BLOOD SYNERGY

RESEARCH REPORT

2022 - 2023

BLOOD SYNERGY TEAM

Chief Investigators

- Prof Erica Wood AO
- Prof Zoe McQuilten
- Prof Peter Cameron
- Prof Jamie Cooper AO
- Prof Michael Reade AM
- Dr Lisa Higgins
- Prof Judith Trotman
- Prof Simon Stanworth
- Ms Linley Bielby

Associate Investigators

- Dr Allison Mo
- Dr Andrew Flint
- Prof Anthony Harris
- Dr Brenton Sanderson
- Prof Craig French
- Prof Enrico Coiera
- A/Prof John Reynolds
- A/Prof Rosemary Sparrow

Partner Investigators

- Prof Biswadev Mitra
- Dr James Winearls
- Prof Jake Shortt
- A/Prof Tina Noutsos
- A/Prof Philip Crispin
- Dr Robert Weinkove

Program, Project Teams & Students

- Dr Elham Ashrafi
- Dr Karina Brady
- Ms Kirsten Caithness
- Ms Sara Carrillo de Albornoz
- Dr Khai Li Chai
- Dr Fiona (Pin-Yen) Chen
- Dr Nicole Eise
- Ms Jennifer Griffiths
- Ms Jessica Guglielmino
- Mrs Helen Haysom
- Dr Kim Huynh
- Dr Adam Irving
- Dr Thao Le
- Dr Aleece MacPhail
- Mr Karthik Mandapaka
- Dr Catriona Parker
- Mr Alex Poole
- Dr Briony Shaw
- Ms Tina van Tonder
- Mr Neil Waters
- Dr Cameron Wellard

Contacts

W: bloodsynergy.org
M: 553 St Kilda Rd Melbourne VIC 3004
E: sphpm.bloodsynergy@monash.edu
X: @BloodSynergy

CONTENT

WELCOME

Prof Erica Wood AO

Principal Investigator

It is a pleasure to share with you this research report from the NHMRC-funded Blood Synergy program.

We established the Blood Synergy in 2020 to address Australia's national transfusion research priorities and deliver ***safer and more appropriate transfusion support for patients, better stewardship of national blood supplies, and reduced costs to the community***. We are attempting to answer these fundamental questions: ***How is blood used in Australia, and how can its use be improved and made more cost-effective?***

Since our last report, and despite the challenges associated with COVID-19, we have made excellent progress across a broad range of projects, from practice surveys and pilot studies to new phase III clinical trials. The research program is structured in streams, from transfusion support for critical bleeding, critical care and blood disorders, to improving the use of immunoglobulins. We have been able to leverage the NHMRC Synergy funding to secure additional NHMRC, MRFF, Australian Research Data Commons and other funding for several major trials and registry-based projects, as well as additional NHMRC PhD scholarships, and we have expanded our collaborations and partnerships, including internationally. We have held two successful Blood Synergy meetings, open to all, to discuss and progress transfusion research. These have been well attended nationally and internationally, both online and in person, and highly productive.

The objective of the NHMRC Synergy grant scheme is "to support outstanding multidisciplinary teams of investigators to work together to answer major questions that cannot be answered by a single investigator". As you can see, we are a truly multidisciplinary team, and this report showcases the work of many people, including PhD students supported by the Blood Synergy, early and mid-career investigators and senior researchers across a range of disciplines, and an experienced research management team. We are guided by our independent Advisory Committee, expertly chaired by Professor Mike Murphy. I thank them all for their hard work and support.

I hope you enjoy reading this Blood Synergy Research Report. Please do get in touch to provide feedback and to discuss your own research ideas – we welcome your input and there are many opportunities for collaboration, now and in the future.

