

## Research questions for the update of the PBM Guidelines (Modules 2-6)

Theme #	Theme	Active question	Population <i>Subgroups</i>	Intervention(s)	Critical outcome(s)
1	Effect of a PBM program	U1-GQ01	All patients <ul style="list-style-type: none"> <li>• <i>Perioperative</i></li> <li>• <i>Medical</i></li> <li>• <i>Critical care</i></li> <li>• <i>Obstetrics and maternity</i></li> <li>• <i>Neonatal and paediatrics</i></li> </ul>	PBM program	<ul style="list-style-type: none"> <li>• Mortality</li> <li>• Transfusion</li> </ul>
2	Effect of RBC transfusion	U1-GQ02	All adult patients <ul style="list-style-type: none"> <li>• <i>Perioperative</i></li> <li>• <i>Medical</i></li> <li>• <i>Critical care</i></li> </ul>	RBC transfusion	<ul style="list-style-type: none"> <li>• Mortality</li> </ul>
		U1-Q25	Neonatal and paediatric patients	RBC (allogeneic) transfusion	<ul style="list-style-type: none"> <li>• Mortality</li> <li>• Composite of mortality and severe morbidity</li> <li>• Neurodevelopmental disability</li> <li>• Necrotising enterocolitis</li> </ul>
3	Restrictive vs. liberal transfusion strategies	U1-GQ03	All patients <ul style="list-style-type: none"> <li>• <i>Perioperative</i></li> <li>• <i>Medical</i></li> <li>• <i>Critical care</i></li> <li>• <i>Obstetrics and maternity</i></li> <li>• <i>Neonatal and paediatrics</i></li> </ul>	Restrictive vs. liberal RBC transfusion	<ul style="list-style-type: none"> <li>• Mortality</li> <li>• Transfusion</li> <li>• Neurodevelopmental disability (<i>neonatal only</i>)</li> <li>• Necrotising enterocolitis (<i>neonatal only</i>)</li> </ul>
4	Optimal Hb threshold for transfusion	U1-Q20	Chronically transfused patients <ul style="list-style-type: none"> <li>• <i>Paediatrics</i></li> <li>• <i>Myelodysplasia</i></li> </ul>	RBC transfusion (at different Hb thresholds)	<ul style="list-style-type: none"> <li>• Mortality/survival</li> <li>• Functional/performance status</li> </ul>
5	Effect of blood component therapy	U1-GQ06	Patients receiving anti-platelet medication <ul style="list-style-type: none"> <li>• <i>Perioperative</i></li> <li>• <i>Medical</i></li> <li>• <i>Critical care</i></li> </ul>	Platelet transfusion	<ul style="list-style-type: none"> <li>• Mortality</li> <li>• Blood component utilisation</li> <li>• Bleeding into critical sites/organs</li> <li>• Major bleeding</li> </ul>
		U1-Q22	Patients with critical bleeding <ul style="list-style-type: none"> <li>• <i>Perioperative</i></li> <li>• <i>Obstetrics</i></li> <li>• <i>Paediatric patients</i></li> </ul>	Cryoprecipitate vs. Fibrinogen concentrate	<ul style="list-style-type: none"> <li>• Mortality</li> <li>• Blood component utilisation</li> </ul>
		U1-Q26	Neonatal and paediatric patients <ul style="list-style-type: none"> <li>• <i>Surgical</i></li> <li>• <i>Trauma</i></li> <li>• <i>Critical illness</i></li> </ul>	1. Platelet transfusion ( <i>preterms and newborns</i> ) 2. Fibrinogen concentrate ( <i>paediatric surgical and trauma patients</i> )	<ul style="list-style-type: none"> <li>• Mortality</li> <li>• Major bleeding</li> <li>• Intraventricular haemorrhage (<i>neonatal only</i>)</li> <li>• Blood component utilisation</li> </ul>

