comparison of study groups	Blinding	Treatment/ measurement bias	Follow-up (ITT)
There was no haemoglobin level that mandated a RBC transfusion, it was at the discretion of the treating physician	There are significant differences in the baseline characteristics of transfused and non transfused patients	No blinding details are reported	It is not clear whether all patients were treated the same	ITT
Overall quality assessment (descriptive) This was a fair quality retrospective cohort study with limitations. As the study is retrospective, patients were not randomised to transfusion. It is also possible, as with other studies of this design, that unmeasured variables may have influenced the results.				

RESULTS					
Outcome	Units RBC Transfused	Transfusion	No transfusion	HR (95% CI)	Statistical Significance
30 day mortality	3 (2–4); median, 25th to 75th percentile	16/95 (16.8)	4/264 (1.5)	5.38 (1.45, 20.0)	p=0.012
MI		20/95 (21.1)	18/264 (6.8)	2.23 (0.98, 5.09)	p=0.056
MI or mortality		26/95 (27.4)	19/264 (7.2)	3.07 (1.43, 6.59)	p=0.004
Clinical importance (1–4) 2 The point estimate of effect is clinically important BUT the confidence interval includes clinically unimportant effects.			Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		
Any other adverse effects None reported					
EXTERNAL VALIDITY					
Generalisability The results of this study are probably generalisable to a wider noncardiac surgery population					
Applicability The study was conducted in Italy and is probably applicable to the Australian healthcare system					
Comment The authors conclude that RBC transfusion is associated with a significantly increased risk of 30 day death, MI, or both.					

STUDY DETAILS				
Reference Bernard AC, Davenport DL, Chang PK, Vaughan TB, Zwischenberger JB. Intraoperative transfusion of 1 U to 2 U packed red blood cells is associated with increased 30-day mortality, surgical-site infection, pneumonia, and sepsis in general surgery patients. J Am Coll Surg. 2009;208(5):931–937				
Affiliation/Source of funds Northfield Laboratories, Wyeth, Pfizer, Eli Lily, Sanofi Aventis, MC3, Avalon, Novalung, Thermasolutions Funding source: Dr Bernard receives funding from Northland Laboratories and is on the speaker's bureaus at Wyeth and Pfizer; Dr Chang is on the speaker's bureaus at Eli Lilly and Company and Sanofi Aventis; Dr Zwischenberger received research funding from MC3 and Avalon and he serves as a consultant to Novalung and ThermaSolutions.				
Study design Prospective cohort study N=125,177	Level of evidence III	Location/setting 121 Hospitals in the USA		
Intervention Intraoperative or postoperative RBC transfusion Sample size N=4,788	Comparator(s) No RBC transfusion Sample size N=120,389			
Population characteristics Patients undergoing major surgical procedures in 121 hospitals as part of the ACS-NSQIP				
Length of follow-up 30 days	Outcome(s) measured Infection, morbidity, mortality			
INTERNAL VALIDITY				
Allocation	Comparison of study groups	Blinding	Treatment/measurement bias	Follow-up (ITT)
The study did not report on how patients were allocated	The study does not report baseline comparisons between the two groups	No blinding details are reported	It is assumed all patients were treated the same	ITT analysis
Overall quality assessment (descriptive) This was a fair quality prospective cohort study with limitations. Because NSQIP is a large national database, the integrity of individual data points is dependent on numerous data-entry sites, and opportunity exits for error at more than one site. Additionally, this is a retrospective study in which decision to transfuse and transfusion volume were not controlled.				

RESULTS					
Outcome	Units RBC Transfused	Transfusion	No transfusion	OR (95% CI)	Statistical Significance
Surgical site infection	1 U intraoperatively 2 U intraoperatively 3–4 U intraoperatively 5–9 U intraoperatively 10+ U intraoperatively > 4 U postoperatively	208/1,343 (15.5) 381/1,903 (38.1) 207/977 (21.2) 75/412 (18.2) 35/153 (22.9) 110/575 (19.1)	5,779/120,389 (4.8)	1.02 1.25 1.19 0.94 1.21 1.19	p>0.05 p<0.05 p<0.05 p<0.05 p<0.05 p<0.05
UTI	1 U intraoperatively 2 U intraoperatively 3–4 U intraoperatively 5–9 U intraoperatively 10+ U intraoperatively > 4 U postoperatively	89/1,343 (6.6) 120/1,903 (6.31) 84/977 (8.6) 33/412 (8.0) 12/153 (7.8) 59/575 (10.3)	1,685/120,389 (1.4)	1.12 1.04 1.33 1.17 1.03 1.73	p<0.05 p<0.05 p<0.05 p<0.05 p<0.05 p<0.05
Pneumonia	1 U intraoperatively 2 U intraoperatively 3–4 U intraoperatively 5–9 U intraoperatively 10+ U intraoperatively > 4 U postoperatively	130/1,343 (9.7) 204/1,903 (10.7) 139/977 (14.2) 66/412 (16.0) 38/153 (24.4) 141/575 (24.5)	1,685/120,389 (1.4)	1.24 1.25 1.41 1.64 2.80 2.71	p<0.05 p<0.05 p<0.05 p<0.05 p<0.05 p<0.05
Sepsis or septic shock	1 U intraoperatively 2 U intraoperatively 3–4 U intraoperatively 5–9 U intraoperatively 10+ U intraoperatively > 4 U postoperatively	263/1,343 (19.6) 466/1,903 (24.5) 284/977 (29.1) 123/412 (29.9) 57/153 (37.3) 250/575 (43.5)	3,852/120,389 (3.2)	1.29 1.53 1.62 1.64 2.29 3.39	p<0.05 p<0.05 p<0.05 p<0.05 p<0.05 p<0.05
Morbidity	1 U intraoperatively 2 U intraoperatively 3–4 U intraoperatively 5–9 U intraoperatively 10+ U intraoperatively > 4 U postoperatively	568/1,343 (42.3) 912/1,903 (47.9) 556/977 (56.9) 242/412 (58.7) 106/153 (69.3) 428/575 (74.4)	11,437/120,389 (9.5)	1.23 1.40 1.68 1.81 2.89 4.80	p<0.05 p<0.05 p<0.05 p<0.05 p<0.05 p<0.05
Mortality	1 U intraoperatively 2 U intraoperatively 3–4 U intraoperatively 5–9 U intraoperatively 10+ U intraoperatively >4 U postoperatively	136/1,343 (10.1) 194/1,903 (10.2) 150/977 (15.4) 67/412 (16.3) 45/153 (29.4) 153/575 (26.6)	1204/120,389 (1.0)	1.32 1.38 1.97 2.17 9.93 2.65	p<0.05 p<0.05 p<0.05 p<0.05 p<0.05 p<0.05
Clinical importance (1–4) Unable to determine			Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		
Any other adverse effects None reported					

EXTERNAL VALIDITY
Generalisability The results of this study are generalisable to a noncardiac surgery population
Applicability The study was conducted in the USA and is probably applicable to the Australian healthcare setting
Comments The authors conclude that intraoperative transfusion of PRBCs increases risk for mortality and several morbidities in general surgery patients.

STUDY DETAILS					
Reference Silva JM Jr, Cezario TA, Toledo DO, Magalhaes DD, Pinto MA, Victoria LG. Complications and prognosis of intraoperative blood transfusion. Rev Bras Anestesiol. 2008;58(5):447–461					
Affiliation/Source of funds Hospital Servidor Publico Estaual, Sao Paulo, Brazil Source of funding not reported					
Study design Prospective cohort study N=80	Level of evidence III-2	Location/setting Sao Paulo, Brazil			
Intervention Differing units of RBC transfusion Sample size N=80	Comparator(s) None				
Population characteristics Patients undergoing general surgery who need blood transfusion					
Length of follow-up Until the end of hospitalisation	Outcome(s) measured Mortality				
INTERNAL VALIDITY					
Allocation	Comparison of study groups	Blinding	Treatment/measurement bias	Follow-up (ITT)	
The study did not report on how patients were allocated	The study does not report baseline comparisons between different transfusion groups	No blinding details are reported	It is assumed all patients were treated the same	ITT analysis	
Overall quality assessment (descriptive) This is a fair quality prospective cohort study with limitations inherent to this type of study design					
RESULTS					
Outcome	Units RBC Transfused	Transfusion	No transfusion	OR (95% CI)	Statistical Significance
Mortality	Increasing	NR	NR	2.22 (1.10, 4.46)	p=0.026
Clinical importance (1–4) 2 The point estimate of effect is clinically important BUT the confidence interval includes clinically unimportant effects.	Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival				
Any other adverse effects None reported					

EXTERNAL VALIDITY
Generalisability The results of this study are generalisable to a noncardiac surgical population
Applicability The study was conducted in Brazil and may not be applicable to the Australian healthcare setting

STUDY DETAILS					
Reference Johnson III ON, Slidell MB, Macsata RA, Faler BJ, Amdur RL, Sidawy AN. Outcomes of surgical management for popliteal artery aneurysms: An analysis of 583 cases. J Vasc Surg. 2008;48(4):845–851					
Affiliation/Source of funds Department of Surgical Services, Veterans' Affairs Medical Center; Department of Surgery, Walter Reed Army Medical Center; Department of Surgery, Georgetown University; Department of Surgery, George Washington University; Washington DC, USA Funding source not reported The authors declared that they had no competing interests					
Study design Retrospective cohort study N=537	Level of evidence III	Location/setting 123 US Veterans' Affairs Medical Centers, USA			
Intervention RBC transfusion Sample size N=NR	Comparator(s) No RBC transfusion Sample size N=NR				
Population characteristics Patients who underwent surgery for popliteal artery aneurysms					
Length of follow-up 30 days after index surgery Survival: 1–2 years post-surgery	Outcome(s) measured Operative morbidity and mortality, early amputation				
INTERNAL VALIDITY					
Allocation	Comparison of study groups	Blinding	Treatment/ measurement bias	Follow-up (ITT)	
The study did not report on how patients were allocated	The study does not report baseline comparisons between different transfusion groups	Patient data de-identified and sent securely to principal investigator using file encryption and password protection	It is not clear whether all patients were treated the same	ITT	
Overall quality assessment (descriptive) This was a fair quality retrospective cohort study with limitations inherent to this study design					
RESULTS					
Outcome	Units RBC Transfused	Transfusion	No transfusion	OR (95% CI)	Statistical Significance
Morbidity and mortality	≥1 unit	NR	NR	4.5 (2.3, 8.9)	p=0.0002
Clinical importance (1–4) 1 A clinically important benefit for the full range of plausible estimates	Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival				

Early amputation	≥ 1 unit	NR	NR	7.2 (1.3, 40.4)	NS
Clinical importance (1–4) 4 The range of estimates defined by the confidence interval includes clinically important effects BUT the range of estimates defined by the confidence interval is also compatible with no effect, or a harmful effect.			Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		
Any other adverse effects None reported					
EXTERNAL VALIDITY					
Generalisability The results of the study may not be generalisable to a wider noncardiac surgical population					
Applicability The study was conducted in the USA and is probably applicable to the Australian healthcare setting					

STUDY DETAILS					
Reference Engoren M, Mitchell E, Perring P, Sferra J. The effect of erythrocyte blood transfusions on survival after surgery for hip fracture. J Trauma. 2008;65(6):1411–1415					
Affiliation/Source of funds Departments of Anesthesiology and Surgery, St Vincent Mercy Medical Center, University of Toledo College of Medicine, Toledo, OH; USA Source of funding: support was provided by St Vincent Mercy Medical Center					
Study design Retrospective cohort study N=229		Level of evidence III		Location/setting Medical centre, Toledo, OH, USA	
Intervention RBC transfusion Sample size N=90			Comparator(s) No RBC transfusion Sample size N=139		
Population characteristics Patients undergoing surgery for hip fracture					
Length of follow-up 30, 90, 120, 365 days			Outcome(s) measured mortality		
INTERNAL VALIDITY					
Allocation	Comparison of study groups	Blinding	Treatment/ measurement bias	Follow-up (ITT)	
The decision to transfuse blood relies on physician decision	The study does not report baseline comparisons between different transfusion groups	No blinding details are reported	It is assumed all patients were treated the same	ITT analysis	
Overall quality assessment (descriptive) This was a poor quality retrospective cohort study. One of the strengths of the study was the use of propensity matching. However, propensity analysis can only control for possible confounders that are variables in the database. Other factor's that may have contributed to a physician's decision to use RBC transfusion are not controlled and may bias the results, thus one cannot exclude the possibility that patients who received RBC transfusion were sicker. As econd limitation of propensity matching is that a variable that affects treatment assignment but not outcome is analysed the same as a variable with similar effect on treatment assignment but a strong relationship to outcome. An additional limitation to the study is the retrospective nature and the chart review. Finally, the causes of death were not known.					
RESULTS					
Outcome	Units RBC Transfused	Transfusion	No transfusion	RR (95% CI)	Statistical Significance
Mortality	Any	31/90 (34.4)	28/139 (20.1)	3.76 (1.22, 11.63)	p=0.02
Clinical importance (1–4) 2 The point estimate of effect is clinically important BUT the confidence interval includes clinically unimportant effects.			Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		

Any other adverse effects None reported
EXTERNAL VALIDITY
Generalisability The results of this study may not be generalisable beyond an orthopaedic surgery population
Applicability The study was conducted in the USA and is probably applicable to the Australian healthcare system
Comments The authors conclude that the use of RBC transfusions in patients undergoing surgical repair of hip fractures was associated with an increased risk of death.

STUDY DETAILS

Reference Rogers J, Kilaru RK, Hosokawa P, Henderson WG, Zinner MJ, Khuri SF. Multivariable predictors of postoperative venous thromboembolic events after general and vascular surgery: results from the patient safety in surgery study. J Am Coll Surg. 2007a;204(6):1211–1221

Affiliation/Source of funds

Department of Surgery and Center for Surgery and Public Health, Brigham and Women's Hospital, Boston; Division of Cardiology, Danbury Hospital, Danbury; National Surgical Quality Improvement Program, Office of Patient Care Services, Department of Veterans Affairs Aurora; University of Colorado Health Outcomes Program, Aurora; VA Boston Healthcare System, West Roxbury; Harvard Medical School and the Brigham and Women's Hospital, Boston, USA

Source of funding: Not reported

Authors declared that they had no competing interests

Study design	Level of evidence	Location/setting
Retrospective cohort study N=184,120	III	128 Veterans Affairs' Medical Centres and 14 private-sector hospitals in the USA

Intervention	Comparator(s)
RBC transfusion > 4 units in 72 hours pre-op Sample size N=NR	No RBC transfusion Sample size N=NR

Population characteristics

Patients undergoing major general or vascular surgery over a 2 year period

Length of follow-up	Outcome(s) measured
30 days after surgery	Venous thromboembolism

INTERNAL VALIDITY

Allocation	Comparison of study groups	Blinding	Treatment/measurement bias	Follow-up (ITT)
The study did not report on how patients were allocated	The study does not report baseline comparisons between different transfusion groups	No blinding details are reported	It is not clear whether all patients were treated the same	1337 (0.7%) patients were excluded from the analysis

Overall quality assessment (descriptive)

This was a fair quality retrospective cohort study with limitations inherent to this study design

RESULTS

Outcome	Units RBC Transfused	Transfusion	No transfusion	OR (95% CI)	Statistical Significance
Venous thromboembolism	>4 units in 72 hours pre-op	NR	NR	1.61 (1.03, 2.51)	p=0.037

Clinical importance (1–4)	Relevance (1–5)
2 The point estimate of effect is clinically important but the confidence interval includes clinically unimportant effects.	1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival

Any other adverse effects None reported
EXTERNAL VALIDITY
Generalisability The results of this study are generalisable to a noncardiac surgery population
Applicability The study was conducted in the USA and is probably applicable to the Australian healthcare setting

STUDY DETAILS				
Reference Ruttinger D, Wolf H, Kuchenhoff H, Jauch KW, Hartl WH. Red cell transfusion: An essential factor for patient prognosis in surgical critical illness? Shock. 2007;28(2):165–171				
Affiliation/Source of funds Department of Surgery, Klinkum Grosshadern, and Institute of Statistics, Ludwig-Maximilian University, Munich, Germany Funding Sources not reported				
Study design Retrospective cohort study N=3037	Level of evidence III	Location/setting Surgical ICU of University Hospital in Germany		
Intervention RBC transfusion Sample size N=1792	Comparator(s) No RBC transfusion Sample size N=1245			
Population characteristics Surgical patients who required intensive care over a 12 year period				
Length of follow-up Not reported	Outcome(s) measured Mortality			
INTERNAL VALIDITY				
Allocation	Comparison of study groups	Blinding	Treatment/measurement bias	Follow-up (ITT)
The study did not report on how patients were allocated	There are significant differences in baseline characteristics between transfused and non transfused patients	No blinding details are reported	It is not clear whether all patients were treated the same	ITT analysis
Overall quality assessment (descriptive) This is a fair quality retrospective cohort study with limitations inherent to this type of study				

RESULTS					
Outcome	Units RBC Transfused	Transfusion	No transfusion	OR (95% CI)	Statistical Significance
Mortality in the ICU	1–2 units	NR	NR	0.68 (0.35, 1.28)	p=0.261
	3–4 units	NR	NR	1.11 (0.52, 2.39)	p=0.793
	5–8 units	NR	NR	1.16 (0.60, 2.26)	p=0.660
	>8 units	NR	NR	0.74 (0.36, 1.51)	p=0.406
Clinical importance (1–4) 4 The range of estimates defined by the confidence interval includes clinically important effects BUT the range of estimates defined by the confidence interval is also compatible with no effect, or a harmful effect.			Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		
ICU LOS	Any	NR	NR	1.50 (1.36, 1.66)	p<0.0001
Clinical importance (1–4) 2 The point estimate of effect is clinically important BUT the confidence interval includes clinically unimportant effects.			Relevance (1–5) 2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention		
Any other adverse effects None reported					
EXTERNAL VALIDITY					
Generalisability The results of this study are generalisable to a noncardiac surgery population					
Applicability The study was conducted in Germany and is probably applicable to the Australian healthcare setting.					
Comments The authors conclude that RBC transfusion during ICU stay may be only a surrogate marker for disease severity and is not causally related to ICU mortality, Relevant side effects of RBC transfusion are presumably small and may only be recognisable in surviving cases.					

STUDY DETAILS

Reference BuSaba NY, Schaumberg DA. Predictors of prolonged length of stay after major elective head and neck surgery. Laryngoscope. 2007;117(10):1756–1763

Affiliation/Source of funds

From the Division of Otolaryngology, VA Boston Health Care System, Boston Massachusetts, USA; the Department of Otology and Laryngology, Harvard Medical School, Boston, Massachusetts, USA; the Department of Otolaryngology-Head and Neck Surgery, Massachusetts Eye and Ear Infirmary, Boston, Massachusetts, USA; the Division of Preventative Medicine, Brigham and Women's Hospital Boston, Massachusetts, USA; and the Schepens Eye Research Institute, Department of Opthalmology, Harvard Medical School, Boston, Massachusetts, USA.

Source of Funding: Not reported

Study design	Level of evidence	Location/setting
Prospective cohort study N=3050	III	Hospitals, USA

Intervention	Comparator(s)
RBC transfusion Sample Size NR	No RBC transfusion Sample Size NR

Population characteristics

Patients undergoing head and neck operations over a 2 year period

Length of follow-up	Outcome(s) measured
Time in hospital	Prolonged hospital LOS

INTERNAL VALIDITY

Allocation	Comparison of study groups	Blinding	Treatment/ measurement bias	Follow-up (ITT)
The study did not report on how patients were allocated	The study does not report baseline comparisons between different transfusion groups	No blinding details are reported	It is not clear whether all patients were treated the same	ITT analysis

Overall quality assessment (descriptive)

This was a fair quality retrospective cohort study with some limitations. One limitation is the use of data from the VHA population, and the findings may not be generalisable to the population at large. The veterans are overwhelmingly male and tend to be older than the average nationwide surgical patient.

RESULTS

Outcome	Units RBC Transfused	Transfusion	No transfusion	OR (95% CI)	Statistical Significance
Prolonged hospital LOS	Any	NR	NR	1.20 (1.10, 1.31)	p<0.0001

Clinical importance (1–4)	Relevance (1–5)
2 The point estimate of effect is clinically important BUT the confidence interval includes clinically unimportant effects.	2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention

Any other adverse effects None reported
EXTERNAL VALIDITY
Generalisability The study may not be generalisable to a younger noncardiac surgical population
Applicability The study was conducted in the USA and is probably applicable to the Australian healthcare setting

STUDY DETAILS				
Reference Weber EWG, Slappendel R, Prins MH, Van Der Schaaf DB, Durieux ME, Strumper D. Perioperative blood transfusions and delayed wound healing after hip replacement surgery: Effects on duration of hospitalization. Anesth Analg. 2005a;100(5):1416–1421				
Affiliation/Source of funds Departments of Anesthesiology and Clinical Epidemiology, University Hospital Maastricht, Maastricht, The Netherlands; Departments of Anesthesiology and Orthopedic Surgery, St Maartens Hospital, Nijmegen, The Netherlands; Department of Anesthesiology, University of Virginia, Charlottesville, Virginia; and Department of Anesthesiology, University Hospital Munster, Munster, Germany. Funding sources not reported				
Study design Prospective cohort study N=444	Level of evidence III	Location/setting Hospital, the Netherlands		
Intervention RBC transfusion Sample size N=92	Comparator(s) No RBC transfusion Sample size N=352			
Population characteristics Patients undergoing total hip replacement over a 1 year period				
Length of follow-up Until hospital discharge	Outcome(s) measured Wound healing disturbances, hospital LOS			
INTERNAL VALIDITY				
Allocation	Comparison of study groups	Blinding	Treatment/ measurement bias	Follow-up (ITT)
RBC transfusions were administered: Hb<8.1g/dL during surgery until 4h post surgery. For patients with cardiovascular disease, transfusion triggers were increased by 0.8g/dL	There are significant differences in baseline characteristics between transfused and non transfused patients	No blinding details are reported	All patients were treated equally according to standard protocol	ITT analysis
Overall quality assessment (descriptive) This was a fair quality prospective cohort study with limitations inherent to this type of study.				

RESULTS					
Outcome	Units RBC Transfused	Transfusion	No transfusion	OR (95% CI)	Statistical Significance
Wound healing disturbances	Any	29/92 (31)	63/352 (18)	2.1 (1.2, 3.5)	p=0.03
Hospital LOS (coefficient [95% CI])	Any	12.3 days	9.8 days	2.2 (1.3, 3.1)	p<0.001
Clinical importance (1–4) 2 The point estimate of effect is clinically important BUT the confidence interval includes clinically unimportant effects.			Relevance (1–5) 2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention		
1 year mortality	Any	NR	NR	1.67 (1.01, 2.89)	p=0.049
Clinical importance (1–4) 2 The point estimate of effect is clinically important BUT the confidence interval includes clinically unimportant effects.			Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		
Any other adverse effects None reorted					
EXTERNAL VALIDITY					
Generalisability The results of this study may not be generalisable to a wider noncardiac surgery patient population					
Applicability The study was conducted in the Netherlands and is probably applicable to the Australian healthcare system					

STUDY DETAILS				
Reference Halm EA, Wang JJ, Boockvar K, Penrod J, Silberzweig SB, Magaziner J, et al. Effects of blood transfusion on clinical and functional outcomes in patients with hip fracture. Transfusion. 2003;43(10):1358–1365				
Affiliation/Source of funds From the Department of health Policy, the Department of medicine, and the Department of geriatrics and Adult Development, Mount Sinai School of Medicine, New York, New York, USA; the Department of Epidemiology and Preventative medicine, University of Maryland School of medicine, Baltimore, Maryland; and the Department of Orthopedics, Hospital for Joint Diseases, New York, New York, USA Funding source: the project was supported by grants from the Agency for healthcare research and Quality (RO1 HS09973 and U18 HS09459-0) and Ortho-Biotech Products, L.P., Raritan, NJ. Additional support was provided by the Robert Wood Johnson Generalist Physician Faculty Scholars Program (EAH) and the National Institute on Aging (Midcareer Investigator Award to ALS)				
Study design Prospective cohort study N=551	Level of evidence III	Location/setting Hospital, New York, USA		
Intervention RBC transfusion Sample Size N=300	Comparator(s) No RBC transfusion Sample Size N=251			
Population characteristics Patients undergoing surgery for hip fracture at 4 hospitals				
Length of follow-up 60 days after hospital discharge	Outcome(s) measured Mortality; readmission; mobility (using the FIM)			
INTERNAL VALIDITY				
Allocation	Comparison of study groups	Blinding	Treatment/ measurement bias	Follow-up (ITT)
The study did not report on how patients were allocated	There are significant differences in baseline characteristics between transfused and non transfused patients	No blinding details are reported	It is not clear whether all patients were treated the same	ITT analysis
Overall quality assessment (descriptive) This was a fair quality prospective cohort study with some limitations. Firstly, because this was an observational study, one needs to be cautious about inferring cause and effect relationships. Second, there was limited information on posthospital processes of care, which may have influenced readmission rates or mobility scores.				

RESULTS					
Outcome	Units RBC Transfused	Transfusion	No transfusion	OR (95% CI)	Statistical Significance
Mortality	Any	14/300 (4.7)	7/251 (2.8)	1.74 (0.51, 5.94)	NS
Clinical importance (1–4) 4 The range of estimates defined by the confidence interval includes clinically important effects BUT the range of estimates defined by the confidence interval is also compatible with no effect, or a harmful effect.			Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		
Readmission	Any	49/300 (16.4)	44/251 (17.7)	0.54 (0.30, 0.97)	S
Clinical importance (1–4) 2 The point estimate of effect is clinically important BUT the confidence interval includes clinically unimportant effects.			Relevance (1–5) 2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention		
FIM score (coefficient [95% CI])	Any	19/300 (6.2)	17/251 (6.9)	0.27 (–0.47, 1.01)	NS
Clinical importance (1–4) 4 The range of estimates defined by the confidence interval includes clinically important effects BUT the range of estimates defined by the confidence interval is also compatible with no effect, or a harmful effect.			Relevance (1–5) 2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention		
Any other adverse effects None reported					
EXTERNAL VALIDITY					
Generalisability The study may not be generalisable to a wider noncardiac surgery population					
Applicability The study was performed in the USA and is probably applicable to the Australian healthcare system					
Comments The authors concluded that postoperative RBC transfusion reduced the risk of readmission but did not decrease mortality or improve mobility score.					

STUDY DETAILS					
Reference Dunne JR, Malone D, Tracy JK, Gannon C, Napolitano LM. Perioperative anemia: An independent risk factor for infection, mortality and resource utilization in surgery. J Surg Res. 2002;102(2):237–244					
Affiliation/Source of funds Department of Surgery, VA Maryland Healthcare System, Baltimore, Maryland; University of Maryland School of Medicine, Baltimore, Maryland; and National Naval Medical centre, Bethesda, Maryland Funding source not reported					
Study design Retrospective cohort study N=6,301	Level of evidence III	Location/setting Hospitals in USA			
Intervention RBC transfusion Sample Size N=NR	Comparator(s) No RBC transfusion Sample Size N=NR				
Population characteristics Patients undergoing noncardiac surgery					
Length of follow-up Not reported	Outcome(s) measured Postoperative pneumonia, 30 day mortality, hospital LOS				
INTERNAL VALIDITY					
Allocation	Comparison of study groups	Blinding	Treatment/measurement bias	Follow-up (ITT)	
The study did not report on how patients were allocated	The study does not report baseline comparisons between different transfusion groups	No blinding details are reported	It is not clear whether all patients were treated the same	ITT analysis	
Overall quality assessment (descriptive) This was a fair quality retrospective cohort study with limitations inherent to this type of study					
RESULTS					
Outcome	Units RBC Transfused	Transfusion	No transfusion	OR (95% CI)	Statistical Significance
Mortality	Any	NR	NR	1.08 (1.04, 1.13)	p<0.001
	>4 units	NR	NR	2.84 (2.07, 3.89)	p<0.001
Risk of infection	Any	NR	NR	1.06 (1.01, 1.11)	p<0.01
	>4 units	NR	NR	9.28 (5.74, 15.00)	p<0.001
Clinical importance (1–4) 1 A clinically important benefit for the full range of plausible estimates	Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival				

Hospital LOS (coefficient [SE])	Any	NR	NR	0.54 (0.10)	p<0.001
	>4 units	NR	NR	7.39 (0.82)	p<0.001
Clinical importance (1–4) Unable to determine			Relevance (1–5) 2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention		
Any other adverse effects None reported					
EXTERNAL VALIDITY					
Generalisability The study is generalisable to a noncardiac surgery population					
Applicability The study was conducted in the USA and is probably applicable to the Australian healthcare setting					

STUDY DETAILS					
Reference Chang H, Hall GA, Geerts WH, Greenwood C, McLeod RS, Sher GD. Allogeneic red blood cell transfusion is an independent risk factor for the development of postoperative bacterial infection. Vox Sang. 2000;78:13–18					
Affiliation/Source of funds Departments of medicine and Surgery, The Toronto Hospital, Mt Sinai Hospital and the Univesity of Toronto; Clinical Epidemiology Unit, Samuel Lunenfeld Research Institute, The Canadian Blood Services, Toronto, Ontario, Canada Funding source not reported					
Study design Prospective cohort study N=1,349	Level of evidence III	Location/setting 11 university teaching hospitals, Canada			
Intervention RBC transfusion Sample Size N=282	Comparator(s) No RBC transfusion Sample Size N=1,067				
Population characteristics Patients undergoing colorectal surgery					
Length of follow-up Not reported	Outcome(s) measured Infection				
INTERNAL VALIDITY					
Allocation	Comparison of study groups	Blinding	Treatment/measurement bias	Follow-up (ITT)	
The study did not report on how patients were allocated	The study does not report baseline comparisons between different transfusion groups	No blinding details are reported	It is not clear whether all patients were treated the same	ITT analysis	
Overall quality assessment (descriptive) This was a fair quality prospective cohort study with limitations inherent to this type of study.					
RESULTS					
Outcome	Units RBC Transfused	Transfusion	No transfusion	OR (95% CI)	Statistical Significance
Postoperative infection (total)	Any	73/282 (25.9)	152/1,067 (14.2)	1.18 (1.05, 1.33)	p=0.007
Clinical importance (1–4) 2 The point estimate of effect is clinically important BUT the confidence interval includes clinically unimportant effects.	Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival				

Wound infection	Any	63/282 (22.3)	144/1,067 (13.5)	1.13 (1.01, 1.54)	p=0.04
Intra-abdominal infection	Any	10/282 (3.5)	8/1,067 (0.7)	1.17 (1.00, 1.38)	p=0.058

Clinical importance (1–4) 4 The range of estimates defined by the confidence interval includes clinically important effects BUT the range of estimates defined by the confidence interval is also compatible with no effect, or a harmful effect	Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival
Any other adverse effects None reported	
EXTERNAL VALIDITY	
Generalisability The results of this study may not be generalisable to a wider noncardiac surgery population	
Applicability The study was conducted in Canada and is applicable to the Australian healthcare setting	
Comments The authors concluded that RBC transfusion is an independent risk factor for the development of postoperative bacterial infection in patients undergoing colorectal surgery	

STUDY DETAILS				
Reference Carson JL, Duff A, Berlin JA, Lawrence VA, Poses RM, Huber EC, et al. Perioperative blood transfusion and postoperative mortality. JAMA. 1998a;279:199–205				
Affiliation/Source of funds From the Division of General Internal Medicine, Departments of Medicine (Dr Carson and Mss Duff and Noveck) and Anesthesia (Dr O'Hara), University of Medicine and Dentistry of New Jersey, Robert Wood Johnson Medical School, New Brunswick; Center for Clinical Epidemiology and Biostatistics, Department of Biostatistics and Epidemiology (Drs Berlin and Strom), and Division of General Internal Medicine, Department of Medicine (Dr Strom), University of Pennsylvania School of Medicine, Philadelphia; Division of General Medicine, Audie Murphy Division, South Texas Veterans Health Care System and Department of Medicine, University of Texas at San Antonio (Dr Lawrence); Division of General Internal Medicine, Department of Medicine, Brown University School of Medicine, Providence, RI, and Memorial Hospital of Rhode Island, Pawtucket (Dr Poses); and Division of General Internal Medicine, Medical College of Virginia, Richmond (Dr Huber). Funding source: This study was supported by award 1R01HS07322 from the Agency for Health Care Policy and Research, Rockville, Md.				
Study design Retrospective cohort study N=8787	Level of evidence III		Location/setting 20 hospitals in the USA	
Intervention RBC transfusion Sample Size N=3699		Comparator(s) No RBC transfusion Sample Size N=5088		
Population characteristics Patients aged ≥60 years undergoing hip fracture surgery over a 10 year period				
Length of follow-up 90 days after operative procedure		Outcome(s) measured 30 and 90 day mortality		
INTERNAL VALIDITY				
Allocation	Comparison of study groups	Blinding	Treatment/measurement bias	Follow-up (ITT)
The study did not report on how patients were allocated	There are significant differences in baseline characteristics between transfused and non transfused patients	No blinding details are reported	It is not clear whether all patients were treated the same	ITT analysis

Overall quality assessment (descriptive)

This was a fair quality retrospective cohort study with limitations. The most important potential limitation of an observational study evaluating the effect of transfusion on mortality is that transfused patients may systematically differ from non-transfused patients in ways that cannot be ascertained or controlled for by a retrospective chart review. Several other limitations should also be considered when interpreting the results of this study. First, the data were collected by medical record review. Second, despite the large sample size (this is the largest study to date to examine this question), inadequate power may still explain our inability to detect a reduction in mortality related to transfusion. Third, this study evaluated the effect of transfusion on mortality, and it is possible that transfusion may affect other outcomes such as morbidity, readmission to the hospital, speed of recovery, and functional status. Fourth, the data for the study were collected over an 11-year period from 20 different hospitals in 4 geographic regions. Data from earlier admissions may not be entirely comparable with data from more recent admissions since surgical procedures, anaesthetic technique, physical therapy, and length of hospital stay may have changed. Fifth, the results may not generalize to other populations of patients or surgical procedures.

RESULTS

Outcome	Units RBC Transfused	Transfusion	No transfusion	OR (95% CI)	Statistical Significance
30 day mortality	Preoperative	NR	NR	1.24 (0.81, 1.90)	NS
30 day mortality	Postoperative	NR	NR	0.96 (0.74, 1.26)	NS
90 day mortality (HR [95% CI])	Postoperative	NR	NR	1.08 (0.90, 1.29)	NS

Clinical importance (1–4)

4 The range of estimates defined by the confidence interval includes clinically important effects BUT the range of estimates defined by the confidence interval is also compatible with no effect, or a harmful effect

Relevance (1–5)

1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival

Any other adverse effects

None reported

EXTERNAL VALIDITY

Generalisability

The results of this study may not be generalisable to a noncardiac surgery population

Applicability

The study was conducted in the USA and is probably applicable to the Australian healthcare system

Comments

The authors concluded that perioperative transfusion in patients with HB levels of ≥8g/dL did not appear to influence the risk of 30- or 90-day mortality in this elderly orthopaedic surgery population

Liberal versus restrictive transfusion strategy

What is the effect of liberal versus restrictive red blood cell transfusion protocols on patient outcomes in a perioperative population?