Prof Michael Murphy

Advisory Committee Chair

The use of blood transfusion is one of the most frequent procedures conducted in hospitals and similar clinical settings. It has significant benefits but also has risks and costs. Reports of avoidable adverse effects of transfusion and inappropriate use of blood, both overuse and underuse, indicate that further efforts are needed to improve transfusion practice. Poor practice may occur because of lack of evidence and uncertainty about the right thing to do because of poor compliance with evidence-based guidelines or due to inadequate resources to implement guidelines. There is much to do to ensure that blood components are collected and used safely and appropriately.

The Advisory Committee is supporting the Blood Synergy program in its aims to identify shortcomings in current practice and to provide new evidence in the form of clinical trials and other studies so that healthcare practitioners have greater certainty and confidence about what is optimal blood transfusion practice and how to deliver it. It is also encouraging the program to showcase its capacity-building capability through the development of young investigators.

As the program is entering its final year, the Advisory Committee has been making recommendations to ensure the program is completed on time and with sufficient high-quality output to justify its continuation either in its current form or as several individually funded projects. One of the important considerations for the future program is the identification of the key themes for further work. The Committee has also been promoting linkage with patient advocacy groups and with similar initiatives internationally to take advantage of the benefits of collaboration and to avoid duplication of effort.

The Committee remains very impressed by what the Blood Synergy Program has achieved so far, and it looks forward to supporting the current program through to its completion. The Committee will also champion the development of a successor program to provide much-needed high-quality evidence in the field of transfusion medicine and its translation into clinical practice.

Addressing Australia's national transfusion research priorities

ABOUT THE PROGRAM

The Blood Synergy is a National Health and Medical Research Council-funded program of research that includes clinical studies, trials, and patient registries concerned with blood transfusion practice and patient outcomes. We're focussing on making better use of blood products and improving outcomes for patients requiring blood in the settings of trauma, critical illness, and blood disease.

Used wisely, blood transfusions save lives. However, limitations still exist in ensuring their best use. A significant challenge is the lack of evidence to guide best practice. Patient blood management (PBM) is an approach that places patient outcomes at the core of blood transfusion. It is international best practice, supported by the World Health Organization, health policy-makers, and professional societies. Yet evidence in many area is inadequate to formulate solid PBM recommendations, including how blood is used, clinical outcomes, patient and clinician preferences, and costs. The result is a potentially inefficient, and ineffective, use of blood, with reduced patient benefit, and potential for harm.

Transfusion support is also not always available when and where it is needed, due to the labile nature of blood components and unexpected bleeding events. Treatment of major haemorrhage may require urgent delivery of large volumes of blood products. Access to these products in out-of-hospital or remote settings is particularly limited. The outcome can be a significant delay in the timely delivery of blood, with the potential for serious clinical consequences.

We are building Australia's transfusion research capacity, bringing together expertise and resources from across clinical and research fields

The Blood Synergy program is addressing these shortcomings by identifying current practice, testing new approaches, and closing evidence gaps, particularly in areas of high-volume use, high risk to patients, and high product costs. Our objective is to make the best use of this most precious national resource and improve patient outcomes.

A key goal is to improve knowledge around how blood is currently used across Australia. To establish the current standard of care, we're using observational studies and expanding our established massive transfusion registry into a national transfusion dataset collating and analysing information on all types of transfusions. Together these data will identify areas of greatest need and improvement.

We're exploring ways to increase access to blood components in prehospital and rural and remote settings by examining products with an extended shelf-life, and we're using interventional studies to evaluate how blood products can be most efficiently and effectively used in the treatment of critical bleeding and critically ill patients.

We're addressing evidence gaps in the management of bleeding and anaemia. We're studying how best to use immunoglobulins and other measures to prevent infections in blood cancer patients. These studies will help identify optimal use of blood products, and improve patient outcomes as well as reduce transfusion risks and costs.

RESEARCH STREAMS

Critical Bleeding

Major haemorrhage is a leading cause of early death. It is often unexpected, and may require large quantities of different blood products urgently – a daily challenge for blood services and health systems. We're expanding our Massive Transfusion Registry into the National Transfusion Dataset, and together with a network of specialists working across prehospital and hospital settings developing new evidence to inform recommendations and guide clinical decision-making on management of critical bleeding.

