

Round 3 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 Grants	Deferred cord clamping to reduce need for neonatal blood transfusion	University of Sydney	\$161,151.10	Prof Helen Liley	To obtain and analyse more data about the babies in APTS, to better support deferred cord clamping as a method to reduce the need for transfusion in babies.	<p>Neonates, particularly if born preterm or with congenital anomalies, are among the paediatric patients most likely to need red cell transfusion. Systematic literature review for the Patient Blood Management Guidelines identified deferred umbilical cord clamping (for 30 seconds to 3 minutes after birth) as one of the few strategies for which there was evidence of potential to reduce transfusion volume and incidence in preterm infants, supporting a practice point. However, several studies, the largest of which is the Australian Placental Transfusion Study (APTS) have since been published and provide much stronger evidence that this is a simple, safe manoeuvre that reduces the proportion of preterm infants who need a blood transfusion by 10%. This striking finding deserves more investigation to understand the mechanism and to encourage the practice. Is it caused by transfusion of blood from the placenta to the baby after birth (which does increase the baby's haemoglobin level in the first week)? Alternatively, placental transfusion may reduce severity of illness in the first weeks after birth. This could lead to fewer blood tests, greater tolerance of anaemia, and better opportunities for babies to make their own red cells.</p> <p>This study aimed to obtain</p> <ol style="list-style-type: none"> 1. Timing of cord clamping, and APTS group allocation predicts the number of blood tests and calculated cumulative sample volume throughout hospital stay. 2. Average haemoglobin in the first week and each subsequent week predicts calculated cumulative sample volume throughout the hospital stay. 3. Cumulative sample volume (independent of APTS group allocation and time to cord clamping) predicts the likelihood of an infant receiving a red cell transfusion and the time to first transfusion (if given). 	No publications received yet

Patient Blood Management Project Grants	Fibrinogen replacement in severe traumatic haemorrhage (FEISTY II)	University of Queensland	\$491,345.80	Dr James Winearls	<p>1. To compare clinical endpoints in a non-inferiority trial of FC vs cryoprecipitate in critical bleeding trauma patients with low fibrinogen levels</p> <p>2. To expand the FEISTY Pilot Trial to other Australian Major Trauma Centres</p>	<p>Over 7000 Australians are treated for severe trauma annually. Haemorrhage secondary to major trauma is a leading cause of potentially preventable death and poor outcomes in Australian adults.</p> <p>Fibrinogen concentrate (FC) is an alternative product used to assist in blood clotting. It is a dry powder form of fibrinogen and can be reconstituted at the bedside and given quickly. The use of a fibrinogen factor concentrate with a long shelf life that is easy to use has enormous implications for both large urban metropolitan areas and remote isolated communities. The FEISTY Pilot trial enrolled 100 patients in four Queensland Major Trauma Centres. The study investigated the bedside assessment of clot strength and subsequently compared fibrinogen replacement with cryoprecipitate to fibrinogen concentrate. Specifically, the study investigated whether it was possible to give cryoprecipitate or fibrinogen concentrate early in the resuscitation of trauma victims, and which could be given faster. The trial showed it was much quicker to administer fibrinogen concentrate to replace low fibrinogen levels in these circumstances.</p> <p>FEISTY II will enrol 2000 patients across Australian and international trauma centres, building on the experience gained doing the FEISTY pilot trial. It will study major trauma patients who require blood products and have evidence of low fibrinogen levels on point of care or laboratory testing. The aim is to compare red blood cell transfusion rates and other clinical outcomes in patients who receive early fibrinogen replacement using cryoprecipitate or fibrinogen concentrate.</p> <p>This proposed study will address a number of key areas highlighted in the 'Patient Blood Management Guidelines Module 1: Critical Bleeding and Massive Transfusion' published by the National Blood Authority where there are evidence gaps and future research is required.</p>	<p>Fibrinogen Early In Severe Trauma study (FEISTY): study protocol for a randomised controlled trial</p> <p>Haemotherapy algorithm for the management of trauma-induced coagulopathy: an Australian perspective</p>
Patient Blood Management Project Grants	Novel fluid alternatives to blood transfusion to treat acute and chronic blood loss	University of Queensland	\$131,246.51	Prof John Fraser	<p>1. To use out sheep models of (a) chronic nonmonomeric anaemia and (b) acute hypovolemic shock, to determine whether novel perfusion fluids are suitable alternatives to RBC transfusion for delivering oxygen to vital tissues.</p> <p>2. To determine whether measures of microvascular blood flow and tissue oxygenation are superior patient – relevant outcome measures compared to haemoglobin levels.</p> <p>The primary objectives of this project are to provide pre-clinical evidence of efficacy of novel plasma expansion fluids</p>	<p>This project set out to determine if novel fluids that enhance blood flow in micro-vessels via haemoglobin-independent mechanisms, which are not reliant on blood cell-mediated viscosity, may achieve adequate tissue oxygenation and waste removal under conditions of moderate to extreme anaemia. This outcome has been demonstrated in small animal experiments, but translation to human studies requires proof of relevance in larger animal models. The sheep models of anaemia will provide evidence for the value of transfusion vs. other modalities in extreme anaemia, and if human trials of novel products are feasible. Furthermore, evidence gaps regarding ideal patient-relevant treatment thresholds and outcome measures point to potential practice changes away from measures of haemoglobin and central blood flow, towards tissue-specific blood flow and oxygen delivery.</p>	<p>An Ovine Model of Hemorrhagic Shock and Resuscitation, to Assess Recovery of Tissue Oxygen Delivery and Oxygen Debt, and Inform Patient Blood Management</p> <p>Recovery of organ-specific tissue oxygen delivery at restrictive transfusion thresholds after fluid treatment in ovine hemorrhagic shock</p>