Level II evidence

<table>
<tr><td colspan="5">STUDY DETAILS</td></tr>
<tr><td colspan="5">Reference Bracey AW, Radovancevic R, Riggs SA, Houston S, Cozart H, Vaughn WK, et al. Lowering the haemoglobin threshold for transfusion in coronary artery bypass procedures: Effect on patient outcome. Transfusion. 1999;39:1070–1077</td></tr>
<tr><td colspan="5">Affiliation/Source of funds
From the Departments of Pathology, Hematology, Surgery, Outcome Management, and Biostatistics and Epidemiology, Texas Heart Institute/St Luke's Episcopal Hospital and Prairie View A&M Collegy of Nursing, Houston, Texas.
Funding source not reported</td></tr>
<tr><td colspan="2">Study design
Randomised controlled trial
N=428</td><td colspan="2">Level of evidence
II</td><td>Location/setting
Heart Institute, USA</td></tr>
<tr><td colspan="2">Intervention
Patients receiving restrictive blood transfusion strategy of Hb <8 g/dL
Sample size N=212</td><td colspan="3">Comparator(s)
Patients receiving liberal blood transfusion strategy of Hb <9 g/dL
Sample size N=216</td></tr>
<tr><td colspan="5">Population characteristics
Patients who underwent first-time, elective CABG surgery</td></tr>
<tr><td colspan="2">Length of follow-up
Length of hospitalisation</td><td colspan="3">Outcome(s) measured
Transfusion incidence, duration of mechanical ventilation, ICU LOS, hospital LOS, morbidity and mortality</td></tr>
<tr><td colspan="5">INTERNAL VALIDITY</td></tr>
<tr><td>Allocation</td><td>Comparison of study groups</td><td>Blinding</td><td>Treatment/ measurement bias</td><td>Follow-up (ITT)</td></tr>
<tr><td>Patients were randomly assigned to study and control groups on the basis of the last digit of their medical record</td><td>There were no significant differences between the demographics, preoperative status, procedure-related variables or blood loss in the study and control groups</td><td>No blinding details are reported in the study</td><td>All patients were treated the same</td><td>ITT analysis</td></tr>
<tr><td colspan="5">Overall quality assessment (descriptive)
This was a fair quality randomised controlled trial</td></tr>
</table>

RESULTS				
Outcome	Restrictive Strategy	Liberal Strategy	OR (95% CI)	Statistical Significance
Transfusion rate, units (mean ± SD)	2.0 ± 2.2	2.5 ± 2.6	NR	p=0.04
Hospital LOS days (mean ± SD)	7.5 ± 2.9	7.9 ± 4.9	NR	NS
Mortality, n/N (%)	3/212 (1.4%)	6/216 (2.7%)	NR	p=0.321
Atrial arrhythmia, n/N (%)	30/212 (14%)	40/216 (19%)	NR	NS
Ventricular arrhythmia, n/N (%)	13/212 (6%)	9/216 (4%)	NR	NS
MI, n/N (%)	1/212 (0.5%)	0/216 (0%)	NR	NS
Neurologic deficit, n/N (%)	11/212 (5%)	9/216 (4%)	NR	NS
Pulmonary complications, n/N (%)	57/212 (27%)	64/216 (30%)	NR	NS
Renal failure, n/N (%)	8/212 (4%)	5/216 (2%)	NR	NS
Infection, n/N (%)	5/212 (2%)	3/216 (1%)	NR	NS
Clinical importance (1–4) 3 The confidence interval does not include any clinically important effects.		Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		
Any other adverse effects None reported				
EXTERNAL VALIDITY				
Generalisability The results of this study are generalisable to a cardiac surgery population				
Applicability The study was conducted in the USA and is probably applicable to the Australian healthcare setting				
Comments The authors concluded that a lower Hb threshold of 8g/dL does not adversely affect patient outcome				

STUDY DETAILS				
Reference Bush RL, Pevec WC, Holcroft JW. A prospective, randomised trial limiting perioperative red blood cell transfusions in vascular patients. Am J Surg 1997;174:143–148				
Affiliation/Source of funds From the Department of Surgery, University of California Davis Medical Centre, Sacramento, California, USA Funding source not reported				
Study design Randomised controlled trial N=99	Level of evidence II	Location/setting University medical Centre, USA		
Intervention Patients receiving restrictive blood transfusion strategy of Hb <9 g/dL Sample size N=50	Comparator(s) Patients receiving liberal blood transfusion strategy of Hb <10 g/dL Sample size N=49			
Population characteristics Patients undergoing elective aortic or infra-inguinal arterial reconstruction				
Length of follow-up Not reported	Outcome(s) measured Myocardial ischaemia, myocardial infarction, death and ICU and hospital LOS			
INTERNAL VALIDITY				
Allocation	Comparison of study groups	Blinding	Treatment/ measurement bias	Follow-up (ITT)
Patients were randomised to study or control group. Sealed envelopes were chosen at random for patient assignment	The study does not report baseline comparisons between different study and control groups	No blinding details are recorded	It is assumed that all patients were treated the same	ITT analysis
Overall quality assessment (descriptive) This was a good quality randomised controlled trial				
RESULTS				

Outcome	Restrictive Strategy	Liberal Strategy	OR (95% CI)	Statistical Significance
Mortality, n/N (%)	4/48 (8%)	4/47 (9%)	NR	NS
Transfusion rate, units (mean ± SD)	2.8 ± 3.1	3.7 ± 3.5	NR	p=0.19
Cardiac morbidity, n/N (%)	8/48 (16%)	8/49 (16%)	NR	NS
MI rate, n/N (%)	2/48 (4%)	1/49 (2%)	NR	p=0.99

Clinical importance (1–4)	Relevance (1–5)
3 The confidence interval does not include any clinically important effects.	1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival

ICU LOS, days (mean ± SD)	4 ± 8	4 ± 4	NR	NS
Hospital LOS, days (mean ± SD)	11 ± 9	10 ± 6	NR	NS
Clinical importance (1–4) 3 The confidence interval does not include any clinically important effects.		Relevance (1–5) 2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention		
Any other adverse effects None reported				
EXTERNAL VALIDITY				
Generalisability The results of this study may not be generalisable to a wider noncardiac surgery population				
Applicability The study was conducted in the USA and is probably applicable to the Australian healthcare setting				
Comments The authors concluded that a lower Hb concentration was tolerated without adverse clinical outcome				

STUDY DETAILS				
Reference Grover M, Talwalker S, Casbard A, Boralessa H, Contreras M, Boralessa H, et al. Silent myocardial ischaemia and haemoglobin concentration: A randomised controlled trial of transfusion strategy in lower limb arthroplasty. Vox Sanguinis. 2006;90:105–112				
Affiliation/Source of funds Chelsea and Westminster Hospital, London, UK; Oldchurch Hospital, Romford, Essex, UK; MRC Clinical Trials Unit, 222 Euston Rd, London, UK; National Blood Service, Colindale Ave, London, UK; National Blood Service, Crescent Drive, Brentwood, Essex, UK; The Royal National Orthopaedic Hospital, Stanmore, Middlesex, UK; Hammersmith Hospital, Du Cane Rd, London, UK Funding source: This study was funded by a grant from the NHS/NBS National Research Review Committee				
Study design Randomised controlled trial N=260	Level of evidence II	Location/setting Acute hospitals, England, UK		
Intervention Patients receiving restrictive blood transfusion strategy of Hb <8 g/dL Sample Size N=109	Comparator(s) Patients receiving liberal blood transfusion strategy of Hb <10 g/dL Sample Size N=109			
Population characteristics Patients undergoing elective hip and knee replacement surgery				
Length of follow-up 72 hours postoperatively	Outcome(s) measured Silent ischaemia, blood loss, Hb concentration, transfusion rate, LOS, AEs and new infections			
INTERNAL VALIDITY				
Allocation	Comparison of study groups	Blinding	Treatment/ measurement bias	Follow-up (ITT)
Patients were randomised perioperatively using permuted blocks that were derived from random number tables.	There was no difference in the baseline demographic characteristics between the two groups	Envelopes containing the number and allocation sequence remained sealed until the patient was assigned to intervention. The patient and technician analysing the Holter tapes were unaware of treatment allocation. The anaesthetists and surgical team responsible for the patient were informed of treatment allocation	All patients were treated the same	ITT analysis

Overall quality assessment (descriptive) This was a fair quality randomised controlled trial				
RESULTS				
Outcome	Restrictive Strategy	Liberal Strategy	OR (95% CI)	Statistical Significance
Silent ischaemia, n/N (%)	21/109 (19%)	26/109 (24%)	MD: –4.6% (–15.5, 6.0%)	p=0.41
DVT, n/N (%)	4/109 (4%)	5/109 (4.6%)	NR	NS
PE, n/N (%)	1/109 (1%)	2/109 (2%)	NR	NS
MI, n/N (%)	1/109 (1%)	0/109 (0%)	NR	NS
Chest infection, n/N (%)	3/109 (3%)	2/109 (2%)	NR	NS
Wound infection, n/N (%)	2/109 (2%)	2/109 (2%)	NR	NS
Mortality, n/N (%)	1/109 (1%)	0/109 (0%)	NR	NS
Clinical importance (1–4) 3 The confidence interval does not include any clinically important effects.		Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		
Hospital LOS, median days (range)	7.3 (5–11)	7.5 (5–13)	NR	NS
Clinical importance (1–4) 3 The confidence interval does not include any clinically important effects.		Relevance (1–5) 2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention		
Any other adverse effects None reported				
EXTERNAL VALIDITY				
Generalisability The results of this study may not be generalisable to a wider noncardiac surgery population				
Applicability The study was conducted in the UK and is applicable to the Australian healthcare system				
Comments The authors concluded that in patients without preoperative evidence of myocardial ischaemia undergoing elective hip and knee replacement surgery, a restrictive transfusion strategy seems unlikely to be associated with an increased incidence of SMI. Use of a restrictive transfusion strategy did not increase length of hospital stay, and use of this strategy would lead to a significant reduction in red cell transfusion in orthopaedic surgery. Our data did not indicate any potential for harm in employing such a strategy in patients with no prior evidence of cardiac ischaemia who were undergoing elective orthopaedic surgery.				

STUDY DETAILS				
Reference Carson JL, Terrin ML, Barton FB, Aaron R, Greenburg AG, Heck DA, et al. A pilot randomised trial comparing symptomatic vs. haemoglobin-level-driven red blood cell transfusions following hip fracture. Transfusion 1998b;38:522–529				
Affiliation/Source of funds From the Division of General Internal Medicine, Department of Medicine, University of Medicine and Dentistry, New Jersey, Robert Wood Johnson Medical School, New Brunswick, New Jersey; the Maryland Medical Research Institute, and the Department of Epidemiology and Preventative Medicine, University of Maryland, Baltimore, Maryland; the Department of Surgery, Miriam Hospital, Providence, Rhode Island; the Department of Orthopedic Surgery, Indiana University, Indianapolis, Indiana; and the Department of Transfusion Medicine, University of Edinburgh, The Royal Infirmary of Edinburgh, Edinburgh, Scotland. Funding source not reported				
Study design Randomised controlled trial N=80	Level of evidence II	Location/setting University hospital, USA and Scotland		
Intervention Patients receiving a restrictive blood transfusion strategy of Hb <8 g/dL Sample size N=40	Comparator(s) Patients receiving a liberal blood transfusion strategy of Hb <10 g/dL Sample Size N=40			
Population characteristics Patients presenting for hip fracture repair with a Hb <10 g/dL in the immediate post operative period				
Length of follow-up 60 days	Outcome(s) measured Death within 60 days or inability to walk 10 feet within 60 days, 30 and 60 day mortality, in-hospital myocardial infarction, thromboembolism, stroke and pneumonia			
INTERNAL VALIDITY				
Allocation	Comparison of study groups	Blinding	Treatment/ measurement bias	Follow-up (ITT)
Patients were randomised by contacting the data coordinating centre's 24 hr automated telephone service.	The baseline demographic characteristics were similar between the two treatment groups	Study nurses collecting information were blind to the transfusion status of the patient.	It appears that all patients were treated the same.	ITT analysis
Overall quality assessment (descriptive) This was a fair quality randomised controlled trial.				

RESULTS				
Outcome	Restrictive Strategy	Liberal Strategy	RR (95% CI)	Statistical Significance
Transfusion rate, median (range)	0 units (0–6)	2 units (0–4)	NR	p<0.001
Death or inability to walk, n/N (%)	16/42 (39.0%)	19/42 (45.2%)	0.9 (0.5, 1.4)	p=0.57
60 day mortality, n/N (%)	5/42 (11.9%)	2/42 (4.8%)	2.5 (0.5, 12.2)	p=0.43
MI rate, n/N (%)	0/42 (0%)	0/42 (0%)	NR	NS
Stroke, n/N (%)	1/42 (2.4%)	0/42	NR	NS
Pneumonia, n/N (%)	2/42 (4.8%)	0/42 (0%)	NR	NS
Thromboembolism, n/N (%)	0/42 (0%)	1/42 (0%)	NR	NS
Clinical importance (1–4) 3 The confidence interval does not include any clinically important effects.		Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		
Hospital LOS, days (mean ± SD)	6.4 ± 3.4	6.3 ± 3.4	NR	NS
Clinical importance (1–4) 3 The confidence interval does not include any clinically important effects.		Relevance (1–5) 2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention		
Any other adverse effects None reported				
EXTERNAL VALIDITY				
Generalisability The results of this study may not be generalisable to a wider noncardiac surgery population				
Applicability The study was conducted in the USA and Scotland and is applicable to the Australian healthcare setting				

STUDY DETAILS				
Reference Foss NB, Kristensen MT, Jensen PS, Palm H, Krasheninnikoff M, Kehlet H. The effects of liberal versus restrictive transfusion thresholds on ambulation after hip fracture surgery. Transfusion. 2009;49:227–234				
Affiliation/Source of funds From the Department of Anesthesia, the Department of Orthopedic Surgery, and the Department of Physiotherapy, Hvidovre University Hospital, Hvidovre; and the Section of Surgical Pathophysiology, Rigshospitalet, Copenhagen University, Copenhagen, Denmark. Funding source: this work received financial support from IMK-almene fond (Copenhagen, Denmark). The authors had no conflict of interest to declare.				
Study design Randomised controlled trial N=120	Level of evidence II	Location/setting University hospital, Denmark		
Intervention Patients receiving a restrictive blood transfusion strategy of Hb <8 g/dL Sample Size N=60	Comparator(s) Patients receiving a liberal blood transfusion strategy of Hb <10 g/dL Sample Size N=60			
Population characteristics Patients with hip fracture				
Length of follow-up 3 days	Outcome(s) measured Cumulated ambulation score, LOS, cardiac complications, infectious complications and mortality			
INTERNAL VALIDITY				
Allocation	Comparison of study groups	Blinding	Treatment/ measurement bias	Follow-up (ITT)
Patients were randomly assigned into 2 groups. The randomisation was done via a computer generated list by a person not affiliated with the project	The randomisation did not succeed in making two completely comparable groups; there were a higher number of patients in the intervention group with an ASA rating of 3 than in the comparator group. there were also fewer patients with pins/screws in the comparator group. All other demographic characteristics were similar between the two groups	Upon inclusion the sealed envelope, containing the transfusion threshold and the patients study number on it, was placed in the patient charts next to the transfusion papers concealing the allocation to both the patient and the physiotherapists conducting the ambulation assessments, making the study double blind	The department's standardised multimodal rehabilitation was instituted in all patients.	ITT analysis

Overall quality assessment (descriptive) This was a good quality randomised controlled trial.				
RESULTS				
Outcome	Restrictive Strategy	Liberal Strategy	RR (95% CI)	Statistical Significance
Need for transfusion, n/N (%)	22/60 (37%)	44/60 (74%)	NR	p<0.01
Transfusion rate, median	2 units	1 unit	NR	p<0.0001
CAS rehabilitation score, median (range)	9 (9–13)	9 (9–15)	NR	p=0.46
Any cardiovascular event, n/N (%)	6/60 (10%)	1/60 (2%)	NR	p=0.05
Any infectious complication, n/N (%)	6/60 (10%)	11/60 (18%)	NR	p=0.19
Thromboembolic event, n/N (%)	1/60 (2%)	2/60 (3%)	NR	p=0.56
30 day mortality, n/N (%)	5/60 (8%)	0/60 (0%)	NR	p=0.02
Clinical importance (1–4) Unable to determine		Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		
Hospital LOS, days (mean ± SD)	17.0 ± 12.9	18.4 ± 14.4	NR	p=0.61
Hospital readmission in 30 days, n/N (%)	9/60 (15%)	11/60 (18%)	NR	p=0.31
Clinical importance (1–4) Unable to determine		Relevance (1–5) 2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention		
Any other adverse effects None reported				
EXTERNAL VALIDITY				
Generalisability The results of this study may not be generalisable to a wider noncardiac surgery population				
Applicability The study was conducted in Denmark and is probably applicable to the Australian healthcare setting				
Comments The authors conclude that although a liberal transfusion trigger did not result in increased ambulation scores, restrictive transfusion thresholds should be treated with caution in elderly high-risk hip fracture patients, until their safety has been proved in larger randomised studies.				

F6 Evidence summaries, Question 6

What is the effect of interventions to increase haemoglobin concentration on morbidity, mortality and need for red blood cell transfusion?

1. Effect of oral iron

Level II evidence: Cardiac studies

<table>
<tr><td colspan="5">STUDY DETAILS</td></tr>
<tr><td colspan="5">Reference Aufricht C, Ties M, Wimmer M, Haschke F, Pietschnig B, Herkner K. Iron supplementation in children after cardiopulmonary bypass for surgical repair of congenital heart disease. Pediatr Cardiol. 1994;15:167–169</td></tr>
<tr><td colspan="5">Affiliation/Source of funds
Department of Paediatric Cardiology, University of Vienna, Austria.
Funding source; Not reported</td></tr>
<tr><td colspan="2">Study design
RCT: n=17</td><td colspan="2">Level of evidence
II</td><td>Location/setting
Hospital in Vienna, Austria</td></tr>
<tr><td colspan="2">Intervention
Iron supplementation:
Postoperative iron supplementation (iron sulfate 5 mg/kg/day) from days 9 to 56
Sample size n=8</td><td colspan="3">Comparator
No active intervention
Sample size n=9</td></tr>
<tr><td colspan="5">Population characteristics
Children (mean age: 6.5 years) admitted for cardiopulmonary bypass</td></tr>
<tr><td colspan="2">Length of follow-up
Outcomes were measured on preoperative (day 0) and postoperative days 9 and 56</td><td colspan="3">Outcomes measured
Need for postoperative blood products and Hb levels (at operation closure, postoperative days 9 and 56)</td></tr>
<tr><td colspan="5">INTERNAL VALIDITY</td></tr>
<tr><td>Allocation</td><td>Results measurement bias</td><td>Blinding analysis</td><td>Treatment/ measurement bias</td><td>Follow-up (ITT)</td></tr>
<tr><td>Report indicates that treatments were randomly allocated, but did not elaborate on the method used</td><td>All patients investigated did not require blood transfusion. There was no difference in post therapy Hb values in both groups</td><td>Anaesthetist and cardiac surgeon performing the surgery were blinded to the trial's purpose to prevent bias on decisions concerning use of blood products during surgery</td><td>It is assumed that all patients were treated the same</td><td>All patients were followed-up and assessed as specified in the protocol. ITT analysis was performed</td></tr>
<tr><td colspan="5">Overall quality assessment (descriptive)
This was a fair quality randomised controlled trial</td></tr>
</table>

RESULTS				
Outcome	Intervention group	Control group	OR (95% CI)	Statistical Significance
Haemoglobin (g/dL)	12.1 ± 1.0	11.8 ± 1.0	NR	NS
Reticulocyte count (%)	11.5 ± 4.3	11.3 ± 4.2	NR	NS
Transferrin saturation (%)	33.5 ± 15.3	18.0 ± 11.9	NR	p<0.05
Free erythrocyte protoporphyrin (ng/mL)	0.57 ± 0.23	0.63 ± 0.69	NR	NS
Ferritin[a] (ng/mL)	22.4 ± 9.5	13.0 ± 6.3	NR	p<0.05
Ferritin ≤12 ng/mL (n/N(%))	0/8 (0%)	5/9 (55%)	NR	p<0.05

Clinical importance (1–4)	Relevance (1–5)
Unable to determine	2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention

EXTERNAL VALIDITY

Generalisability

This study was performed in children and may not be generalisable to an adult population

Applicability

The study was conducted in Austria and is probably applicable to the Australian healthcare setting

Comments

The authors conclude that anaemic children after cardiopulmonary bypass for surgical repair of congenital heart disease thus benefit from iron supplementation within the first postoperative weeks.

This study reports mean Hb levels at various time points and not changes in Hb levels.

STUDY DETAILS				
Reference Crosby L, Palarski VA, Cottington E, Cmolik B. Iron supplementation for acute blood loss anaemia after coronary artery bypass surgery: A randomised, placebo-controlled study. Heart Lung. 1994;23:493–499.				
Affiliation/Source of funds Cardiac and Pulmonary Rehab Services and the department of Surgery, Allegheny General Hospital, Pittsburgh; the cardiac Rehabilitation Department, Allegheny Valley Hospital, Natrona Heights; and the Allegheny Singer Research Institute, Pittsburgh. Funding source: Supported by a grant from the Allegheny Singer Research Institute.				
Study design Randomised controlled trial N = 128	Level of evidence II	Location/setting Perioperative acute care hospital and a surgery clinic for a single cardiothoracic physician group in the USA		
Intervention Iron supplementation: Postoperative treatment with oral iron (50 mg/day) N=28 Postoperative treatment with oral iron (200 mg/day) N=34	Comparator No treatment N=33 Placebo treatment N=26			
Population characteristics Males and postmenopausal females aged >50 years undergoing CABP surgery				
Length of follow-up Patients were followed up for 8 weeks	Outcomes measured Haemoglobin and ferritin levels at different time points			
INTERNAL VALIDITY				
Allocation	Results measurement bias	Blinding analysis	Treatment/ measurement bias	Follow-up (ITT)
Patients were randomised in a double-blind manner with a computer generated table of random numbers	No differences in baseline characteristics between the groups. Groups were compared with repeated analysis of variance	The study was double blinded	All patients were treated the same	Of the 128 patients randomised, 3 subjects did not complete the study and 4 were disqualified because of poor compliance or medical reasons resulting in 121 patients included in the analysis.
Overall quality assessment (descriptive) This was a fair quality randomised controlled trial. This study had several limitations. First the time interval, which allowed for a mean elapsed time of 59 days after surgery was based on convenience for subjects. Second the use of serum iron and ferritin as indicators of total body iron stores is recognised to be less than ideal. Third, a small percentage of the late visit laboratory analysis may not have been completed under identical conditions. Finally, aspirin or other antiplatelet and reinfused shed mediastinal blood were not controlled, which may have				

influenced the results.				
RESULTS				
Outcome	Intervention group	Control group	OR (95% CI)	Statistical Significance
Haemoglobin (g/dL) 6 days	NR	NR	NR	NS
Haemoglobin (g/dL) 59 days	NR	NR	NR	NS
Ferritin (ng/ml) 59 days	NR	NR	NR	NS
Clinical importance (1–4) Unable to determine		Relevance (1–5) 2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention		
EXTERNAL VALIDITY				
Generalisability The study was performed in adult patients undergoing coronary artery bypass surgery and is generalisable to a wider perioperative cardiac surgery population				
Applicability The study was conducted in the USA and is probably applicable to the Australian healthcare setting				
Comments The authors conclude that the use of oral iron supplements for the treatment of acute blood loss anaemia after uncomplicated coronary artery bypass surgery did not assist in restoring red blood cell mass or help maintain total body iron stores.				

STUDY DETAILS				
Reference Del Campo C, Lukman H, Mehta H, McKenzie FN. Iron therapy after cardiac operation: one prescription less? J Thorac Cardiovasc Surg. 1982;84:631–635				
Affiliation/Source of funds Division of Cardiovascular and Thoracic Surgery, University Hospital, London, Ontario, Canada. Funding source not reported				
Study design RCT: n=37	Level of evidence II	Location/setting University Hospital, Canada		
Intervention Iron supplementation: Patients receiving post operative oral iron (325 mg tid) Sample size n=18	Comparator No active intervention Sample size n=16			
Population characteristics Adult patients undergoing elective CABP				
Length of follow-up 6 weeks	Outcomes measured Hb levels			
INTERNAL VALIDITY				
Allocation	Results measurement bias	Blinding analysis	Treatment/ measurement bias	Follow-up (ITT)
Report indicates that treatments were randomly allocated upon discharge, but did not elaborate on the method used	There were no difference in baseline Hb and iron levels between the two groups	No blinding details are reported	Patients received a blood transfusion when there Hb fell below 10 g/dL. It is assumed patients were otherwise treated the same	ITT analysis was performed
Overall quality assessment (descriptive) This was a poor quality randomised controlled trial				
RESULTS				
Outcome	Intervention group	Control group	OR (95% CI)	Statistical Significance
Haemoglobin (g/dL) 10 days	11.3 ± 1.2	11.7 ± 1.0	NR	p>0.1
Haemoglobin (g/dL) 6 weeks	14.4 ± 1.2	14.8 ± 1.0	NR	p>0.1

Clinical importance (1–4)	Relevance (1–5)
Unable to determine	2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention
EXTERNAL VALIDITY	
Generalisability This study is probably generalisable to a wider perioperative cardiac surgery population	
Applicability The study was conducted in Canada and is probably applicable to the Australian healthcare setting	
Comments The authors conclude that iron therapy did not modify the haematologic picture, and they conclude that it is not necessary in the average patient after a cardiac operation.	

Level II evidence: Noncardiac studies

STUDY DETAILS				
Reference Andrews CM, Lane DW, Bradley JG. Iron pre-load for major joint replacement. Transfus Med. 1997;7:281–286				
Affiliation/Source of funds Scarborough Hospital, Woodlands Drive, Scarborough, North Yorkshire. , UK Funding source: the Wishbone Trust for funding purchase of the HemoCue haemoglobinometer				
Study design RCT: n=75	Level of evidence II	Location/setting Hospital, UK		
Intervention Iron supplementation: Preoperative treatment with oral iron (200 mg bid) Sample size n=35	Comparator No active intervention: Preoperative treatment with placebo tablets Sample size n=40			
Population characteristics Adult patients undergoing THR or TKR				
Length of follow-up NR	Outcomes measured Change in Hb concentration, units of blood transfused			
INTERNAL VALIDITY				
Allocation	Results measurement bias	Blinding analysis	Treatment/ measurement bias	Follow-up (ITT)
Patients were randomised using a system of sequentially numbered sealed envelopes	There were no difference in baseline demographic chartacteristics between the two groups	No blinding details are reported	Patients were transfused on the day of surgery at the discretion of the anaesthetist and thereafter if the HB fell below 10 g/dL	6 patients were excluded from the iron group after randomisation.
Overall quality assessment (descriptive) This was a fair quality randomised controlled trial				
RESULTS				
Outcome	Intervention group	Control group	OR (95% CI)	Statistical Significance
Change in Hb[a] (g/dL)	–0.4	–1.3	NR	p<0.001
Mean units of blood transfused	1.7	1.8	NR	NS
Repeat transfusions (n/N)	0/35	3/40	NR	NS
Clinical importance (1–4) Unable to determine		Relevance (1–5) 2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention		

EXTERNAL VALIDITY
Generalisability This study was performed in patients undergoing orthopaedic surgery and may not be generalisable to a wider perioperative noncardiac surgery population
Applicability The study was conducted in the UK and is probably applicable to the Australian healthcare setting
Comments The authors conclude that iron supplementation in patients without obvious anaemia protects against a fall in Hb during the immediate postoperative period, suggesting a widespread underlying depletion of iron stores in this groupo despite a normal Hb. Preoperative iron supplements may reduce transfusion requirements as part of a co-ordinated strategy in this group of patients. The data from this study was not included in development of recommendations for this question as it offered only Level IV evidence for the intervention relevant to Question 3 and higher level evidence was available.

STUDY DETAILS				
Reference Lidder PG, Sanders G, Whitehead E, Douie WJ, Mellor N, Lewis SJ, Hosie KB. Preoperative oral iron supplementation reduces blood transfusion in colorectal surgery—a prospective, randomised, controlled trial. Ann R Coll Surg Engl. 2007;89:418–421				
Affiliation/Source of funds Department of Colorectal Surgery, Derriford Hospital, Plymouth, UK Funding source: none reported				
Study design RCT: n=45	Level of evidence II	Location/setting Hospital, UK		
Intervention Iron supplementation: Preoperative treatment with oral iron (200 mg tid) Sample size n=23	Comparator No active intervention: No treatment (standard care) Sample size n=22			
Population characteristics Patients undergoing surgery for colorectal cancer. It is unclear if all patients had preoperative anaemia				
Length of follow-up NR	Outcomes measured Hb concentration, need for blood transfusion			
INTERNAL VALIDITY				
Allocation	Results measurement bias	Blinding analysis	Treatment/ measurement bias	Follow-up (ITT)
Patients were randomised by telephone to a distant centre, to recive ferrous sulphate until surgery or standard care	There were no difference between the two groups in terms of age, sex, operative procedure, operative duration, estimated blood loss or tumor stage	The clinical team (surgeons, nurses, anaesthetists) were blinded to treatment allocation	Postoperatively, patients underwent standard care including adherence to a transfusion protocol	A total of 4 patients (2 from each group) were excluded from the study and subsequent analysis
Overall quality assessment (descriptive) This was a good quality randomised controlled trial				
RESULTS				

Outcome	Intervention group	Control group	OR (95% CI)	Statistical Significance
Number of patients transfused (n/N (%))	6/23 (26%)	13/22 (59%)	0.24 (0.06, 1.01)	p<0.031
Total units transfused	15	47	Absolute difference: 32 units	NR
Mean units transfused (range)	0 (0–4)	2 (0–11)	NR	p<0.031

Clinical importance (1–4)	Relevance (1–5)
Unable to determine	2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention
EXTERNAL VALIDITY	
Generalisability This study was performed in patients undergoing colorectal surgery for malignancies and may not be generalisable to a wider perioperative noncardiac surgery population	
Applicability The study was conducted in the UK and is probably applicable to the Australian healthcare setting	
Comments The authors conclude that preoperative iron supplementation in patients undergoing colorectal surgery offers a simple, inexpensive method of reducing blood transfusions	

STUDY DETAILS				
Reference Mundy GM, Birtwistle SJ, Power RA. The effect of iron supplementation on the level of haemoglobin after lower limb arthroplasty. J Bone Jt Surg Ser B. 2005;87:213–217				
Affiliation/Source of funds Glenfield Hospital, Leicester, England, UK Funding source: This study was funded by the Wishbone Trust. The authors declared that no benefits in any form have been or will be received from a commercial party related directly or indirectly to the subject of the article				
Study design RCT: n=99	Level of evidence II	Location/setting Hospital, UK		
Intervention Iron supplementation: Oral ferrous sulphate (200 mg containing 65 mg elemental iron) thrice daily for 3 weeks, beginning on postoperative day 2 Sample size n=61	Comparator No active intervention: Non-active placebo of intervention administered similarly for same duration Sample size n=59			
Population characteristics Patients undergoing elective primary total hip or knee arthroplasty				
Length of follow-up 6 weeks	Outcomes measured Hb concentration			
INTERNAL VALIDITY				
Allocation	Results measurement bias	Blinding analysis	Treatment/ measurement bias	Follow-up (ITT)
Patients were randomised based on scientific tables. Numbers chosen from rows of 10; even numbers allocated the intervention, and odd to placebo. Hospital research pharmacist contracted to assign treatment allocation	There were no difference between the two groups in terms of baseline demographics	Surgeons and patients were blinded	It appears that all patients were treated the same	A cohort of 120 patients was randomised, but 21 were excluded after randomisation due to non-compliance and meeting exclusion criteria. Of these, complete data were available for 91 patients
Overall quality assessment (descriptive) This was a good quality randomised controlled trial				

RESULTS				
Outcome	Intervention group	Control group	OR (95% CI)	Statistical Significance
Percentage recovery in Hb 3 weeks after surgery (men)	85.1%	86.6%	NR	p=0.45
Percentage recovery in Hb 3 weeks after surgery (women)	86.7%	88.5%	NR	p=0.35
Further percentage recovery in Hb 6 weeks after surgery (men)	6%	3%	NR	p<0.01
Further percentage recovery in Hb 6 weeks after surgery (women)	5%	1.5%	NR	p<0.05
Clinical importance (1–4) Unable to determine		Relevance (1–5) 2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention		
EXTERNAL VALIDITY				
Generalisability This study was performed in patients undergoing orthopaedic surgery and may not be generalisable to a wider perioperative noncardiac surgery population				
Applicability The study was conducted in the UK and is probably applicable to the Australian healthcare setting				
Comments The authors conclude that the administration of iron supplements after elective total hip or total knee arthroplasty does not appear to be worthwhile				

STUDY DETAILS				
Reference Weatherall M, Maling TJ. Oral iron therapy for anaemia after orthopaedic surgery: Randomised clinical trial. ANZ J Surg. 2004;74:1049–1051				
Affiliation/Source of funds Department of Medicine, Wellington School of medicine and Health Sciences and Wellington Hospital, Wellington South, Wellington, New Zealand Funding source: The research was funded by the New Zealand Lottery Grants Board and the Wellington School of Medicine and Health Sciences				
Study design RCT: n=72	Level of evidence II	Location/setting Hospital, New Zealand		
Intervention Iron supplementation: Post-surgical iron therapy Ferrous sulphate (325 mg) once daily for 10 weeks post-surgery Sample size n=36	Comparator Folic acid: Folic acid (5 mg) once daily for 10 weeks post-surgery Sample size n=36			
Population characteristics Patients who underwent elective hip or knee replacement surgery with normal iron and folic acid stores				
Length of follow-up 10 weeks	Outcomes measured Hb level, QoL assessed via VAS			
INTERNAL VALIDITY				
Allocation	Results measurement bias	Blinding analysis	Treatment/ measurement bias	Follow-up (ITT)
Randomised allocation based on computer generated random ordering of bottles. Newly recruited patients were allocated the next bottle number in the generated sequence by phone contact with the principal researcher	There were no differences between the two groups in terms of baseline demographics	Patients and investigators were blinded and similar bottles were used as packaging for the tablets but the tablet preparations were not identical in appearance. Controlling the appearance of both tablets was deemed unnecessary since the darkening of stools as a side effect of iron therapy would have revealed the treatment allocation to patients and investigators	It appears that all patients were treated the same	72 patients were randomised (n=36 in each group); 5 patients withdrew before the first outcome measurement time point and were not included in any analysis

<table>
<tr><td colspan="5">Overall quality assessment (descriptive)
This was a fair quality randomised controlled trial</td></tr>
<tr><td colspan="5">RESULTS</td></tr>
<tr><td>Outcome</td><td>Intervention group</td><td>Control group</td><td>OR (95% CI)</td><td>Statistical Significance</td></tr>
<tr><td>Hb level (g/L)</td><td>132.8 ± 13.4</td><td>128.0 ± 10.6</td><td>Difference: 4.8 (–1.2, 6.8)</td><td>p=0.15</td></tr>
<tr><td colspan="2">Clinical importance (1–4)
Unable to determine</td><td colspan="3">Relevance (1–5)
2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention</td></tr>
<tr><td>QoL (mm, 100 mm VAS)</td><td>78.6 ± 18.2</td><td>77.4 ± 17.0</td><td>NR</td><td>p=0.78</td></tr>
<tr><td colspan="2">Clinical importance (1–4)
Unable to determine</td><td colspan="3">Relevance (1–5)
1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival</td></tr>
<tr><td colspan="5">EXTERNAL VALIDITY</td></tr>
<tr><td colspan="5">Generalisability
This study was performed in patients undergoing orthopaedic surgery and may not be generalisable to a wider perioperative noncardiac surgery population</td></tr>
<tr><td colspan="5">Applicability
The study was conducted in New Zealand and is probably applicable to the Australian healthcare setting</td></tr>
<tr><td colspan="5">Comments
The authors conclude that iron taken after elective hip or knee replacement surgery does not result in higher haemoglobin 10 weeks after surgery, or a faster rate of increase in haemoglobin than a control treatment</td></tr>
</table>

Level III evidence: Noncardiac studies

<table>
<tr><td colspan="5">STUDY DETAILS</td></tr>
<tr><td colspan="5">Reference Cuenca J, Garcia-Erce JA, Martinez F, Cardona R, Perez-Serrano L, Munoz M. Preoperative haematinics and transfusion protocol reduce the need for transfusion after total knee replacement. Int J Surg. 2007;5:89–94</td></tr>
<tr><td colspan="5">Affiliation/Source of funds
Department of Orthopaedic and Trauma Surgery, and Department of Haematology, University Hospital “Miguel Servet”, Avenida Isabel la Catolica, Zaragoza, Spain
Funding source: None reported</td></tr>
<tr><td colspan="2">Study design
Historical control
n=312</td><td colspan="2">Level of evidence
III-3</td><td>Location/setting
Hospital, Spain</td></tr>
<tr><td colspan="3">Intervention
Iron supplementation:
Preoperative treatment with iron (256 mg/day), Vitamin C (1000 mg/day) and folic acid (5 mg/day)
Sample size n=156</td><td colspan="2">Comparator
No treatment
Sample size n=156</td></tr>
<tr><td colspan="5">Population characteristics
Unilateral TKR patients</td></tr>
<tr><td colspan="3">Length of follow-up
NR</td><td colspan="2">Outcomes measured
Hb concentration, number of patients transfused, transfusion index, hospital LOS</td></tr>
<tr><td colspan="5">INTERNAL VALIDITY</td></tr>
<tr><td>Allocation</td><td>Results measurement bias</td><td>Blinding analysis</td><td>Treatment/ measurement bias</td><td>Follow-up (ITT)</td></tr>
<tr><td>All patients scheduled for elective TKR were interviewed by the surgeon at least 1 month before surgery to enter in a blood saving protocol. A previous series of TKR patients who met the inclusion criteria and underwent surgery before the blood saving protocol was implemented</td><td>There were no statistically significant differences between groups regarding age, gender, anaesthetic risk, Hb at preop assessment and hospital LOS</td><td>The study was not blinded</td><td>It is unclear if all patients were treated the same</td><td>ITT analysis</td></tr>
</table>

Overall quality assessment (descriptive) This was a fair quality historical control study				
RESULTS				
Outcome	Intervention group	Control group	OR (95% CI)	Statistical Significance
Postoperative haemoglobin (mg/dL)	10.8 ± 1.4	10.5 ± 1.2	NR	p<0.05[a]
Rate of blood transfusion (n/N [%]) Preoperative Hb <130 g/L Preoperative Hb >130 g/L	9/156 (5.8%) 19.3% 2.4%	50/156 (32.0%) 61.5% 26.1%	OR=0.13 [0.05, 0.28]	p<0.01 χ^2=10.6, p<0.01 χ^2=28.9, p<0.001
Clinical importance (1–4) 1 A clinically important benefit for the full range of plausible estimates		Relevance (1–5) 2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention		
Transfusion index (units/transfused patient)	1.78 ± 0.44	2.22 ± 0.65	NR	p<0.05
Length of hospital stay (days)	11 ± 5	12 ± 4	NR	NS
Clinical importance (1–4) 1 Unable to determine		Relevance (1–5) 2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention		
EXTERNAL VALIDITY				
Generalisability This study was performed in patients undergoing orthopaedic surgery and may not be generalisable to a wider perioperative noncardiac surgery population				
Applicability The study was conducted in Spain and is probably applicable to the Australian healthcare setting				

