# Round 1 Project Summary, Publications, aims and objectives

Grant type	Project Title	Administering Institute	Amount (inc. GST)	Principal Chief Investigator	Project Aims/Objectives	Project Summary	Publications
Patient Blood management Project Grant	Effects of antenatal haemoglobin and obstetric transfusion on adverse maternal outcomes	University of Sydney	\$160,930.00	Prof Jane Ford	To use linked whole population data (biomarker, hospitalisations, births, deaths pathology, blood bank) for obstetric patients to ascertain antenatal risk markers for transfusion, and among women transfused, identify adverse outcomes.	Around 1 in 10 women suffer excessive bleeding after childbirth and 15% of these women will have a red blood cell transfusion. Obstetric transfusion rates are increasing, against a backdrop of decreasing use in other patient groups. While red cell transfusion is a potentially lifesaving treatment, blood transfusion is not without complication, and there is insufficient evidence to guide practice in terms of identifying the women that will benefit, the optimal timing, the amount transfused and clinically meaningful patient-centred outcomes. Only 4 of 56 recommendations in recently released Obstetric and Maternity Patient Blood Management (PBM) guidelines had any evidence (Grade C) to inform practice, with the remaining recommendations based on expert opinion.  This project would address two of the gaps identified in Obstetric and Maternity PBM guidelines:  1) in maternity patients, the Hb and ferritin levels that are associated with optimal maternal and foetal outcomes; and  2) in bleeding patients, the effect of transfusion on patient centred outcomes, including mortality, morbidity, postnatal recovery, quality of life, functional status, breastfeeding and psychological health.  Using population level data on Hb and ferritin levels, transfusion and subsequent outcomes (morbidity, mortality, readmission and breastfeeding), adjusted for covariates, this project will address these research gaps. On completion of this project the results will be translated into information for patient counselling, monitoring, and treatment; clinician education and transfusion reduction strategies; and form evidence for revised patient blood management guidelines.  To address the knowledge gaps in obstetric transfusion, the team collaborated with the New South Wales (NSW) Clinical Excellence Commission (CEC) and the Australian Red Cross Blood Service (ARCBS) to explore transfusion use in NSW. The team has established a number of large, linked population datasets with core maternity data linked to antenatal screening, pathology and A	Outcomes associated with transfusion in low-risk women with obstetric haemorrhage  The association between haemoglobin levels in the first 20 weeks of pregnancy and pregnancy outcomes  Haemoglobin trajectories during pregnancy and associated outcomes using pooled maternity and hospitalization data from two tertiary hospitals  Validation of anaemia, haemorrhage and blood disorder reporting in hospital data in New South Wales, Australia  Reporting of gestational diabetes and other maternal medical conditions