					that enhance microvascular function and to demonstrate the feasibility of incorporating microvascular function and tissue oxygenation outcomes that are relevant to patient recovery into Patient Blood Management treatment decisions and outcomes measures	
Immunoglobulin Project Grants	Immunoglobulin use in chronic lymphocytic leukaemia and non-Hodgkin lymphoma – the ICAN study	Monash University	\$494,220.10	Dr Zoe McQuilten	<p>To conduct a national cohort study of Ig use and patient outcomes in CLL and NHL using the research infrastructure of two national clinical quality registries</p> <p>Immunoglobulin therapy (made from plasma) is commonly used to prevent infections by replacing protective antibodies. The use of immunoglobulin therapy for patients with CLL and NHL is one of the most common and fastest growing indications in Australia. Due to introduction of novel treatments for CLL and other non-Hodgkin lymphoma, which have a greater effect on suppressing antibody levels and for longer, it is likely that the demand for immunoglobulin therapy for this patient group will continue to grow.</p> <p>Although immunoglobulin is commonly used to prevent infection for patients with CLL and other NHL, there is limited evidence from clinical studies to guide clinicians on which patients are most likely to benefit, when treatment should be commenced or for how long. Furthermore, the role of other strategies to prevent infection, such as prophylactic antibiotics and immunisations, have not been well studied.</p> <p>Working with the Australian Lymphoma and Related Disease Registry and the newly established Chronic Lymphocytic Leukaemia Registry, this project will collect data on current use of immunoglobulin replacement and other infection prevention strategies as well as patient-centred outcomes in patients with CLL and NHL in Australia. Findings from the study will provide up-to-date local data on current practice for immunoglobulin replacement and outcomes. In a subgroup, the study will also collect serial peripheral blood samples to perform novel immune-profiling studies.</p> <p>This study will include:</p> <ol style="list-style-type: none"> 1. Up-to-date local data on current standard of care for infection prophylaxis and infection outcomes, in the era of novel therapies for CLL and NHL to inform clinicians and policymakers. 2. Identifying areas for improvement – where practice is not aligned with guidelines or evidence, and where observed variation is linked to differences in patient outcomes – including infection rates and quality of life. We will also be able to better understand the extent of variation in Ig use that does not impact on clinical outcomes. 3. Better targeting of infection prophylaxis strategies for CLL and NHL based on patient, disease and treatment factors in the era of novel therapies. 	No publications received yet