STUDY DETAILS				
Reference Okuyama M, Ikeda K, Shibata T, Tsukahara Y, Kitada M, Shimano T. Preoperative iron supplementation and intraoperative transfusion during colorectal cancer surgery. Sur Today. 2005;35:36–40				
Affiliation/Source of funds Department of Surgery, Toyonaka Municipal Hospital Toyonaka, Osaka, Japan Funding source: none reported				
Study design Retrospective cohort study n=116	Level of evidence III-2	Location/setting Toyonaka Municipal Hospital, Osaka, Japan		
Intervention Iron supplementation: Preoperative oral iron therapy (200 mg/day) Sample size n=32	Comparator No treatment: Sample size n=84			
Population characteristics Anaemic colorectal cancer surgery patients (Hb <10 g/dL)				
Length of follow-up Not reported	Outcomes measured Hb concentration, number of patients transfused			
INTERNAL VALIDITY				
Allocation	Results measurement bias	Blinding analysis	Treatment/ measurement bias	Follow-up (ITT)
The study does not report how patients were allocated to treatment	There were no differences between the two groups in terms of baseline demographics	No blinding details are reported	The criteria for transfusion were an intraoperative Hb of about 7 g/dL with unstable haemodynamics.	ITT analysis
Overall quality assessment (descriptive) This was a fair quality retrospective cohort study.				
RESULTS				
Outcome	Intervention group	Control group	OR (95% CI)	Statistical Significance
Preoperative haemoglobin (mg/dL)	10.1 ± 1.3	8.9 ± 1.3	NR	p<0.0001
Postoperative haemoglobin (mg/dL)	9.5 ± 1.0	9.5 ± 1.5	NR	p=0.82
Clinical importance (1–4) Unable to determine	Relevance (1–5) 2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention			

Rate of intraoperative blood transfusion (n/N [%])	3/32 (9.4%)	23/84 (27.4%)	OR= 0.27 (0.05, 1.03)	p<0.05
Clinical importance (1–4) 2 The point estimate of effect is clinically important BUT the confidence interval includes clinically unimportant effects.		Relevance (1–5) 2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention		
EXTERNAL VALIDITY				
Generalisability This study was performed in anaemic patients undergoing colorectal cancer surgery and may not be generalisable to a wider perioperative noncardiac surgery population				
Applicability The study was conducted in Japan and may not be applicable to the Australian healthcare setting				
Comments The authors conclude that iron supplementation for at least 2 weeks before colorectal cancer surgery increases Hb and Ht values in anaemic patients, and reduces the need for intraoperative transfusion				

2. Effect of intravenous iron

Level III evidence: Noncardiac studies

STUDY DETAILS				
Reference Cuenca J, Garcia-Erce JA, Munoz M, Izuel M, Martinez AA, Herrera A. Patients with pertrochanteric hip fracture may benefit from preoperative intravenous iron therapy: a pilot study. Transfusion. 2004;44:1447–1452				
Affiliation/Source of funds From the Departments of Orthopaedic and Trauma Surgery, Haematology, and Pharmacy, "Miguel Servet" University Hospital, Zaragoza; and GIEMSA, School of Medicine, University of Malaga, Malaga, Spain Funding source: None reported				
Study design Historical control n=157	Level of evidence III-3	Location/setting Univerity hospital, Spain		
Intervention Iron supplementation: Preoperative iron (100 mg); 2–3 doses before surgery Sample size n=55	Comparator No treatment No preoperative iron therapy Sample size n=102			
Population characteristics Patients undergoing hip fracture repair surgery				
Length of follow-up 30 days	Outcomes measured Hb concentration, number of patients transfused, transfusion rate, infection rate, 30 day mortality, hospital LOS			
INTERNAL VALIDITY				
Allocation	Results measurement bias	Blinding analysis	Treatment/ measurement bias	Follow-up (ITT)
Patients undergoing surgery for PHF repair between Oct 2002 and Mar 2003 received IV iron. A previous series of PHF patients, operated on between Jan 2000 and Dec 2001 who had not received IV iron served as controls	There were no statistically significant differences between in respect to patient's age, sex and perioperative Hb	The study was not blinded	It is unclear if all patients were treated the same	ITT analysis

Overall quality assessment (descriptive) This was a fair quality historical control study				
RESULTS				
Outcome	Intervention group	Control group	OR (95% CI)	Statistical Significance
Postoperative haemoglobin level (g/dL)	9.5 ± 1.7	9.6 ± 1.6	NR	NS
Number of patients transfused (n/N (%))	24/55 (43.6%)	57/102 (55.9%)	NR	NS
Transfusion rate (units per patient)	0.89 ± 1.22	1.27 ± 1.34	NR	NS
Clinical importance (1–4) 1 Unable to determine		Relevance (1–5) 2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention		
Number of infections (n/N (%))	9/55 (16.4%)	34/102 (33.3)	NR	p<0.001
30 day mortality (n/N (%))	5/55 (8.9%)	17/102 (16.7%)	NR	p=0.22
Clinical importance (1–4) 1 Unable to determine		Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		
Length of hospital stay (days)	12.6 ± 4.4	14.3 ± 3.6	NR	NS
Clinical importance (1–4) 1 Unable to determine		Relevance (1–5) 2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention		
EXTERNAL VALIDITY				
Generalisability This study was performed in patients undergoing orthopaedic surgery and may not be generalisable to a wider perioperative noncardiac surgery population				
Applicability The study was conducted in Spain and is probably applicable to the Australian healthcare setting				
Comment The authors conclude that the administration of IV iron sucrose seems to reduce blood transfusion requirements in patients with PHF and is associated with a lower postoperative morbidity				

STUDY DETAILS				
Reference Cuenca J, Garcia-Erce JA, Martinez F, Solano VM, Molina J, Munoz M. Role of parenteral iron in the management of anaemia in the elderly patient undergoing displaced subcapital hip fracture repair: Preliminary data. Arch Orthop Trauma Surg. 2005;125:342–347				
Affiliation/Source of funds From the Departments of Orthopaedic and Trauma Surgery, Haematology and Haemotherapy, and Preventative Medicine, "Miguel Servet" University Hospital, Zaragoza; and Department of Orthopaedic and Trauma Surgery, Hospital of Barbastro, Huesca, Spain Funding source: None reported				
Study design Historical control n=77	Level of evidence III-3	Location/setting Univerity hospital, Spain		
Intervention Iron supplementation: Preoperative IV iron (100 mg); 2–3 doses before surgery Sample size n=20	Comparator No treatment No preoperative iron therapy Sample size n=57			
Population characteristics Patients undergoing hip fracture repair surgery				
Length of follow-up 30 days	Outcomes measured Hb concentration, number of patients transfused, transfusion rate, infection rate, 30 day mortality, hospital LOS			
INTERNAL VALIDITY				
Allocation	Results measurement bias	Blinding analysis	Treatment/ measurement bias	Follow-up (ITT)
Patients >65 y with a DSHF admitted between Oct 2002 and Mar 2003 received IV iron. A previous series of DSHF patients, operated on between Jan 2000 and Dec 2001 who had not received IV iron served as controls	There were no statistically significant differences between in respect to patient's age, sex, ASA classification or perioperative Hb	The study was not blinded	It is unclear if all patients were treated the same	ITT analysis
Overall quality assessment (descriptive) This was a fair quality historical control study				

RESULTS				
Outcome	Intervention group	Control group	OR (95% CI)	Statistical Significance
Postoperative haemoglobin level (g/dL)	9.6 ± 1.3	10.1 ± 1.4	NR	p=0.178
Number of patients transfused (n/N (%))	3/20 (15.0%)	21/57 (36.8%)	NR	p=0.059
Transfusion rate (units per patient)	0.26 ± 0.65	0.77 ± 1.09	NR	p=0.18
Clinical importance (1–4) 1 Unable to determine		Relevance (1–5) 2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention		
Number of infections (n/N (%))	3/20 (15.0%)	19/57 (33.3%)	NR	p=0.099
30 day mortality (n/N (%))	0/20 (0.0%)	11/57 (19.3%)	NR	p=0.034
Clinical importance (1–4) 1 Unable to determine		Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		
Length of hospital stay (days)	11.9 ± 2.1	14.1 ± 3.1	NR	p=0.004
Clinical importance (1–4) 1 Unable to determine		Relevance (1–5) 2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention		
EXTERNAL VALIDITY				
Generalisability This study was performed in patients undergoing orthopaedic surgery and may not be generalisable to a wider perioperative noncardiac surgery population				
Applicability The study was conducted in Spain and is probably applicable to the Australian healthcare setting				
Comment The authors conclude that preoperative parenteral iron administration could be a safe and effective way to reduce the transfusion requirements in DSHF patients. This reduction in the transfusion requirements is accompanied by a reduction in the morbid-mortality rate and LOS.				

STUDY DETAILS				
Reference Munoz M, Naveira E, Seara J, Palmer H, Cuenca J, Garcia-Erce JA. Role of parenteral iron in transfusion requirements after total hip replacement. A pilot study. Transfus Med. 2006;16:137–142				
Affiliation/Source of funds GIEMSA, School of Medicine, University of Malaga, Postoperative Care Unit, Orthopaedic Surgery, and Anaesthesiology, Clinica Santa Elena, Torremolinos, Malaga, Spain Funding source: This study was supported by a grant FIS PI 02/1826 from Instituto de Salud Carlos III (Spain) and the European Union				
Study design Historical control n=46	Level of evidence III	Location/setting Univerity hospital, Spain		
Intervention Iron supplementation: Postoperative IV iron (100 mg/day) for 3 days starting after surgery Sample size n=24	Comparator No treatment No postoperative iron therapy Sample size n=22			
Population characteristics Patients undergoing THR surgery				
Length of follow-up Time in hospital	Outcomes measured Number of patients transfused, transfusion rate, infection rate, hospital LOS			
INTERNAL VALIDITY				
Allocation	Results measurement bias	Blinding analysis	Treatment/ measurement bias	Follow-up (ITT)
Patients undergoing surgery for THR received iron therapy postoperatively; a retrospective series of THR patients who did not receive iron was the control group	There were no statistically significant differences between in respect to patient's age, sex, comorbidities, type of anaesthesia	The study was not blinded	All patients were treated the same; however, blood transfusion was given according to a transfusion protocol when Hb level fell below 8 g/dL or symptoms of acute anaemia were present	ITT analysis
Overall quality assessment (descriptive) This was a fair quality historical control study				

RESULTS				
Outcome	Intervention group	Control group	OR (95% CI)	Statistical Significance
Number of patients transfused (n/N (%))	11/24 (46%)	16/22 (73%)	NR	p=0.07
Transfusion rate (units per patient)[b]	0.96 ± 1.12	1.68 ± 1.17	NR	p=0.04
Transfusion rate (units per patient)	1.12 ± 1.17	2.18 ± 0.98	NR	p=0.019
Clinical importance (1–4) 1 Unable to determine		Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		
Number of infections (n/N (%))	2/24 (8%)	5/22 (23%)	NR	p=0.23
In-hospital mortality (n/N (%))	0/24 (0%)	1/22 (4%)	NR	p=0.49
Clinical importance (1–4) 1 Unable to determine		Relevance (1–5) 2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention		
Length of hospital stay (days)	10.1 ± 4.4	11.4 ± 3.4	NR	p=0.29
Clinical importance (1–4) 1 Unable to determine		Relevance (1–5) 2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention		
EXTERNAL VALIDITY				
Generalisability This study was performed in patients undergoing orthopaedic surgery and may not be generalisable to a wider perioperative noncardiac surgery population				
Applicability The study was conducted in Spain and is probably applicable to the Australian healthcare setting				
Comment The authors conclude that postoperative parenteral iron administration could be a safe and effective way to reduce the transfusion requirements in THR patients.				

3. Effect of intravenous iron versus oral iron

Level II evidence: Cardiac studies

STUDY DETAILS

Reference Madi-Jebara SN, Sleilaty GS, Achouh PE, Yazigi AG, Haddad FA, Hayek GM, et al. Postoperative intravenous iron used alone or in combination with low-dose erythropoietin is not effective for correction of anaemia after cardiac surgery. J Cardiothorac Vasc Anesth. 2004;18:59–63				
Affiliation/Source of funds From the Departments of Anesthesiology and Thoracic and Cardiovascular Surgery, Hotel-Dieu de France, Universite Saint-Joseph, Beirut, Lebanon Funding source: None reported				
Study design RCT n=157	Level of evidence II	Location/setting Univerity hospital, Lebanon		
Intervention Iron supplementation: A postoperative single dose of EPO (300 U/kg) and IV iron (200 mg/day) Sample size n=40 IV iron alone (200 mg/day) Sample size n=40	Comparator No treatment Patients received placebo Sample size n=40			
Population characteristics CPB patients who had post-pump Hb in the range 7–10 g/dL				
Length of follow-up 30 days	Outcomes measured Hb and ferritin levels			
INTERNAL VALIDITY				
Allocation	Results measurement bias	Blinding analysis	Treatment/ measurement bias	Follow-up (ITT)
Treatment allocation blocks were distributed among surgeons according to caseload	There were no statistically significant differences in baseline demographic characteristics between groups	Double-blind study	It is unclear if all patients were treated the same	A total of 26 patients were transfused and excluded from the study and further analysis
Overall quality assessment (descriptive) This was a good quality randomised controlled trial				
RESULTS				
Outcome	Intervention group	Control group	OR (95% CI)	Statistical Significance
Need for transfusions (n/N (%)	10/40 (25%)	9/40 (22%)	NR	NS
Transfusion rate (units/person)	2.3	2.3	NR	NS
Hb day 30 (g/dL)	12.18 ± 1.04	11.87 ± 1.21	NR	NS

Ferritin day 15 (ng/mL)	489.45 ± 303.24	253.72 ± 154.27	NR	p<0.001
Clinical importance (1–4) 1 Unable to determine		Relevance (1–5) 2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention		
EXTERNAL VALIDITY				
Generalisability This study was performed in patients undergoing cardiac surgery and is generalisable to a perioperative cardiac surgery population				
Applicability The study was conducted in Lebanon and may not be applicable to the Australian healthcare setting				
Comment The authors conclude that postoperative intravenous iron supplementation alone or in combination with EPO is not effective in correcting anaemia after cardiac surgery				

STUDY DETAILS				
Reference Karkouti K, McCluskey SA, Ghannam M, Salpeter MJ, Quirt I, Yau TM. Intravenous iron and recombinant erythropoietin for the treatment of postoperative anaemia. Can J Anesth. 2006a; 53:11–19				
Affiliation/Source of funds From the Departments of Anaesthesia, Health Policy, Management , and Evaluation, Division of Hematology, and the Division of Cardiac Surgery, University of Toronto, University Health Network, Toronto, Ontario, Canada Funding source: The Physicians' Services Incorporated, Ontario, Canada, funded this study. Ortho Biotech donated recombinant erythropoietin. K Karkouti is supported in part by the Canadian Institutes of Health Research and the Canadian Blood Services. TM Yau is supported in part by the Canadian Institutes of Health research and the Heart and Stroke Foundation of Ontario. K Karkouti and SA McCluskey have received research funding and speakers' fees from Ortho Biotech				
Study design RCT n=38	Level of evidence II	Location/setting Tertiary/quarternary care hospital affiliated with the University of Toronto, Canada		
Intervention Iron supplementation: A postoperative single dose of EPO (300 U/kg) and IV iron (200 mg/day) for 3 days plus oral iron (150 mg/day) Sample size n=12 IV iron alone (200 mg/day) plus oral iron (150 mg/day) Sample size n=13	Comparator Control group received oral iron (150 mg/day) N=13 Sample size n=13			
Population characteristics Adult patients who underwent open heart surgery, total hip arthroplasty or spinal fusion with Hb range 7–9 g/dL				
Length of follow-up 7 days	Outcomes measured Hb levels			
INTERNAL VALIDITY				
Allocation	Results measurement bias	Blinding analysis	Treatment/ measurement bias	Follow-up (ITT)
A restricted stratified randomisation scheme was used to allocate the patients to the 3 treatment arms. Randomisation was by a computer generated table of random numbers	There were no statistically significant differences in baseline demographic characteristics between groups	An unblinded pharmacist prepared all medication according to the randomisation schedule to ensure blinding of other study peronnel	It is unclear if all patients were treated the same	A total of 7 patients were lost to follow-up and were excluded from the analysis
Overall quality assessment (descriptive) This was a fair quality randomised controlled trial				

RESULTS				
Outcome	Intervention group	Control group	OR (95% CI)	Statistical Significance
Need for transfusion (n/N (%))	2/13 (15.4%)	4/13 (30.1%)	NR	NS
Hb day 42 (g/dL)	12.7 ± 0.6	12.0 ± 1.3	NR	NS
Ferritin day 7 (ng/mL)	513 ± 221	311 ± 286	NR	NS
Clinical importance (1–4) 1 Unable to determine		Relevance (1–5) 2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention		
EXTERNAL VALIDITY				
Generalisability This study was performed in patients undergoing cardiac surgery or orthopaedic surgery and is generalisable to a wider perioperative surgery population				
Applicability The study was conducted in Canada and is probably applicable to the Australian healthcare setting				
Comment The authors conclude that early postoperative treatment with iv iron alone or in combination with EPO does not appear to accelerate early recovery from postoperative anaemia				

Level II evidence: Noncardiac studies

<table>
<tr><td colspan="5">STUDY DETAILS</td></tr>
<tr><td colspan="5">Reference Kim YH, Chung HH, Kang SB, Kim SC, Kim YT. Safety and usefulness of intravenous iron sucrose in the management of preoperative anaemia in patients with menorrhagia: a phase IV, open-label, prospective, randomised study. Acta Haematol. 2009;121:37–41</td></tr>
<tr><td colspan="5">Affiliation/Source of funds
Department of Obstetrics and Gynecology, College of Medicine, Seoul National University; Department of Obstetrics and Gynecology, College of Medicine, Ewha Woman's University, and Department of Obstetrics and Gynecology, Yonsel University College of Medicine, Seoul, Korea
Funding source: None reported</td></tr>
<tr><td colspan="2">Study design
RCT
n=76</td><td colspan="2">Level of evidence
II</td><td>Location/setting
Univerity hospital, Seoul, Korea</td></tr>
<tr><td colspan="3">Intervention
Preoperative IV iron therapy: weight x [target Hb – actual Hb] x 2.4 ÷ 500 mg 3 times weekly for 3 weeks
Sample size n=39</td><td colspan="2">Comparator
Oral iron (80 mg/day) for 3 weeks before surgery
Sample size n=37</td></tr>
<tr><td colspan="5">Population characteristics
Menorrhagic patients with established iron deficient anaemia scheduled to undergo surgical treatment</td></tr>
<tr><td colspan="3">Length of follow-up
Not reported</td><td colspan="2">Outcomes measured
Hb concentration, ferritin concentration</td></tr>
<tr><td colspan="5">INTERNAL VALIDITY</td></tr>
<tr><td>Allocation</td><td>Results measurement bias</td><td>Blinding analysis</td><td>Treatment/ measurement bias</td><td>Follow-up (ITT)</td></tr>
<tr><td>Patients were randomised according to a computer-generated randomisation table</td><td>There were no statistically significant differences in baseline demographic characteristics between groups</td><td>Open label study</td><td>It is unclear if all patients were treated the same</td><td>Per protocol analysis for efficacy and ITT for safety. A total of 20 patients were excluded from the efficacy analysis</td></tr>
<tr><td colspan="5">Overall quality assessment (descriptive)
This was a poor quality randomised controlled trial</td></tr>
</table>

RESULTS				
Outcome	Intervention group	Control group	OR (95% CI)	Statistical Significance
Postoperative Hb level (g/dL)	10.5 ± 1.4	8.6 ± 1.4	NR	p<0.0001
Postoperative ferritin level (μg/L)	231.4 ± 561.7	9.7 ± 10.3	NR	p<0.0001
Clinical importance (1–4) 1 Unable to determine		Relevance (1–5) 2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention		
EXTERNAL VALIDITY				
Generalisability This study was performed in women undergoing surgery for menorrhagia and may not be generalisable to a wider perioperative noncardiac surgical population				
Applicability The study was conducted in Korea and may not be applicable to the Australian healthcare setting				
Comment The authors conclude that preoperative intravenous iron administration is more effective than oral iron and is as safe as oral iron therapy in the correction of preoperative anaemia due to menorrhagia				

4. Effect of erythropoietin with or without iron

Level I evidence: Noncardiac studies

<table>
<tr><td colspan="5">STUDY DETAILS</td></tr>
<tr><td colspan="5">Reference Devon KM, McLeod RS. Pre and perioperative erythropoietin for reducing allogeneic blood transfusions in colorectal cancer surgery. Cochrane Database Syst Rev 2009;(1): CD007148. DOI: 10.1002/14651858.pub2</td></tr>
<tr><td colspan="5">Affiliation/Source of funds:
Department of Surgery, University of Toronto, Mount Sinai Hospital, Toronto, Canada; Division of General Surgery, Mount Sinai Hospital, Toronto, Canada
Funding source: No external funding sources; authors declared that they had no conflict of interest</td></tr>
<tr><td colspan="2">Study design: Systematic Review
N = 4 studies</td><td colspan="2">Level of evidence: I</td><td>Location/setting: NA</td></tr>
<tr><td colspan="5">Population characteristics: Studies were included if it was a randomised controlled trial of erythropoietin versus placebo or no treatment/standard of care. The study must have reported one of the primary or secondary outcomes and included anaemic patients undergoing surgery for colorectal cancer</td></tr>
<tr><td colspan="2">Length of follow-up: NA</td><td colspan="3">Outcome(s) measured: Proportion of transfused patients, transfusion rate, Hb levels, 30 day and/or hospital mortality, thrombotic events</td></tr>
<tr><td colspan="5">INTERNAL VALIDITY</td></tr>
<tr><td>Allocation
Assessed</td><td>Comparison of study groups
Studies were compared by meta-analysis</td><td>Blinding
Assessed</td><td>Treatment/measurement bias
Assessed</td><td>Follow-up (ITT)
ITT analysis.</td></tr>
<tr><td colspan="5">Overall quality assessment (descriptive):
This study was a good quality systematic review.</td></tr>
<tr><td colspan="5">RESULTS</td></tr>
<tr><td colspan="2">Outcome</td><td colspan="2">RR (95% CI)</td><td>Statistical significance</td></tr>
<tr><td colspan="2">Mortality</td><td colspan="2">2.12 (0.59, 7.65)</td><td>NS</td></tr>
<tr><td colspan="2">Thrombotic complications</td><td colspan="2">1.71 (0.41, 7.08)</td><td>NS</td></tr>
<tr><td colspan="2">Clinical importance (1–4)
4 The range of estimates defined by the confidence interval includes clinically important effects BUT the range of estimates defined by the confidence interval is also compatible with no effect, or a harmful effect.</td><td colspan="3">Relevance (1–5)
1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival.</td></tr>
<tr><td colspan="2">Risk of transfusion</td><td colspan="2">0.92 (0.65, 1.31)</td><td>NS</td></tr>
<tr><td colspan="2">Clinical importance (1–4)
4 The range of estimates defined by the confidence interval includes clinically important effects BUT the range of estimates defined by the confidence interval is</td><td colspan="3">Relevance (1–5)
2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention</td></tr>
</table>

also compatible with no effect, or a harmful effect.		
Outcome	MD (95% CI)	Statistical significance
Transfusion rate	–1.3 (–1.85, –0.75)	S
Clinical importance (1–4) 2 The point estimate of effect is clinically important BUT the confidence interval includes clinically unimportant effects.	Relevance (1–5) 2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention	
Any other adverse effects None reported		
EXTERNAL VALIDITY		
Generalisability The studies were performed in patients undergoing surgery for colorectal cancer and may not be generalisable to other types of surgeries		
Applicability The study is most likely applicable to the Australian healthcare setting.		
Comments The authors concluded that there is no sufficient evidence to date to recommend pre and perioperative erythropoietin use in colorectal cancer surgery.		

STUDY DETAILS				
Reference Laupacis A, Fergusson D; International Study of Perioperative Transfusion (ISPOT) Investigators. Erythropoietin to minimise perioperative blood transfusion: A systematic review of randomized trials. Transfus Med. 1998;8:309–317				
Affiliation/Source of funds: Clinical Epidemiology Unit, Loeb Research Institute, Ottowa Civic Hospital, Ontario Canada Funding source: Dr Laupacis is the recipient of the First Fellowship from the International Societ y of Technology Assessment in Health Care, funded by the PPP Medical Trust, UK; The Ottowa Coordinating Centre has received funding from Janssen Ortho Inc., Canada; the Australian Group from the National Health and Medical Research Council and the Hunter Area Pathology Services; the French Group from Haemonetics France, Ortho Diagnostics France and University Segalen Bordeaux II; the Scottish Group from the Scottish National Blood Transfusion Service; and the group from the United States from the Baxter Healthcare Corporation Biotech Group and the Emory Center for Clinical Evaluation Services.				
Study design: Systematic Review N = 5 studies	Level of evidence: I	Location/setting: NA		
Population characteristics: Patients undergoing orthopaedic or cardiovascular surgery who did not donate autologous blood before surgery				
Length of follow-up: NA	Outcome(s) measured: Risk of blood transfusion (in orthopaedic and cardiovascular surgery)			
INTERNAL VALIDITY				
Allocation Assessed	Comparison of study groups Studies were compared by meta-analysis	Blinding Assessed	Treatment/measurement bias Assessed	Follow-up (ITT) ITT analysis.
Overall quality assessment (descriptive): The study was a fair quality systematic review. The authors clearly define the research question and scope of the review. The authors provide a summary of characteristics of individual studies (i.e. intervention route, dose, frequency, study population, etc) and a quality rating (JADAD scale), but do not include commentary on the quality of the included studies. It is unclear if sources of heterogeneity were explored or data were pooled appropriately				
RESULTS				
Outcome	OR (95% CI)	Statistical significance		
Transfusion rate – cardiovascular surgery	0.36 (0.24, 0.56)	S		
Transfusion rate – orthopaedic surgery	0.25 (0.06, 1.04)	S		
Clinical importance (1–4) 1 A clinically important benefit for the full range of plausible estimates	Relevance (1–5) 2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention			
Any other adverse effects None reported				

EXTERNAL VALIDITY
Generalisability The studies were performed in patients undergoing cardiovascular and orthopaedic surgeries and may not be generalisable to other types of surgeries
Applicability The study is most likely applicable to the Australian healthcare setting.
Comments The authors concluded that erythropoietin decreases exposure to allogeneic blood transfusion in patients undergoing orthopaedic and cardiac surgeries.

Level II evidence: Cardiac studies

<table>
<tr><td colspan="5">STUDY DETAILS</td></tr>
<tr><td colspan="5">Reference D'Ambra MN, Gray RJ, Hillman R, Jones JW, Kim HC, Rawitscher R, Schnaper H, et al. Effect of recombinant human erythropoietin on transfusion risk in coronary bypass patients. Ann Thorac Surg. 1997;64:1686–1693</td></tr>
<tr><td colspan="5">Affiliation/Source of funds
Cardiac Anaesthesia Group, Massachusetts General Hospital, Boston Massachusetts; Division of Cardiac Surgery, Cedar-Sinai, Medical Center, Los- Angeles, California; Department of Medicine, Maine Medical Centre, South Portland, Maine; Department of Surgery, Baylor College of Medicine and Veterans Administration Medical Centre, Houston Texas; Robert Wood Johnson Medical School, New Brunswick, New Jersey; Robert Wood Johnson Pharmaceutical Research Institute, Raritan, New Jersey; Harvard Medical School, Boston, Massachusetts, Ritter Heart Institute, Toledo Ohio and University of Alabama Medical Centre, Birmingham
Funding source: This study was funded by grants from the RW Johnson Pharmaceutical Research Institute, Raritan New Jersey and Rowland Foundation, Cambridge Massachusetts</td></tr>
<tr><td colspan="2">Study design
RCT
n=182</td><td colspan="2">Level of evidence
II</td><td>Location/setting
A total of 9 hospitals in the USA</td></tr>
<tr><td colspan="3">Intervention
Erythropoietin (EPO-α,300 IU/kg and oral iron (325 mg tid) 5 days before and 2 days after surgery
Sample size n=63
Erythropoietin (EPO-α,150 IU/kg and oral iron (325 mg tid) 5 days before and 2 days after surgery
Sample size n=63</td><td colspan="2">Comparator
Placebo and oral iron (325 mg tid)
Sample size n=56</td></tr>
<tr><td colspan="5">Population characteristics
Patients scheduled for coronary artery bypass grafting who had not received blood transfusion before study commencement.</td></tr>
<tr><td colspan="3">Length of follow-up
Outcome measurements were taken at baseline (with 7 days of administering first dose), preoperatively, daily postoperatively</td><td colspan="2">Outcomes measured
Mortality (all-cause), adverse events, thrombotic or vascular events, Need for perioperative blood transfusion, number of blood units transfused/ transfused patient, changes in Hb levels and time to discharge</td></tr>
<tr><td colspan="5">INTERNAL VALIDITY</td></tr>
<tr><td>Allocation</td><td>Results measurement bias</td><td>Blinding analysis</td><td>Treatment/ measurement bias</td><td>Follow-up (ITT)</td></tr>
<tr><td>Patients were stratified by centre and allocated treatment based on a computer generated randomisation code</td><td>There were no statistically significant differences in baseline demographic characteristics between groups</td><td>Patients and investigators were blinded to treatment allocations but investigators were aware of volume of interventions administered.</td><td>It is unclear if all patients were treated the same</td><td>A total of 24 patients were excluded from analysis</td></tr>
<tr><td colspan="5">Overall quality assessment (descriptive)</td></tr>
</table>

<table>
<tr><td colspan="6">This was a good quality randomised controlled trial</td></tr>
<tr><td colspan="6">RESULTS</td></tr>
<tr><td>Outcome</td><td>EPO Dose</td><td>Intervention group</td><td>Control group</td><td>OR (95% CI)</td><td>Statistical Significance</td></tr>
<tr><td rowspan="2">Need for transfusions (n/N(%))
(Patients with a HCT value >24% were not transfused unless clinically indicated)</td><td>300 IU/kg</td><td>20/60 (33%)</td><td rowspan="2">25/60 (42%)</td><td>OR: 0.7 (0.31, 1.57)</td><td rowspan="2">P=0.054</td></tr>
<tr><td>150 IU/kg</td><td>17/61 (28%)</td><td>OR: 0.54 (0.24, 1.23)</td></tr>
<tr><td colspan="3">Clinical importance (1–4)
4 The range of estimates defined by the confidence interval includes clinically important effects BUT the range of estimates defined by the confidence interval is also compatible with no effect, or a harmful effect.</td><td colspan="3">Relevance (1–5)
2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention</td></tr>
<tr><td rowspan="2">Total units transfused (mean ± SD)</td><td>300 IU/kg</td><td>1.42 ± 2.78</td><td rowspan="2">1.33 ± 2.01</td><td>NA</td><td rowspan="2">P=0.797</td></tr>
<tr><td>150 IU/kg</td><td>1.69 ± 3.62</td><td>NA</td></tr>
<tr><td rowspan="2">Hb change baseline to preoperative (g/dL)</td><td>300 IU/kg</td><td>0.25 ± 0.11</td><td rowspan="2">–0.07 ± 0.12</td><td>NA</td><td>NS</td></tr>
<tr><td>150 IU/kg</td><td>–0.08 ± 0.10</td><td>NA</td><td>NS</td></tr>
<tr><td rowspan="2">Hb change preoperative to postoperative (g/dL)</td><td>300 IU/kg</td><td>–4.58 ± 0.21</td><td rowspan="2">–4.87 ± 0.23</td><td>NA</td><td>NS</td></tr>
<tr><td>150 IU/kg</td><td>–4.33 ± 0.21</td><td>NA</td><td>NS</td></tr>
<tr><td rowspan="2">Hb change postoperative to discharge (g/dL)</td><td>300 IU/kg</td><td>0.81 ± 0.18</td><td rowspan="2">0.56 ± 0.20</td><td>NA</td><td>NS</td></tr>
<tr><td>150 IU/kg</td><td>0.72 ± 0.18</td><td>NA</td><td>NS</td></tr>
<tr><td colspan="3">Clinical importance (1–4)
1 Unable to determine</td><td colspan="3">Relevance (1–5)
2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention</td></tr>
<tr><td rowspan="2">Mortality (all cause, n/N [%])</td><td>300 IU/kg</td><td>3/63 (4.8%)</td><td rowspan="2">0/56 (0%)</td><td>NR</td><td rowspan="2">P=0.06</td></tr>
<tr><td>150 IU/kg</td><td>4/63 (6.3%)</td><td>NR</td></tr>
<tr><td colspan="3">Clinical importance (1–4)
1 Unable to determine</td><td colspan="3">Relevance (1–5)
1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival</td></tr>
</table>

Thrombotic or vascular complications (n/N [%])	300 IU/kg	18/63 (28.6%)	16/56 (28.6%)	OR: 1.0 (0.42, 2.4)	NS
	150 IU/kg	11/63 (17.5%)		OR: 0.53 (0.20, 1.37)	

Clinical importance (1–4)	Relevance (1–5)
4 The range of estimates defined by the confidence interval includes clinically important effects BUT the range of estimates defined by the confidence interval is also compatible with no effect, or a harmful effect.	1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival

EXTERNAL VALIDITY

Generalisability

This study was performed in patients undergoing CABG and is probably generalisable to a wider perioperative cardiac surgical population

Applicability

The study was conducted in the USA and is probably applicable to the Australian healthcare setting

Comment

The authors conclude that a lower incidence of exposure to allogenic blood transfusions was observed in both EPO treated groups compared with the placebo group.

On internal peer review by the Clinical Reference Group conducting the systematic review, the population in this study was found to be non-anaemic and was not used to inform clinical guidance for this question.

STUDY DETAILS				
Reference Podesta A, Carmagnini E, Parodi E, Dottori V, Crivellari R, Barberis L, et al. Elective coronary and valve surgery without blood transfusion in patients treated with recombinant human erythropoietin (epoietin-α). Minerva Cardioangiol. 2000;48:341–347				
Affiliation/Source of funds From the Cattedra di Cardiochirugia, Universita degli Studi, Genova; Divisione Cardiochirurgica, Ospedale S. Martino, Genova; Ospedale S. Salvatore, Santbia, Italy Funding source: No funding sources were reported				
Study design RCT n=60	Level of evidence II	Location/setting A total of 9 hospitals in the USA		
Intervention Erythropoietin (EPO-α,10,000 IU SC twice weekly) and oral iron 3 weeks preoperatively Sample size n=30	Comparator Oral iron 3 weeks preoperatively Sample size n=30			
Population characteristics Patients scheduled for open heart surgery				
Length of follow-up Outcomes were measured before therapy, the day before surgery, on the day of surgery, days 1, 2, 3 and postoperatively and on discharge	Outcomes measured Need for blood transfusion, mortality, Hb concentration			
INTERNAL VALIDITY				
Allocation	Results measurement bias	Blinding analysis	Treatment/ measurement bias	Follow-up (ITT)
Method of treatment allocation is not reported	There were no statistically significant differences in baseline demographic characteristics between groups	No blinding details are reported	It is unclear if all patients were treated the same	ITT analysis used
Overall quality assessment (descriptive) This was a fair quality randomised controlled trial				

RESULTS					
Outcome	EPO Dose	Intervention group	Control group	OR (95% CI)	Statistical Significance
Need for transfusions (n/N [%]) (HCT values between 25 and 27% were indicative of transfusion if associated with age >60 years; transfusion threshold NR for ≤60 years)	10,000 IU , sc twice weekly for 3 weeks preoperatively	1/30 (3.33%)	26/30 (86%)	OR: 0.005 (0.0001, 0.055)	P<0.0001
Clinical importance (1–4) 1 A clinically important benefit for the full range of plausible estimates			Relevance (1–5) 2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention		
Pre-treatment Hb (g/dL)	10,000 IU , sc twice weekly for 3 weeks preoperatively	13.95 ± 1.23	14.22 ± 1.04	NA	P=0.38
Post-treatment Hb (before surgery) (g/dL)		15.92 ± 1.31	14.03 ± 1.05	NA	P<0.0001
Discharge Hb (g/dL)		11	9	NA	p≤0.05
Clinical importance (1–4) Unable to determine			Relevance (1–5) 2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention		
Mortality (n/N (%))	10,000 IU , sc twice weekly for 3 weeks preoperatively	1/30 (3.33%)	0/30 (0%)	NR	NS
Clinical importance (1–4) Unable to determine			Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		

EXTERNAL VALIDITY
Generalisability This study was performed in patients undergoing heart surgery and is probably generalisable to a wider perioperative cardiac surgical population
Applicability The study was conducted in Italy and is probably applicable to the Australian healthcare setting
Comment The authors conclude that the syudy confirms the effectiveness of EPO in reducing postoperative need for homologous blood transfusion. The conclusion is that EPO can be used as an alternative to blood transfusion or in association with predeosit and in the treatment of basal anaemia. On internal peer review by the Clinical Reference Group conducting the systematic review, the population in this study was found to be non-anaemic and was not used to inform clinical guidance for this question.