						trajectories through pregnancy and adverse outcomes post-transfusion.	
Patient Blood management Project Grant	Fibrinogen Replacement in Severe Traumatic Haemorrhage	University of Queensland	\$190,274.70	Dr James Winearls	1. To investigate the feasibility of fibrinogen replacement in severe traumatic haemorrhage utilising either fibrinogen concentrate (FC) or Cryoprecipitate.  2. Compare time to administration of fibrinogen replacement between FC and Cryoprecipitate.  3. To investigate the effects of fibrinogen replacement utilising either FC or Cryoprecipitate on fibrinogen levels during traumatic haemorrhage.  4. Investigating the feasibility of implementing the study protocol in a pilot multicentre study.  5. Use the data generated in the pilot study to inform on logistical considerations and guide planning of a large definitive multicentre study with patient centred outcome measures as primary endpoint	There are over 7000 Australians who are treated for severe trauma in hospitals annually. Major haemorrhage in the setting of severe trauma is associated with significantly poorer outcomes and increased rates of death. Severe trauma is also known to cause a decrease in the factors within the blood that helps clots to form and stop bleeding. There is good evidence to suggest that this loss of clotting factors is also associated with worse outcomes, and it is proposed that early replacement of these factors may reduce haemorrhage and improve outcomes.  Fibrinogen is one of the key clotting factors that needs to be replaced in severe traumatic haemorrhage.  Currently fibrinogen is replaced using cryoprecipitate. Cryoprecipitate is a blood product made from blood donated by health donors and is a precious resource. This blood product can take a significant amount of time to administer as it is frozen and stored in the blood bank. This makes timely administration of cryoprecipitate difficult as it needs to be thawed.  The large doses of cryoprecipitate utilised in traumatic haemorrhage place a significant strain on local blood banks in issuing requested units in a timely manner and on national blood supply agencies in maintaining and providing adequate stocks to individual blood banks. In addition, the size of Australia makes supplying and maintaining adequate stocks of 'fresh' allogenic blood products logistically challenging.  Fibrinogen concentrate (FC) is an alternative product used to assist in blood clotting. It is stored in powder form and can be reconstituted at the bedside and given quickly. It is hypothesised that it will be significantly quicker to administer FC than cryoprecipitate, which will reduce haemorrhage time and improve patient outcomes. The use of a fibrinogen factor concentrate that has a long shelf life and is easy to use has enormous implications for both large urban metropolitan areas and remote isolated communities.  This pilot study included 100 patients from 4 major trauma centres in Quee	Fibrinogen Early In Severe Trauma studY (FEISTY): study protocol for a randomised controlled trial  Haemotherapy algorithm for the management of trauma-induced coagulopathy: an Australian perspective  Fibrinogen Early In Severe Trauma studY (FEISTY): results from an Australian multicentre randomised controlled pilot trial - PMC (nih.gov)  A novel method to quantify fibrin–fibrin and fibrin–α2-antiplasmin cross-links in thrombi formed from human trauma patient plasma - ScienceDirect - FEISTY patient samples were used for this research  Cryoprecipitate transfusion in trauma patients attenuates hyperfibrinolysis and restores normal clot structure and stability: Results from a laboratory sub-study of the FEISTY trial - PMC (nih.gov) - FEISTY patient samples were used for this research

						This study aimed to address several key areas highlighted in the 'Patient Blood Management Guidelines Module 1: Critical Bleeding and Massive Transfusion'	
Patient Blood management Project Grant	Iron need in pregnancy and after birth	University of Adelaide	\$153,035.63	Prof Bernd Froessler	To assess whether two different doses of antenatal intravenous iron administration (500 mg and 100mg ferric carboxymaltose) are equivalent in replenishing and sustaining iron stores successfully in pregnant iron deficient women.	Iron deficiency is a common nutritional deficiency amongst women of childbearing age. Iron deficiency in pregnancy and around the time of delivery is associated with significant maternal, foetal and infant morbidity, including premature birth, foetal growth restriction, still-birth and infection.  Women with iron deficiency anaemia are at risk of requiring red blood cell transfusion, and having cardiovascular problems, reduced physical and mental (understanding and functioning) performance, reduced immune function, tiredness and depressive episodes in pregnancy and around the time of delivery.  Intravenous (IV) iron is an effective treatment option for iron deficiency and generally well tolerated. Different doses of IV iron have been studied but it remains unclear if there is an optimal dose and what this dose might be for the short and longer term.  This study assessed whether one intravenous iron administration of 500 or 1000 mg ferric carboxymaltose replenishes and sustains iron stores successfully when given to pregnant iron deficient women.  The research aimed to identify the right dose of iron required to get women through pregnancy, labour and the time after delivery. This could improve the well-being of mothers, reduce the need for blood transfusions and protect babies from the adverse effects of iron deficiency. This may have critical and long-lasting implications for growth and development, particularly for the foetal brain.	Testing equivalence of two doses of intravenous iron to treat iron deficiency in pregnancy: A randomised controlled trial - Froessler
Patient Blood Management Seed Grants	Clinical characteristics of geriatric patients transfused within 24 hours of emergency	University of Sunshine Coast	\$54,802.00	Dr Geoff Simon	To characterise patients aged 65 years and above who received red cell transfusions within 24 hours of ED presentation, in the context of red cell use for younger ED presentations, and overall red cell use	Australian and international studies report that over 50% of the red cell supply is used in people 65 years of age and older. This group represents the fastest growing age cohort in Australia and many western countries, with the number of people in Australia aged over 65 expected to increase from 3.2 million in 2012 to 5.8 million in 2031 and to 11.1 million by 2061.	Outcomes of restrictive versus liberal transfusion strategies in older adults from nine randomised controlled trials: a systematic review and meta-analysis