Critical Illness

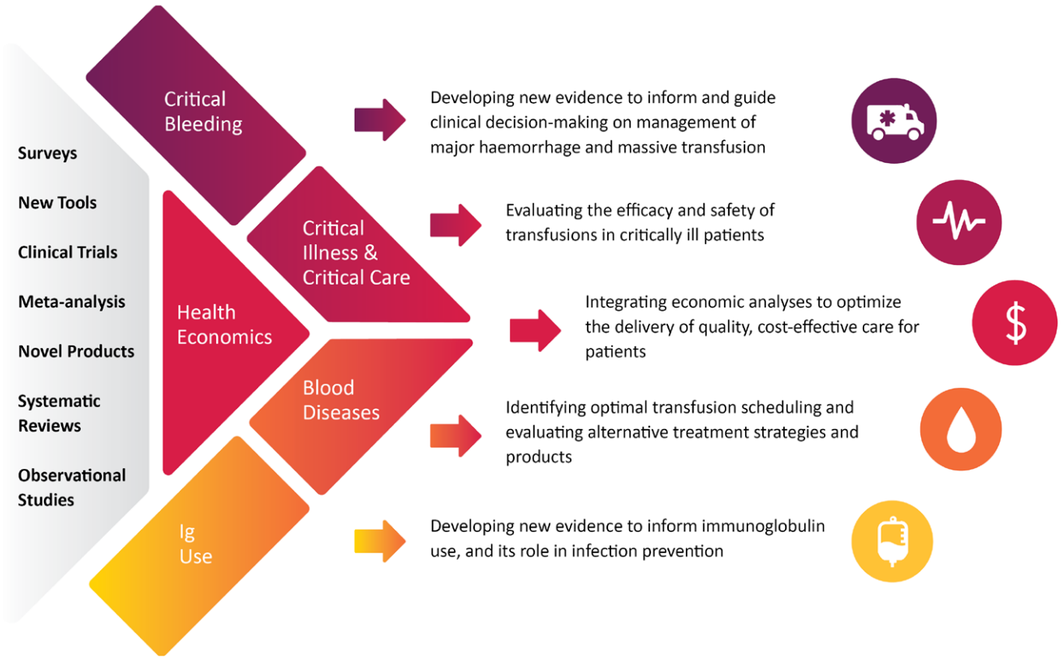
Critically ill patients in intensive care often receive blood transfusions, yet major evidence gaps still exist regarding the optimal use of blood components and other therapies in this context. We are conducting observational and interventional studies to evaluate the efficacy and safety of transfusions in critically ill patients, providing data that will inform policy and guide clinical decision-making in transfusion support for patients in the critical care setting.

Blood Diseases

Patients with blood cancers and other blood diseases are the major users of red cell and platelet products. However, much of the evidence base for transfusion practice in this area is weak and in some cases, outdated, as treatments of these disorders have advanced significantly in recent years. We are investigating optimal transfusion and alternative treatment strategies and products, to improve clinical management and outcomes, and reduce transfusion risks.

Immunoglobulin Use

Immunoglobulin (Ig) therapy, made from plasma, is used to treat patients with a wide range of conditions; for patients with blood cancers, it is generally used to prevent or treat infections. Ig use accounts for over half of Australia's national blood budget, but supply is limited and its use continues to grow. Our research investigates the efficient and effective use of Ig, including optimal duration of use, clinical outcomes for patients receiving Ig, and other interventions to manage infectious risks.



Health Economics

Our health economic analyses are conducted alongside each research stream, embedded within each of the research projects. This approach provides important new information to improve health system performance and deliver quality, cost-effective care for patients.