STUDY DETAILS				
Reference Sowade O, Warnke H, Scigalla P, Sowade B, Franke W, Messinger D, Gross J. Avoidance of allogeneic blood transfusions by treatment with epoetin beta (recombinant human erythropoietin) in patients undergoing open-heart surgery. Blood. 1997;89:411–418				
Affiliation/Source of funds From the Clinic od heart Surgery and Institute of Pathological and Clinical Biochemistry, Medical Faculty (Charite), Humboldt University, Berlin; Department of Anaesthesiology, Hospital Berlin-Kaulsdorf, Germany; and Department of Clinical Research, Boehringer Mannheim GmbH, Mannheim, Germany. Funding source: Supported by Boehringer Mannheim GmbH, Germany				
Study design RCT n=76	Level of evidence II	Location/setting Hospital Germany		
Intervention Erythropoietin (EPO-β, 500 U/kg delivered on 5 days over 2 weeks) and oral iron (300 mg/day) 2 weeks preoperatively Sample size n=38	Comparator Placebo and oral iron (300 mg/day) 2 weeks preoperatively Sample size n=38			
Population characteristics Patients undergoing elective open heart surgery				
Length of follow-up	Outcomes measured Need for blood transfusion, units of blood transfused, haematological parameters, parameters of iron metabolism			
INTERNAL VALIDITY				
Allocation	Results measurement bias	Blinding analysis	Treatment/ measurement bias	Follow-up (ITT)
Medication was assigned to patients on the basis of chronological enrolment of patients and the sequential order of the blinded medication in a randomisation list, determined by a random algorithm	There were no statistically significant differences in baseline demographic characteristics between groups	The trial was performed under double blind conditions: neither the transfusing anaesthetists nor the surgeons were aware of the haematologic values measured at baseline and the changes during the treatment phase required to maintain blinding	All patients were treated the same	A total of 36 patients per group were included in the efficacy analysis
Overall quality assessment (descriptive) This was a fair quality randomised controlled trial				

RESULTS				
Outcome	Intervention group	Control group	OR (95% CI)	Statistical Significance
Pre-treatment Hb (g/dL)	14.31 ± 0.98	13.78 ± 1.03	NA	NS
Day of surgery Hb (g/dL; difference [95% CI])	15.84 ± 1.11	13.97 ± 1.06	NA	P<0.001
Postoperative day 7 Hb (g/dL; difference [95% CI])	13.41 ± 2.11	11.99 ± 1.80	NA	P<0.05
Pre-treatment ferritin (ng/mL)	145 ± 126	118 ± 77	NA	NS
Day of surgery ferritin (ng/mL; difference [95% CI])	78 ± 70	148 ± 83	NA	P<0.001
Postoperative day 7 ferritin (ng/mL; difference [95% CI])	319 ± 267	309 ± 252	NA	NS
Transfusion rate (units/person)	0.44	1.67	NA	P=0.0002
Clinical importance (1–4) Unable to determine		Relevance (1–5) 2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention		
Need for transfusions (n/N [%])	4/36 (11.1%)	19/36 (52.8%)	0.11 (0.02, 0.42)	P=0.0003
Clinical importance (1–4) 2 The point estimate of effect is clinically important BUT the confidence interval includes clinically unimportant effects.		Relevance (1–5) 2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention		
Fever/infection	1/36 (2.8%)	4/36 (11.1%)	0.23 (0.004, 2.51)	NR
Clinical importance (1–4) 2 The point estimate of effect is clinically important BUT the confidence interval includes clinically unimportant effects.		Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		
Mortality	4/36 (11.1%)	4/36 (11.1%)	NR	NR
Clinical importance (1–4) Unable to determine		Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		

EXTERNAL VALIDITY
Generalisability This study was performed in patients undergoing heart surgery and is probably generalisable to a wider perioperative cardiac surgical population
Applicability The study was conducted in Germany and is probably applicable to the Australian healthcare setting
Comments On internal peer review by the Clinical Reference Group conducting the systematic review, the population in this study was found to be non-anaemic and was not used to inform clinical guidance for this question.

Level II evidence: Noncardiac studies

<table>
<tr><td colspan="5">STUDY DETAILS</td></tr>
<tr><td colspan="5">Reference Canadian Orthopedic Perioperative Erythropoietin Study Group. Effectiveness of perioperative recombinant human erythropoietin in elective hip replacement. Lancet. 1993;341:1227–1232.</td></tr>
<tr><td colspan="5">Affiliation/Source of funds
Members of the Canadian Orthopaedic Perioperative Erythropoietin Study Group are: University of Western Ontario, London, Ontario; University of Montreal; University of British Columbia, Vancouver; Dalhousie University, Halifax; University of Toronto, Toronto.
Funding source: This study was sponsored by the medical Research Council of Canada and R. W. Johnson Pharmaceutical Research Institute, Canada, through an MRC University-Industry Grant, #UI-11092.</td></tr>
<tr><td colspan="2">Study design
RCT
n=208</td><td colspan="2">Level of evidence
II</td><td>Location/setting
University-affiliated Hospital/Tertiary care centres, Canada</td></tr>
<tr><td colspan="3">Intervention
EPO (300 U/kg) 14 days before surgery and oral iron (300 mg tid) 21 days before surgery
Sample size n=77
EPO (300 U/kg) 5 days before and 3 days after surgery and oral iron (325 mg tid) 21 days before surgery
Sample size n=53</td><td colspan="2">Comparator
Placebo 14 days before surgery and oral iron (300 mg tid) 21 days before surgery
Sample size n=78</td></tr>
<tr><td colspan="5">Population characteristics
Anaemic patients scheduled for elective unilateral hip replacement aged l<84 years</td></tr>
<tr><td colspan="3">Length of follow-up
3 weeks postoperatively</td><td colspan="2">Outcomes measured
Need for perisurgical blood transfusion, mean change in Hb (baseline to pre-surgery), thrombotic events</td></tr>
<tr><td colspan="5">INTERNAL VALIDITY</td></tr>
<tr><td>Allocation</td><td>Results measurement bias</td><td>Blinding analysis</td><td>Treatment/ measurement bias</td><td>Follow-up (ITT)</td></tr>
<tr><td>Patients were randomly allocated to treatment groups using computer generated randomisation schedules at the coordinating centre</td><td>There were no statistically significant differences in baseline demographic characteristics between groups</td><td>All study personnel and patients were blinded to treatment allocations. An unrelated unblinded physician reviewed patients' Hb level for safety</td><td>It was reported that some patients in one centre were provided with enteric-coated iron tablets instead of non-enteric coated iron. There was no difference in the need for transfusion or the prevalence of anaemia in both groups</td><td>ITT analysis: all patients were included in the safety and efficacy analysis regardless of their adherence to the treatment regimen</td></tr>
</table>

Overall quality assessment (descriptive) This was a good quality randomised controlled trial					
RESULTS					
Outcome	EPO Dose	Intervention group	Control group	OR (95% CI)	Statistical Significance
Need for blood transfusion (n/N %))	300 IU/kg 14d prior to surgery	18/77 (23%)	34/78 (44%)	NR	P=0.007
	300 IU/kg 9d prior to surgery	16/53 (30%)		NR	
Clinical importance (1–4) Unable to determine			Relevance (1–5) 2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention		
DVT (n/N (%))	300 IU/kg 14d prior to surgery	8/77 (10.4%)	5/78 (6.4%)	1.69 (0.46, 6.89)	NS
	300 IU/kg 9d prior to surgery	8/53 (15.1)		2.59 (0.69, 10.66)	
Clinical importance (1–4) 4 The range of estimates defined by the confidence interval includes clinically important effects BUT the range of estimates defined by the confidence interval is also compatible with no effect, or a harmful effect.			Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		
EXTERNAL VALIDITY					
Generalisability This study was performed in patients undergoing orthopaedic surgery and may not be generalisable to a wider perioperative noncardiac surgical population					
Applicability The study was conducted in Canada and is most likely applicable to the Australian healthcare setting					
Comment The authors concluded that erythropoietin given for 14 days perioperatively decreases the need for transfusion in patients undergoing elective hip arthroplasty.					

STUDY DETAILS					
Reference Christodoulakis M, Tsiftsis DD, for the Hellenic Surgical Oncology Perioperative EPO Study Group. Preoperative epoetin alfa in colorectal surgery: A randomised controlled study. Ann Surg Oncol. 2005;12:718–725					
Affiliation/Source of funds Department of Surgical Oncology, University Hospital, Medical School University of Crete, Herakleion, Greece. Funding source: None reported					
Study design RCT n=223		Level of evidence II		Location/setting Hospital, Greece	
Intervention EPO (EPO-α,300 IU/kg/day) and oral iron (200 mg/day) 10 days before and 1 day after surgery Sample size n=67 EPO (EPO-α,150 IU/kg/day) and oral iron (200 mg/day) 10 days before and 1 day after surgery Sample size n=69		Comparator Control group receiving oral iron (200 mg/day) Sample size n=68			
Population characteristics Colorectal cancer patients who were anaemic and scheduled for surgery					
Length of follow-up 15 days after surgery		Outcomes measured Need for blood transfusion, and units of blood transfused per patient			
INTERNAL VALIDITY					
Allocation	Results measurement bias	Blinding analysis	Treatment/ measurement bias	Follow-up (ITT)	
The randomisation method was not reported	There were no statistically significant differences in baseline demographic characteristics between groups	This was an open label study. Patients in the treatment groups were blinded to dose of EPO received	All patients were treated the same	Per protocol analysis performed for efficacy with 204 patients	
Overall quality assessment (descriptive) This was a fair quality randomised controlled trial					
RESULTS					
Outcome	EPO Dose	Intervention group	Control group	OR (95% CI)	Statistical Significance
Need for perioperative transfusion (n/N (%))	150 IU/kg	34/69 (49.3%)	36/68 (52.2%)	NR	NR
	300 IU/kg	25/67 (37.3%)		NR	NR
Need for postoperative	150 IU/kg	33/69 (47.8%)	36/68	NR	NR

transfusion (n/N (%))	300 IU/kg	27/67 (40.3%)	(52.2%)	NR	NR
Transfusion rate perioperatively (U/person)	150 IU/kg	1.19 ± 1.46	1.34 ± 1.59	NA	NS P=0.016
	300 IU/kg	0.81 ± 1.22		NA	
Transfusion rate postoperatively (U/person)	150 IU/kg	1.10 ± 1.42	1.35 ± 1.58	NA	NS P=0.023
	300 IU/kg	0.87 ± 1.21		NA	

Clinical importance (1–4)	Relevance (1–5)
Unable to determine.	2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention

EXTERNAL VALIDITY

Generalisability

This study was performed in patients with colorectal cancer undergoing colorectal surgery and may not be generalisable to a wider perioperative noncardiac surgical population

Applicability

The study was conducted in Greece and may not be applicable to the Australian healthcare setting

Comment

Perioperative EPO increases haemoglobin levels and hematocrit in colorectal surgery patients. These effects are associated with a reduced need for perioperative and postoperative transfusions.

STUDY DETAILS		
Reference Faris PM, Ritter MA, Abels RI; Mooreville, Indiana and American Erythropoietin Study Group. The effects of recombinant human erythropoietin on perioperative transfusion requirements in patients having a major orthopaedic operation. J Bone Joint Surg Ser A. 1996;78:62–72		
Affiliation/Source of funds The authors were affiliated with the Centre for Hip and Knee Surgery Mooresville, Indiana; RW Johnson Pharmaceutical Research Institute, Raritan New Jersey; University of Alabama at Birmingham, Birmingham, Alabama; Dartmouth-Hitchcock Medical Centre, Hanover, New Hampshire; Gunderson Clinic, La Crosse, Wisconsin; Arthritis Association of Minneapolis, Minneapolis, Minnesota; Dakota Medical Center, Fargo, North Dakota; Emory Clinic, Atlanta, Georgia; Anderson Orthopedic Research Institute, Arlington, Virginia; Sarasota Memorial Hospital, Sarasota, Florida; Massachussetts General Hospital, Boston, Massachussetts; Maine Medical Centre, Portland, Maine; Hospital for Joint Diseases, New York; University Health Center, Burlington, Vermont; DeKalb Orthopedic Clinic, Decatur, Georgia; Veterans Affairs Medical Center, Houston, Texas; University of Kentucky, Lexington, Kentucky; Hughston Sports medicine Foundation, Columbus, Georgia; The Hospital for Special Surgery, New York; University of Arizona, Tucson, Arizona; University of Wisconsin, Madison, Wisconsin. Funding source: Although none of the authors have received or will receive benefits for personal or professional use from a commercial party related directly or indirectly to the subject of this article, benefits have been or will be received but are directed solely to a research fund, foundation, educational institution, or other non-profit organisation with which one or more of the authors are associated. Funds were received in total or partial support of the research or clinical study presented in this article. The funding source was the R. W. Johnson Pharmaceutical Research Institute, Raritan, New Jersey		
Study design RCT n=200	Level of evidence II	Location/setting Hospital, USA
Intervention EPO (300 IU/kg/day) 10 days before surgery and oral iron (325 mg tid) throughout the study Sample size n=71 EPO (100 IU/kg/day) 10 days before surgery and oral iron (325 mg tid) throughout the study Sample size n=69	Comparator Placebo and oral iron (325 mg tid) Sample size n=69	
Population characteristics Patients scheduled for major orthopaedic surgery		
Length of follow-up 4 weeks after surgery	Outcomes measured Need for blood transfusion, units of blood transfused, morbidity	

INTERNAL VALIDITY				
Allocation	Results measurement bias	Blinding analysis	Treatment/ measurement bias	Follow-up (ITT)
Random assignment of treatment group but method not described	There were no statistically significant differences in baseline demographic characteristics between groups	Patients and investigators were blinded to treatment allocations	All patients were treated the same	Patients who had scheduled surgery and were administered 14 of the 15 doses of treatment assigned to them were included in the efficacy analysis (n=185/200). All patients who received 1 dose of treatment were included in the safety analysis (n=200)

Overall quality assessment (descriptive)

This was a good quality randomised controlled trial

RESULTS

Outcome	EPO Dose	Intervention group	Control group	OR (95% CI)	Statistical Significance
Need for transfusion (n/N (%))	300 IU/kg/day	9/54 (17%)	36/67 (54%)	NR	P<0.001
	100 IU/kg/day	16/64 (25%)		NR	P<0.001
Transfusion rate (U/person)	300 IU/kg/day	0.37 ± 0.96	1.42 ± 1.67	NA	P=0.007
	100 IU/kg/day	0.58 ± 1.15		NA	P=0.005

Clinical importance (1–4)	Relevance (1–5)
Unable to determine.	2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention

Thrombotic and vascular events (n/N (%))	300 IU/kg/day	2/60 (3%)	6/69 (9%)	0.36 (0.03, 2.14)	P=0.40
	100 IU/kg/day	3/71 (4%)		0.46 (0.07, 2.29)	

Clinical importance (1–4)	Relevance (1–5)
4 The range of estimates defined by the confidence interval includes clinically important effects BUT the range of estimates defined by the confidence interval is also compatible with no effect, or a harmful effect.	1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival

EXTERNAL VALIDITY
Generalisability This study was performed in patients undergoing orthopaedic surgery and may not be generalisable to a wider perioperative noncardiac surgical population
Applicability The study was conducted in the USA and may not be applicable to the Australian healthcare setting
Comment The authors conclude that these data suggest that recombinant human erythoropoietin, administered before and after major orthopaedic operations, can minimise the need for homologous red blood cell transfusion.

STUDY DETAILS				
Reference Feagan BG, Wong CJ, Kirkley A, Johnston DWC, Smith FC, Whitsitt P, et al. Erythropoietin with iron supplementation to prevent allogeneic blood transfusion in total hip joint arthroplasty. A randomised controlled trial. Ann Intern Med. 2000;133:845–854				
Affiliation/Source of funds The authors of this study were affiliated with the London Clinical Trials Research Group, London UK; University of Western Ontario; University of Alberta; Sir William Osler Health Institute, Ontario; Lakeridge Health Ottawa, Ontario; and Janssen-Ortho Inc Toronto, Canada. Funding source: Janssen-Ortho Inc, a manufacturer of epoetin alfa, provided input to the study design, conduct and reporting. This article was co-authored by two employees and share-owners of this company				
Study design RCT n=214	Level of evidence II	Location/setting Teaching and community hospitals, Canada		
Intervention EPO (40 000 U) as a weekly injection 4 weeks before surgery and oral iron (150 mg tid) 42 days before surgery until discharge Sample size=46 EPO (20 000 U) as a weekly injection 4 weeks before surgery and oral iron (150 mg tid) 42 days before surgery until discharge Sample size n=86	Comparator Placebo as a weekly injection 4 weeks before surgery and oral iron (150 mg tid) 42 days before surgery until discharge Sample size n=82			
Population characteristics Anaemic patients undergoing primary hip arthroplasty				
Length of follow-up 5 days after surgery	Outcomes measured Need for transfusion, units transfused, hospital LOS, Hb levels			
INTERNAL VALIDITY				
Allocation	Results measurement bias	Blinding analysis	Treatment/ measurement bias	Follow-up (ITT)
Patients randomised to 3 arms of the study using computer generated schedule, in blocks of 13; allocation ratio = 3:5:5 (high dose EPO: low dose EPO: placebo)	There were no statistically significant differences in baseline demographic characteristics between groups	Patients and investigators were blinded to treatment allocation	All patients were treated the same	A total of 201/214 patients were included in the efficacy analysis. None were lost to follow-up
Overall quality assessment (descriptive) This was a good quality randomised controlled trial				

RESULTS					
Outcome	EPO Dose	Intervention group	Control group	OR (95% CI)	Statistical Significance
Need for transfusion (n/N (%))	40 000 U/week	5/44 (11.4%)	35/78 (44.9%)	NR	P=0.001
	20 000U/week	18/79 (22.8%)		NR	P=0.003
Preoperative increase in Hb (g/dL)	40 000 U/week	19.5 g/dL	1.2 g/dL	NA	P<0.001
	20 000U/week	17.2 g/dL		NA	P<0.001
Clinical importance (1–4) Unable to determine			Relevance (1–5) 2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention		
Thromboembolic disease (n/N (%))	40 000 U/week	2/44 (4.5%)	6/78 (8.0%)	0.57 (0.05, 3.4)	NR
	20 000U/week	5/79 (6.3%)		0.81 (0.19, 3.35)	NR
Clinical importance (1–4) 4 The range of estimates defined by the confidence interval includes clinically important effects BUT the range of estimates defined by the confidence interval is also compatible with no effect, or a harmful effect.			Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		
EXTERNAL VALIDITY					
Generalisability This study was performed in patients undergoing orthopaedic surgery and may not be generalisable to a wider perioperative noncardiac surgical population					
Applicability The study was conducted in Canada and is most likely applicable to the Australian healthcare setting					
Comment The authors conclude epoetin alfa was effective compared with placebo in reducing allogenic transfusion in patients undergoing hip arthroplasty. On internal peer review by the Clinical Reference Group conducting the systematic review, the population in this study was found to be non-anaemic and was not used to inform clinical guidance for this question.					

STUDY DETAILS					
Reference Goldberg MA, McCutchen JW, Jove M, Di Cesare P, Friedman RJ, Poss R, Guilfoyle M, Frei D, Young D. A safety and efficacy comparison study of two dosing regimens of epoetin alfa in patients undergoing major orthopaedic surgery. Am J Orthoped. 1996;25:544–552					
Affiliation/Source of funds Department of Medicine, Hematology/Oncology Division, Harvard Medical School; Brigham and Women's Hospital, Harvard Medical School, Boston, Massachussetts; Jewett Orthopedic Clinic, Winter Park, Florida; Orthopedic Section, Dekalb Medical Center, Decatur, Georgia; Musculoskeletal Research Center, Arthritis Services, Hospital for Joint Diseases, New York, New York; Orthopedic Surgery, Medical University of South Carolina, Charleston, South Carolina; The R. W. Johnson Pharmaceutical Research Institute, Raritan, New Jersey. Funding source: None reported					
Study design RCT n=145		Level of evidence II		Location/setting Hospitals, USA	
Intervention EPO (600 IU/kg) as a weekly injection 3 weeks before surgery and oral iron (200 mg/day) throughout the study Sample size n=73		Comparator EPO (300 IU/kg) as a daily injection 10 days before surgery until 4 days after surgery and oral iron (200 mg/day) throughout the study Sample size n=72			
Population characteristics Mild to moderate anaemic patients scheduled for major elective hip or knee surgery					
Length of follow-up Patients were followed up from study entrance to hospital discharge		Outcomes measured Hb concentration, need for transfusion, units of blood transfused			
INTERNAL VALIDITY					
Allocation	Results measurement bias	Blinding analysis	Treatment/ measurement bias	Follow-up (ITT)	
Treatment was randomly allocated using computer generated randomisation code	There were no statistically significant differences in baseline demographic characteristics between groups	Open label study- patients and investigators were aware of treatment allocations	All patients were treated the same	A total of 5 patients were removed from the efficacy analysis.	
Overall quality assessment (descriptive) This was a fair quality randomised controlled trial					
RESULTS					
Outcome	EPO Dose	Intervention group	Control group	OR (95% CI)	Statistical Significance
Preoperative increase in	600 IU/week	1.44 ± 1.03	No control	NA	NS

Hb (g/dL)	300 IU/day	0.73 ± 0.87		NA	
Peri-surgical decrease in Hb (g/dL)[e]	600 IU/week	–2.94 ± 1.45	No control	NA	NS
	300 IU/day	–2.3 ± 1.3		NA	
Need for transfusion	600 IU/week	11/69 (16%)	No control	NR	NS
	300 IU/day	14/71 (20%)		NR	
Transfusion rate (U/person)	600 IU/week	0.33 ± 0.87	No control	NA	NS
	300 IU/day	0.30 ± 0.64		NA	

Clinical importance (1–4)	Relevance (1–5)
Unable to determine	2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention

EXTERNAL VALIDITY

Generalisability

This study was performed in patients undergoing orthopaedic surgery and may not be generalisable to a wider perioperative noncardiac surgical population

Applicability

The study was conducted in the USA and is probably applicable to the Australian healthcare setting

Comment

The authors conclude that these data showed the weekly regimen of epoietin alfa to be at least as efficacious as the daily regimen and more .convenient.

STUDY DETAILS				
Reference Heiss MM, Tarabichi A, Delanoff C, Allgayer H, Jauch KW, Hernandez-Richter T, et al. Perisurgical erythropoietin application in anemic patients with colorectal cancer: A double-blind randomized study. Surgery. 1996; 119:523–527				
Affiliation/Source of funds The authors were affiliated with the Department of Surgery, Klinikum Grosshadern, Transfusion Center 3 Med Department and Institute of Surgical Research, Ludwig Maximilians University, Munich and the Cilag GmbH, Sulzbach, Germany Funding source: None reported				
Study design RCT n=30	Level of evidence II	Location/setting Hospital, Germany		
Intervention EPO (150 IU/kg) SC injection every 2 days starting 10 days before surgery until 2 days after surgery and oral iron (200 mg/day) and folate (5 mg/day) throughout the study Sample size n=20	Comparator Placebo as SC injection every 2 days starting 10 days before surgery until 2 days after surgery and oral iron (200 mg/day) and folate (5 mg/day) throughout the study Sample size n=10			
Population characteristics Patients with moderate anaemia undergoing colorectal cancer surgery				
Length of follow-up Patients were followed up from study entrance to hospital discharge	Outcomes measured Need for blood transfusion, units of blood transfused, Hb concentration, morbidity and mortality			
INTERNAL VALIDITY				
Allocation	Results measurement bias	Blinding analysis	Treatment/ measurement bias	Follow-up (ITT)
Randomised assignment indicated but not described	There were no statistically significant differences in baseline demographic characteristics between groups	Both patients and investigators were blinded to treatment allocation; placebo was prepared to be identical in administration and features to study drug	All patients were treated the same	30 patients were randomised (2:1) to receive EPO or the control. All randomised patients were followed up in the control group and 17 patients were evaluated in the intervention group
Overall quality assessment (descriptive) This was a fair quality randomised controlled trial				

RESULTS				
Outcome	Intervention group	Control group	OR (95% CI)	Statistical Significance
Need for transfusion (n/N (%))	9/17 (53%)	4/10 (40%)	NR	NR
Transfusion rate (U/person)	1.82 ± 0.8	1.80 ± 0.97	NA	NR
Preoperative increase in Hb (g/dL)	0.4	0.1	NA	P=0.065

Clinical importance (1–4)	Relevance (1–5)
Unable to determine	2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention

EXTERNAL VALIDITY

Generalisability

This study was performed in patients with colorectal cancer undergoing colorectal surgery and may not be generalisable to a wider perioperative noncardiac surgical population

Applicability

The study was conducted in Germany and is probably applicable to the Australian healthcare setting

Comment

The authors conclude that these results indicate that haematopoiesis in anaemic patients with colorectal cancer can be stimulated by erythropoietin; however, clinical efficacy is to be expected only in selected patients with high iron availability, which calls for further studies combining erythropoieitin and parenteral iron application.

STUDY DETAILS				
Reference Kettelhack C, Hones C, Messinger D, Schlag PM. Randomised multicentre trial of the influence of recombinant human erythropoietin on intraoperative and postoperative transfusion need in anaemic patients undergoing right hemicolectomy for carcinoma. Br J Surg. 1998;85:63–67				
Affiliation/Source of funds The authors were affiliated with the Department of Surgery and Surgical Oncology, Robert Rossle Hospital and Tumour Institute, Humboldt Universoty, Berlin; and Boehringer Mannheim, Mannheim, Germany Funding source: None reported				
Study design RCT n=109 enrolled	Level of evidence II	Location/setting 16 hospitals in Germany		
Intervention EPO (as epoetin β 20 000 U) as SC injection every day starting 5–10 days before surgery until 4 days after surgery and oral iron throughout the study as well as IV iron 1 day after surgery Sample size n=48	Comparator Placebo as SC injection every day starting 5–10 days before surgery until 4 days after surgery and oral iron throughout the study as well as IV iron 1 day after surgery Sample size n=54			
Population characteristics Anaemic patients with colon cancer 35 years or older undergoing colorectal surgery				
Length of follow-up Last follow-up was 3 months after surgery	Outcomes measured Need for blood transfusion, morbidity			
INTERNAL VALIDITY				
Allocation	Results measurement bias	Blinding analysis	Treatment/ measurement bias	Follow-up (ITT)
Randomised assignment indicated but not described	There were some statistically significant differences in baseline demographic characteristics between groups	Both patients and investigators were blinded to treatment allocation	All patients were treated the same	109 patients were recruited; of these, 102 were included in the final analysis. Seven patients were excluded from the study before its conclusion due to adverse events. patients meeting the exclusion criteria (preoperative transfusion, no confirmation of colonic cancer)
Overall quality assessment (descriptive) This was a fair quality randomised controlled trial				

RESULTS				
Outcome	Intervention group	Control group	OR (95% CI)	Statistical Significance
Need for transfusion (n/N (%))	16/48 (33%)	15/54 (28%)	NR	P=0.27
Clinical importance (1–4) Unable to determine		Relevance (1–5) 2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention		
EXTERNAL VALIDITY				
Generalisability This study was performed in patients with colorectal cancer undergoing colorectal surgery and may not be generalisable to a wider perioperative noncardiac surgical population				
Applicability The study was conducted in Germany and is probably applicable to the Australian healthcare setting				
Comment The authors conclude that despite the perioperative administration of EPO, it was not possible to reduce the intraoperative and postoperative transfusion need.				

STUDY DETAILS				
Reference Kosmadakis N, Messaris E, Maris A, Katsaragakis S, Leandros E, Konstadoulakis MM, Androulakis G. Perioperative erythropoietin administration in patients with gastrointestinal tract cancer: Prospective randomised double-blind study. Ann Surg. 2003;237:417–421				
Affiliation/Source of funds The authors were affiliated with the First Department of Propaedeutic Surgery, Hippokation General Hospital, Athens Medical School, University of Athens, Athens, Greece Funding source: None reported				
Study design RCT n=63	Level of evidence II	Location/setting Hospital, Greece		
Intervention EPO (300 IU/kg) as SC injection every day starting 7 days before surgery until 6 days after surgery and intravenous iron (100 mg) throughout the study Sample size n=31	Comparator Placebo as SC injection every day starting 7 days before surgery until 6 days after surgery and intravenous iron (100 mg) throughout the study Sample size n=32			
Population characteristics Moderately anaemic patients aged 40–90 years undergoing surgery for non-metastatic gastrointestinal tract malignancies				
Length of follow-up Not reported	Outcomes measured Need for blood transfusion, Hb concentration, hospital LOS			
INTERNAL VALIDITY				
Allocation	Results measurement bias	Blinding analysis	Treatment/ measurement bias	Follow-up (ITT)
Randomised assignment indicated but not described	There were no statistically significant differences in baseline demographic characteristics between groups	Both patients and investigators were blinded to treatment allocation	All patients were treated the same	75 patients enrolled over 16 months and included in randomisation. 12 were excluded for non-fulfilment of inclusion criteria or personal reasons. There were 31 and 32 patients in the study and control groups respectively
Overall quality assessment (descriptive) This was a good quality randomised controlled trial				

RESULTS				
Outcome	Intervention group	Control group	OR (95% CI)	Statistical Significance
Need for intra-surgical transfusion (n/N (%))	9/31 (29%)	19/32 (59.3%)	NR	S
Need for postoperative transfusion (n/N (%))	1/31 (3.2%)	9/32 (28%)	NR	P=0.001
Hb level at discharge (g/dL)	12.1 ± 0.12	11.1 ± 0.15	NA	P=0.0001
Hospital LOS (days)	10 ± 0.5	13 ± 0.9	NA	P=0.022

Clinical importance (1–4)	Relevance (1–5)
Unable to determine	2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention

EXTERNAL VALIDITY

Generalisability

This study was performed in patients undergoing surgery for GI tract malignancies and may not be generalisable to a wider perioperative noncardiac surgical population

Applicability

The study was conducted in Greece and is probably applicable to the Australian healthcare setting

Comment

The authors conclude that patients with gastrointestinal tract cancer and mild anaemia benefit from perioperative EPO administration in terms of stimulated erythropoiesis, reduction in the number of blood transfusions, and a favourable outcome.

STUDY DETAILS				
Reference Larson B, Bremme K, Clyne N, Nordstrom L. Preoperative treatment of anemic women with epoetin beta. Acta Obstet Gynecol Scand. 2001;80:559–562				
Affiliation/Source of funds The authors were affiliated with the Departments of Obstetrics and Gynaecology and Nephrology, Karolinska Hospital, Stockholm and Roche AB, Stockholm, Sweden Funding source: None reported				
Study design RCT n=31	Level of evidence II	Location/setting Hospital, Greece		
Intervention EPO (as epoetin β 5 000 U) as SC injection twice a week and oral iron (100 mg bid) 4 weeks before surgery Sample size n=15	Comparator Control group receiving oral iron (100 mg bid) 4 weeks before surgery Sample size n=16			
Population characteristics Anaemic women with uterine myoma undergoing hysterectomy				
Length of follow-up Outcomes were measured before treatment was initiated, after 4 weeks of therapy (before surgery) and 2 weeks postoperatively	Outcomes measured Infection, hospital LOS, Hb concentrations			
INTERNAL VALIDITY				
Allocation	Results measurement bias	Blinding analysis	Treatment/ measurement bias	Follow-up (ITT)
Randomised assignment indicated but not described	No baseline measurement details are reported	This was an open labelled study	All patients were treated the same	32 patients were initially enrolled and randomised. One patient from the intervention group had to be excluded due to high preoperative Hb levels
Overall quality assessment (descriptive) This was a fair quality randomised controlled trial				
RESULTS				

Outcome	Intervention group	Control group	OR (95% CI)	Statistical Significance
Pre-surgery Hb concentration (g/dL)	12.6 ± 1.3	12.0 ± 1.4	NA	P=0.007
Postoperative Hb concentration[g] (g/dL)	11.6 ± 1.4	11.7 ± 0.6	NA	NS

Infection rate (n/N (%))	1/15 (6.66%)	2/16 (12.5%)	NA	NR
Hospital LOS (days)	6.4 ± 2.4	8.1 ± 7.1	NA	NS

Clinical importance (1–4) Unable to determine	Relevance (1–5) 2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention

EXTERNAL VALIDITY

Generalisability

This study was performed in anaemic women with uterine myoma undergoing hysterectomy and may not be generalisable to a wider perioperative noncardiac surgical population

Applicability

The study was conducted in Sweden and is probably applicable to the Australian healthcare setting

Comment

The authors conclude that there was a significantly greater increase in Hb with iron in combination with EPO, although in most cases iron only seemed to be as efficacious as iron + EPO in correcting anaemia in myoma patients preoperatively

STUDY DETAILS				
Reference Qvist N, Boesby S, Wolff B, Hansen CP. Recombinant human erythropoietin and haemoglobin concentration at operation and during the postoperative period: Reduced need for blood transfusions in patients undergoing colorectal cancer surgery—prospective double blind placebo controlled study. World J Surg. 1999;23:30–35				
Affiliation/Source of funds Department of Surgical Gastroenterology, Odense University Hospital, Sdr. Boulevard 29, DK 5000 Odense C, Denmark; Department of Surgical Gastroenterology, Glostrup University Hospital, Ndr. Ringvej 29-69, DK 2600 Denmark Funding source: Test medicine and funding was provided by Janssen-Cilag, Copenhagen, Denmark				
Study design RCT n=100	Level of evidence II	Location/setting Hospital, Denmark		
Intervention EPO (300 IU/kg/day) as SC injection for 4 days before surgery then erythropoietin (150 IU/kg/day) until 6 days after surgery and oral iron (200 mg/day) for the 4 days before surgery Sample size n=38	Comparator Placebo as SC injection 4 days before until 6 days after surgery and oral iron (200 mg/day) for the 4 days before surgery Sample size n=43			
Population characteristics Anaemic patients with colorectal cancer undergoing colorectal surgery				
Length of follow-up Measurements were taken before study entry, on the day before and day of surgery, postoperative days 3 and 7, and at hospital discharge	Outcomes measured Need for blood transfusion, morbidities			
INTERNAL VALIDITY				
Allocation	Results measurement bias	Blinding analysis	Treatment/ measurement bias	Follow-up (ITT)
Randomised assignment indicated but not described	There were no statistically significant differences in baseline demographic characteristics between groups	Patients and investigators were blinded to treatment allocation	All patients were treated the same	100 patients were initially randomised. Of these, 19 were excluded from analysis (11 from intervention group; 8 from control) because of protocol violation (11), personal reasons (6) and death after surgery due to widespread neoplastic disease (2)
Overall quality assessment (descriptive) This was a good quality randomised controlled trial				

RESULTS				
Outcome	Intervention group	Control group	OR (95% CI)	Statistical Significance
Need for transfusion (n/N (%))	13/38 (35%)	23/43 (53%)	NR	NS[h]
Transfusion rate (U/person)	0.3	1.6	NA	P<0.05
Post-surgery Hb concentration (median (range))	7.8 (5.5, 9.2)	7.2 (4.6, 8.5)	NA	P<0.05
Discharge Hb concentration (median (range))	7.8 (5.9, 8.8)	7.2 (5.4, 8.6)	NA	P<0.02
Hospital LOS (days)	10.5	10.9	NR	NS[h]

Clinical importance (1–4)	Relevance (1–5)
Unable to determine	2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention

EXTERNAL VALIDITY

Generalisability

This study was performed in patients with colorectal cancer undergoing colorectal surgery and may not be generalisable to a wider perioperative noncardiac surgical population

Applicability

The study was conducted in Denmark and is probably applicable to the Australian healthcare setting

Comment

The authors conclude that the Hb concentration at the time of surgery and the week following surgery was significiantly higher in the group of patients receiving EPO perioperatively compared to the placebo group together with a significant lower use of blood transfusions in the EPO group.

STUDY DETAILS				
Reference Rohling RG, Zimmerman AP, Breymann C. Intravenous versus oral iron supplementation for preoperative stimulation by haemoglobin synthesis using recombinant human erythropoietin. J Hematother Stem Cell Res. 2000;9:497–500				
Affiliation/Source of funds Institute of Anesthesiology, Department of Cranio-Maxillofacial Surgery, and Department of Obstetrics and Gynecology, Division of Obstetrics and Perinatal Physiology, University Hospital, Zurich, Switzerland Funding source: None reported				
Study design RCT n=12	Level of evidence II	Location/setting Hospital, Switzerland		
Intervention EPO (200 U/kg) and IV iron (200 mg) twice weekly 3 weeks before surgery until 3 days before surgery Sample size n=6	Comparator EPO (200 U/kg) twice weekly 3 weeks before surgery until 3 days before surgery and oral iron (160 mg/day) until surgery Sample size n=6			
Population characteristics Healthy patients with Hb <14 g/dL undergoing elective surgery with a potential blood loss of 500 mL				
Length of follow-up 3 days after surgery	Outcomes measured Hb and ferritin levels			
INTERNAL VALIDITY				
Allocation	Results measurement bias	Blinding analysis	Treatment/ measurement bias	Follow-up (ITT)
Randomised assignment indicated but not described	There were no statistically significant differences in baseline demographic characteristics between groups	No blinding details are reported	All patients were treated the same	ITT
Overall quality assessment (descriptive) This was a fair quality randomised controlled trial				
RESULTS				
Outcome	Intervention group	Control group	OR (95% CI)	Statistical Significance
Preoperative increase in Hb (g/dL)	2.5 ± 0.7	2.0 ± 1.0	NR	NS
End-of-treatment ferritin (μg/L)	266.8 ± 144.3	34.0 ± 47.6	NR	P<0.001
Clinical importance (1–4) Unable to determine	Relevance (1–5) 2 Evidence of an effect on a surrogate outcome that			

	has been shown to be predictive of patient-relevant outcomes for the same intervention
EXTERNAL VALIDITY	
Generalisability The results of this study may not be generalisable to a wider perioperative noncardiac surgical population	
Applicability The study was conducted in Switzerland and is probably applicable to the Australian healthcare setting	
Comment The authors conclude that intravenous iron significantly boosts the hematopoietic response to EPO and prevents iatrogenic iron depletion in otherwise healthy candidates for elective surgery. On internal peer review by the Clinical Reference Group conducting the systematic review, the population in this study was found to be non-anaemic and was not used to inform clinical guidance for this question.	