	department (ED) presentation					Despite the geriatric population consuming more than 50% of the available red cell supply, most evidence relating to this group pertains to oncology and elective surgical settings. Geriatric blood use in the Emergency Department, a key entry point to the health system, is poorly characterised which leads to Patient Blood Management (PBM) evidence gaps. Clinical scenarios covered in the PBM guidelines, including massive transfusion, iron deficiency anaemia, surgery and others, are relevant in the geriatric setting. Clinicians dealing with the geriatric population in emergency scenarios are often acutely aware of the lower 3 physiological reserves of this cohort, and may treat more aggressively to deal with reductions in blood volume and haemoglobin in anticipation of better clinical outcomes. The approaches recommended by PBM guidelines are therefore often opposite to the intuitive approach of the emergency physician when dealing with the geriatric population.  This one-year pilot study aimed to gather baseline data from patients aged 65 years and older who received a transfusion within 24 hours of presentation to the Emergency Department (ED) at the Sunshine Coast Hospital and Health Service. Concurrently an international literature review explored current evidence regarding geriatric red cell use in emergency settings.  Data was analysed to determine demographic and clinical characteristics of geriatric patients who receive red cell transfusions within 24 hours of presentation at the ED, including reason for presentation and comorbidities and to explore elements that may be predictors of red cell transfusion, and those that might be used to guide early management of geriatric patients.	Impact and implications of the ageing population on anaemia management, patient blood management and unplanned blood use - University of the Sunshine Coast, Queensland dissertation)
Patient Blood Management Seed Grants	Improving blood sampling practice for critically ill children undergoing cardiac surgery	Griffith University	\$54,078.20	A/Prof Deborah Long	To audit current blood sampling practice for critically ill children undergoing cardiac surgery     To evaluate the impact of a closed-loop blood sampling system +/- bundled strategies on infection outcomes and blood sample volumes	Arterial catheters (AC) are widely used in anaesthesia and critical care to facilitate continuous monitoring of blood pressure and to sample arterial blood of critically ill patients. About 250,000 Australians need an arterial catheter each year, of which approximately 2,300 are children undergoing cardiac surgery. However, the presence and use of an arterial catheter may lead to a number of complications, including anaemia following blood sampling (low red blood cell count) and arterial catheter-associated bloodstream infection and arterial damage. These complications are associated with patient suffering, prolonged hospitalisation, expensive healthcare costs and increased mortality. Compared to adults, children are more susceptible to anaemia, risks associated with transfusion and infection. Implementation of evidence-based blood sampling practices and reducing the risk of catheter related blood stream infection in critically ill children is a top priority. Closed loop systems may be the key to minimising the risk of unnecessary blood loss and infection through	Patient blood management in critically ill children undergoing cardiac surgery: A cohort study