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6	Trigger for blood component therapy	U1-GQ04	All patients <ul style="list-style-type: none"> <li>• Perioperative</li> <li>• Medical</li> <li>• Critical care</li> <li>• Obstetrics and maternity</li> <li>• Neonatal and paediatrics</li> </ul>	Platelet transfusion	<ul style="list-style-type: none"> <li>• Mortality</li> <li>• Bleeding in previously non-bleeding patients (including intracranial haemorrhage for neonates)</li> <li>• Bleeding into critical sites/organs</li> <li>• ischaemic/thromboembolic events</li> <li>• Blood component utilisation</li> </ul>
		U1-GQ05	Patients with acquired abnormalities of haemostasis <ul style="list-style-type: none"> <li>• Perioperative</li> <li>• Medical</li> <li>• Critical care</li> <li>• Obstetrics and maternity</li> <li>• Neonatal and paediatrics</li> </ul>	<ol style="list-style-type: none"> <li>1. Plasma transfusion or prothrombinex (at an INR threshold)</li> <li>2. Cryoprecipitate or fibrinogen concentrate (at a specific fibrinogen level)</li> <li>3. Platelet transfusion (at a specific platelet count) (included in GQ04)<sup>Error!</sup> Bookmark not defined.</li> <li>4. Blood component therapy based on viscoelastic testing</li> </ol>	<ul style="list-style-type: none"> <li>• Mortality</li> <li>• Major bleeding</li> <li>• Intracranial haemorrhage (<i>neonatal only</i>)</li> <li>• Ischaemic or thromboembolic events</li> <li>• Blood component utilisation</li> </ul>
7	Effect of cessation of medications that affect haemostasis	U1-Q17	<ol style="list-style-type: none"> <li>1. Surgical patients</li> <li>2. Patients undergoing invasive procedures</li> </ol>	Anti-coagulants and anti-platelet therapy, including aspirin, clopidogrel, direct-acting anti-coagulants, warfarin	<ul style="list-style-type: none"> <li>• Mortality</li> <li>• Transfusion</li> <li>• Procedure-related bleeding</li> <li>• Reoperation for bleeding</li> <li>• Ischaemic or thromboembolic events</li> </ul>
8	Effect of non-transfusion interventions	U1-Q16	Surgical patients <ul style="list-style-type: none"> <li>• Preoperative</li> <li>• Intraoperative</li> <li>• Postoperative</li> </ul>	1. Iron therapy (oral and/or parenteral)	<ul style="list-style-type: none"> <li>• Mortality</li> <li>• RBC transfusion</li> </ul>
		U1-Q19	Medical patients <ul style="list-style-type: none"> <li>• Haematology oncology</li> <li>• Renal</li> <li>• Congestive heart failure</li> </ul>	<ol style="list-style-type: none"> <li>1. ESAs</li> <li>2. Iron therapy (oral or parenteral IV or IM)</li> <li>3. Combination of these</li> </ol>	<ul style="list-style-type: none"> <li>• Mortality</li> <li>• RBC transfusion</li> <li>• Ischaemic or thromboembolic events</li> </ul>
		U1-Q21	Critically ill patients	<ol style="list-style-type: none"> <li>1. Iron therapy (parenteral IV)</li> <li>2. ESAs</li> <li>3. Combination of these</li> </ol>	<ul style="list-style-type: none"> <li>• Mortality</li> <li>• RBC transfusion</li> <li>• Ischaemic or thromboembolic events</li> </ul>
		U1-Q23	Obstetrics and maternity patients	1. Iron therapy (oral and/or parenteral IV)	<ul style="list-style-type: none"> <li>• Mortality (maternal)</li> <li>• Transfusion</li> <li>• Measures of fetal outcome</li> </ul>

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9	Effect of blood conservation strategies	U1-Q18	Surgical patients Patients undergoing invasive procedures (TXA only) • <i>Obstetrics</i>	1. Cell salvage (perioperative) 2. Deliberate induced hypotension 3. POC testing for coagulation status and Hb 4. Restrictive sampling 5. Administration of antifibrinolytics (TXA, aprotinin) and DDAVP	• Mortality • Transfusion
		U1-Q24	Obstetrics and maternity patients • <i>Bleeding patients (postpartum/ante partum haemorrhage, placenta problems, ectopic pregnancy, miscarriage)</i>	1. Viscoelastic testing 2. Administration of antifibrinolytics (TXA only) 3. Cell salvage (intraoperative) 4. Interventional radiology (iliac balloon catheters or embolisation only)	• Mortality (maternal) • Transfusion
		U1-Q27	Neonatal patients Paediatric patients • <i>Surgical (cardiac, burns, transplantation, orthopaedic)</i> • <i>Critical illness (ECMO/ECLS, trauma)</i>	<u>Preterm and newborn</u> 1. Placental transfusion <u>Infant/child/adolescent – surgical</u> 1. Deliberate controlled/induced hypotension 2. Cell salvage (intraoperative) 3. Viscoelastic testing 4. Administration of antifibrinolytics (TXA, aprotinin) <u>Infant/child/adolescent – critical illness</u> 1. Viscoelastic testing	<u>Preterm and newborn</u> • Composite death and/or major morbidity • Transfusion • Mortality • Neurodevelopmental outcomes <u>Infant/child/adolescent – surgical/critical illness</u> • Mortality • Transfusion • Neurodevelopmental outcomes • Major bleeding • Intraventricular haemorrhage (neonatal only)

Abbreviations: DDAVP, desmopressin; ECLS, extracorporeal life support; ECMO, extracorporeal membrane oxygenation; ESA, erythrocyte-stimulating agents; Hb, haemoglobin; IM, intramuscular; IV, intravenous; IVIg, intravenous immunoglobulin; LBW, low birth weight; NSAID, non-steroidal anti-coagulant; POC, point-of-care; RBC, red blood cell; TXA, tranexamic acid.