STUDY DETAILS				
Reference Tsuji Y, Kambayashi JI, Shiba E, Sakon M, Kawasaki T, Mori T. Effect of recombinant human erythropoietin on anaemia after gastrectomy: A pilot study. Eur J Surg Act Chir. 1995;161:29–33				
Affiliation/Source of funds Department of Surgery H.Osaka University Medical School, Osaka, Japan Funding source: EPO was provided by the KIRIN Brewery Company Ltd. of Tokyo, Japan				
Study design RCT n=10	Level of evidence II	Location/setting Hospital, Japan		
Intervention EPO (200 IU/kg/day) and IV iron (40 mg/day) for 7 days before until 14 days after surgery Sample size n=5	Comparator Controls receiving IV iron (40 mg/day) for 7 days before until 14 days after surgery Sample size n=5			
Population characteristics Patients with gastric cancer undergoing distal gastrectomy				
Length of follow-up Blood was drawn for outcome measurements on days 14, 7 and 1 before surgery and 1,4,10, 14 and 28 after the surgery	Outcomes measured Hb levels			
INTERNAL VALIDITY				
Allocation	Results measurement bias	Blinding analysis	Treatment/ measurement bias	Follow-up (ITT)
Randomised assignment indicated but not described	There were no statistically significant differences in baseline demographic characteristics between groups	Blinding details were not reported	All patients were treated the same	At postoperative day 14, only 2/5 patients were evaluated for efficacy measures in the control group. On day 28, only 4/5 patients were evaluated in the intervention group
Overall quality assessment (descriptive) This was a poor quality randomised controlled trial				
RESULTS				
Outcome	Intervention group	Control group	OR (95% CI)	Statistical Significance
Postoperative Hb concentration[i] (g/dL)	200 IU/kg/day	14.0 ± 1.0	10.8 ± 1.5	NA
Clinical importance (1–4) Unable to determine	Relevance (1–5) 2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention			

EXTERNAL VALIDITY
Generalisability This study was performed in patients undergoing surgery for gastric cancer and may not be generalisable to a wider perioperative noncardiac surgical population
Applicability The study was conducted in Japan and may not be applicable to the Australian healthcare setting
Comment The authors conclude that EPO prevented postoperative anaemia after gastrectomy as judged by packed cell volume, haemoglobin concentration, and red cell count. EPO given before and after surgery therefore, has the potential to reduce the need for homologous blood transfusion. The small sample size and larger operative blood loss in the control group is noted. Intervention: Median 338ml (220-450ml) Control: Median 434ml (300-600ml). On internal peer review by the Clinical Reference Group conducting the systematic review, the population in this study was found to be non-anaemic and was not used to inform clinical guidance for this question.

STUDY DETAILS				
Reference Weber EWG, Slappendel R, Hemon Y, Mahler S, Dalen T, Rouwet E, et al. Effects of epoetin alfa on blood transfusions and postoperative recovery in orthopaedic surgery: The European Epoetin Alfa Trial (EEST). Eur J Anaesthesiol. 2005b;22:249–257				
Affiliation/Source of funds Sint Maartenskliniek, Nijmegen; Hopital Ste-Marguerite, Marseille, France; Kreiskrankenhaus, Langenau, Germany; Norrlands Universitetssjukhus, Umea, Sweden; medisch Spectrum Twente, Enschede; Maasland Ziekenhuis, Sittard; Ikazia Ziekenhuis, Rotterdam; Environ Netherlands BV Zeist, The Netherlands Funding source: This trial was sponsored by Ortho Biotech Europe and P.v.d.A. at the time of the study was an employee of the sponsoring company				
Study design RCT n=704	Level of evidence II		Location/setting Hospitals in The Netherlands, France, Germany, Sweden, Belgium, Australia	
Intervention EPO (as epoetin α 40 000 IU) as SC injection once weekly and oral daily iron for 3 weeks before surgery Sample size n=467	Comparator Controls receiving oral daily iron for 3 weeks before surgery Sample size n=237			
Population characteristics Mild to moderate anaemic patients undergoing elective major orthopaedic surgery				
Length of follow-up Outcome measurements were taken at study entry, before surgery, 1 day after surgery, at hospital discharge and at a follow-up visit scheduled 4–6 weeks after surgery	Outcomes measured Need for blood transfusion, number of units transfused, infection rate, Hb levels, hospital LOS			
INTERNAL VALIDITY				
Allocation	Results measurement bias	Blinding analysis	Treatment/ measurement bias	Follow-up (ITT)
Patients were randomised in blocks of 9 per hospital, by a telephone operated interactive voice randomisation system in a ratio of 1:2 (control: intervention)	There were no statistically significant differences in baseline demographic characteristics between groups	Open label Allocation of interventions was not concealed	All patients were treated the same	This study initially enrolled 733 patients collectively in 6 countries. The ITT analysis included 704 patients Patients who had surgery postponed for >10 days were excluded. Included population=695 patients. Patients excluded due to surgery delay were not included in the analysis

Overall quality assessment (descriptive) This was a fair quality randomised controlled trial				
RESULTS				
Outcome	Intervention group	Control group	OR (95% CI)	Statistical Significance
Need for transfusion (n/N (%))[j]	55/460 (12%)	108/235 (46%)	NR	P<0.05
Transfusion rate (U/person)	2.36 ± 1.95	2.41 ± 1.24	NA	NS
Preoperative increase in Hb (g/dL)	2.1	0	NA	P<0.05
Postoperative Hb (g/dL)	11.4 ± 1.4	9.7 ± 1.2	NA	P<0.05
Postoperative Hb (4–6 weeks)	12.3 ± 1.0	11.9 ± 0.9	NA	P<0.05
Clinical importance (1–4) Unable to determine		Relevance (1–5) 2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention		
EXTERNAL VALIDITY				
Generalisability This study was performed in patients undergoing orthopaedic surgery and may not be generalisable to a wider perioperative noncardiac surgical population				
Applicability The study was conducted in Europe and is probably applicable to the Australian healthcare setting				
Comment The authors conclude that EPO increases perioperative Hb concentration in mild-to-moderately anaemic patients and thus reduces transfusion requirments. Patients receiving blood transfusions require a longer hospitalisation than non-transfused patients.				

STUDY DETAILS				
Reference Green D, Lawler M, Rosen M, Bloom S, Duerden M, Turba R, et al. Recombinant human erythropoietin: Effect on the functional performance of anemia orthopaedic patients. Arch Phys Med Rehabil. 1996;77:242–246				
Affiliation/Source of funds From the Department of Physical Medicine and Rehabilitation and Department of Medicine, Rehabilitation Institute and Northwestern University Medical School, Chicago, USA Funding source: This trial was supported by Orthobiotech, Raritan, NJ, USA				
Study design RCT n=27	Level of evidence II	Location/setting Chicago, Illinois, USA/Rehabilitation Institute		
Intervention EPO (100 IU/kg) as a subcutaneous injection 3 times a week for 8 weeks and oral iron (325 mg tid) throughout the study Sample size n=460	Comparator Placebo as a subcutaneous injection 3 times a week for 8 weeks and oral iron (325 mg tid) throughout the study Sample size n=13			
Population characteristics Patients rehabilitating after orthopaedic surgery at least 2 weeks previously with Hb <10 g/dL				
Length of follow-up Weekly blood counts were obtained for the duration of the study (8 weeks)	Outcomes measured Mean Hb levels at postoperative weeks 4 and 8			
INTERNAL VALIDITY				
Allocation	Results measurement bias	Blinding analysis	Treatment/ measurement bias	Follow-up (ITT)
Randomly assigned based on a table of random numbers	Groups' demographics were reported to be not significantly different. However, the gender balance between groups was reported was numerically close to be significantly different (by virtue of p value).	The patients was well as the investigators were unaware of patient treatment assignment or the results of haematological indices	All patients were treated the same	27 patients were initially randomised, 3 patients were lost to follow-up
Overall quality assessment (descriptive) This was a good quality randomised controlled trial				

RESULTS				
Outcome	Intervention group	Control group	OR (95% CI)	Statistical Significance
Postoperative Hb (week 4)	12.6 ± 1.5	11.0 ± 1.5	NA	P=0.02
Postoperative Hb (week 8)	13.5 ± 1.4	11.7 ± 1.7	NA	P=0.01
FIM (mobility)	6.10 ± 0.31	5.69 ± 0.63	NA	NS
Clinical importance (1–4) Unable to determine		Relevance (1–5) 2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention		
EXTERNAL VALIDITY				
Generalisability This study was performed in patients undergoing orthopaedic surgery and may not be generalisable to a wider perioperative noncardiac surgical population				
Applicability The study was conducted in the USA and is probably applicable to the Australian healthcare setting				
Comment The authors conclude that although Hb increases more rapidly in anemic orthopaedic patients treated with EPO, equally rapid functional improvement occurs in those who receive only iron therapy.				

F7 Evidence summaries, Question 7

What is the effect of rFVIIa (prophylaxis or treatment) on morbidity, mortality and transfusion rate?

Level I evidence

<table>
<tr><td colspan="3">STUDY DETAILS</td></tr>
<tr><td colspan="3">Reference Ranucci M, Isgro G, Soro G, Conti D, De Toffol B. Efficacy and safety of recombinant activated factor VII in major surgical procedures: Systematic review and meta-analysis of randomized clinical trials. Arch Surg. 2008b;143(3):296–304</td></tr>
<tr><td colspan="3">Affiliation/Source of funds One study author was a principal investigator on the Registry-Base Case Study on The Use of Recombinant Activated Factor VII in Trauma Patients sponsored by Novo Nordisk</td></tr>
<tr><td>Study design</td><td colspan="2">Level of evidence</td></tr>
<tr><td>Systematic review of level II studies
(7 primary studies)</td><td colspan="2">Level I</td></tr>
<tr><td colspan="2">Intervention</td><td>Comparator</td></tr>
<tr><td colspan="2">Prophylactic rFVIIa
Dosage varied from 20 to 120 μg/kg</td><td>Placebo</td></tr>
<tr><td colspan="3">Population characteristics</td></tr>
<tr><td colspan="3">Surgical patients (pelvic trauma, cardiovascular, prostatectomy, liver resection, liver transplantation)</td></tr>
<tr><td colspan="3">Outcomes measured</td></tr>
<tr><td colspan="3">Mortality, transfusion requirements, thromboembolic events</td></tr>
<tr><td colspan="3">Overall quality assessment (descriptive)</td></tr>
<tr><td colspan="3">Good: clinical research question was clearly defined, with pre-specified inclusion/exclusion criteria. Quality assessment of included studies was performed and statistical methods for pooling data were appropriate, with sources of heterogeneity explored</td></tr>
</table>

RESULTS		
Outcome	Summary	Statistical significance
Mortality (Level II evidence)	Mortality rates were not different between prophylactic rFVIIa and placebo-treated patients (OR_p 0.99, 95% CI:[0.37, 2.68]; I^2=0%, p=0.94)	p=0.99
Clinical importance 4	Clinical relevance 1	
Morbidity (Level II evidence)	Thromboembolic complication rates were not different between prophylactic rFVIIa and placebo-treated patients (OR_p 1.32, 95% CI:[0.69, 2.52]; I^2=0%, p=0.99)	p=0.40
Clinical importance 4	Clinical relevance 1	
Transfusion requirements (Level II evidence)	Prophylaxis with rFVIIa reduced the likelihood of receiving allogeneic red blood cells (OR_p 0.29, 95% CI:[0.10, 0.80]; I^2=60%, p=NR) Subgroup analysis found that only patients receiving at least 50 µg/kg rFVIIa had a significant benefit in terms of reduction in transfusion requirements (OR_p 0.43, 95% CI:[0.23, 0.78], p=0.006)	p=0.02
Clinical importance 1	Clinical relevance 1	
EXTERNAL VALIDITY		
Generalisability		
Populations of included studies considered similar to guideline target population		
Applicability		
Reduced – primary studies performed in Europe – therefore difference to Australian/New Zealand healthcare systems		
Comments		
The findings of this systematic review suggest that prophylactic rFVIIa is beneficial in terms of reducing the need for allogeneic RBC transfusion. However, no definitive conclusions can be made regarding the effect of prophylactic rFVIIa on mortality or morbidity – the wide CI for the OR_p shows that included studies are not sufficiently powered for these outcomes		

Abbreviations: CI, confidence intervals; OR_p, pooled odds ratio; RBC, red blood cells; rFVIIa, recombinant activated factor VIIa

STUDY DETAILS			
Reference Warren O, Mandal K, Hadjianastassiou V, Knowlton L, Panesar S, John K, et al. Recombinant activated factor VII in cardiac surgery: A systematic review. Ann Thorac Surg. 2007;83(2):707–714			
Affiliation/Source of funds Funding not reported			
Study design	**Level of evidence**		
Systematic review of Level II (2 primary studies) and III-2 (4 primary) studies	Level II and III-2		
Intervention rFVIIa: Dosage ranged from 18 to 90 µg/kg		**Comparator** Placebo	
Population characteristics Cardiac surgery patients (complex non-coronary cardiac surgery, various procedures, aortic dissection)			
Outcomes measured Mortality, blood loss, transfusion requirements, morbidity (thromboembolic effects)			
Overall quality assessment (descriptive) Poor: quality assessment of included primary studies not performed, characteristics and results of included studies inadequately summarised			
RESULTS			
Outcome	**Summary**		**Statistical significance**
Morbidity (Level II and III-2)	Treatment with rFVIIa—Aggregated adverse event rate for thromboembolic events was 5.3% in adult patients. Rate NR for control patients (inter study heterogeneity not assessed)		Not reported
Clinical importance Not determined		**Clinical relevance** 1	
Blood loss/transfusion requirements (Level II)	In one study of infants <1year (n=82), prophylactic rFVIIa had no effect on volumes of transfusion products required In one small (underpowered) study of adult patients (n=19), 13 units of allogeneic blood were transfused in the group who received prophylactic rFVIIa vs. 105 units in the placebo group (RR, any transfusion=0.26)		p=0.037
Clinical importance Not determined		**Clinical relevance** 1	
Time to chest closure (Level II)	In one study of infants <1year (n=82), prophylactic rFVIIa significantly increased the time to chest closure		p=0.02
Clinical importance Not determined		**Clinical relevance** 1	
EXTERNAL VALIDITY			
Generalisability Populations of included studies considered similar to guideline target population			
Applicability Reduced – primary studies performed in Europe – therefore difference to Australian/New Zealand healthcare systems			
Comment Findings from one small study included in this systematic review suggest that prophylactic rFVIIa has the potential to reduce transfusion requirements in adult patients. However, this small study is inadequately powered to detect the effects of rFVIIa			

Abbreviations: NR, not reported; rFVIIa, recombinant activated factor VIIa; RR, relative risk

STUDY DETAILS		
Reference Zangrillo A, Mizzi A, Biondi-Zoccai G, Bignami E, Calabro MG, Pappalardo F, et al. Recombinant activated factor VII in cardiac surgery: A meta-analysis. J Cardiothorac Vasc Anesth. 2009;23(1):34–40		
Affiliation/Source of funds Funding not reported		
Study design	**Level of evidence**	
Systematic review of Level II (1 primary study) and III-2 studies (4 primary studies)	Level II and Level III-2	
Intervention Prophylactic and therapeutic rFVIIa: Dosage ranged from 18 to 90 µg/kg		**Comparator** Placebo
Population characteristics Cardiac surgery patients (cardiopulmonary bypass, various procedures)		
Outcomes measured Mortality, surgical re-exploration, and morbidity (stroke, MI, AKI)		
Overall quality assessment (descriptive) Fair: quality assessment of included studies not performed		
RESULTS		
Outcome	**Summary**	**Statistical significance**
Mortality (Level II and III-2)	rFVIIa=15% vs. control=15%; OR_p=0.96[a] (95% CI:[0.50, 1.86]) (I^2=0% with 298 patients included in 5 studies)	p=0.90
Clinical importance 4	**Clinical relevance** 1	
Morbidity (Level II and III-2)	Rate of thromboembolic events (MI, stroke and DVT): rFVIIa = 9% vs. control=6%; OR_p=1.62 [a] (95% CI:[0.68, 3.86]) (I^2=0% with 298 patients included in 5 studies) Rate of perioperative stroke: rFVIIa=5% vs. control=1.4%; OR_p=3.17 [a] (95% CI:[0.83, 12.10]), (I^2=0% with 298 patients included in 5 studies) Rate of MI: rFVIIa=4.5% vs. control=6.5%; OR_p=0.70 [a] (95% CI:[0.21, 2.29]), (I^2=0% with 218 patients included in 4 studies) Rate of acute kidney injury: rFVIIa=15% vs. control=9%; OR_p=1.86 [a] (95% CI:[0.81, 4.31]), (I^2=39% with 228 patients included in 3 studies)	p=0.28(NS) p=0.09 (NS) p=0.55 (NS) p=0.15 (NS)
Clinical importance Thromboembolic events=4 perioperative stroke=4 MI=4 AKI=4	**Clinical relevance** 1	
Surgical re-exploration (Level II and III-2)	Rate of re-exploration: rFVIIa=13% vs. control=57%; OR_p=0.25 [a] (95% CI:[0.01, 7.01]), (I^2=90% with 150 patients included in 3 studies)	p=0.42 (NS)
Clinical importance 4	**Clinical relevance** 1	
EXTERNAL VALIDITY		

Generalisability Populations of included studies considered similar to guideline target population
Applicability Reduced – primary studies performed in Europe – therefore difference to Australian/New Zealand healthcare systems
Comments Results suggest that rFVIIa may reduce the rate of surgical exploration after cardiac surgery, although this difference was not statistically significant. There was also significant heterogeneity among the three studies that reported this outcome. Furthermore, this potential benefit should be considered with awareness of a possible increase in the risk of thromboembolic events. The use of rFVIIa appears to have no effect on mortality, but this result was also not statistically significant. For all the OR_p values reported in this systematic review, the CIs were broad and captured the value of no effect (i.e. 1.00). No definitive conclusions can be drawn from this systematic review due to the absence of statistical significance. Studies included in this systematic review were not adequately powered to measure the effects of rFVIIa

Abbreviations: AKI, acute kidney injury; CI, confidence intervals; MI, myocardial infarction; NS, not significant; OR_p, pooled odds ratio; rFVIIa, recombinant activated factor VIIa

Level II evidence

STUDY DETAILS				
Reference Essam MA. Prophylactic administration of recombinant activated factor VII in coronary revascularization surgery. Internet J Anesthesiol. 2007;13(1). http://www.ispub.com/ostia/index.php?xmlPrinter=true&xmlFilePath=journals/ija/vol13n1/factor.xml				
Affiliation/Source of funds None reported				
Study design	Level of evidence	Location/setting		
Single-centre, randomised, placebo-controlled trial	Level II	Saudi Arabia/Hospital		
Intervention	Comparator			
Prophylactic rFVIIa, dose=90 µg/kg following weaning off cardiopulmonary bypass N=15	Placebo N=15			
Population characteristics Elective cardiac revascularisation patients who underwent cardiopulmonary bypass				
Length of follow-up	Outcomes measured			
24 hours	Transfusion requirements, chest tube drainage, haemoglobin levels			
INTERNAL VALIDITY				
Allocation	Results	Blinding analysis	Treatment/measurement bias	Follow-up (ITT)
Randomisation using sealed enveloped	Baseline characteristics similar for both treatment groups	Blinding not reported	None	All patients followed up
Overall quality assessment (descriptive) Fair				
RESULTS				
Outcome	Intervention group	Comparator group	Statistical significance	
Transfusion requirements (24 hrs) (mean ± SD)	RBC: 316.6 ± 333.6 FFP: 60 ± 94.8 Platelets: 40 ± 69.6	RBC: 516.66 ± 175.93 FFP: 270 ± 181.06 Platelets: 106.6 ± 67.78	p=0.047 p=0.004 p=0.021	
Clinical importance Not determined		Clinical relevance 1		
Chest tube drainage (24 hrs) (mean ± SD)	435 mL (SD: 93.86)	620.33 mL (SD: 108.33)	p=0.001	
Clinical importance Not determined		Clinical relevance 1		

Hb Levels[a] (g/dl) (mean ± SD)	Baseline Hb=12.56 (SD: 0.79) T1 Hb (off CPB)=8.66 (SD: 0.47) T2 Hb (CICU admission)=9.26 (SD: 0.68) T3 Hb (12 hrs CICU)=9.71 (SD: 0.61) T4 Hb (24 hrs CICU)=9.9 (SD 0.74)	Baseline Hb=12.56 (SD: 1.22) T1 Hb (off CPB)=8.53 (SD: 0.72) T2 Hb (CICU admission)=9.27 (SD: 0.82) T3 Hb (12 hrs CICU)=9.51 (SD : 0.63) T4 Hb (24 hrs CICU)=9.03 (SD 2.26)	p=0.985 p=0.34 p=0.959 p=0.098 p=0.159
Clinical importance Not determined		Clinical relevance 1	
EXTERNAL VALIDITY			
Generalisability Patient population similar to guideline target population			
Applicability Reduced – Study conducted in Saudi Arabia – some differences to Australian/ New Zealand health care systems			
Comments Small study – underpowered, with no blinding reported. The wide range of standard deviation (SD) values reported for outcomes indicate that the data set is skewed. Therefore, definitive conclusions cannot be made about the effect of rFVIIa owing to the absence of statistical analysis appropriate for skewed data.			

Abbreviations: CICIU, coronary intensive care unit; CPB, cardiopulmonary bypass; FFP, fresh frozen plasma; Hb, haemoglobin; rFVIIa, recombinant activated factor VIIa; RBC, red blood cells; SD, standard deviation

[a] Hb measured at several time points: T1 = off CPB prior to study drug administration;T2 = on CICIU admission; T3 = 12 hours post CICU admission; and T4 = 24 hours post CICU admission.

STUDY DETAILS				
Reference Gill R, Herbertson M, Vuylsteke A, Olsen PS, von Heymann C, Mythen M, et al. Safety and efficacy of recombinant activated factor VII. A randomized placebo-controlled trial in the setting of bleeding after cardiac surgery. Circulation. 2009;120:21–27				
Affiliation/Source of funds Clinical trial sponsored by Novo Nordisk. All study authors were compensated by Novo Nordisk				
Study design	Level of evidence	Location/setting		
Multi-centre, randomised, double-blind, placebo-controlled trial	Level II	13 countries/hospital		
Intervention	Comparator			
Postoperative, therapeutic rFVIIa, dose=40 µg/kg, N=35 or 80 µg/kg, N=69	Placebo N=68			
Population characteristics Postoperative, cardiac surgery patients who underwent cardiopulmonary bypass				
Length of follow-up	Outcomes measured			
30 days	Mortality, morbidity, re-operation, transfusion requirements			
INTERNAL VALIDITY				
Allocation	Results	Blinding analysis	Treatment/measurement bias	Follow-up (ITT)
Randomisation through an interactive voice response system	Baseline characteristics similar for all treatment groups	Double-blind	None	7 of 179 randomised patients not dosed with rFVIIa or placebo
Overall quality assessment (descriptive) Fair				
RESULTS				
Outcome	Intervention group	Comparator group	Statistical significance	
Mortality (proportion)	40 µg/kg=11% 80 µg/kg=9%	6%	p=NR	
Clinical importance Not determined		Clinical relevance 1		
Morbidity (proportion) (critical SAEs)	40 µg/kg=14% 80 µg/kg=12%	7%	p=0.25 p= 0.43	
Clinical importanc Not determined		Clinical relevance 1		
Re-operation (proportion)	40 µg/kg=14% 80 µg/kg=12%	25%	p=0.21 p=0.04	
Clinical importance Not determined		Clinical relevance 1		

Allogeneic blood transfusion (mL, 25–75% IQR)	40 µg/kg=640 (0–1920) 80 µg/kg=500 (0–1750)	825 (326.5–1893)	p=0.047 p=0.042
Clinical importance Not determined		Clinical relevance 1	
EXTERNAL VALIDITY			
Generalisability Patient population similar to guideline target population			
Applicability Reduced—Study conducted in several countries—some to differences to Australian/ New Zealand health care systems			
Comments Small study, inadequate powering to detect genuine effects of rFVIIa			

Abbreviations: IQR, interquartile range; NR, not reported; rFVIIa, recombinant activated factor VIIa; SAE, serious adverse event

STUDY DETAILS				
Reference Johansson PI, Eriksen K, Nielsen SL, Rojkjaer R, Alsbjorn B. Recombinant FVIIa decreases perioperative blood transfusion requirement in burn patients undergoing excision and skin grafting—results of a single centre pilot study. Burns. 2007;33(4):435–440				
Affiliation/Source of funds Study supported by an unrestricted educational grant from Novo Nordisk				
Study design	**Level of evidence**		**Location/setting**	
Single-centre, randomised, double-blind, placebo-controlled trial	Level II		Denmark/Hospital	
Intervention		**Comparator**		
rFVIIa, prophylactically, 40 µg/kg as IV bolus injection immediately prior to surgery, and second dose (40 µg/kg) 90 minutes later N=9		No rFVIIa – same placebo regimen before and after surgery as intervention group N=9		
Population characteristics Patients with thermal burns aged ≥18 years, scheduled to have full thickness burn wound excision of >10% of total body surface area and skin grafting				
Length of follow-up		**Outcomes measured**		
30 days		Mortality (survival rate on day 30); adverse events; ICU and hospital LOS		
INTERNAL VALIDITY				
Allocation	**Results**	**Blinding analysis**	**Treatment/measurement bias**	**Follow-up (ITT)**
Randomisation using permuted blocks derived from random number tables	Baseline characteristics similar for both treatment groups except age: RfVIIa vs. placebo: Median age (range)=38 years(19–81) vs. 54 years (22–85)	Double-blind	None	All patients followed up
Overall quality assessment (descriptive) Fair				
RESULTS				
Outcome	**Intervention group**	**Comparator group**	**Statistical significance**	
Mortality (proprotion) (survival at day 30)	100%	66.7%	p=0.20	
Clinical importance Not determined		**Clinical relevance** 1		

Postoperative complications	Wound infection n=2 Sepsis (days) 20 Pnemonia n=6 ALI n=2 MOF n=3 TE n=0	Wound infection n=2 Sepsis (days) 62 Pnemonia n=5 ALI n=1 MOF n=7 TE n=0	p=0.71 p=0.44 p=0.50 p=0.50 p=0.08 NA
Clinical importance Not determined		**Clinical relevance** 1	
ICU LOS (days ; median, range)	4 (0–63)	8 (0–37)	p=0.59
Clinical importance Not determined		**Clinical relevance** 1	
Hospital LOS (days ; median, range)	49 (33–110)	36 (28-72)	p=0.22
Clinical importance Not determined		**Clinical relevance** 1	
EXTERNAL VALIDITY			
Generalisability Patient population similar to guideline target population			
Applicability Reduced—Study conducted in Denmark—some differences to Australian/ New Zealand health care systems			
Comments Small study, therefore underpowered to detect effects of rFVIIa. Results suggest trend towards reduced multiple organ failure in patients who received rFVIIa			

Abbreviations: ICU, intensive care unit; LOS, length of stay; N/A, not applicable; rFVIIa, recombinant activated factor VIIa; TE, thromboembolic event

STUDY DETAILS				
Reference Ma B, Wang ZN, Zhang BR, Xu ZY, Yang LX, Chen KB, Li J. Effect of recombinant activated factor VIIa on early recovery of patients undergoing cardiac valve replacement under cardiopulmonary bypass: A randomized double-blind placebo-controlled trial. Acad J Second Mil Med Univ. 2006;27(10):1110–1113.				
Affiliation/Source of funds Not assessed – study reported in foreign language paper				
Study design	Level of evidence	Location/setting		
Single-centre, randomised, double-blind, placebo-controlled trial	Level II	China/Hospital		
Intervention	Comparator			
Prophylactic rFVIIa, 40 µg/kg, N=11	Placebo, N=11			
Population characteristics Unknown—study reported in foreign language paper				
Length of follow-up	Outcomes measured			
Unknown—study reported in foreign language paper	Morbidity, transfusion requirements; blood loss; ICU LOS, hospitalisation costs			
INTERNAL VALIDITY				
Allocation	Results	Blinding analysis	Treatment/measurement bias	Follow-up (ITT)
Unknown		Double-blind	Unknown	Unknown
Overall quality assessment (descriptive) Not assessed—information not available, foreign language paper				
RESULTS				
Outcome	Intervention group	Comparator group	Statistical significance	
Mortality	No deaths	No deaths	Not applicable	
Clinical importance Not determined		Clinical relevance 1		
Morbidity Cerbral infarction MI DVT PE	No events	No events	Not applicable	
Clinical importance Not determined		Clinical relevance 1		

Transfusion requirements			
RBC (units, mean±SD)	3.5±2.2	6.3±3.1	p<0.01
Plasma (units, mean±SD)	5.5±3.5	4.8±4.7	Not significant
Platelets (units, mean±SD)	3.4±2.2	7.5±3.2	p<0.01
Cryoprecipitate (units, mean±SD)	0.9±1.0	1.1±1.7	p value NR
Total blood use (units, mean±SD)	13.1±4.6	19.5±7.1	p<0.05
Total blood use (volume, mean±SD)	2120.3±621.7	3417.7±735.2	Not significant
Clinical importance Not determined		**Clinical relevance** 1	
Blood loss (mL, mean±SD)	338±42.1	342±50.3	NR
Clinical importance Not determined		**Clinical relevance** 1	
ICU LOS (days, mean±SD)	2.7±0.5	3.3±0.7	p<0.05
Clinical importance Not determined		**Clinical relevance** 1	
Hospitalisation costs (Chinese RMB, mean±SD)	71356.3±11437.6	66772.0±19272.0	NR
Clinical importance Not determined		**Clinical relevance** 1	
EXTERNAL VALIDITY			
Generalisability Unknown—limited patient details in English abstract			
Applicability Limited—study conducted in China—difference to Australian and New Zealand healthcare systems			
Comments Small study, therefore underpowered to detect effects of rFVIIa. Results suggest that patients who receive rFVIIa may have some transfusion requirements reduced (RBC, platelets), with a trend towards reduced ICU LOS. No definitive conclusions can be made due to the underpowering			

Abbreviations: ICU, intensive care unit; LOS, length of stay; NR, not reported; RBC, red blood cells; rFVIIa, recombinant activated factor VIIa; SD, standard deviation

Reference Pihusch M, Bacigalupo A, Szer J, Von Depka Prondzinski M, Gaspar-Blaudschun B, Hyveled L, et al. Recombinant activated factor VII in treatment of bleeding complications following hematopoietic stem cell transplantation. J Thromb Haemost. 2005;3(9):1935–1944.				
Affiliation/Source of funds Two authors employed by Novo Nordisk, manufacturers of Novoseven® (rFVIIa)				
Study design	Level of evidence		Location/setting	
Multi-centre, randomised, double-blind, placebo-controlled trial	Level II		Europe and Australia/Hospital	
Intervention		Comparator		
rFVIIa: three different dosing regimens: Cohort 1=40 µg/kg , every 6h for 36h, N=20 Cohort 2=80 µg/kg, every 6h for 36h, N=26 Cohort 3=160 µg/kg, every 6h for 36h, N=31 rFVIIa used therapeutically for bleeding complications following hematopoietic stem cell transplantation		Placebo N=23		
Population characteristics				
Patients ≥12 yrs receiving allogeneic hematopoietic stem cell grafts. Patients admitted for a variety of haematological and oncological disorders at various stages of their diseases Patients included if they had mild bleeding for >3 full consecutive days or with severe or serious bleeding episodes Mild bleeding: defined as minor bleeding that does not required RBC transfusion over routine transfusion needs Severe bleeding: defined as haemorrhage causing rapid decrease in hematocrit level necessitating ≥1 units of RBC per day over routine transfusion needs Serious bleeding: Life-threatening haemorrhage – defined as massive bleeding causing severe hemodynamic compromise or bleeding into a vital organ				
Length of follow-up		Outcomes measured		
96 h following initial dose		Mortality, morbidity, transfusion requirements, change in bleeding status		
INTERNAL VALIDITY				
Allocation	Results	Blinding analysis	Treatment/measurement bias	Follow-up (ITT)
Computer-generated	Baseline characteristics were similar across treatment groups. Some variability across treatment groups with regard to primary bleeding site	Double-blind	None reported	All patients followed up
Overall quality assessment (descriptive) Fair				

RESULTS					
Outcome	Intervention group			Comparator group	Statistical significance
Mortality (within 96 h study period) [n (%)]	Cohort 1 0	Cohort 2 0	Cohort 3 1(3.2)	Placebo 1 (4.4)	Not reported
Clinical importance Not determined			Clinical relevance 1		
Morbidity [n (%)] TE SAE[a]	Cohort 1 1 (5) 2 (10)	Cohort 2 0 5 (19.2)	Cohort 3 2 (6.5) 3 (9.7)	Placebo 0 3 (13)	Not reported
Clinical importance Not determined			Clinical relevance 1		
Transfusion requirements	Data not presented, but authors report that there was no overall significant trend towards reduced RBC, platelet concentrates or FFP requirements with increasing dose in actively bleeding patients or in patients with haemorrhagic cystitis or moderate or severe bleeding within 96 h after initial administration of rFVIIa				
Clinical importance Not determined			Clinical relevance 1		
Bleeding status[b] [n (%)] (38 h post initial dosing) Stopped Decreased Unchanged or worsened	Cohort 1 6 (30.0) 4 (20.0) 10 (50.0)	Cohort 2 14 (53.8) 7 (26.9) 5 (19.2)	Cohort 3 4 (12.9) 9 (29.0) 17 (54.8)	Placebo 5 (21.7) 8 (34.8) 9 (39.1)	Authors report no significant difference in proportion of patients who stopped bleeding between each treatment group and Placebo
Clinical importance Not determined			Clinical relevance 1		
EXTERNAL VALIDITY					
Generalisability Patient population similar to guideline target population					
Applicability Reduced – Study conducted in several countries – some with differences to Australian/New Zealand health care systems					
Comments Small study, therefore underpowered to detect effects of rFVIIa. Trend towards increased number of patients who stopped bleeding in 80 µg/kg rFVIIa treatment group, with increased SAE In this group. Transfusion requirements apparently unaffected. No definitive conclusions can be made from this study due to the small sample size and lack of powering					

Abbreviations: FFP, fresh frozen plasma; RBC, red blood cells; rFVIIa, recombinant activated factor VIIa; SAE, serious adverse event.

[a] Serious adverse events described by study authors: death, threat to life of patient, in-patient hospitalisation or prolongation of existing hosopitalisation, persistent or significant disability or incapacity; important medical events that may not result in death, be life threatening, or require hospitalisation may be considered an SAE when, based upon appropriate medical judgement, they may jeopardise the patient or subject and may require medical or surgical intervention to prevent one of the outcomes.