						<ul> <li>(i) reducing wastage of line clearance volumes (blood and fluid) and</li> <li>(ii) reducing exposure of administration and monitoring set to external environment.</li> <li>Anaemia and related transfusions, as well as catheter associated bloodstream infection cost the Australian healthcare system millions of dollars each year, yet there is currently no high-quality evidence from independent trials to guide decision making and practice on this topic. This project aimed to audit blood loss through current sampling practice in the paediatric cardiac surgery population and conduct a high quality, pilot randomised controlled trial, to test the feasibility of undertaking a full-scale efficacy trial, and obtain preliminary data.</li> </ul>	
Immunoglobulin Project Grants	Towards a better understanding of doctors' treatment patterns and immunoglobulin use in Australian children with Kawasaki disease: an opportunity for improvement?	Murdoch Children's Research Institute	\$271,309.5	Prof David Burgner	1. To determine the incidence, and seasonal and geographical clustering of Kawasaki disease in Australia 2. To understand the variability in the patterns of intravenous immunoglobulin (IVIg) treatment of Kawasaki disease among Australian doctors 3. To determine whether particular clinical features of patients with Kawasaki disease at presentation can predict response to IVIg therapy and cardiac outcomes.	Kawasaki disease (KD) is a potentially life-threatening childhood condition. It is the most common cause of acquired heart disease in Australian children and may cause coronary artery disease and heart attack in childhood. The true Australian incidence of KD is however unknown with the current best estimate of ~200 cases annually likely to be a significant underestimate. The only evidence-based treatment is one or more large doses of intravenous immunoglobulin (IVIg), an expensive and scarce resource derived from blood donors.  Currently little is known about IVIG use in KD in Australia; key unanswered questions include  (i) whether IVIG is used appropriately in terms of timing and dose,  (ii) (iii) what criteria are used for IVIG re-treatment, and  (iiii) (iii) what adjunctive treatment is given.  Attempts to identify those at risk of poor outcome and IVIG treatment failure perform poorly in mixed populations outside Japan (such as Australia) and local data are needed. There is significant variation in clinicians' management of KD, including timing and nature of treatment of those failing initial IVIg, and an increasing use of adjunctive agents such as corticosteroids and biological drugs. It should be possible to develop disease stratification scores to identify high and low risk patients who may benefit from different treatment protocols. These findings would rationalise IVIg usage and avoid unnecessary use of IVIG in some cases.  The study combined:  - A retrospective review of KD incidence in Australia using data available from the Australian Red Cross Blood Bank IVIg database (2008-present). The data included basic demographics to define the current epidemiology in Australia.  - A national survey of KD management by doctors investigating decisions in different clinical KD scenarios to provide greater	Epidemiology of Kawasaki disease in Australia using two nationally complete datasets  Prospective characterisation of SARS-CoV-2 infections among children presenting to tertiary paediatric hospitals across Australia in 2020: a national cohort study  Coronavirus and Kawasaki disease in children: it's an intriguing but unproven link  FDG-PET imaging in a child with Kawasaki disease: systemic and coronary artery inflammation without dilatation  Variation in the management of Kawasaki disease in Australia and New Zealand: A survey of paediatricians

Immunoglobulin Project Grants	Oral antibiotics or intravenous immunoglobulin to reduce infections in patients with blood cancers	Monash University	\$434,453.80	Prof Erica Wood	1. To conduct a feasibility trial to inform a definitive RCT comparing prophylactic antibiotics with IVIg to prevent infections in patients with hypogammaglobulinaemia secondary to haematologic malignancies  2. To perform a systematic review of the role of prophylactic oral antibiotics compared with IVIg, and  3. To conduct an international survey of current practice of interventions to reduce infection.	understanding of IVIg prescription patterns due to a lack of national guidelines, with international collaboration to facilitate international benchmarking.  A prospective study of all patients with KD treated in Australia over a 3-year period, identified from IVIg requests to the Red Cross Blood Service. Data included clinical features, treatment and outcomes, with the finding aimed at providing a detailed picture of IVIG use, variations in clinical practice, comparisons to international standards and identification of clinical features that may help stratify risk in KD.  An improved understanding of the current epidemiological and treatment patterns for KD in Australia will help inform the development and implementation of standardised management protocols based on best evidence and international practice. This will optimise management- particularly IVIG use in KD.  The findings aim to provide a platform to establish a KD registry, for ongoing prospective monitoring of IVIG management, particularly in the face of newer interventions. The registry would foster research related to biomarkers in KD to enhance understanding, including IVIG responsiveness and risk stratification. The findings aim to facilitate optimal outcomes for children with KD and judicious use of resources.  The RATIONAL (Role of antibiotic therapy or IVIg on infections in haematology) project aimed to understand whether oral antibiotics can be used instead of intravenous immunoglobulin (IVIg, a blood product made from human plasma) to reduce the risk of infections in people with blood cancers.  Some blood cancers, or the medications used to treat them, can cause low levels of immunoglobulins (antibodies) in the blood, resulting in increased risks of serious infection. Over 20% of all IVIg issued in Australia is used to try to prevent infections in patients with blood cancers.  Even though blood products like IVIg used in Australia are very safe, they do still carry some risks and should only be used when really needed. IVIg is also expensive	Managing hypogammaglobulinaemia secondary to haematological malignancies in Australia and New Zealand: a clinician survey  Rational: A randomised controlled feasibility trial comparing prophylactic immunoglobulin with antibiotics in patients with acquired hypogammaglobulinemia secondary to haematological malignancies  Interventions to reduce infections in patients with hematological malignancies: a systematic review and meta-analysis  Immunoglobulin replacement vs prophylactic antibiotics for hypogammaglobulinemia secondary to hematological malignancy - PMC (nih.gov)
						In some countries, for patients with low immunoglobulin levels, a trial of oral antibiotics is used before commencing IVIg, to see whether	prophylactic antibiotics for hypogammaglobulinemia secondary to