						4. Identification of novel immune markers to improve infection risk stratification of CLL patients.	
Patient Blood Management Seed Grants	Concealing treatment in pregnancy anaemia randomised trials: can it be used?	University of New South Wales	\$50,737.50	Dr Amanda Henry	<p>1. To determine the feasibility and effectiveness of blinding treatment allocation to IV iron or saline placebo infusion using an opaque sleeve covering the syringe and giving set.</p> <p>2. To assess the acceptability of blinding/use of placebo intravenous infusions to patients and clinicians, treatment side-effects and adherence, and HRQoL measures in women receiving IV versus oral iron in a blinded, randomised fashion. The scientific objective of the project is to provide proof-in-principle of ability to effectively blind patients and clinicians to IDA treatment (IV or oral) received, thereby offering a mechanism to reduce evaluation bias regarding treatment effectiveness in future large-scale clinical trials.</p>	<p>Iron-deficiency anaemia (IDA) affects approximately 1 in 7 Australian pregnant women. IDA has been associated with adverse maternal and infant health outcomes. Optimal treatment for improving maternal wellbeing and decreasing blood transfusion remains uncertain, with research largely focused on improvements in haematological indices.</p> <p>An issue with prior randomised trials of IV versus oral iron is lack of patient and clinician blinding to treatment received. This makes it difficult to address the relevant Obstetrics and Maternity Patient Blood Management evidence gaps of the relationship between different levels of anaemia and functional and performance levels, the degree of anaemia that is clinically relevant, and the clinically relevant degree of anaemia that equates to 'optimisation' of Haemoglobin (Hb). This is because unless women and clinicians are totally neutral regarding treatment modality, awareness of treatment received is likely to influence answers to scales that assess the relationship between different levels of anaemia and functional and performance levels, or how soon a clinician will declare the first-line treatment "failed" and give second-line intravenous therapy. Knowledge of prior treatment and clinician perception of this, may also influence seemingly objective clinical outcomes such as diagnosis and treatment of postpartum haemorrhage, and decision to give a red cell transfusion.</p> <p>This pilot study will conduct a randomised, blinded trial of intravenous FCM versus oral elemental iron for treating IDA in late pregnancy (enrolment 26+0-32+6 weeks gestation). Fifty women with IDA (defined as Hb Perinatal outcome data) will be recorded.</p> <p>The primary outcome will demonstrate the proportion of women that correctly identify treatment allocation. Secondary outcomes will include: 1) Proportion of clinicians that correctly identify treatment allocation. 2) Change in SF-36 scores over time 3) Treatment adverse effects 4) Treatment adherence 5) Proportion with persistent IDA in late pregnancy (Hb).</p>	No publication is listed yet
Patient Blood Management Seed Grants	Transfusion strategies for low platelets	Australian National University	\$73,799.00	Dr Philip Crispin	To generate data in support of further clinical trials into the effect of readily available frozen or lyophilised blood components to improve haemostasis in severely thrombocytopenic patients.	<p>Platelets are transfused in patients with low platelet counts either to control bleeding, or prophylactically in the setting of severely reduced platelets during chemotherapy. Although platelet transfusion is proven to reduce bleeding in leukaemia patients with very low counts, severe bleeding still occurs above the current platelet count trigger for transfusion, suggesting that other measures, such as platelet function and interaction with clotting proteins may also be important.</p>	<p>Cryoprecipitate as an alternative to platelet transfusion in thrombocytopenia</p> <p>Achieving haemostasis in thrombocytopenia in remote settings: an in vitro comparison of frozen and lyophilized products</p>

Platelets collected from blood donors for transfusion are logistically difficult. Platelets cannot be stored cold and this limits storage to only 5 days. After initial testing and transport, they are therefore only available in hospitals for about three days prior to expiry, and because demand fluctuates, expiration rates of platelet bags is high.

Ideally, alternatives with longer shelf lives would be available to replace platelet transfusion. One currently available product, cryoprecipitate, is a concentrate of clotting factors stored frozen for 12 months and readily available. It is mostly used to replace the clotting protein fibrinogen, and fibrinogen has been shown to correct the tendency to bleed using rotational thromboelastography (a laboratory based whole blood clotting assay) as well as platelet transfusions. Frozen platelets have also been used in some trials, and by the military, and appear to be very effective at stopping bleeding despite not increasing the platelet count.

This study will transfuse patients with very low platelet counts, with either platelets, cryoprecipitate (and then platelets), or frozen platelets. Blood samples taken before and after each transfusion will be evaluated for platelet count and platelet function by flow cytometry, rotational thromboelastometry (TEG) and behaviour in platelet flow chambers. TEG is now used to predict bleeding in trauma and cardiac surgery routinely. This whole blood assay, so the final results comprise changes to interactions between any blood components that may occur. There have been mixed reports previously on the ability to predict bleeding with very low platelet count by thromboelastometry. The platelet flow chamber is similar in that it can use whole blood, but the rate of flow can be varied to more physiological levels – an important consideration as platelets interact differently with clotting proteins depending on the amount of fluid shear stress.

OFFICIAL

OFFICIAL