[b] Results unavailable for two patients

STUDY DETAILS				
Reference Pugliese F, Ruberto F, Summonti D, Perrella S, Cappannoli A, Tosi A, et al. Activated recombinant factor VII in orthotopic liver transplantation. Transplant Proc. 2007;39(6):1883–1885				
Affiliation/Source of funds Details of study funding not reported				
Study design	**Level of evidence**		**Location/setting**	
Single-centre, randomised, double-blind, placebo-controlled trial	Level II		Italy/Hospital	
Intervention		**Comparator**		
Prophylactic rFVIIa, N=10 40 μg/kg given as single bolus prior to anaesthesia induction		Placebo N=10		
Population characteristics Patients scheduled for orthotopic liver transplant, with Hb>8 mg/dL, INR>1.5, fibrinogen >100 mg/dL				
Length of follow-up		**Outcomes measured**		
6 hr after bolus administration		Mortality, morbidity, Transfusion requirements, blood loss, ICU LOS **Note:** Blood transfusions administered as follows: 800 mL FFP if INR>1.5 and 200 mL RBC when Hb<10 g/dL		
INTERNAL VALIDITY				
Allocation	**Results**	**Blinding analysis**	**Treatment/measurement bias**	**Follow-up (ITT)**
Not reported	INR was different between rFVIIa and placebo groups at bolus administration: 1.9 vs. 1.6, p<0.21	Double-blind	None	All patients followed up
Overall quality assessment (descriptive) Poor				
RESULTS				
Outcome	**Intervention group**	**Comparator group**	**Statistical significance**	
Mortality	No deaths	No deaths	Not applicable	
Clinical importance Not determined		**Clinical relevance** 1		
Morbidity	No TEs	No TEs	Not applicable	
Clinical importance Not determined		**Clinical relevance** 1		

Transfusion requirements (mL)			
RBC during hepatectomy	120	240	p<0.049
RBC during anahepatic phase	180	330	p<0.17
FFP 1hr after bolus	0	240	p<0.001
FFP during hepatectomy	280	600	p<0.001
FFP during anahepatic phase	320	560	p<0.16
Clinical importance Not determined		**Clinical relevance** 1	
Blood loss (mL)			
During hepatectomy	160	280	p<0.049
During anahepactic phase	310	470	p<0.001
After vascular unclamping	270	390	p<0.049
Clinical importance Not determined		**Clinical relevance** 1	
ICU LOS (days, mean ± SD)	4.8±1.3	5.2±1.2	p=not significant
Clinical importance Not determined		**Clinical relevance** 1	
EXTERNAL VALIDITY			
Generalisability Patient population similar to guideline target population			
Applicability Reduced – Study performed in Italy – therefore difference in healthcare system to Australia/New Zealand			
Comments Small study, therefore underpowered to detect effects of rFVIIa. However, results suggest rFVIIa prophylaxis in these patients may reduce blood loss and transfusion requirements, without impacting on mortality or increasing the risk of thromboembolic events. No definitive conclusions can be made due to the small study size			

Abbreviations: CICIU, coronary intensive care unit; CPB, cardiopulmonary bypass; FFP, fresh frozen plasma; Hb, haemoglobin; ICU, intensive care unit; INR, international normalised ratio; IQR, interquartile range; LOS, length of stay; NR, not reported; RBC, red blood cells; rFVIIa, recombinant activated factor VIIa; SAE, serious adverse event; SD, standard deviation; TE, thromboembolic event

STUDY DETAILS				
Reference Sachs B, Delacy D, Green J, Graham RS, Ramsay J, Kreisler N, et al. Recombinant activated factor VII in spinal surgery: A multicenter, randomized, double-blind, placebo-controlled, dose-escalation trial. Spine. 2007;32(21):2285–2293				
Affiliation/Source of funds Funds from Novo Nordisk Inc., Princeton, NJ were received in support of this study				
Study design	**Level of evidence**		**Location/setting**	
Multi-centre, randomised, double-blind, placebo-controlled trial	Level II		USA/Hospital	
Intervention		**Comparator**		
rFVIIa: three different dosing regimens: Cohort 1=3 x 30 µg/kg, N=12 Cohort 2=3 x 60 µg/kg, N=12 Cohort 3 = 3 x 120 µg/kg, N=12 rFVIIa used therapeutically when bleeding trigger reached (see below) and given at 2 hour intervals		**Placebo** Cohort 1, N=4 Cohort 2, N=4 Cohort 3, N=5 Total N=13		
Population characteristics				
Patients 15 to 70 years of age, scheduled to undergo elective spinal fusion surgery of 3 or more motion segments by posterior approach. Patients screened for eligibility prior to surgery, but not randomised to treatment unless a bleeding trigger was reached during surgery: 10% loss of estimated blood volume, with a total expected loss of at least 20% of estimated blood volume before the end of surgery				
Length of follow-up		**Outcomes measured**		
30 days post surgery		Mortality; Morbidity, transfusion requirements, blood loss Note: RBC administered during and after surgery when Hb fell <9 g/dL; FFP given when microvascular bleeding observed and prothrombin or partial prothrombin time was 1.5x normal; Platelets given when microvascular bleeding observed and platelet count < 75,000/mm^3		
INTERNAL VALIDITY				
Allocation	**Results**	**Blinding analysis**	**Treatment/measurement bias**	**Follow-up (ITT)**
Methods not reported	No difference between treatment groups at study inception	Double-blind	None	All patients followed up
Overall quality assessment (descriptive) Fair				

RESULTS					
Outcome	Intervention group		Comparator group		Statistical significance
Mortality (%)	Cohort 1: n=1 (8) Cohort 2: n=0 Cohort 3: n=0		n=0		Not reported
Clinical importance Not determined			Clinical relevance 1		
Morbidity (%) Stroke MI Troponin 1 increased Visual acuity reduction Bardycardia Pleural effusion Seroma Postoperative infection	Cohort 1 1(8) 0 0 0 0 0 1(8) 1(8)	Cohort 2 0 1(8) 1(8) 0 0 1(8) 0 0	Cohort 3 0 0 0 0 0 0 0 0	Placebo 0 0 0 1(8) 1(8) 0 0 0	Not reported for any morbidity outcomes
Clinical importance Not determined			Clinical relevance 1		
Total transfusion volume[a] (mL, adjusted mean[b] 95% CI)	Cohort 1 258 (67,991) p=0.002	Cohort 2 89 (16,496) p<0.001	Cohort 3 287 (112,736) p<0.001	Placebo 1488 (971,2279)	Note : p values based on ratio of rFVIIa results to placebo result
Clinical importance Cohort 1 vs placebo: 2 Cohort 2 vs placebo: 1 Cohort 3 vs placebo: 1			Clinical relevance 1		
Units of blood products (combined RBC, FFP, cryoprecipitate, platelets; adjusted mean[b])	Cohort 1 1.1 p=0.03	Cohort 2 1.3 p=0.03	Cohort 3 0.8 p=0.03	Placebo 5	Note : p values based on ratio of rFVIIa results to placebo result
Clinical importance Not determined			Clinical relevance 1		
Units of RBC	Cohort 1 0.9 p=0.002	Cohort 2 1.2 p=0.012	Cohort 3 0.8 p=0.033	Placebo 1.6	Note : p values based on ratio of rFVIIa results to placebo result
Clinical importance Not determined			Clinical relevance 1		

Blood loss (mL, adjusted mean[b], 95%CI)	Cohort 1 1120 (647,1938) p=0.001	Cohort 2 400 (151,1059) p<0.001	Cohort 3 824 (435,1558) p<0.001	Placebo 2536 (1869,3441)	Note : p values based on ratio of rFVIIa results to placebo result
Clinical importance Cohort 1 vs placebo: 2 Cohort 2 vs placebo: 1 Cohort 3 vs placebo: 1			Clinical relevance 1		
EXTERNAL VALIDITY					
Generalisability Patient population similar to guideline target population					
Applicability Reduced – Study conducted in USA – some differences to Australian/New Zealand healthcare systems					
Comments Small study, therefore underpowered to detect effects of rFVIIa. However, results suggest that rFVIIa reduces transfusion requirements and blood loss, with no impact morbidity. A regimen of 3 x 60 μg/kg appears to most effective. There was 1 death in the rFVIIa treatment groups and none in the placebo group, but no definitive conclusions can be regarding the impact of rFVIIa on mortality due to the small sample size in this study					

Abbreviations: CI, confidence interval; FFP, fresh frozen plasma; RBC, red blood cells; rFVIIa, recombinant activated factor VIIa;
[a] Total transfusion volume for RBC, autologous RBC, cell saver, fresh frozen plasma, cryoprecipitates, platelets.
[b] Mean adjusted for number of spinal segments fused, duration of surgery and initial blood volume

F8 Evidence summaries, Question 8

What is the effect of fresh frozen plasma, cryoprecipitate, fibrinogen concentrate, and/or platelet transfusion on patient outcome?

Effect of fresh frozen plasma: Level I evidence

<table>
<tr><td colspan="5">STUDY DETAILS</td></tr>
<tr><td colspan="5">Reference Casbard AC, Williamson LM, Murphy MF, Rege K, Johnson T. The role of prophylactic fresh frozen plasma in decreasing blood loss and correcting coagulopathy in cardiac surgery. A systematic review. Anaesthesia. 2004;59:550–558.</td></tr>
<tr><td colspan="5">Affiliation/Source of funds
Medical Research Council Clinical Trials Unit, 222 Euston Rd, London, UK; University of Cambridge, Vational Blood Service, Cambridge, UK; National Blood Service, John Radcliffe Hospital, Headington, Oxford, UK; Papworth Hospital, Papworth, Everard, Cambridgeshire, UK; Medical Research Council Biostatistics Unit, Institute of Public Health, University Forrie Site, Cambridge, UK.
Funding source: the study was funded by the national Blood Service</td></tr>
<tr><td colspan="2">Study design
Systematic review of RCTs (6 primary Level II studies)</td><td colspan="2">Level of evidence
I</td><td>Location/setting
USA, 3 Germany, Israel, Amsterdam</td></tr>
<tr><td colspan="3">Intervention
Prophylactic administration of FFP</td><td colspan="2">Comparator(s)
Placebo or no FFP</td></tr>
<tr><td colspan="5">Population characteristics
Cardiac surgery</td></tr>
<tr><td colspan="3">Length of follow-up
NA</td><td colspan="2">Outcome(s) measured
Blood loss at 24 hours, platelet count, fibrinogen, Hb, PT, activated partial thromboplastin time</td></tr>
<tr><td colspan="5">INTERNAL VALIDITY</td></tr>
<tr><td>Allocation</td><td>Comparison of study groups</td><td>Blinding</td><td>Treatment/ measurement bias</td><td>Follow-up (ITT)</td></tr>
<tr><td>Of the six studies, one study randomised patients using a list of random numbers, one used block randomisation, and one a computer generated sequence. 3 studies did not report the randomisation method</td><td>It is not clear in the report how the studies compared with each other or how each treatment arm within each study compared</td><td>Investigato: yes in 2 studies, no in 2 studies and unclear in 2 studies.
Carers: yes in 1 study, no in one study and not clear in 4 studies</td><td>Not clear</td><td>ITT analysis was used in 4 studies and per protocol analysis in 2 studies</td></tr>
</table>

Overall quality assessment (descriptive) This was a good quality systematic review				
RESULTS				
Outcome	FFP	Placebo	SMD (95% CI)	Statistical Significance
Blood loss at 24 hours	NR	NR	-0.01 (-0.22, 0.20)	P=0.95
Clinical importance (1–4) 3 The confidence interval does not include any clinically important effects		Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		
Platelet count	NR	NR	0.24 (0.01, 0.48)	P=0.05
Fibrinogen	NR	NR	0.47 (0.06, 0.87)	P=0.02
Clinical importance (1–4) 2 The point estimate of effect is clinically important BUT the confidence interval includes clinically unimportant effects.		Relevance (1–5) 2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention		
Haemoglobin	NR	NR	-0.06 (-0.38, 0.27)	P=0.74
Activated partial thromboplastin time	NR	NR	-0.27 (-0.51, -0.02)	P=0.15
Clinical importance (1–4) 4 The range of estimates defined by the confidence interval includes clinically important effects BUT the range of estimates defined by the confidence interval is also compatible with no effect, or a harmful effect		Relevance (1–5) 2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient-relevant outcomes for the same intervention		
Any other adverse effects None reported				
EXTERNAL VALIDITY				
Generalisability The results of this study is generalisable to a cardiac surgery population				
Applicability The studies are probably applicable to the Australian healthcare setting				
Comment The authors conclude that none of the studies found showed any benefit of administering prophylactic intraoperative FFP during coronary artery bypass surgery. The size and design, and the small numbers of subjects in the included studies mean that this review is inconclusive, and will be unlikely to affect current practice until further evidence comes to light				

Effect of fresh frozen plasma: Level III evidence

<table>
<tr><td colspan="5">STUDY DETAILS</td></tr>
<tr><td colspan="5">Reference Sarani B, Dunkman J, Dean L, Sonnad S, Rohrbach JI, Gracias VH. Transfusion of fresh frozen plasma in critically ill surgical patients is associated with an increased risk of infection. Crit Care Med. 2008;36:1114–1118.</td></tr>
<tr><td colspan="5">Affiliation/Source of funds
From the Division of Traumatology and Surgical Critical care, Department of Surgery, University of Pennsylvania, School of medicine, Philadelphia, USA
Funding source: supported in part by the Division of Traumatology and Surgical Care, University of Pennsylvania, School of Medicine, Philadelphia, USA</td></tr>
<tr><td colspan="2">Study design
Retrospective cohort study
N=2,438</td><td colspan="2">Level of evidence
III</td><td>Location/setting
Surgical intensive care unit of a university hospital in the USA</td></tr>
<tr><td colspan="3">Intervention
FFP
Sample size N=380</td><td colspan="2">Comparator(s)
No FFP
Sample size N=2058</td></tr>
<tr><td colspan="5">Population characteristics
Non-trauma patients admitted to the surgical intensive care unit</td></tr>
<tr><td colspan="3">Length of follow-up
Not reported</td><td colspan="2">Outcome(s) measured
Infections</td></tr>
<tr><td colspan="5">INTERNAL VALIDITY</td></tr>
<tr><td>Allocation</td><td>Comparison of study groups</td><td>Blinding</td><td>Treatment/ measurement bias</td><td>Follow-up (ITT)</td></tr>
<tr><td>The study does not report on how patients were allocated</td><td>There are significant difference in baseline demographic characteristics between patients receiving FFP and those who did not.</td><td>No blinding details are rported</td><td>It is not clear whether all patients were treated the same</td><td>ITT analysis</td></tr>
<tr><td colspan="5">Overall quality assessment (descriptive)
This was a fair quality retrospective cohort study with some limitations. Baecause this study was not a randomised study, the possible effect of other unmeasured confounding variables cannot be excluded. Moreover, there were significant differences in the characteristics that were recorded between the two groups, although multivariate analysis was used to control for the noted disparties. Furthermore, the retrospective study design precludes establishing a causal relationship between FFP transfusion and infectious complications, and a one institute design limits heterogeneity. The study design also precludes determining the reason underlying the FFP transfusion or its impact on coagulation variables.</td></tr>
</table>

RESULTS				
Outcome	FFP transfusion	No FFP transfusion	OR (95% CI)	Statistical Significance
Infection	69/380 (18.2)	125/2,058 (6.1)	1.04 (1.01, 1.07)	p<0.01
Clinical importance (1–4) 2 The point estimate of effect is clinically important BUT the confidence interval includes clinically unimportant effects.		Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		
Any other adverse effects None reported				
EXTERNAL VALIDITY				
Generalisability The study results are most likely generalisable to a wider noncardiac surgical population				
Applicability The study was conducted in the USA and is probably applicable to the Australian healthcare setting				
Comment The authors concluded that transfusion of FFP is associated with an increased risk of infection in critically ill surgical patients				

Effect of platelets: Level III evidence

<table>
<tr><td colspan="5">STUDY DETAILS</td></tr>
<tr><td colspan="5">Reference Karkouti K, Wijeysundera DN, Yau TM, Callum JL, Meineri M, Wasowicz M, et al. Platelet transfusions are not associated with increased morbidity or mortality in cardiac surgery. Can J Anesth. 2006b;53(3):279–287.</td></tr>
<tr><td colspan="5">Affiliation/Source of funds
From the Departments of Anesthesia, Health Policy, Management, and Evaluation, Cardiac Surgery, and Haematology, University Health Network, University of Toronto, Toronto, Ontario, Canada
Funding source: K. Karkouti is supported in part by the Canadian Institutes of Health Research and the Canadian Blood Services; D.N. Wijeysundera is supported in part by the Canadian Institutes of Health Research; T.M. Yau is supported in part by the Canadian Institutes of Health Research and the Heart and Stroke Foundation of Ontario; W.S. Beattie is the R. Frasier Elliot Chair of Cardiac Anesthesia at the University Health Network. No third party funding was used for this study, None of the authors have any affiliation with or financial involvement in any organisation or entity with a direct financial interest in the subject manner or materials discussed in the manuscript.</td></tr>
<tr><td colspan="2">Study design
Retrospective cohort study
N=11,459</td><td colspan="2">Level of evidence
III</td><td>Location/setting
General Hospital, Canada</td></tr>
<tr><td colspan="2">Intervention
Platelets
Sample size N=2,174</td><td colspan="3">Comparator(s)
No platelets
Sample size N=9,285</td></tr>
<tr><td colspan="5">Population characteristics
Patients who underwent cardiac surgery at a single institution over a 5 year period</td></tr>
<tr><td colspan="2">Length of follow-up
Not reported</td><td colspan="3">Outcome(s) measured
Low output syndrome, stroke, acute renal failure, MI, sepsis, in-hospital death</td></tr>
<tr><td colspan="5">INTERNAL VALIDITY</td></tr>
<tr><td>Allocation</td><td>Comparison of study groups</td><td>Blinding</td><td>Treatment/ measurement bias</td><td>Follow-up (ITT)</td></tr>
<tr><td>Indications for platelet transfusion included a platelet count of <50x10^9/L, ongoing haemorrhage after complete reversal of heparin and a platelet count of <80x10^9/L, or ongoing haemorrhage after prolonged CPB irrespective of platelet count</td><td>There were significant differences in baseline demographics between patients receiving and not receiving platelets</td><td>No blinding details are reported</td><td>Some patients also received RBC transfusion as well as FFP transfusion</td><td>ITT analysis</td></tr>
</table>

Overall quality assessment (descriptive) This was a fair quality retrospective cohort study with limitations inhersnt to this study design				
RESULTS				
Outcome	Platelets	No Platelets	OR (95% CI)	Statistical Significance
Low output syndrome	53/924 (5.7)	57/924 (6.2)	NR	p=0.7
Myocardial infarction	37/924 (4.0)	29/924 (3.1)	NR	p=0.3
Stroke	13/924 (1.4)	17/924 (1.8)	NR	p=0.5
Renal failure	12/294 (1.3)	19/294 (2.1)	NR	p=0.2
Sepsis	20/294 (2.2)	21/294 (2.3)	NR	p=0.9
Death	20/294 (2.2)	23/294 (2.5)	NR	p=0.6
Clinical importance (1–4) 3 The confidence interval does not include any clinically important effects.		Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		
Any other adverse effects None reported				
EXTERNAL VALIDITY				
Generalisability The results of this study are generalisable to a cardiac surgery population				
Applicability The study was conducted in Canada and is applicable to the Australian healthcare setting				
Comment The authors concluded that transfusion of leukoreduced platelets in cardiac surgery is not associated with adverse clinical outcomes when adjustments are made for important confounders				

STUDY DETAILS				
Reference McGrath T, Koch CG, Xu M, Li L, Mihaljevic T, Figueroa P, Blackstone EH. Platelet transfusion in cardiac surgery does not confer increased risk for adverse morbid outcomes. Ann Thorac Surg. 2008;86:543–553.				
Affiliation/Source of funds Departments of Cardiothoracic Anesthesia, Quantitative Health Sciences, Thoracic and cardiovascular Surgery, Laboratory Medicine and Clinical Pathology, and Outcomes Research, Clevelend Clinic Cleveland, Ohio, USA Funding source: all financial support was obtained within the Department of Cardiothoracic Anesthesia. There was no external source of funding for this project.				
Study design Retrospective cohort study N=29,487	Level of evidence III	Location/setting Clevelend Clinic, USA		
Intervention Platelets Sample size N=3,599	Comparator(s) No platelets Sample size N=25,888			
Population characteristics Patients who underwent isolated CABG, an isolated valve procedure, or a combined CABG and valve procedure requiring CPB				
Length of follow-up Not reported	Outcome(s) measured In-hospital mortality, cardiac, pulmonary, renal, and neurologic morbidities, serious infection, and re-exploration for bleeding. A composite outcome of adverse events consisted of in-hospital mortality, cardiac morbidity, respiratory insufficiency, renal morbidity, serious infection and neurologic morbidity			
INTERNAL VALIDITY				
Allocation	Comparison of study groups	Blinding	Treatment/ measurement bias	Follow-up (ITT)
The study does not reort how patients were allocated	There were significant differences in baseline demographics between patients receiving and not receiving platelets	No blinding details are reported	It is not clear if all patients were treated the same	ITT analysis
Overall quality assessment (descriptive) This was a fair quality retrospective cohort study with limitations. Inherent to non-randomised studies, the inability to capture every intraoperative and postoperative process-of-care events and the potential for unobserved or unknown confounders may have influenced the reported findings. Another limitation intrinsic to all cohort investigations concerns that association or correlation does not prove causality.				

RESULTS				
Outcome	Platelets	No Platelets	OR (95% CI)	Statistical Significance
Hospital mortality[a]	121/3,599 (3.4)	207/25,888 (0.8)	0.74 (0.58, 0.95)	p=0.017
Composite outcome[b]	416/2,774 (15.0)	478/2,774 (17.2)	NR	p=0.024
Hospital death[b]	57/2,774 (2.1)	85/2,774 (3.1)	NR	p=0.017
Clinical importance (1–4) 2 The point estimate of effect is clinically important BUT the confidence interval includes clinically unimportant effects		Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		
Cardiac morbidity[b]	67/2,774 (2.4)	49/2,774 (1.8)	NR	p=0.09
Pulmonary morbidity[b]	248/2,774 (9.0)	274/2,774 (9.9)	NR	p=0.23
Renal morbidity[b]	37/2,774 (1.3)	41/2,774 (1.5)	NR	p=0.65
Clinical importance (1–4) 3 The confidence interval does not include any clinically important effects		Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		
Neurological morbidity[b]	63/2,774 (2.3)	89/2,774 (3.2)	NR	p=0.033
Serious infection[b]	115/2,774 (4.2)	148/2,774 (5.3)	NR	p=0.037
Return to OR for bleeding[b]	195/2,774 (7.0)	69/2,774 (2.5)	NR	p<0.001
Clinical importance (1–4) 2 The point estimate of effect is clinically important BUT the confidence interval includes clinically unimportant effects		Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival		
Any other adverse effects None reported				
EXTERNAL VALIDITY				
Generalisability The results of the study are generalisable to a cardiac surgery population				
Applicability The study was performed in the USA and is probably applicable to the Australian healthcare setting				

STUDY DETAILS				
Reference Spiess BD, Royston D, Levy JH, Fitch J, Dietrich W, Body S, et al. Platelet transfusions during coronary artery bypass graft surgery are associated with serious adverse outcomes. Transfusion. 2004;44(8):1143–1148.				
Affiliation/Source of funds From the Department of Anesthesiology, Virginia Commonwealth University/Medical College of Virginia Campus, Riscmond, Virginia; the Department of Anesthesia, Harefield Hospital, London, UK; the department of Anesthesiology, Emory University, Atlanta, Georgia; the Department of Anesthesiology, University of Oklahoma, Oklahoma City, Oklahoma; the Department of Anesthesiology, Munich Heart Institute, Munich, Germany; the Department of Anesthesiology, Harvard Medical School, Boston, Massachusetts; the Department of Anesthesia, University of Western Ontario, London, Ontario, Canada; and Global Statistics, Bayer Corporation, West Haven, Connecticut. Funding source not reported				
Study design Retrospective cohort study N=1,720	Level of evidence III	Location/setting Medical institutions in Denmark, Israel and USA		
Intervention Platelets Sample size N=284	Comparator(s) No platelets sample size N=1,436			
Population characteristics Patients undergoing CABG surgery				
Length of follow-up Not reported	Outcome(s) measured MI, stroke, 30 day mortality, pulmonary dysfunction, low cardiac output syndrome (congestive failure), infection			
INTERNAL VALIDITY				
Allocation	Comparison of study groups	Blinding	Treatment/ measurement bias	Follow-up (ITT)
The study does not reort how patients were allocated	There were significant differences in baseline demographics between patients receiving and not receiving platelets	No blinding details are reported	Patients could also receive RBC transfusion. Aprotinin was administered to some patients	ITT analysis
Overall quality assessment (descriptive) This was a fair quality retrospective cohort study with limitations inherent to this type of study design				

<table>
<tr><td colspan="5">RESULTS</td></tr>
<tr><td>Outcome</td><td>Platelets</td><td>No Platelets</td><td>OR (95% CI)</td><td>Statistical Significance</td></tr>
<tr><td>30 day mortality</td><td>NR</td><td>NR</td><td>4.76 (1.65, 13.73)</td><td>p=0.009</td></tr>
<tr><td colspan="2">Clinical importance (1–4)
1 A clinically important benefit for the full range of plausible estimates</td><td colspan="3">Relevance (1–5)
1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival</td></tr>
<tr><td>Stroke</td><td>NR</td><td>NR</td><td>2.56 (0.99, 6.67)</td><td>p=0.054</td></tr>
<tr><td colspan="2">Clinical importance (1–4)
4 The range of estimates defined by the confidence interval includes clinically important effects BUT the range of estimates defined by the confidence interval is also compatible with no effect, or a harmful effect</td><td colspan="3">Relevance (1–5)
1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival</td></tr>
<tr><td colspan="5">Any other adverse effects
None reported</td></tr>
<tr><td colspan="5">EXTERNAL VALIDITY</td></tr>
<tr><td colspan="5">Generalisability
The results of this study are generalisable to a cardiac surgery population</td></tr>
<tr><td colspan="5">Applicability
The study is probably applicable to the Australian health care setting</td></tr>
<tr><td colspan="5">Comment
The authors concluded that platelet transfusion in the perioperative period of CABG was associated with increased risk for serious adverse events.</td></tr>
</table>

F9 Evidence summaries, Question 9

At what INR (or PT/APTT) for fresh frozen plasma, fibrinogen level for cryoprecipitate, platelet count for platelet concentrates should patients be transfused to avoid risks of significant adverse events?

<table>
<tr><td colspan="5">STUDY DETAILS</td></tr>
<tr><td colspan="5">Reference Dillon JF, Simpson KJ, Hayes PC. Liver biopsy and bleeding time: An unpredictable event. J Gastroenterol Hepatol. 1994;9:269–271.</td></tr>
<tr><td colspan="5">Affiliation/Source of funds:
Liver Research Laboratories, Department of Medicine, Royal Infirmary, Edinburgh, Scotland.
Funding source: None reported.</td></tr>
<tr><td colspan="2">Study design: Prospective cohort study
N = 51 (60 procedures)</td><td>Level of evidence: II</td><td colspan="2">Location/setting: Hospital, Scotland, UK</td></tr>
<tr><td colspan="5">Population characteristics: Patients referred for laproscopic liver biopsy.</td></tr>
<tr><td colspan="3">Length of follow-up: Not reported</td><td colspan="2">Outcome(s) measured: Bleeding complications</td></tr>
<tr><td colspan="5">INTERNAL VALIDITY</td></tr>
<tr><td>Allocation

Patients with different levels of coagulopathy.</td><td>Comparison of study groups
There may be some differences between patients. Coefficients of correlation were calculated for PT and platelet count and bleeding time.</td><td>Blinding

No blinding details were recorded</td><td>Treatment/measurement bias
Patients who had significant coagulopathy, considered to be a contraindication to blind percutaneous liver biopsy, did not have it corrected prophylactically. In 2 patients on warfarin therapy which could not be discontinued, the level of anticoagulation was reduced to the lowest acceptable limit and the biopsy performed (PTR 2.1).</td><td>Follow-up (ITT)

ITT analysis.</td></tr>
<tr><td colspan="5">Overall quality assessment (descriptive):
This study was a fair quality prospective cohort study with limitations inherent to this type of study.</td></tr>
</table>

<table>
<tr><td colspan="5">RESULTS</td></tr>
<tr><td>Outcome</td><td>Risk Measure</td><td>Coagulation test</td><td>Correlation</td><td>Statistical significance</td></tr>
<tr><td rowspan="2">Bleeding time</td><td rowspan="2">correlation</td><td>PTR</td><td>none</td><td>-</td></tr>
<tr><td>Platelet count</td><td>none</td><td>-</td></tr>
<tr><td colspan="3">Clinical importance (1–4)
Unable to determine</td><td colspan="2">Relevance (1–5)
1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival.</td></tr>
<tr><td colspan="5">Any other adverse effects
None reported</td></tr>
<tr><td colspan="5">EXTERNAL VALIDITY</td></tr>
<tr><td colspan="5">Generalisability
The study was performed in patients receiving liver biopsies and may not be generalisable to patients undergoing other invasive procedures</td></tr>
<tr><td colspan="5">Applicability
The study was performed in the UK and is most likely applicable to the Australian healthcare setting.</td></tr>
<tr><td colspan="5">Comment
The authors conclude that mild to moderate coagulopathy (PT <2.1; platelet count >55 x 10^9/L) does not appear to be associated with prolonged bleeding following liver biopsy. Equally, normality of these coagulation studies does not indicate an absence of risk for post liver biopsy bleeding.</td></tr>
</table>

STUDY DETAILS

Reference McVay PA, Toy PT. Lack of increased bleeding after liver biopsy in patients with mild hemostatic abnormalities. Am J Clin Pathol. 1990;94:747–753.

Affiliation/Source of funds:

Blood Bank, San Francisco General Hospital Medical Centre, and Department of Laboratory Medicine, University of California San Francisco, San Francisco, California, USA.

Funding source: This study was supported in part by Public Health Service Transfusion Academic Award (K07HL01270) from the National Heart, Lung and Blood Institute, National Institutes of Health.

Study design: Retrospective cohort study N = 177 procedures	Level of evidence: III	Location/setting: San Francisco General Hospital Medical Centre, USA.

Population characteristics: Patients who underwent percutaneous liver biopsy.

Length of follow-up: Not reported	Outcome(s) measured: Incidence of bleeding complications

INTERNAL VALIDITY

Allocation	Comparison of study groups	Blinding	Treatment/measurement bias	Follow-up (ITT)
Patients with differing PTs.	There may be some differences between patients with different baseline PT. A two-tailed Fisher-Irwin exact test was used to compare proportions, and a two-tailed Student's t-test was used to compare means.	No blinding details were recorded	All patients appear to be treated the same. Patients were excluded if they received prophylactic FFP.	114 (112 patients) procedures were excluded due to incomplete data

Overall quality assessment (descriptive):

This study was a fair quality retrospective cohort study with limitations inherent to this type of study.

RESULTS

Outcome	Risk Measure	PT Range (seconds)	Rate	OR	Statistical significance
Incidence of bleeding complications	n/N (%)	Normal: ≤11.5	4/100 (4.0%)	Ref	-
		Mildly prolonged: 11.6-13.5	4/65 (6.2%)	1.57 (0.38, 6.52)	0.5316
		Moderately prolonged: 13.6-15.7	0/11 (0.0%)	-	-

Outcome	Risk Measure	Platelet count, x 10^9/L	Rate	OR	Statistical significance
Incidence of bleeding complications	n/N (%)	Normal: ≥100	5/157 (3.2%)	Ref	
		Mildl thrombocytopenia: 50-99	1/18 (5.6%)	1.79 (0.20, 16.17)	0.605
		Moderate/marked thrombocytopenia: 16, 48	2/2 (100%)	-	-

Clinical importance (1–4)	Relevance (1–5)
4 The range of estimates defined by the confidence interval includes clinically important effects BUT the range of estimates defined by the confidence interval is also compatible with no effect, or a harmful effect.	1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival.

Any other adverse effects

None reported

EXTERNAL VALIDITY

Generalisability

The study was performed in patients undergoing liver biopsy and so the data may not be generalisable to patients undergoing other invasive procedures

Applicability

The study was performed in the USA and is most likely applicable to the Australian healthcare setting.

Comment

The data from this study suggest that a PT prolonged less than 1.5 times mid range normal (4 seconds) is not associated with increased risk of bleeding complications after percutaneous liver bospy. Although the number of patients with platelets 50-99 x 10^9/L was low, in light of other published data, the authours conclude that mild thrombocytopenia, without risk factors for dysfunctional platelets, does not significantly increase the risk of bleeding after biopsy.

STUDY DETAILS					
Reference Misra S, Gyamlani G, Swaminathan S, Buehrig CK, Bjamason H, McKusick MA, et al. Safety and diagnostic yield of transjugular renal biopsy. J Vasc Interv Radiol. 2008;19(4):546–551.					
Affiliation/Source of funds: The Department of Radiology and the Division of Nephrology, Mayo Clinic Rochester, USA. Funding source: None of the Authors declared a conflict of interest.					
Study design: Retrospective cohort study N = 38 (38 procedures)		Level of evidence: III		Location/setting: Mayo Clinic Rochester, USA.	
Population characteristics: Patients who underwent transjugular renal biopsy.					
Length of follow-up: Not reported		Outcome(s) measured: Renal haematoma			
INTERNAL VALIDITY					
Allocation Patients with differing INRs and platelet counts.	Comparison of study groups There may be some differences between patients with different baseline INRs and platelet counts. Statistical analysis was paired or unpaired t-test for continuous data and Fisher exact test for categorical data.	Blinding No blinding details were recorded	Treatment/measurement bias An attempt was made to correct the patient's INR to less than 1.8 and platelet count to more than 50 x 10^9/L before the procedure. Patients with a decreased platelet count underwent transfusion with 6 pack units of platelets. After transfusion, the platelet count was determined and if the platelets remanined below 50 x 10^9/L, another 6 U platelets was transfused during the procedure. Patients with an increased INR underwent transfusion with 2 U FFP.	Follow-up (ITT) ITT analysis used.	
Overall quality assessment (descriptive): This study was a fair quality retrospective cohort study with limitations inherent to this type of study.					
RESULTS					

Outcome	Risk Measure	INR	Rate	OR	Statistical significance
Incidence of renal haematoma	n/N (%)	INR ≤1.4	9/27 (33.3%)	Ref	-
		INR >1.4	4/11 (36.4%)	1.14 (0.29, 4.50)	0.8486
Outcome	Risk Measure	Platelet count, x 10^9/L	Rate	OR	Statistical significance
Incidence of renal haematoma	n/N (%)	≤75	7/21 (33.3%)	0.92 (0.26, 3.25)	0.8927
		>75	6/17 (35.3%)	Ref	-

Clinical importance (1–4)	Relevance (1–5)
4 The range of estimates defined by the confidence interval includes clinically important effects BUT the range of estimates defined by the confidence interval is also compatible with no effect, or a harmful effect.	1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival.
Any other adverse effects None reported	
EXTERNAL VALIDITY	
Generalisability The study was performed in patients undergoing transjugular renal biopsy and so the data may not be generalisable to patients undergoing other invasive procedures	
Applicability The study was performed in the USA and is most likely applicable to the Australian healthcare setting.	
Comment Patients with a platelet count of less than or equal to 75 x 10^9/L or those with an elevated INR of more than 1.4 after transfusion were not at increased risk of hematoma formation.	

STUDY DETAILS					
Reference Ray CE, Shenoy SS. Patients with thrombocytopenia: outcome of radiologic placement of central venous access devices. Radiology. 1997;204(1):97–99.					
Affiliation/Source of funds: Department of Radiology, Roswell Park Cancer Institute Buffalo, NY, USA and Millard Filmore Hospital, Buffalo, NY, USA. Funding source: None reported.					
Study design: Prospective cohort study N = 105 (112 procedures)		Level of evidence: II		Location/setting: Hospital, USA	
Population characteristics: Patients receiving catheters, arm port systems and chest port systems placed radiologically.					
Length of follow-up: Not reported		Outcome(s) measured: Success and complication rates			
INTERNAL VALIDITY					
Allocation Patients with different levels of coagulopathy. A) platelets <50 x 10^9/L; B) 50-100 x 10^9/L; C) >100 x 10^9/L	Comparison of study groups There may be some differences between patients. P values were calculated with one tailed student t test to compare groups A and B separately with C.	Blinding No blinding details were recorded	Treatment/measurement bias Patients in group A received a transfusion of 1 unit of single-donor platelets during placement of venous access devices, while patients in groups B and C did not receive transfusions.	Follow-up (ITT) 7 placement procedures were excluded from analysis because the patients were in group A and did not receive platelet transfusion during implantation (n=5) or were in group B and received platelets (n=2).	
Overall quality assessment (descriptive): This study was a fair quality prospective cohort study with limitations inherent to this type of study.					
RESULTS					
Outcome	Risk Measure	Platelet count, x 10^9/L	Rate	OR	Statistical significance
Immediate complications	n/N (%)	<50 x 10^9/L	2/37 (5.4%)	>50: 1.87 (0.26, 13.94) >100: 1.83 (0.16, 21.10)	0.5343 0.6286
		50-100 x 10^9/L	1/35 (2.9%)	>100: 0.94 (0.06, 15.67) <100 vs >100: 1.39 (0.14, 13.88)	0.9663 0.7784
		>100 x 10^9/L	1/33 (3.0%)	Ref	-

Delayed complications (1-56 days post procedure	n/N (%)	<50 x 10^9/L	16/37 (43.2%)	>50: 1.49 (0.70, 3.17) >100: 1.75 (0.70, 4.39)	0.2989 0.2990
		50-100 x 10^9/L	13/35 (37.1%)	>100: 1.36 (0.53, 3.52) <100 vs >100: 1.55 (0.68, 3.55)	0.5725 0.2990
		>100 x 10^9/L	10/33 (30.3%)	Ref	-

Clinical importance (1–4)	Relevance (1–5)
4 The range of estimates defined by the confidence interval includes clinically important effects BUT the range of estimates defined by the confidence interval is also compatible with no effect, or a harmful effect.	1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival.

Any other adverse effects

None reported

EXTERNAL VALIDITY

Generalisability

The study was performed in patients receiving radiologic placement of central venous access devices and may not be generalisable to patients undergoing other invasive procedures

Applicability

The study was performed in the USA and is most likely applicable to the Australian healthcare setting.

Comment

The authors conclude that patients with thrombocytopenia show no demonstrable increase in immediate or delayed complications after radiologic placement of central venous access devices. Since intraproceduaral platelet transfusions elevated the platelet count only slightly (mean 11.5 x 10^9/L), it is possible that patients with severe thrombocytopaemia may not require platelet transfsion.

STUDY DETAILS		
Reference Fisher NC, Mutimer DJ. Central venous cannulation in patients with liver disease and coagulopathy—a prospective audit. Intensive Care Med. 1999;25:481–485.		
Affiliation/Source of funds: Liver Unit, Queen Elizabeth Hospital, Birmingham, UK. Funding source: None reported.		
Study design: Prospective cohort study N = 283 (658 procedures)	Level of evidence: II	Location/setting: Hospital, UK
Population characteristics: Patients undergoing CV cannulation episodes with liver disease where the prothrombin international normalised ratio (INR) was 1.5 or more and/or the platelet count was 150 or less x 10^9/L.		
Length of follow-up: Not reported	Outcome(s) measured: Vascular complications defined as major (haemothrorax or any other haemodynamically significant or life threatening haemorrhage) or minor (superficial haematoma, either visible or palpable, or superficial oozing from the cannulation site persisting for more than 24 h but withour haemodynamic consequence).	

INTERNAL VALIDITY				
Allocation Patients with different levels of coagulopathy.	Comparison of study groups There may be some differences between patients. Statistical analyses were done using Mann-Whitney U-test, Chi-squared test with Yates's correction and multivariate logistic regression analysis as appropriate.	Blinding No blinding details were recorded	Treatment/measurement bias All patients were treated the same.	Follow-up (ITT) ITT analysis
Overall quality assessment (descriptive): This study was a good quality prospective cohort study with limitations inherent to this type of study.				

RESULTS

Outcome	Risk Measure	Platelet count	Rate	OR	Statistical significance
Superficial haematoma	n/N (%)	<50 x 10^9/L	12/146 (8.2%)	1.26 (0.64, 2.49)	0.5089
		≥50 x 10^9/L	34/512 (6.6%)	Ref	-
Ooze	n/N (%)	<50 x 10^9/L	7/146 (4.8%)	3.17 (1.13, 8.90)	0.0282
		≥50 x 10^9/L	8/512 (1.6%)	Ref	-

Outcome	Risk Measure	INR	Rate	OR	Statistical significance
Superficial haematoma	n/N (%)	>5	17/137 (12.4%)	2.40 (1.28, 4.50)	0.0062
		<5	29/521 (5.6%)	Ref	-
Ooze	n/N (%)	>5	3/137 (2.2%)	0.95 (0.26, 3.41)	0.9369
		<5	12/521 (2.3%)	Ref	-

Clinical importance (1–4)	Relevance (1–5)
4 The range of estimates defined by the confidence interval includes clinically important effects BUT the range of estimates defined by the confidence interval is also compatible with no effect, or a harmful effect.	1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival.

Any other adverse effects

None reported

EXTERNAL VALIDITY

Generalisability

The study was performed in patients with liver disease receiving CV cannulation and may not be generalisable to patients undergoing other invasive procedures

Applicability

The study was performed in the UK and is most likely applicable to the Australian healthcare setting.