						Are prophylactic (preventive) oral antibiotics equivalent to immunoglobulin replacement in reducing the risk of serious infections in adults with blood cancers?  What is the role of other measures, such as vaccination against infectious diseases, in this setting?  Together, these questions aimed to provide answers to help guide more efficient and effective use of IVIg in Australia and help patients with blood cancers get better care, while also reducing risks and costs.	Advances   American Society of Hematology (ashpublications.org)
Immunoglobulin Seed Grants	Improving the use of intravenous immunoglobulin (IVIg) in children with neurological disorders	The University of Sydney	\$50,837.60	Prof Russell Dale	1. To improve understanding of tolerability and outcomes in children with neurological disease given IVIg  2. To identify gaps in the National guidelines and provoke a discussion about the health economic costs of IVIg administration in children with potentially serious neurological conditions.	Intravenous immunoglobulin is an expensive product, which can treat immune deficiency or autoimmune/inflammatory conditions. IVIg is being increasingly used to treat autoimmune or inflammatory disorders of the nervous system. Children with these conditions often present with acute weakness, blindness, or encephalopathy.  Previously this research team has conducted a major review of the use of IVIg for neurological conditions between 2000 and 2014 at the largest children's Hospital in New South Wales. IVIg was administered to 1264 children at the hospital during the time period, and 196 of these children had neurological disorders (15.5%).  This project completed the data collection and analysis for the next year. This core data source was used to investigate the following:  1. Identify adherence of current practice to guidelines and identify indications that were not in the current guidelines. For example, the autoimmune encephalitis syndrome, anti-NMDAR encephalitis, which was 'discovered' in 2007 and is the prototypic autoimmune encephalitis syndrome, is not specifically recognised as an indication for IVIG administration, although there is clear evidence that this is an autoimmune disorder.  2. The cost of IVIg administration in our institute for neurological indications was over 2.5million Australian dollars. Performing a secondary analysis aimed to identify the relative cost according to indication which would help inform practice and identify opportunities for economic efficiencies.  3. Children receiving IVIg for neurological indications may be particularly vulnerable to certain adverse effects such as aseptic meningitis. Detailed case notes review would identify the adverse events using CTCAE v3.0. This would identify the relative risk of allergic phenomenon and serious adverse events, if they exist.  4. Using the Modified Rankin Scale and using ethically approved follow-up mechanisms (LNR/15/SCHN/218), follow-up was extended to mean 52 months post onset of disease (median 36 months), and 88% of	Intravenous immunoglobulin in paediatric neurology: safety, adherence to guidelines, and long-term outcome  Clinical course, therapeutic responses and outcomes in relapsing MOG antibody-associated demyelination