PROGRAM AT A GLANCE

The program of research encompasses:

Major Haemorrhage Management

- Developing a National Transfusion Dataset (NTD), through expansion of the Australian & New Zealand Massive Transfusion Registry (ANZ MTR)
- Integration of prehospital haemorrhage and transfusion datasets

Access And Use Of Blood Products For Critical Bleeding

- Modelling demand and availability of blood products
- Uptake and impact of point-of-care testing on coagulation management and blood use

New Approaches To Massive Transfusion Support

- FEISTY II: Fibrinogen concentrate for the treatment of critical bleeding
- Development of clinical decision-support systems for critical bleeding

Transfusion Support In Critically Ill Patients

- Observational studies of blood product use in intensive care
- Platelet transfusion thresholds in critically ill patients

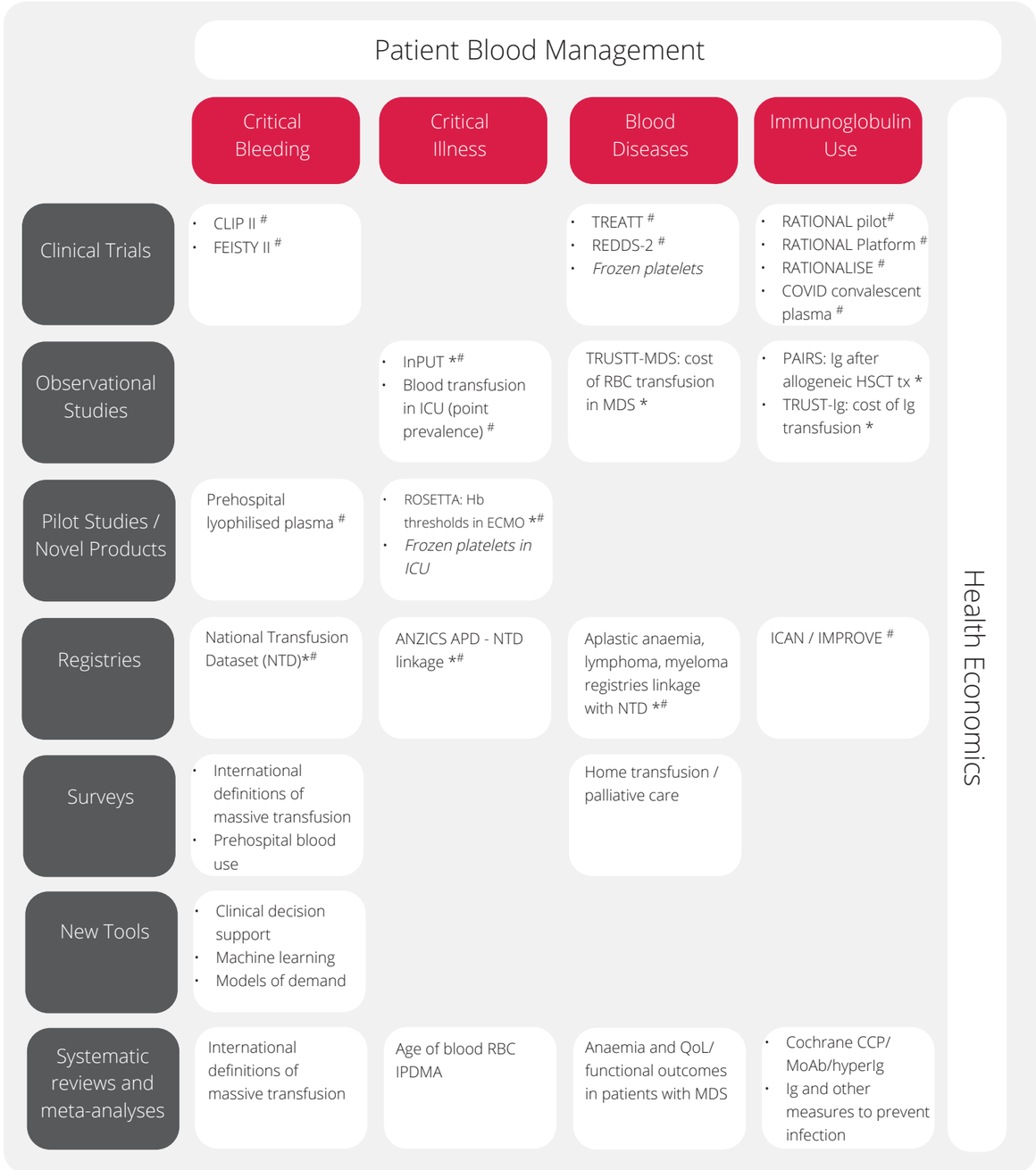
Management Of Anaemia And Bleeding In Haematologic Malignancies