Comment

The authors conclude that in patients with liver failure, the presence of a raised INR or PT ratio should not be considered an absolute contra-indication to CV cannulation. There remains little evidence that FFP should be transfused beforehand. However, caution should be exercised in patients with combined coagulopathies including low platelet counts and in those undergoing haemofiltration or dialysis with regional anticoagulation.

STUDY DETAILS

Reference Weigand K, Encke J, Meyer FJ, Hinkel UP, Munder M, Stremmel W, Zahn A. Low levels of prothrombin time (INR) and platelets do not increase the risk of significant bleeding when placing central venous catheters. Med Klin. 2009;104:331–335.

Affiliation/Source of funds:

Department of Gastroenterology and Hepatology, Department of Cardiology and Pulmonology, Department of Nephrology and Department of Hematology, Oncology and Rheumatology, University Hospital Heidelberg, Germany. Johanna-Etienne-Krankenhaus, Neuss, Germany.

Funding source: None reported.

Study design: Prospective cohort study N = 196	Level of evidence: II	Location/setting: Two medical ICUs and one haematology intermediate care ward in Germany.

Population characteristics: Patients >18 years that were undergoing CVC insertion electively or in case of emergency.

Length of follow-up: Not reported	Outcome(s) measured: Bleeding complications by Hb drop

INTERNAL VALIDITY

Allocation	Comparison of study groups	Blinding	Treatment/measurement bias	Follow-up (ITT)
Patients with differing levels of haemostsis.	There may be some differences between patients with different levels of haemostatsis. For calculation of significance, Mann-Whitney rank sum test was used..	No blinding details were recorded	It is assumed that all patients were treated the same.	ITT analysis used.

Overall quality assessment (descriptive):

This study was a fair quality prospective cohort study with limitations inherent to this type of study.

RESULTS

Outcome	Risk Measure	Haematology paramter	RR	Statistical significance
Significant drop in Hb	RR	Platelets ≤50 x 10^9	0.282	P=0.252
		PT≤50%	0.863	P=0.900

Clinical importance (1–4)	Relevance (1–5)
Unable to determine	2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient relevant outcomes for the same intervention.

Any other adverse effects

None reported

EXTERNAL VALIDITY
Generalisability The study was performed in patientsplacement of central venous catheters and may not be generalisable to patients undergoing other invasive procedures
Applicability The study was performed in the Germany and is most likely applicable to the Australian healthcare setting.
Comment These findings demonstrate that coagulation disorders with altered prothrombin time (INR) or platelets.do not increase the risk of significant bleeding when inserting a central venous catheter. Therefore, the prophylactic correction of coagulation by transfusion of blood products or coagulation factors is not necessary before central venous catheter insertion.

STUDY DETAILS				
Reference Foster PF, Moore LR, Sankary HN, Hart ME, Ashmann MK, Williams JW. Central venous catheterization in patients with coagulopathy. Arch Surg. 1992;127:273–275.				
Affiliation/Source of funds: Department of General Surgery, Section of Transplantation Surgery, Rush-Presbyterian-St Luke's Medical Centre, Chicago, USA. Funding source: None reported.				
Study design: Retrospective cohort study N = 40 (259 procedures)	Level of evidence: III	Location/setting: Medical Centre, USA		
Population characteristics: Forty liver transplant recipients with coagulopathy who underwent central venous catheter insertions.				
Length of follow-up: Not reported	Outcome(s) measured: Serious bleeding complicatins			
INTERNAL VALIDITY				
Allocation Patients with different levels of coagulopathy.	Comparison of study groups There may be some differences between patients. Statistical methods were not stated.	Blinding No blinding details were recorded	Treatment/measurement bias It is assumed that all patients were treated the same.	Follow-up (ITT) ITT analysis.
Overall quality assessment (descriptive): This study was a fair quality retrospective cohort study with limitations inherent to this type of study.				
RESULTS				
Outcome	Risk Measure	Coagulation test	Rate	Statistical significance
Serious complications	Rate	Any	0/202	-
Clinical importance (1–4) Unable to determine			Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival.	
Any other adverse effects None reported				
EXTERNAL VALIDITY				
Generalisability The study was performed in liver transplant patients undergoing central venous catheter placement and may not be generalisable to patients undergoing other invasive procedures				
Applicability The study was performed in the USA and is most likely applicable to the Australian healthcare setting.				

Comment

The authors conclude that the lack of bleeding documented in this study, even in patients with marked simultaneous derangements of coagulation test results, the experienced clinician using simple precautions and techniques may safely undertake emergency, percutaneous subclavian and internal jugular venous catheterisation. Furthermore, these attempts need not be preceeded by infusion of blood products or medications to correct the coagulopathy.

STUDY DETAILS

Reference Doerfler ME, Kaufman B, Goldenberg AS. Central venous catheter placement in patients with disorders of hemostasis. Chest. 1996;110:185–188.

Affiliation/Source of funds:

Division of Pulmonary/Critical Care Medicine and Haematology and the Department of Anaesthesiology, New York University School of Medicine, NEW York, USA.

Funding source: None reported.

Study design: Retrospective cohort study N = 76	Level of evidence: III	Location/setting: University Teaching Hospital, USA

Population characteristics: Patients with disorders of haemostasis who required central venous access for clinical management.

Length of follow-up: Not reported	Outcome(s) measured: Complication rates

INTERNAL VALIDITY

Allocation	Comparison of study groups	Blinding	Treatment/measurement bias	Follow-up (ITT)
Patients with disorders of haemostatsis defined as platelet count <100 x 10^9/L and PT of ≥1.2 x midpoint for the laboratory's normal range.	There may be some differences between patients. Groups were compared using logistic regression	No blinding details were recorded	No patient receieved platelets or FFP prior to the procedure. It is assumed that all patients were treated the same in other respects.	ITT analysis.

Overall quality assessment (descriptive):

This study was a good quality retrospective cohort study with limitations inherent to this type of study.

RESULTS

Outcome	Risk Measure	Coagulation test	Rate	Statistical significance
Serious complications	Rate	PT	0/76	-
		Platelet count	0/42	-
Bleeding	Logistic regression	Platelet count	-	S

Clinical importance (1–4)	Relevance (1–5)
Unable to determine	1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival.

Any other adverse effects

None reported

EXTERNAL VALIDITY
Generalisability The study was performed in patients undergoing central venous catheter placement and may not be generalisable to patients undergoing other invasive procedures
Applicability The study was performed in the USA and is most likely applicable to the Australian healthcare setting.
Comment In this analysis, the platelet count was the only risk factor statistically associated with even minor bleeding. The platelet count associated with this risk in this series was $<38 \times 10^9$/L. The authors conclude that central venous cannualtion can be safely performed by experienced physicians in patients with disorders of haemostatsis. They do not believe that the routine administratin of blood products to correct haemostatic abnormalities is warranted under these conditions. Platelets should be available for patients with very low platelet counts in case bleeding is a problem.

STUDY DETAILS				
Reference Martin JH, Rosser CJ, Linebach RF, McCullough DL, Assimos DG. Are coagulation studies necessary before percutaneous nephrostomy? Tech Urol. 2000;6(3):205–207.				
Affiliation/Source of funds: Department of Urology, Wake Forest University School of Medicine, Winston-Salem, North Carolina, USA. Funding source: None reported.				
Study design: Retrospective cohort study N = 180		Level of evidence: III		Location/setting: University Teaching Hospital, USA
Population characteristics: Patients undergoing PCN with platelet counts >100 x 10^9/L.				
Length of follow-up: Not reported		Outcome(s) measured: Haemorrhagic complication rates		
INTERNAL VALIDITY				
Allocation Patients with platelet count >100 x 10^9/L divided into patients with a normal PT and patients with an abnormal PT.	Comparison of study groups There may be some differences between patients. Groups were compared using Fisher's and Student's t-tests, and multivariate analysis with logistic regression and linear regression.	Blinding No blinding details were recorded	Treatment/measurement bias It is assumed that all patients were treated the same in other respects.	Follow-up (ITT) ITT analysis.
Overall quality assessment (descriptive): This study was a fair quality retrospective cohort study with limitations inherent to this type of study.				
RESULTS				

Outcome	Risk Measure	PT	Rate	Statistical significance
Haemorrhagic complication rate	Rate	≤13.9	NR	-
		>13.9	NR	0.203

Clinical importance (1–4)	Relevance (1–5)
Unable to determine	1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival.

Any other adverse effects
None reported

EXTERNAL VALIDITY
Generalisability The study was performed in patients undergoing PCN and may not be generalisable to patients undergoing other invasive procedures
Applicability The study was performed in the USA and is most likely applicable to the Australian healthcare setting.
Comment The authors concluded that the routine assessment of coagulation studies before PCN in unnecessary. The low prevalence of coagulation abnormalities, the low overall bleeding complication rate associated with this procedure, and the lack of correlation abnormalities and haemorrhagic complications support this position.

STUDY DETAILS				
Reference Mainwaring CJ, Natarajan A, Peckham C, Readett D, Singhal R, Vazzalwar R, Vora AJ. Untreated thrombocytopenia and lumbar puncture-related bleeding risk at diagnosis of childhood acute lymphoblastic leukaemia (ALL). Poster Presentation 201, British Society for Haematology Conference; Glasgow; 1998 April 27–30.				
Affiliation/Source of funds: Department of Haematology, The Childrens Hospital, Western Bank, Sheffield, UK. Funding source: None reported.				
Study design: Retrospective cohort study N = 134		Level of evidence: III		Location/setting: Hospital, UK
Population characteristics: Children with ALL				
Length of follow-up: Not reported		Outcome(s) measured: Minor bleeding		
INTERNAL VALIDITY				
Allocation Patients with platelet count >50 x 10^9/L compared with patients with platelet count <50 x 10^9/L.	Comparison of study groups There may be some differences between patients. It is not stated how groups were compared	Blinding No blinding details were recorded	Treatment/measurement bias 12 patients with platelet count <50 x 10^9/L received a platelet transfusion prior to LP in view of haemorrhagic symptoms or signs.	Follow-up (ITT) Of the 134 patients, only 51 did not have comprehensive data available and were therefore excluded from the analysis.
Overall quality assessment (descriptive): This study was a fair quality retrospective cohort study with limitations inherent to this type of study.				
RESULTS				

Outcome	Risk Measure	Platelet count	Rate	Statistical significance
Haemorrhagic complication rate	Rate	<50 x 10^9/L	8/37 (21.6%)	NR
		≥50 x 10^9/L	NR	-

Clinical importance (1–4)	Relevance (1–5)
Unable to determine	1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival.

Any other adverse effects
None reported

EXTERNAL VALIDITY
Generalisability The study was performed in children with ALL undergoing lumbar puncture and may not be generalisable to adult patients or patients undergoing other invasive procedures
Applicability The study was performed in the UK and is most likely applicable to the Australian healthcare setting.
Comment The authors concluded that the study indicates that transfusion of platelet concentrates prior to LP in children with significant thrombocytopenia is not justified as a routine measure.

STUDY DETAILS

Reference Howard SC, Gajjar A, Ribeiro RC, Rivera GK, Rubnitz JE, Sandlund JT, et al. Safety of lumbar puncture for children with acute lymphoblastic leukemia and thrombocytopenia. JAMA. 2000;284(17):2222–2224.

Affiliation/Source of funds:

Departments of Hematology-Oncology, Biostatisitcs and Epidemiology, Pathology and Anesthesiology, St Jude Chilkdren's Research Hospital, and Department of Pediatrics, University of Tennessee College of Medicine, Memphis, Tenn USA; Department of Pediatrics, Stanford University, School of Medicine, Stanford, Calif.

Funding source: This study was supported in part by Cancer Center Support (CORE) grant CA-21765 from the National Cancer Institute; by a Center of Excellence grant from the State of Tennessee; and by the American Lebanese Syrian Associated Charities, Memphis, Tennessee.

Study design: Retrospective cohort study N = 958	Level of evidence: III	Location/setting: St Jude Children's Research Hospital, Memphis, Tennessee, USA.

Population characteristics: Children with newly diagnosed acute lymphoblastic leukemia.

Length of follow-up: Not reported	Outcome(s) measured: Incidence of serious complications

INTERNAL VALIDITY

Allocation	Comparison of study groups	Blinding	Treatment/measurement bias	Follow-up (ITT)
Differing platelet counts. Groups consisted of Platelet counts (x 10^9): 1-5; 6-10; 11-20; 21-30; 31-40; 41-50; 51-100; >100.	There may be some differences between patients with different baseline platelet counts. The 95% CI's for the probability of serious complications were calculated.	No blinding details were recorded	All patients appear to be treated the same.	ITT analysis used.

Overall quality assessment (descriptive):

This study was a good quality retrospective cohort study with limitations inherent to this type of study.

RESULTS

Outcome	Risk Measure	Platelet count, x 10^9/L	Rate (%, 95%CI)	Statistical significance
Incidence of serious complications	95% CI	1-5	0 (0, 40.19)	No serious complications were observed at any platelet count. One can be 95% confident that these intervals contain the true proportion of serious complications.
		6-10	0 (0, 13.21)	
		11-20	0 (0, 2.05)	
		21-30	0 (0, 1.49)	
		31-40	0 (0, 1.48)	
		41-50	0 (0, 1.27)	
		51-100	0 (0, 0.10)	
		>100	0 (0, 0.07)	

Clinical importance (1–4)	Relevance (1–5)
1 A clinically important benefit for the full range of plausible estimates	1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival.
Any other adverse effects None reported	
EXTERNAL VALIDITY	
Generalisability The study was performed in children undergoing lumbar puncture. The data from this study may not be generalisable to adulot patients or patients undergoing other invasive procedures	
Applicability The study was performed in the USA and is most likely applicable to the Australian healthcare setting.	
Comment In summary, no serious lumbar puncture complications were found in this review, despite the fact that 18% of procedures were performed in patients with platelet counts 50 x 10^9/L or less. However, platelet counts were 10 x 10^9/l in only 0.36% of instances. The authors conclude that children with acute lymphoblastic leukemia do not require prophylactic platelet transfusion for lumbar puncture if the platelet count is greater than 10 x 10^9/L.	

STUDY DETAILS				
Reference Vavricka SR, Walter RB, Irani S, Halter J, Schanz U. Safety of lumbar puncture for adults with acute leukemia and restrictive prophylactic platelet transfusion. Ann Hematol. 2003;82:570–573.				
Affiliation/Source of funds: Department of Internal Medicine, University Hospital of Zurich, Zurich Switzerland and Clinical Research Division, Fred Hutchison Cancer Research Center, Seattle, Washington, USA. Funding source: None reported.				
Study design: Retrospective cohort study N = 66	Level of evidence: III	Location/setting: University Hospital Zurich, Switzerland		
Population characteristics: Patients with acute leukaemia who underwent one or more therapeutic or prophylactic lumbar punctures.				
Length of follow-up: Not reported	Outcome(s) measured: Traumatic lumbar puncture (LP)			
INTERNAL VALIDITY				
Allocation Patients with differing platelet levels.	Comparison of study groups There may be some differences between patients with different platelet levels. Groups were compared using non-parametric statistical tests.	Blinding No blinding details were recorded	Treatment/measurement bias 37 patients had platelet counts below 20 x 10^9/L and received platelets according to the institution's transfusion criteria. Afterwards, the effect of transfusion was verified with a 1-h-post-transfusion count, and the LP was performed only when platelet counts increased to values higher than 20 x 10^9/L.	Follow-up (ITT) ITT analysis used.
Overall quality assessment (descriptive): This study was a fair quality retrospective cohort study with limitations inherent to this type of study.				
RESULTS				
Outcome	Risk Measure	Platelet count	OR (95% CI)	Statistical significance
Traumatic LP	Chi-square	Lower	9.46	P<0.005
Clinical importance (1–4) Unable to determine			Relevance (1–5) 2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient relevant outcomes for the same intervention.	

Outcome	Risk Measure	Platelet count, x 10^9/L	Rate	OR	Statistical significance
Serious complications	% (95% CI)	20-30	0 (0, 10.0)	-	NS
		30-50	0 (0, 8.81)	-	NS
		50-100	0 (0, 8.22)	-	NS
		>100	0 (0, 1.87)	-	NS
Clinical importance (1–4) 1 A clinically important benefit for the full range of plausible estimates			Relevance (1–5) 2 Evidence of an effect on a surrogate outcome that has been shown to be predictive of patient relevant outcomes for the same intervention.		
Any other adverse effects None reported					
EXTERNAL VALIDITY					
Generalisability The study was performed in patients undergoing lumbar puncture and may not be generalisable to patients undergoing other invasive procedures					
Applicability The study was performed in the Switzerland and is most likely applicable to the Australian healthcare setting.					
Comment No serious haemorrhagic complications occurred, but there was a significant trend towards a higher percentage of traumatic procedures in patients with lowest platelet count. Although not associated with serious clinical bleeding events in this study, the increased occurrence of traumatic procedures may indicate an increased risk of more serious haemorrhagic complications, implying a trigger not lower than 20 x 10^9/L for prophylactic transfusions of platelets in adult patients with acute leukaemia undergoing LP.					

STUDY DETAILS				
Reference Ruell J, Karuvattil R, Wynn R, Will A. Platelet count has no influence on traumatic and bloody lumbar puncture in children undergoing intrathecal chemotherapy [letter]. Br J Haematol. 2007;136(2):347–348.				
Affiliation/Source of funds: Department of Haematology, Pendlebury Hospital, Manchester, UK. Funding source: None reported.				
Study design: Retrospective cohort study N = 54 (738 procedures)		Level of evidence: III		Location/setting: Pendlebury Hospital, Manchester, UK.
Population characteristics: Paediatric patients with haematological malignancy who underwent a total of 738 lumbar puncture procedures.				
Length of follow-up: Not reported		Outcome(s) measured: Traumatic and bloody lumbar puncture		
INTERNAL VALIDITY				
Allocation Patients with differing platelet counts.	Comparison of study groups There may be some differences between patients with different baseline platelet counts. No method for statistical analysis was reported.	Blinding No blinding details were recorded	Treatment/measurement bias It is assumed that all patients were treated the same.	Follow-up (ITT) ITT analysis used.
Overall quality assessment (descriptive): This study was a fair quality retrospective cohort study with limitations inherent to this type of study.				
RESULTS				
Outcome	Risk Measure	Platelet count	R^2	Statistical significance
Risk of traumatic or bloody LP	Correlation	any	0.004	NS
Clinical importance (1–4) Unable to determine			Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival.	
Any other adverse effects None reported				

EXTERNAL VALIDITY
Generalisability The study was performed in children undergoing lumbar puncture. The data from this study may not be generalisable to adulot patients or patients undergoing other invasive procedures
Applicability The study was performed in the UK and is most likely applicable to the Australian healthcare setting.
Comment This study and existing evidence in the literature would support the safety of performing LPs with platelet counts ≥30 x 10^9/L.

STUDY DETAILS				
Reference Darcy MD, Kanterman RY, Kleinhoffer MA, Vesely TM, Picus D, Hicks ME, Pilgram TK. Evaluation of coagulation tests as predictors of angiographic bleeding complications. Radiology. 1996;198:741–744.				
Affiliation/Source of funds: Mallinckrodt Institute of Radiology, Washington University School of Medicine, St Louis, USA. Funding source: None reported.				
Study design: Prospective cohort study N = 1,000		Level of evidence: II	Location/setting: University hospital in USA	
Population characteristics: Patients who underwent femoral arterial puncture for a diagnostic or therapeutic vascular procedure.				
Length of follow-up: Not reported		Outcome(s) measured: Complication rates		
INTERNAL VALIDITY				
Allocation Patients with normal and abnormal coagulation tests (PT, platelet count).	Comparison of study groups There may be some differences between patients with normal and abnormal coagulation tests. Groups were compared using multivariate analysis	Blinding No blinding details were recorded	Treatment/measurement bias FFP was given to 5 patients to reverse the effects of warfarin.	Follow-up (ITT) ITT analysis.
Overall quality assessment (descriptive): This study was a good quality prospective cohort study with limitations inherent to this type of study.				
RESULTS				

Outcome	Risk Measure	Coagulation test	OR	Statistical significance
Haemotoma	OR	PT	-	P=0.999
		Platelet count	9.328	P=0.002

Clinical importance (1–4)	Relevance (1–5)
1 A clinically important benefit for the full range of plausible estimates	1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival.

Any other adverse effects
None reported

EXTERNAL VALIDITY
Generalisability The study was performed in patients undergoing angiography and may not be generalisable to patients undergoing other invasive procedures
Applicability The study was performed in the USA and is most likely applicable to the Australian healthcare setting.
Comment Abnormal PTs do not correlate with an increased risk of postangiographic haematoma, but a low platelet count is associated with more bleeding complications. Patients with a platelet count of less than 100 x 10^9/L were more than nine times as likely to develop a medium or large haematoma as those with a count of more than 100 x 10^9/L.

STUDY DETAILS					
Reference Weiss SM, Hert RC, Gianola FJ, Clark JG, Crawford SW. Complications of fiberoptic bronchoscopy in thrombocytopenic patients. Chest. 1993;104:1025–1028.					
Affiliation/Source of funds: Fred Hutchison Cancer Research Centre and University of Washington Medical Centre, Division of Pulmonary and Critical Care Medicine, Seattle, USA. Funding source: This investigation was supported by Public Health Service Grants CA-18029, CA-47748 and CA-15704 from the National Cancer Institute.					
Study design: Prospective cohort study N = 47 (66 procedures)		Level of evidence: II		Location/setting: A single BMT Centre, USA	
Population characteristics: Bone marrow transplant (BMT) recipients undergoing diagnostic fibreoptic bronchoscopy (FOB) with bronchoalveolar lavage (BAL).					
Length of follow-up: Not reported		Outcome(s) measured: Complication rates			
INTERNAL VALIDITY					
Allocation Patients with thrombocytopenia.	Comparison of study groups There may be some differences between patients. Statistical methods were not stated.	Blinding No blinding details were recorded	Treatment/measurement bias Patients received platelet transfusions routinely in an attempt to maintain counts >20 x 10^9/L. It is assumed that all patients were treated the same in other respects.	Follow-up (ITT) ITT analysis.	
Overall quality assessment (descriptive): This study was a fair quality prospective cohort study with limitations inherent to this type of study.					
RESULTS					

Outcome	Risk Measure	Platelet count, x 10^9/L	Rate	OR	Statistical significance
Complication rate	n/N (%)	<20 x 10^9/L	2/13 (15%)	>100: 1.27 (0.10, 16.41)	0.8533
		20-50 x 10^9/L	3/31 (10%)	>100: 0.75 (0.07, 8.21) <50 vs >50: 0.81 (0.18, 3.72)	0.8137 0.7883
		50-100 x 10^9/L	2/14 (14%)	>100: 1.17 (0.09, 14.98) <100 vs >100: 0.96 (0.10, 8.86)	0.9058 0.9718
		>100 x 10^9/L	1/8 (13%)	Ref	-

Clinical importance (1–4)	Relevance (1–5)
4 The range of estimates defined by the confidence interval includes clinically important effects BUT the range of estimates defined by the confidence interval is also compatible with no effect, or a harmful effect.	1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival.

Any other adverse effects None reported
EXTERNAL VALIDITY
Generalisability The study was performed in BMT patients undergoing fibreoptic bronchoscopy with bronchoalveolar lavage and may not be generalisable to patients undergoing other invasive procedures
Applicability The study was performed in the USA and is most likely applicable to the Australian healthcare setting.
Comment In summary, these data support the statement that FOB with BAL may be performed with relative safety despite the presence of significant thrombocytopenia. The authors' experience suggests that routine platelet transfusion before FOB with BAL in all patients with thrombocytopenia may not be necessary.

STUDY DETAILS				
Reference Wolf AT, Wasan SK, Saltzman JR. Impact of anticoagulation on rebleeding following endoscopic therapy for nonvariceal upper gastrointestinal hemorrhage. Am J Gastroenterol. 2007;102:290–296.				
Affiliation/Source of funds: Division of Gastroenterology and Department of Medicine, Brigham and Women's Hospital Harvard Medical School, Boston, Massachusetts. Funding source: The study was supported by a grant from the American College of Gastroenterology.				
Study design: Retrospective cohort study N = 246		Level of evidence: III		Location/setting: Large tertiary care teaching hospital in USA
Population characteristics: Adult patients who received endoscopic therapy for nonvariceal upper gastrointestinal haemorrhage.				
Length of follow-up: Not reported		Outcome(s) measured: Rebleeding		
INTERNAL VALIDITY				
Allocation Patients with differing INR values.	Comparison of study groups There may be some differences between patients with different INRs. Groups were compared using multivariate analysis	Blinding No blinding details were recorded	Treatment/measurement bias It is assumed that all patients were treated the same.	Follow-up (ITT) A total of 11 patients were excluded from the analysis because endoscopic haemostasis coulod not be achieved, and an additional 2 patients were excluded because INRs were not obtained prior to endoscopy.
Overall quality assessment (descriptive): This study was a fair quality retrospective cohort study with limitations inherent to this type of study.				

RESULTS				
Outcome	Risk Measure	INR	OR (95% CI)	Statistical significance
Rebleeding	OR	1.3-1.6	1.21 (0.53, 2.75)	P=0.66
		1.7-2.0	0.55 (0.17, 1.85)	P=0.34
		2.1-2.5	<0.001 (<0.001, >999)	P=0.98
		>2.5	0.42 (0.67, 2.56)	P=0.35
Clinical importance (1–4) 1 A clinically important benefit for the full range of plausible estimates			Relevance (1–5) 1 Evidence of an effect on patient-relevant clinical outcomes, including benefits and harms, and quality of life and survival.	
Any other adverse effects None reported				

EXTERNAL VALIDITY
Generalisability The study was performed in patients with upper gastrointestinal haemorrhage receiving endoscopic therapy and may not be generalisable to patients undergoing other invasive procedures
Applicability The study was performed in the USA and is most likely applicable to the Australian healthcare setting.
Comment The study found that mild to moderate anticoagulation does not increase the risk of rebleeding following endoscopic therapy for nonvariceal upper gastrointestinal hemorrhage. In addition, INR was not a significant predictor of transfusion requirement, length of hospital stay, surgery to control bleeding, or mortality. These findings suggest that endoscopic therapy is appropriate in mildly to moderately anticoagulated patients.

References

1 National Health and Medical Research Council and Australasian Society of Blood Transfusion. Clinical practice guidelines on the use of blood components (red blood cells, platelets, fresh frozen plasma, cryoprecipitate). Canberra, ACT: NHMRC, 2001. http://www.nhmrc.gov.au/_files_nhmrc/file/publications/synopses/cp78.pdf

2 National Health and Medical Research Council. NHMRC additional levels of evidence and grades for recommendations for developers of guidelines. Canberra, ACT: NHMRC, 2009. http://www.nhmrc.gov.au/guidelines/consult/consultations/add_levels_grades_dev_guidelines2.htm

3 National Health and Medical Research Council. NHMRC standards and procedures for externally developed guidelines. Canberra, ACT: NHMRC, 2007. http://www.nhmrc.gov.au/publications/synopses/nh56syn.htm

4 National Health and Medical Research Council. A guide to the development, implementation and evaluation of clinical practice guidelines. Canberra, ACT: NHMRC, 1999. http://www.nhmrc.gov.au/publications/synopses/cp30syn.htm

5 National Health and Medical Research Council. How to use the evidence: assessment and application of scientific evidence. Canberra, ACT: NHMRC, 2000. http://www.nhmrc.gov.au/publications/synopses/cp69syn.htm

6 Ahn HJ, Chung SK, Dhong HJ, Kim HY, Ahn JH, Lee SM, et al. Comparison of surgical conditions during propofol or sevoflurane anaesthesia for endoscopic sinus surgery. Br J Anaesth. 2008;100:50–54.

7 Hall JE, Ng WS, Smith S. Blood loss during first trimester termination of pregnancy: comparison of two anaesthetic techniques. Br J Anaesth. 1997;78:172–174.

8 Albertin A, La Colla L, Gandolfi A, Colnaghi E, Mandelli D, Gioia G, et al. Greater peripheral blood flow but less bleeding with propofol versus sevoflurane during spine surgery. A possible physiologic model. Spine. 2008;33:2017–2022.

9 Okuyucu S, Inanoglu K, Akkurt CO, Akoglu E, Dagli S. The effect of anesthetic agents on perioperative bleeding during tonsillectomy: propofol-based versus desflurane-based anesthesia. Otolaryngol Head Neck Surg. 2008;138:158–161.

10 Rodgers A, Walker N, Schug S, et al. Reduction of postoperative mortality and morbidity with epidural or spinal anaesthesia: results from overview of randomised trials. BMJ. 2000;321:1493.

11 Richman JM, Rowlingson AJ, Maine DN, Courpas GE, Weller JF, Wu CL. Does neuraxial anesthesia reduce intraoperative blood loss? A meta-analysis. J Clin Anesth. 2006;18,427–435.

12 Modig J, Karlstrom G. Intra- and postoperative blood loss and haemodynamics in total hip replacement when performed under lumbar epidural versus general anaesthesia. Eur J Anaesthesiol. 1987;4:345–355.

13 Keith I. Anaesthesia and blood loss in total hip replacement. Anaesthesia. 1977;32:444–450.

14 Sharrock NE, Salvati EA. Hypotensive epidural anesthesia for total hip arthroplasty: a review. Acta Orthop Scand. 1996;67:91–107.

15 Jellish WS, Shea JF. Spinal anaesthesia for spinal surgery. Best Pract Res Clin Anaesthesiol. 2003;17:323–334.

16 Mauermann WJ, Shilling AM, Zuo Z. A comparison of neuraxial block versus general anesthesia for elective total hip replacement: a meta-analysis. Anesth Analg. 2006;103:1018–1025.

17 Modig J. Regional anaesthesia and blood loss. Acta Anaesthesiol Scand Suppl. 1988; 89: 44–48.

18 Parker MJ, Handoll HH, Griffiths R. Anaesthesia for hip fracture surgery in adults. Cochrane Database Syst Rev. 2004;(4):CD000521.

19 Kakiuchi M. Reduction of blood loss during spinal surgery by epidural blockade under normotensive general anesthesia. Spine. 1997;22:889–894.

20 Twyman R, Kirwan T, Fennelly M. Blood loss reduced during hip arthroplasty by lumbar plexus block. J Bone Joint Surg Br. 1990;72:770–771.

21 Stevens RD, Van Gessel E, Flory N, Fournier R, Gamulin Z. Lumbar plexus block reduces pain and blood loss associated with total hip arthroplasty. Anesthesiol. 2000;93:115–121.

22 Ballantyne JC, Kupelnick B, McPeek B, Lau J. Does the evidence support the use of spinal and epidural anesthesia for surgery? J Clin Anesth. 2005;17:382–391.

23 Rigg JR, Jamrozik K, Myles PS, Silbert BS, Peyton PJ, Parsons RW, et al. Epidural anaesthesia and analgesia and outcome of major surgery: a randomised trial. Lancet. 2002;359:1276–1282.

24 Park WY, Thompson JS, Lee KK. Effect of epidural anesthesia and analgesia on perioperative outcome. A randomized, controlled veterans' affairs cooperative study. Ann Surg. 2001;234:560–571.

25 Rashiq S, Finegan BA. The effect of spinal anesthesia on blood transfusion rate in total joint arthroplasty. Can J Surg. 2006;49:391–396.

26 Spiess BD, Spence RK, Shander A, editors. Perioperative transfusion medicine. 2nd ed. Chapter 32. Lippincott Williams Wilkins, 2006: 436.

27 Ferraris VA, Ferraris SP, Saha SP, Hessel II EA, Haan CK, Royston BD, et al. Perioperative blood transfusion and blood conservation in cardiac surgery: The Society of Thoracic Surgeons and The Society of Cardiovascular Anesthesiologists clinical practice guideline. Ann Thorac Surg. 2007;83(5 Suppl):S27–S86.

28 Freedman J, Luke K, Monga N, Lincoln S, Koen R, Escobar M, et al. A provincial program of blood conservation: The Ontario Transfusion Coordinators (ONTraC). Transfus Apher Sci. 2005;33:343–349.

29 DeAnda A Jr, Baker KM, Roseff SD, Green JA, Mccarthy H, Aron T, Spiess BD. Developing a blood conservation program in cardiac surgery. Am J Med Qual. 2006;21:230–237.

30 Freedman J, Luke K, Escobar M, Vernich L, Chiavetta JA. Experience of a network of transfusion coordinators for blood conservation (Ontario Transfusion Coordinators [ONTraC]). Transfusion. 2008;48:237–250.

31 Brevig J, McDonald J, Zelinka ES, Gallagher T, Jin R, Grunkemeier GL. Blood transfusion reduction in cardiac surgery: multidisciplinary approach at a community hospital. Ann Thorac Surg. 2009;87:532–539.

32 Bui LL, Smith AJ, Bercovici M, Szalai JP, Hanna SS. Minimising blood loss and transfusion requirements in hepatic resection. HPB (Oxford). 2002;4(1):5–10.

33 Bolan CD, Rick ME, Polly DW Jr. Transfusion medicine management for reconstructive spinal repair in a patient with von Willebrand's disease and a history of heavy surgical bleeding. Spine. 2001;26:E552–E556.

34 Alghamdi AA, Davis A, Brister S, Corey P, Logan A. Development and validation of Transfusion Risk Understanding Scoring Tool (TRUST) to stratify cardiac surgery patients according to their blood transfusion needs. Transfusion. 2006;46:1120–1129.

35 Ghaffarinejad MH, Fazelifar AF, Shirvani SM, Asdaghpoor E, Fazeli F, Bonakdar HR, et al. The effect of preoperative aspirin use on postoperative bleeding and perioperative myocardial infarction in patients undergoing coronary artery bypass surgery. Cardiol J. 2007;14:453–457.

36 Gerrah R, Elami A, Stamler A, Smirnov A, Stoeger Z. Preoperative aspirin administration improves oxygenation in patients undergoing coronary artery bypass grafting. Chest. 2005;127:1622–1626.

37 Gulbins H, Malkoc A, Ennker IC, Ennker J. Preoperative platelet inhibition with ASA does not influence postoperative blood loss following coronary artery bypass grafting. Thorac Cardiovasc Surg. 2009;57:18–21.

38 Kamran M, Ahmed A, Dar MI, Khan AB. Effect of aspirin on postoperative bleeding in coronary artery bypass grafting. Ann Thorac Cardiovasc Surg. 2008;14:224–229.

39 Ascione R, Ghosh A, Rogers CA, Cohen A, Monk C, Angelini GD. In-hospital patients exposed to clopidogrel before coronary artery bypass graft surgery: a word of caution. Ann Thorac Surg. 2005;79:1210–1216.

40 Berger JS, Frye CB, Harshaw Q, Edwards FH, Steinhubl SR, Becker RC. Impact of clopidogrel in patients with acute coronary syndromes requiring coronary artery bypass surgery: a multicenter analysis. J Am Coll Cardiol. 2008;52:1693–1701.

41 Chu MW, Wilson SR, Novick RJ, Stitt LW, Quantz MA. Does clopidogrel increase blood loss following coronary artery bypass surgery? Ann Thorac Surg. 2004;78:1536–1541.

42 Kapetanakis EI, Medlam DA, Petro KR, Haile E, Hill PC, Dullum MK, et al. Effect of clopidogrel premedication in off-pump cardiac surgery: are we forfeiting the benefits of reduced hemorrhagic sequelae? Circulation. 2006;113:1667–1674.

43 Shim JK, Choi YS, Oh YJ, Bang SO, Yoo KJ, Kwak YL. Effects of preoperative aspirin and clopidogrel therapy on perioperative blood loss and blood transfusion requirements in patients undergoing off-pump coronary artery bypass graft surgery. J Thorac Cardiovasc Surg. 2007;134:59–64.

44 Song SW, Youn YN, Yi G, Lee S, Yoo KJ. Effects of continuous administration of clopidogrel before off-pump coronary artery bypass grafting in patients with acute coronary syndrome. Circ J. 2008;72:626–632.

45 Kang W, Theman TE, Reed JF, Stoltzfus J, Weger N. The effect of preoperative clopidogrel on bleeding after coronary artery bypass surgery. J Surg Educ. 2007;64:88–92.

46 Picker SM, Kaleta T, Hekmat K, Kampe S, Gathof BS. Antiplatelet therapy preceding coronary artery surgery: implications for bleeding, transfusion requirements and outcome. Eur J Anaesthesiol. 2007;24:332–339.

47 Weightman WM, Gibbs NM, Weidmann CR, Newman MA, Grey DE, Sheminant MR, et al. The effect of preoperative aspirin-free interval on red blood cell transfusion requirements in cardiac surgical patients. J Cardiothorac Vasc Anesth. 2002;16:54–58.

48 Burger W, Chemnitius JM, Kneissl GD, Rücker G. Low-dose aspirin for secondary cardiovascular prevention—cardiovascular risks after its perioperative withdrawal versus

bleeding risks with its continuation—review and meta-analysis. J Intern Med. 2005;257:399–414.

49 Dunn AS, Turpie AG. Perioperative management of patients receiving oral anticoagulants: a systematic review. Arch Intern Med. 2003;163:901–908.

50 Nematullah A, Alabousi A, Blanas N, Douketis JD, Sutherland SE. Dental surgery for patients on anticoagulant therapy with warfarin: a systematic review and meta-analysis. J Can Dent Assoc. 2009;75:41-41i.

51 Krishnan B, Shenoy NA, Alexander M. Exodontia and antiplatelet therapy. J Oral Maxillofac Surg. 2008;66:2063–2066.

52 Slappendel R, Weber EWG, Benraad B, Dirksen R, Bugter ML. Does ibuprofen increase perioperative blood loss during hip arthroplasty? Eur J Anaesthesiol. 2002;19:829–831.