						patients had follow-up for longer than 12 months. This research aimed to define the level of disability in this cohort to establish the 'disease severity' during the acute disease, and at final follow-up.  A significant proportion of children receiving IVIg have autoimmune CNS demyelination (n=36). The research team aimed to perform detailed analysis of these patients to determine if IVIg provides additional benefit to 'steroids only' which is considered the standard of care in the treatment of acute CNS demyelination. It is recognised that some patients with CNS demyelination do not adequately respond to steroids, and IVIg or plasma exchange is typically used. This subgroup analysis would identify specific questions that would lead to a large national paediatric study into the use of IVIg in paediatric CNS demyelination.	
Patient Blood management Early Career Research Grant (Scholarship)	A series of studies on a new clotting test in pregnant women to optimise the management of bleeding	The University of Queensland	\$33,000.00	Dr Julie Lee	1. To enable improved haemostasis management in the parturient by generating normal values for the obstetric population and by examining the correlation between ROTEM® parameters, transfusion requirements and the probability of PPH.  2. Associations between ROTEM® and transfusion requirement, estimated blood loss, and other outcomes for analysis  3. To examine the relationship between FIBTEM and fibrinogen in patients with abnormal coagulation or exposure to anticoagulant drugs.  4. To test the hypothesis that ROTEM® Platelet can be used to assess the severity of platelet dysfunction in preeclamptic patients and that there is a utility for ROTEM® Platelet testing in women prior to the administration of regional anaesthesia or urgent delivery to reduce morbidity and mortality from post-partum haemorrhage.  This study aimed to quantify the changes in platelet function and aggregation in women with preeclampsia and this would be	Rotational thromboelastometry (ROTEM®) is a point-of-care diagnostic device which provides rapid and specific clotting assessment. The use of ROTEM® is well established in liver and open-heart surgery, but not yet in the obstetric setting.  There is increasing use of ROTEM® for the monitoring of clotting in patients with massive haemorrhage, but there remains limited data on reference ranges in uncomplicated pregnancies and subsequently limited understanding of the effect of complicated pregnancies on ROTEM® interpretation.  In this project, ROTEM® values would be obtained from women presenting to the labour ward and from patients presenting for an elective Caesarean section. A ROTEM® sample of 3.5mL of blood would be obtained to process the standard ROTEM® panel. Standard coagulation profiles would be taken for patients with complicated pregnancies to allow correlation with ROTEM® values. Complicated pregnancies would include patients with pre-existing clotting disorders and all pregnancy-related conditions.  Previous small-scale studies have reported ROTEM® values in non-pregnant women, normal pregnancies, postpartum and in active labour, but not in obstetric patients with pre-eclampsia, pregnancy-induced low platelets, liver disease, blood clotting disorders or other pathologies. Pre-eclampsia is a pregnancy-specific syndrome associated with low platelet count and platelet dysfunction. ROTEM® Platelet is a new module for platelet function testing which would be available in late 2016. This third study would also analyse platelet function in obstetric patients presenting with pre-eclampsia. These values would be compared with published reference ranges to further the understanding of clotting changes in complicated pregnancies, in order to enable improved blood transfusion management in the pre-eclamptic patient. ROTEM® Platelet values would be obtained from labouring women presenting to the labour ward with pre-eclampsia.	The influence of obesity on coagulation in healthy term pregnancy as assessed by rotational thromboelastometry  Baseline parameters for rotational thromboelastometry in healthy labouring women: a prospective observational study  Baseline parameters for rotational thromboelastometry (ROTEM-Æ) in healthy pregnant Australian women: a comparison of labouring and non-labouring women at term  Baseline parameters for rotational thromboelastometry (ROTEM-Æ) in healthy women undergoing elective caesarean delivery: a prospective observational study in Australia

correlated to the platelet count and standard coagulation profile with data collected on demographics, medication history, gestation, delivery outcomes, severity of pre-eclampsia, transfusion requirement, whether an MTP was activated, treatment instituted for pre-eclampsia and neonatal outcomes.

5. The focus of the audit was to compare the amount and distribution of blood products used intra-operatively pre- and post-implementation of ROTEM® thromboelastometry and to identify the type of procedures requiring blood transfusions, whether it was elective or emergency surgery, the use of ICS and MTP intra-operatively and whether or not ROTEM® was utilised to guide the transfusion of blood products

Standard coagulation profiles would be taken for these patients to allow correlation with ROTEM® values. These patients routinely have a full blood count performed upon presentation to the labour ward, which would include a platelet count. These platelet count results would be retrieved from the laboratory database to also correlate with the ROTEM® Platelet results.

These three prospective observational studies aimed to add to the current knowledge and enable improved blood transfusion management in the pregnant patient by generating normal values for the obstetric population and by examining the correlation between ROTEM® parameters, transfusion requirements and the probability of severe bleeding following childbirth. There exists a gap in evidence to be filled by these proposed studies in the field of transfusion medicine, which can potentially benefit the obstetric population and lead to optimisation of blood transfusion practices. ROTEM® values can be derived within minutes and are potentially useful for guiding rapid transfusion management. Where test results are not derived within a reasonable time-frame, unnecessary or inappropriate transfusion of blood products may occur and this can be prevented with the use of ROTEM®, the more rapid test.