53 Robinson CM, Christie J, Malcolm-Smith N. Nonsteroidal antiinflammatory drugs, perioperative blood loss, and transfusion requirements in elective hip arthroplasty. J Arthroplasty. 1993;8:607–610.

54 An HS, Mikhail WE, Jackson WT, Tolin B, Dodd GA. Effects of hypotensive anesthesia, nonsteroidal antiinflammatory drugs, and polymethylmethacrylate on bleeding in total hip arthroplasty patients. J Arthroplasty. 1991;6:245–250.

55 Ozao-Choy J, Tammaro Y, Fradis M, Weber K, Divino CM. Clopidogrel and bleeding after general surgery procedures. Am Surg. 2008;74:721–725.

56 Devani P, Lavery KM, Howell CJ. Dental extractions in patients on warfarin: is alteration of anticoagulant regime necessary? Br J Oral Maxillofac Surg. 1998;36:107–111.

57 Campbell JH, Alvarado F, Murray RA. Anticoagulation and minor oral surgery: should the anticoagulant regimen be altered? J Oral Maxillofac Surg. 2000;58:131–135.

58 El-Jack SS, Ruygrok PN, Webster MW, Stewart JT, Bass NM, Armstrong GP, et al. Effectiveness of manual pressure hemostasis following transfemoral coronary angiography in patients on therapeutic warfarin anticoagulation. Am J Cardiol. 2006;97:485–488.

59 Wysokinski WE, McBane RD, Daniels PR, Litin SC, Hodge DO, Dowling NF, Heit JA. Periprocedural anticoagulation management of patients with nonvalvular atrial fibrillation. Mayo Clin Proc 2008;83:639–645.

60 McLemore EC, Harold KL, Cha SS, Johnson DJ, Fowl RJ. The safety of open inguinal herniorraphy in patients on chronic warfarin therapy. Am J Surg. 2006;192:860–864.

61 Shander A, Knight K, Thurer R, Adamson J, Spence R. Prevalence and outcomes of anaemia in surgery: a systematic review of the literature. Am J Med. 2004;116 Suppl 7A:58S–69S.

62 DeFoe GR, Ross CS, Olmstead EM, Surgenor SD, Fillinger MP, Groom RC, et al. Lowest hematocrit on bypass and adverse outcomes associated with coronary artery bypass grafting. Northern New England Cardiovascular Disease Study Group. Ann Thorac Surg. 2001;71:769–776.

63 Gombotz H, Rehak PH, Shander A, Hofmann A. Blood use in elective surgery: the Austrian benchmark study. Transfusion. 2007;47:1468–1480.

64 Koch CG, Weng YS, Zhou SX, Savino JS, Mathew JP, Hsu PH, et al. Prevalence of risk factors, and not gender per se, determines short- and long-term survival after coronary artery bypass surgery. J Cardiothorac Vasc Anesth. 2003;17:585–593.

65 Kulier A, Levin J, Moser R, Rumpold-Seitlinger G, Tudor IC, Snyder-Ramos SA, et al. Impact of preoperative anaemia on outcome in patients undergoing coronary artery bypass graft surgery. Circulation. 2007;116:471–479.

66 Lee RJ, Shih KN, Lee SH, Shyu KG, Chiu CZ, Lin SC, et al. Predictors of long-term outcomes in patients after elective stent implantation for unprotected left main coronary artery disease. Heart Vessels. 2007;22:99–103.

67 Parr KG, Patel MA, Dekker R, Levin R, Glynn R, Avorn J, et al. Multivariate predictors of blood product use in cardiac surgery. J Cardiothorac Vasc Anesth. 2003;17:176–181.

68 Rady MY, Ryan T, Starr NJ. Perioperative determinants of morbidity and mortality in elderly patients undergoing cardiac surgery. Crit Care Med. 1998;26:225–235.

69 Surgenor SD, DeFoe GR, Fillinger MP, Likosky DS, Groom RC, Clark C, et al. Intraoperative red blood cell transfusion during coronary artery bypass graft surgery increases the risk of postoperative low-output heart failure. Circulation. 2006;114 Suppl 1:I43–I48.

70 Swenne CL, Lindholm C, Borowiec J, Carlsson M. Surgical-site infections within 60 days of coronary artery by-pass graft surgery. J Hosp Infect. 2004;57:14–24.

71 Zindrou D, Taylor KM, Bagger JP. Preoperative haemoglobin concentration and mortality rate after coronary artery bypass surgery. Lancet. 2002;359:1747–1748.

72 Conlon NP, Bale EP, Herbison GP, McCarroll M. Postoperative anemia and quality of life after primary hip arthroplasty in patients over 65 years old. Anesth Analg. 2008;106:1056–1061.

73 Foss NB, Kristensen MT, Kehlet H. Anaemia impedes functional mobility after hip fracture surgery. Age Ageing. 2008;37:173–178.

74 Halm EA, Wang JJ, Boockvar K, Penrod J, Silberzweig SB, Magaziner J, et al. The effect of perioperative anaemia on clinical and functional outcomes in patients with hip fracture. J Orthop Trauma. 2004;18:369–374.

75 Meltomaa SS, Makinen JI, Taalikka MO, Helenius HY. Incidence, risk factors and outcome of infection in a 1-year hysterectomy cohort: a prospective follow-up study. J Hosp Infect. 2000;45:211–217.

76 Myers E, Grady P, Dolan AM. The influence of preclinical anaemia on outcome following total hip replacement. Arch Orthop Trauma Surg. 2004;124:699–701.

77 Wallis JP, Wells AW, Whitehead S, Brewster N. Recovery from postoperative anaemia. Transfus Med. 2005;15:413–418.

78 Wolters U, Wolf T, Stutzer H, Schroder Y, Pichlmaier H. Risk factors, complications, and outcome in surgery: a multivariate analysis. Eur J Surg. 1997;163:563–568.

79 Bell ML, Grunwald GK, Baltz JH, McDonald GO, Bell MR, Grover FL, et al. Does preoperative hemoglobin independently predict short-term outcomes after coronary artery bypass graft surgery? Ann Thorac Surg. 2008;86:1415–1423.

80 Cladellas M, Bruguera J, Comin J, Vila J, de Jaime E, Marti J, et al. Is preoperative anaemia a risk marker for in-hospital mortality and morbidity after valve replacement? Eur Heart J. 2006;27:1093–1099.

81 Fang WC, Helm RE, Krieger KH, Rosengart TK, DuBois WJ, Sason C, et al. Impact of minimum hematocrit during cardiopulmonary bypass on mortality in patients undergoing coronary artery surgery. Circulation. 1997;96(9 Suppl):II-194–II-199.

82 Ferraris VA, Ferraris SP, Edwards FH, Guyton RA, Reitz BA. Risk factors for postoperative morbidity. J Thorac Cardiovasc Surg. 1996;111:731–741.

83 Habib RH, Zacharias A, Schwann TA, Riordan CJ, Durham SJ, Shah A. Adverse effects of low hematocrit during cardiopulmonary bypass in the adult: should current practice be changed? J Thorac Cardiovasc Surg. 2003;125:1438–1450.

84 Habib RH, Zacharias A, Schwann TA, Riordan CJ, Engoren M, Durham SJ, et al. Role of hemodilutional anemia and transfusion during cardiopulmonary bypass in renal injury after coronary revascularization: implications on operative outcome. Crit Care Med. 2005;33:1749–1756.

85 Higgins TL, Estafanous FG, Loop FD, Beck GJ, Blum JM, Paranandi L. Stratification of morbidity and mortality outcome by preoperative risk factors in coronary artery bypass patients. A clinical severity score. JAMA. 1992;267:2344–2348.

86 Karkouti K, Wijeysundera DN, Yau TM, Callum JL, Cheng DC, Crowther M, et al. Acute kidney injury after cardiac surgery: focus on modifiable risk factors. Circulation. 2009;119:495–502.

87 Karkouti K, Wijeysundera DN, Beattie WS. Risk associated with preoperative anemia in cardiac surgery: a multicenter cohort study. Circulation. 2008a;117:478–484.

88 Karkouti K, Wijeysundera DN, Yau TM, McCluskey SA, Van Rensburg A, Beattie WS. The influence of baseline hemoglobin concentration on tolerance of anemia in cardiac surgery. Transfusion. 2008b;48:666–672.

89 Karkouti K, Djaiani G, Borger MA, Beattie WS, Fedorko L, Wijeysundera D, et al. Low hematocrit during cardiopulmonary bypass is associated with increased risk of perioperative stroke in cardiac surgery. Ann Thorac Surg. 2005;80:1381–1387.

90 Litmathe J, Boeken U, Feindt P, Gams E. Predictors of homologous blood transfusion for patients undergoing open heart surgery. Thorac Cardiovasc Surg. 2003;51:17–21.

91 McKechnie RS, Smith D, Montoye C, Kline-Rogers J, O'Donnell MJ, DeFranco AC, et al. Prognostic implication of anemia on hospital outcomes after percutaneous coronary intervention. Circulation. 2004;110:271–277.

92 Reinecke H, Trey T, Wellmann J, Heidrich J, Fobker M, Wichter T, et al. Haemoglobin-related mortality in patients undergoing percutaneous coronary interventions. Eur Heart J. 2003;24:2142–2150.

93 Beattie WS, Karkouti K, Wijeysundera DN, Tait G. Risk associated with preoperative anemia in noncardiac surgery: a single-center cohort study. Anesthesiology. 2009;110:574–581.

94 Carson JL, Noveck H, Berlin JA, Gould SA. Mortality and morbidity in patients with very low postoperative Hb levels who decline blood transfusion. Transfusion. 2002;42:812–818.

95 Dunkelgrun M, Hoeks SE, Welten GM, Vidakovic R, Winkel TA, Schouten O, et al. Anemia as an independent predictor of perioperative and long-term cardiovascular outcome in patients scheduled for elective vascular surgery. Am J Cardiol. 2008;101:1196–1200.

96 Gruson KI, Aharonoff GB, Egol KA, Zuckerman JD, Koval KJ. The relationship between admission hemoglobin level and outcome after hip fracture. J Orthop Trauma. 2002;16:39–44.

97 Lawrence VA, Silverstein JH, Cornell JE, Pederson T, Noveck H, Carson JL. Higher Hb level is associated with better early functional recovery after hip fracture repair. Transfusion. 2003;43:1717–1722.

98 Lunn JN, Elwood PC. Anaemia and surgery. Br Med J. 1970;3:71–73.

99 Marcantonio ER, Goldman L, Orav EJ, Cook EF, Lee TH. The association of intraoperative factors with the development of postoperative delirium. Am J Med. 1998;105:380–384.

100 Rogers SO, Kilaru RK, Hosokawa P, Henderson WG, Zinner MJ, Khuri SF. Multivariable predictors of postoperative venous thromboembolic events after general and vascular surgery: results from the patient safety in surgery study. J Am Coll Surg. 2007a;204:1211–1221.

101 Stoller ML, Wolf JS, St Lezin MA. Estimated blood loss and transfusion rates associated with percutaneous nephrolithotomy. J Urol. 1994;152(6 Pt 1):1977–1981.

102 Saleh E, McClelland DB, Hay A, Semple D, Walsh TS. Prevalence of anaemia before major joint arthroplasty and the potential impact of preoperative investigation and correction on perioperative blood transfusions. Br J Anaesth. 2007;99:801–808.

103 Wu WC, Schifftner TL, Henderson WG, Eaton CB, Poses RM, Uttley G, et al. Preoperative hematocrit levels and postoperative outcomes in older patients undergoing noncardiac surgery. JAMA. 2007;297:2481–2488.

104 Surgenor SD, Kramer RS, Olmstead EM, Ross CS, Sellke FW, Likosky DS, et al. The association of perioperative red blood cell transfusions and decreased long-term survival after cardiac surgery. Anesth Analg. 2009;108:1741–1746.

105 Hortal J, Munoz P, Cuerpo G, Litvan H, Rosseel PM, Bouza E; European Study Group on Nosocomial Infections, European Workgroup of Cardiothoracic Intensivists. Ventilator-associated pneumonia in patients undergoing major heart surgery: an incidence study in Europe. Crit Care. 2009;13(3):R80.

106 Cislaghi F, Condemi AM, Corona A. Predictors of prolonged mechanical ventilation in a cohort of 5123 cardiac surgical patients. Eur J Anaesthesiol. 2009;26:396–403.

107 Scott BH, Seifert FC, Grimson R. Blood transfusion is associated with increased resource utilisation, morbidity and mortality in cardiac surgery. Ann Card Anaesth. 2008;11:15–19.

108 Ranucci M, Bozzetti G, Ditta A, Cotza M, Carboni G, Ballotta A. Surgical reexploration after cardiac operations: why a worse outcome? Ann Thorac Surg. 2008a;86:1557–1562.

109 Murphy GJ, Reeves BC, Rogers CA, Rizvi SI, Culliford L, Angelini GD. Increased mortality, postoperative morbidity, and cost after red blood cell transfusion in patients having cardiac surgery. Circulation. 2007;116:2544–2552.

110 Rogers MA, Blumberg N, Heal JM, Hicks GL. Increased risk of infection and mortality in women after cardiac surgery related to allogeneic blood transfusion. J Womens Health (Larchmt). 2007b;16:1412–1420.

111 Koch CG, Li L, Duncan AI, Mihaljevic T, Loop FD, Starr NJ, et al. Transfusion in coronary artery bypass grafting is associated with reduced long-term survival. Ann Thorac Surg. 2006a;81:1650–1657.

112 Koch CG, Li L, Duncan AI, Mihaljevic T, Cosgrove DM, Loop FD, Starr NJ, Blackstone EH. Morbidity and mortality risk associated with red blood cell and blood-component transfusion in isolated coronary artery bypass grafting. Crit Care Med. 2006b;34:1608–1616.

113 Koch CG, Li L, Van Wagoner DR, Duncan AI, Gillinov AM, Blackstone EH. Red cell transfusion is associated with an increased risk for postoperative atrial fibrillation. Ann Thorac Surg. 2006c;82:1747–1756.

114 Koch CG, Khandwala F, Li L, Estafanous FG, Loop FD, Blackstone EH. Persistent effect of red cell transfusion on health-related quality of life after cardiac surgery. Ann Thorac Surg. 2006d;82:13–20.

115 El Solh AA, Bhora M, Pineda L, Dhillon R. Nosocomial pneumonia in elderly patients following cardiac surgery. Respir Med. 2006;100:729–736.

116 Augoustides JG, Pochettino A, McGarvey ML, Cowie D, Weiner J, Gambone AJ, et al. Clinical predictors for mortality in adults undergoing thoracic aortic surgery requiring deep hypothermic circulatory arrest. Ann Card Anaesth. 2006;9:114–119.

117 Banbury MK, Brizzio ME, Rajeswaran J, Lytle BW, Blackstone EH. Transfusion increases the risk of postoperative infection after cardiovascular surgery. J Am Coll Surg. 2006;202:131–138.

118 Kuduvalli M, Oo AY, Newall N, Grayson AD, Jackson M, Desmond MJ, et al. Effect of perioperative red blood cell transfusion on 30-day and 1-year mortality following coronary artery bypass surgery. Eur J Cardiothorac Surg. 2005;27:592–598.

119 Olsen MA, Sundt TM, Lawton JS, Damiano J, Hopkins-Broyles D, Lock-Buckley P, Fraser VJ. Risk factors for leg harvest surgical site infections after coronary artery bypass graft surgery. J Thorac Cardiovasc Surg. 2003;126:992–999.

120 Bucerius J, Gummert JF, Borger MA, Walther T, Doll N, Onnasch JF, et al. Stroke after cardiac surgery: a risk factor analysis of 16,184 consecutive adult patients. Ann Thorac Surg. 2003;75:472–478.

121 Chelemer SB, Prato BS, Cox PM, O'Connor GT, Morton JR. Association of bacterial infection and red blood cell transfusion after coronary artery bypass surgery. Ann Thorac Surg. 2002;73:138–142.

122 Engoren MC, Habib RH, Zacharias A, Schwann TA, Riordan CJ, Durham SJ. Effect of blood transfusion on long-term survival after cardiac operation. Ann Thoac Surg. 2002;74:1180–1186.

123 Leal-Noval SR, Rincón-Ferrari MD, García-Curiel A, Herruzo-Avilés A, Camacho-Larana P, Garnacho-Montero J, Amaya-Villar R. Transfusion of blood components and postoperative infection in patients undergoing cardiac surgery. Chest. 2001;119:1461–1468.

124 Soleimani M, Hosseini SY, Aliasgari M, Dadkhah F, Lashay A, Amini E. Erectile dysfunction after prostatectomy: an evaluation of the risk factors. Scand J Urol Nephrol. 2009;43:277-281.

125 Garcia-Alvarez F, Al-Ghanem R, Garcia-Alvarez I, Lopez-Baisson A, Bernal M. Risk factors for postoperative infections in patients with hip fracture treated by means of Thompson arthroplasty. Arch Gerontol Geriatr. 2009;50:51–55. Epub 2009 Feb 23.

126 Fuks D, Piessen G, Huet E, Tavernier M, Zerbib P, Michot F, et al. Life-threatening postoperative pancreatic fistula (grade C) after pancreaticoduodenectomy: incidence, prognosis, and risk factors. Am J Surg. 2009;197:702–709.

127 Bursi F, Barbieri A, Politi L, Di Girolamo A, Malagoli A, Grimaldi T, et al. Perioperative red blood cell transfusion and outcome in stable patients after elective major vascular surgery. Eur J Vasc Endovasc Surg. 2009;37:311–318.

128 Bernard AC, Davenport DL, Chang PK, Vaughan TB, Zwischenberger JB. Intraoperative transfusion of 1 U to 2 U packed red blood cells is associated with increased 30-day mortality, surgical-site infection, pneumonia, and sepsis in general surgery patients. J Am Coll Surg. 2009;208:931–937.

129 Silva JM, Cezario TA, Toledo DO, Magalhaes DD, Pinto MA, Victoria LG. Complications and prognosis of intraoperative blood transfusion. Rev Bras Anestesiol. 2008;58:447–461.

130 Johnson ON, Slidell MB, Macsata RA, Faler BJ, Amdur RL, Sidawy AN. Outcomes of surgical management for popliteal artery aneurysms: an analysis of 583 cases. J Vasc Surg. 2008;48:845–851.

131 Engoren M, Mitchell E, Perring P, Sferra J. The effect of erythrocyte blood transfusions on survival after surgery for hip fracture. J Trauma. 2008;65:1411–1415.

132 Ruttinger D, Wolf H, Kuchenhoff H, Jauch KW, Hartl WH. Red cell transfusion: an essential factor for patient prognosis in surgical critical illness? Shock. 2007;28:165–171.

133 BuSaba NY, Schaumberg DA. Predictors of prolonged length of stay after major elective head and neck surgery. Laryngoscope. 2007;117:1756–1763.

134 Weber EW, Slappendel R, Prins MH, van der Schaaf DB, Durieux ME, Strumper D. Perioperative blood transfusions and delayed wound healing after hip replacement surgery: effects on duration of hospitalization. Anesth Analg. 2005;100:1416–1421.

135 Halm EA, Wang JJ, Boockvar K, Penrod J, Silberzweig SB, Magaziner J, et al. Effects of blood transfusion on clinical and functional outcomes in patients with hip fracture. Transfusion. 2003;43:1358–1365.

136 Dunne JR, Malone D, Tracy JK, Gannon C, Napolitano LM. Perioperative anemia: an independent risk factor for infection, mortality and resource utilization is surgery. J Surg Res. 2002;102:237–244.

137 Chang H, Hall GA, Geerts WH, Greenwood C, McLeod RS, Sher GD. Allogeneic red blood cell transfusion is an independent risk factor for the development of postoperative bacterial infection. Vox Sang. 2000;78:13–18.

138 Carson JL, Duff A, Berlin JA, Lawrence VA, Poses RM, Huber EC, et al. Perioperative blood transfusion and postoperative mortality. JAMA 1998a;279:199–205.

139 Glenngard AH, Persson U, Soderman C. Costs associated with blood transfusions in Sweden—the societal cost of autologous, allogeneic and perioperative RBC transfusion. Transfus Med. 2005;15:295–306.

140 Lubarsky DA, Hahn C, Bennett DH, Smith LR, Bredehoeft SJ, Klein HG, Reves JG. The hospital cost (fiscal year 1991/1992) of a simple perioperative allogeneic red blood cell transfusion during elective surgery at Duke University. Anesth Analg. 1994;79:629–637.

141 Bracey AW, Radovancevic R, Riggs SA, Houston S, Cozart H, Vaughn WK, et al. Lowering the haemoglobin threshold for transfusion in coronary artery bypass procedures: effect on patient outcome. Transfusion. 1999;39:1070–1077.

142 Bush RL, Pevec WC, Holcroft JW. A prospective, randomized trial limiting perioperative red blood cell transfusions in vascular patients. Am J Surg. 1997;174:143–148.

143 Grover M, Talwalker S, Casbard A, Boralessa H, Contreras M, Brett S, et al. Silent myocardial ischaemia and haemoglobin concentration: a randomized controlled trial of transfusion strategy in lower limb arthroplasty. Vox Sang. 2006;90:105–112.

144 Carson JL, Terrin ML, Barton FB, Aaron R, Greenburg AG, Heck DA, et al. A pilot randomized trial comparing symptomatic vs. hemoglobin-level-driven red blood cell transfusions following hip fracture. Transfusion. 1998b;38:522–529.

145 Foss NB, Kristensen MT, Jensen PS, Palm H, Krasheninnikoff M, Kehlet H. The effects of liberal versus restrictive transfusion thresholds on ambulation after hip fracture surgery. Transfusion. 2009;49:227–234.

146 Aufricht C, Ties M, Wimmer M, Haschke F, Pietschnig B, Herkner K. Iron supplementation in children after cardiopulmonary bypass for surgical repair of congenital heart disease. Pediatr Cardiol. 1994;15:167–169.

147 Crosby L, Palarski VA, Cottington E, Cmolik B. Iron supplementation for acute blood loss anemia after coronary artery bypass surgery: a randomized, placebo-controlled study. Heart Lung. 1994;23:493–499.

148 Del Campo C, Lukman H, Mehta H, McKenzie FN. Iron therapy after cardiac operation: one prescription less? J Thorac Cardiovasc Surg. 1982;84:631–633.

149 Andrews CM, Lane DW, Bradley JG. Iron pre-load for major joint replacement. Transfus Med. 1997;7:281–286.

150 Lidder PG, Sanders G, Whitehead E, Douie WJ, Mellor N, Lewis SJ, Hosie KB. Preoperative oral iron supplementation reduces blood transfusion in colorectal surgery—a prospective, randomised, controlled trial. Ann R Coll Surg Engl. 2007;89:418–421.

151 Mundy GM, Birtwistle SJ, Power RA. The effect of iron supplementation on the level of haemoglobin after lower limb arthroplasty. J Bone Joint Surg Br. 2005;87:213–217.

152 Weatherall M, Maling TJ. Oral iron therapy for anaemia after orthopaedic surgery: randomized clinical trial. ANZ J Surg. 2004;74:1049–1051.

153 Cuenca J, Garcia-Erce JA, Martinez F, Cardona R, Perez-Serrano L, Munoz M. Preoperative haematinics and transfusion protocol reduce the need for transfusion after total knee replacement. Int J Surg. 2007;5:89–94.

154 Okuyama M, Ikeda K, Shibata T, Tsukahara Y, Kitada M, Shimano T. Preoperative iron supplementation and intraoperative transfusion during colorectal cancer surgery. Surg Today. 2005;35:36–40.

155 Cuenca J, Garcia-Erce JA, Munoz M, Izuel M, Martinez AA, Herrera A. Patients with pertrochanteric hip fracture may benefit from preoperative intravenous iron therapy: a pilot study. Transfusion. 2004;44:1447–1452.

156 Cuenca J, Garcia-Erce JA, Martinez AA, Solano VM, Molina J, Munoz M. Role of parenteral iron in the management of anaemia in the elderly patient undergoing displaced subcapital hip fracture repair: preliminary data. Arch Orthop Trauma Surg. 2005;125:342–347.

157 Munoz M, Naveira E, Seara J, Palmer JH, Cuenca J, Garcia-Erce JA. Role of parenteral iron in transfusion requirements after total hip replacement. A pilot study. Transfus Med. 2006;16:137–142.

158 Madi-Jebara SN, Sleilaty GS, Achouh PE, Yazigi AG, Haddad FA, Hayek GM, et al. Postoperative intravenous iron used alone or in combination with low-dose erythropoietin is not effective for correction of anemia after cardiac surgery. J Cardiothorac Vasc Anesth. 2004;18:59–63.

159 Karkouti K, McCluskey SA, Ghannam M, Salpeter MJ, Quirt I, Yau TM. Intravenous iron and recombinant erythropoietin for the treatment of postoperative anaemia. Can J Anesth. 2006a;53:11–19.

160 Kim YH, Chung HH, Kang SB, Kim SC, Kim YT. Safety and usefulness of intravenous iron sucrose in the management of preoperative anemia in patients with menorrhagia: a phase IV, open-label, prospective, randomised study. Acta Haematol. 2009;121:37–41.

161 Devon KM, McLeod RS. Pre and perioperative erythropoietin for reducing allogeneic blood transfusions in colorectal cancer surgery. Cochrane Database Syst Rev. 2009;(1):CD007148.

162 Laupacis A, Fergusson D; International Study of Perioperative Transfusion (ISPOT) Investigators. Erythropoietin to minimize perioperative blood transfusion: a systematic review of randomized trials. Transfus Med. 1998;8:309–317.

163 D'Ambra MN, Gray RJ, Hillman R, Jones JW, Kim HC, Rawitscher R, et al. Effect of recombinant human erythropoietin on transfusion risk in coronary bypass patients. Ann Thorac Surg. 1997;64:1686–1693.

164 Podesta A, Carmagnini E, Parodi E, Dottori V, Crivellari R, Barberis L, et al. Elective coronary and valve surgery without blood transfusion in patients treated with recombinant human erythropoietin (epoetin-α). Minerva Cardioangiol. 2000;48:341–347.

165 Sowade O, Warnke H, Scigalla P, Sowade B, Franke W, Messinger D, Gross J. Avoidance of allogeneic blood transfusions by treatment with epoetin beta (recombinant human erythropoietin) in patients undergoing open-heart surgery. Blood. 1997;89:411–418.

166 Canadian Orthopedic Perioperative Erythropoietin Study Group. Effectiveness of perioperative recombinant human erythropoietin in elective hip replacement. Lancet. 1993;341:1227–1232.

167 Christodoulakis M, Tsiftsis DD; Hellenic Surgical Oncology Perioperative EPO Study Group. Preoperative epoetin alfa in colorectal surgery: a randomised, controlled study. Ann Surg Oncol. 2005;12:718–725.

168 DeAndrade JR, Frei D, Young D, Larholt K. Epoetin alfa reduces allogeneic transfusions in subjects undergoing orthopaedic surgery [abstract]. Mid-America Orthopedic Association, 1996. Cited by: Laupacis A, Fergusson D; International Study of Perioperative Transfusion (ISPOT) Investigators. Erythropoietin to minimize perioperative blood transfusion: a systematic review of randomized trials. Transfus Med. 1998;8:309–317.

169 Faris PM, Ritter MA, Abels RI; American Erythropoietin Study Group. The effects of recombinant human erythropoietin on perioperative transfusion requirements in patients having a major orthopaedic operation. J Bone Joint Surg Am. 1996;78:62–72.

170 Feagan BG, Wong CJ, Kirkley A, Johnston DW, Smith FC, Whitsitt P, et al. Erythropoietin with iron supplementation to prevent allogeneic blood transfusion in total hip joint arthroplasty. A randomized controlled trial. Ann Intern Med. 2000;133:845–854.

171 Goldberg MA, McCutchen JW, Jove M, Di Cesare P, Friedman RJ, Poss R, et al. A safety and efficacy comparison study of two dosing regimens of epoetin alfa in patients undergoing major orthopaedic surgery. Am J Orthop (Belle Mead NJ). 1996;25:544–552.

172 Heiss MM, Tarabichi A, Delanoff C, Allgayer H, Jauch KW, Hernandez-Richter T, et al. Perisurgical erythropoietin application in anemic patients with colorectal cancer: a double-blind randomized study. Surgery. 1996;119:523–527.

173 Kettelhack C, Hones C, Messinger D, Schlag PM. Randomized multicentre trial of the influence of recombinant human erythropoietin on intraoperative and postoperative transfusion need in anaemic patients undergoing right hemicolectomy for carcinoma. Br J Surg. 1998;85:63–67.

174 Kosmadakis N, Messaris E, Maris A, Katsaragakis S, Leandros E, Konstadoulakis MM, Androulakis G. Perioperative erythropoietin administration in patients with gastrointestinal tract cancer: prospective randomized double-blind study. Ann Surg. 2003;237:417–421.

175 Larson B, Bremme K, Clyne N, Nordstrom L. Preoperative treatment of anemic women with epoetin beta. Acta Obstet Gynecol Scand. 2001;80:559–562.

176 Qvist N, Boesby S, Wolff B, Hansen CP. Recombinant human erythropoietin and haemoglobin concentration at operation and during the postoperative period: reduced need for blood transfusions in patients undergoing colorectal cancer surgery—prospective double-blind placebo-controlled study. World J Surg. 1999;23:30–35.

177 Rohling RG, Zimmermann AP, Breymann C. Intravenous versus oral iron supplementation for preoperative stimulation of hemoglobin synthesis using recombinant human erythropoietin. J Hematother Stem Cell Res. 2000;9:497–500.

178 Tsuji Y, Kambayashi J, Shiba E, Sakon M, Kawasaki T, Mori T. Effect of recombinant human erythropoietin on anaemia after gastrectomy: a pilot study. Eur J Surg. 1995;161:29–33.

179 Weber EW, Slappendel R, Hemon Y, Mahler S, Dalen T, Rouwet E, et al. Effects of epoetin alfa on blood transfusions and postoperative recovery in orthopaedic surgery: the European Epoetin Alfa Trial (EEST). Eur J Anaesthesiol. 2005b;22:249–257.

180 Green D, Lawler M, Rosen M, Bloom S, Duerden M, Turba R, et al. Recombinant human erythropoietin: effect on the functional performance of anemia orthopedic patients. Arch Phys Med Rehabil. 1996;77:242–246.

181 Warren O, Mandal K, Hadjianastassiou V, Knowlton L, Panesar S, John K, et al. Recombinant activated factor VII in cardiac surgery: a systematic review. Ann Thorac Surg. 2007;83:707–714.

182 Zangrillo A, Mizzi A, Biondi-Zoccai G, Bignami E, Calabro MG, Pappalardo F, et al. Recombinant activated factor VII in cardiac surgery: a meta-analysis. J Cardiothorac Vasc Anesth. 2009;23:34–40.

183 Ranucci M, Isgro G, Soro G, Conti D, De Toffol B. Efficacy and safety of recombinant activated factor VII in major surgical procedures: systematic review and meta-analysis of randomized clinical trials. Arch Surg. 2008b;143(3):296–304.

184 Essam MA. Prophylactic administration of recombinant activated factor VII in coronary revascularization surgery. Internet J Anesthesiol. 2007;13(1). http://www.ispub.com/ostia/index.php?xmlPrinter=true&xmlFilePath=journals/ija/vol13n1/factor.xml.

185 Gill R, Herbertson M, Vuylsteke A, Olsen PS, von Heymann C, Mythen M, et al. Safety and efficacy of recombinant activated factor VII: a randomized placebo-controlled trial in the setting of bleeding after cardiac surgery. Circulation. 2009;120:21–27.

186 Ma B, Wang ZN, Zhang BR, Xu ZY, Yang LX, Chen KB, Li J. Effect of recombinant activated factor VIIa on early recovery of patients undergoing cardiac valve replacement under cardiopulmonary bypass: a randomized double-blind placebo-controlled trial. Acad J Second Mil Med Univ. 2006;27:1110–1113.

187 Alavi AA, Jalali SM, Rasouli MR, Eghtesadi-Araghi P. Administration of recombinant activated factor VII in major thoracic operations. Arch Surg. 2008;143:1021.

188 Johansson PI, Eriksen K, Nielsen SL, Rojkjaer R, Alsbjorn B. Recombinant FVIIa decreases perioperative blood transfusion requirement in burn patients undergoing excision and skin grafting—results of a single centre pilot study. Burns. 2007;33:435–440.

189 Pihusch M, Bacigalupo A, Szer J, Von Depka Prondzinski M, Gaspar-Blaudschun B, Hyveled L, et al. Recombinant activated factor VII in treatment of bleeding complications following hematopoietic stem cell transplantation. J Thromb Haemost. 2005;3:1935–1944.

190 Pugliese F, Ruberto F, Summonti D, Perrella S, Cappannoli A, Tosi A, et al. Activated recombinant factor VII in orthotopic liver transplantation. Transplant Proc. 2007;39:1883–1885.

191 Sachs B, Delacy D, Green J, Graham RS, Ramsay J, Kreisler N, et al. Recombinant activated factor VII in spinal surgery: a multicenter, randomized, double-blind, placebo-controlled, dose-escalation trial. Spine. 2007;32:2285–2293.

192. Casbard AC, Williamson LM, Murphy MF, Rege K, Johnson T. The role of prophylactic fresh frozen plasma in decreasing blood loss and correcting coagulopathy in cardiac surgery. A systematic review. Anaesthesia. 2004;59:550–558.

193. Sarani B, Dunkman WJ, Dean L, Sonnad S, Rohrbach JI, Gracias VH. Transfusion of fresh frozen plasma in critically ill surgical patients is associated with an increased risk of infection. Crit Care Med. 2008;36:1114–1118.

194. Karkouti K, Wijeysundera DN, Yau TM, Callum JL, Meineri M, Wasowicz M, et al. Platelet transfusions are not associated with increased morbidity or mortality in cardiac surgery. Can J Anaesth. 2006b;53:279–287.

195. McGrath T, Koch CG, Xu M, Li L, Mihaljevic T, Figueroa P, Blackstone EH. Platelet transfusion in cardiac surgery does not confer increased risk for adverse morbid outcomes. Ann Thorac Surg. 2008;86:543–553.

196. Spiess BD, Royston D, Levy JH, Fitch J, Dietrich W, Body S, et al. Platelet transfusions during coronary artery bypass graft surgery are associated with serious adverse outcomes. Transfusion. 2004;44:1143–1148.

197 Dillon JF, Simpson KJ, Hayes PC. Liver biopsy bleeding time: an unpredictable event. J Gastroenterol Hepatol. 1994;9:269–271.

198 McVay PA, Toy PT. Lack of increased bleeding after liver biopsy in patients with mild hemostatic abnormalities. Am J Clin Pathol. 1990;94:747–753.

199 Misra S, Gyamlani G, Swaminathan S, Buehrig CK, Bjarnason H, McKusick MA, et al. Safety and diagnostic yield of transjugular renal biopsy. J Vasc Interv Radiol. 2008;19(4):546–551.

200 Ray CE, Shenoy SS. Patients with thrombocytopenia: outcome of radiologic placement of central venous access devices. Radiology. 1997;204:97–99.

201 Fisher NC, Mutimer DJ. Central venous cannulation in patients with liver disease and coagulopathy—a prospective audit. Intensive Care Med. 1999;25:481–485.

202 Weigand K, Encke J, Meyer FJ, Hinkel UP, Munder M, Stremmel W, Zahn A. Low levels of prothrombin time (INR) and platelets do not increase the risk of significant bleeding when placing central venous catheters. Med Klin (Munich). 2009;104:331–335.

203 Foster PF, Moore LR, Sankary HN, Hart ME, Ashmann MK, Williams JW. Central venous catheterization in patients with coagulopathy. Arch Surg. 1992;127:273–275.

204 Doerfler ME, Kaufman B, Goldenberg AS. Central venous catheter placement in patients with disorders of hemostasis. Chest. 1996;110:185–188.

205 Martin JH, Rosser CJ, Linebach RF, McCullough DL, Assimos DG. Are coagulation studies necessary before percutaneous nephrostomy? Tech Urol. 2000;6:205–207.

206 Mainwaring CJ, Natarajan A, Peckham C, Readett D, Singhal R, Vazzalwar R, Vora AJ. Untreated thrombocytopenia and lumbar puncture-related bleeding risk at diagnosis of childhood acute lymphoblastic leukemia (ALL) [abstract]. In: Poster Presentations, Conference of the British Society for Haematology; April 27–30 1998; Glasgow, Scotland. Poster 201.

207 Howard SC, Gajjar A, Ribeiro RC, Rivera GK, Rubnitz JE, Sandlund JT, et al. Safety of lumbar puncture for children with acute lymphoblastic leukemia and thrombocytopenia. JAMA. 2000;284:2222–2224.

208 Vavricka SR, Walter RB, Irani S, Halter J, Schanz U. Safety of lumbar puncture for adults with acute leukemia and restrictive prophylactic platelet transfusion. Ann Hematol. 2003;82:570–573.

209 Ruell J, Karuvattil R, Wynn R, Will A. Platelet count has no influence on traumatic and bloody lumbar puncture in children undergoing intrathecal chemotherapy. Br J Haematol. 2007;136:347–348.

210 Darcy MD, Kanterman RY, Kleinhoffer MA, Vesely TM, Picus D, Hicks ME, Pilgram TK. Evaluation of coagulation tests as predictors of angiographic bleeding complications. Radiology. 1996;198:741–744.

211 Weiss SM, Hert RC, Gianola FJ, Clark JG, Crawford SW. Complications of fiberoptic bronchoscopy in thrombocytopenic patients. Chest. 1993;104:1025–1028.

212 Wolf AT, Wasan SK, Saltzman JR. Impact of anticoagulation on rebleeding following endoscopic therapy for nonvariceal upper gastrointestinal hemorrhage. Am J Gastroenterol. 2007;102:290–296.