- Alternatives to conventional platelet transfusion to prevent and manage bleeding
- Optimising red blood cell transfusion strategies in myelodysplasia

Immunoglobulin Use

- Observational studies of immunoglobulin use in patients with blood cancers
- Immunoglobulin therapy versus antibiotics for the prevention and treatment of infection
- Convalescent plasma for treatment of SARS-CoV-2 infection (COVID-19)

PROJECTS



* Blood Syngery co-funded; # Independent funds obtained; *Projects in preparation*

FEISTY II TRIAL

Fibrinogen Early In Severe Trauma

A phase III randomised clinical trial examining fibrinogen replacement (fibrinogen concentrate versus cryoprecipitate) in severely injured trauma patients with major haemorrhage and hypofibrinogenemia

In people affected by severe trauma and critical bleeding, the timely transfusion of blood products can be lifesaving. Early replacement of fibrinogen, an important blood clotting protein, may help to reduce bleeding in these situations. The FEISTY II trial compares the two available blood products commonly used for fibrinogen replacement during major haemorrhage, with the aim to inform clinicians and policy-makers about how best to deliver blood product support to improve outcomes for individual patients following major trauma.

FEISTY II is a phase III randomised trial which will enrol 850 patients from Australian and New Zealand major trauma centres, with a primary patient outcome of days alive out of hospital at day 90 after injury. Severely injured trauma patients who require blood transfusion and have evidence of low fibrinogen levels will be randomised to receive either fibrinogen concentrate or cryoprecipitate.

FEISTY II is coordinated by the Australian and New Zealand Intensive Care Research Centre (ANZIC-RC), and led by **Prof Zoe McQuilten, Dr James Winearls** and Dr James Moore. The study is endorsed by the Blood Synergy, as well as the Australian and New Zealand Intensive Care Society Clinical Trials Group (ANZICS-CTG), the Australian College of Emergency Medicine Clinical Trials Network (ACEM-CTN), the Australasian Trauma Society (ATS) and Australian and New Zealand Association for the Surgery of Trauma (ANZAST). The first trial site (Gold Coast University Hospital) opened to recruitment in November 2022, with up to 12 further sites open by the end of 2023, and a target of 25 sites in total by 2024. The FEISTY II trial is funded by grants from the MRFF and National Blood Authority.

ROSETTA PILOT

Red Cell Transfusion In ECMO

Extracorporeal membrane oxygenation (ECMO) provides critical cardiac and respiratory support to patients with life-threatening heart or lung disease, and is a procedure that is often accompanied by repeated red blood cell (RBC) transfusion. The current practice of RBC transfusion in intensive care generally follows what is regarded as a 'restrictive' approach, where transfusion is triggered by haemoglobin (Hb) levels of <70 g/L. Yet there is a lack of evidence to support this practice in ECMO patients despite their unique physiology, higher likelihood of anaemia, greater exposure to blood products, and higher mortality compared to the general critical care population. To address this, the ROSETTA trial is assessing which of the 'restrictive' or 'liberal' (Hb < 90 g/L) threshold policies translates into improved outcomes for ECMO patients. It is a phase II, registry-embedded, open-label, randomised pilot trial examining the feasbility and safety of comparing two different transfusion strategies in patients on ECMO. The ROSETTA pilot trial is led by **A/Prof Hergen Buscher** and **Prof Zoe McQuilten**, funded by the Australian and New Zealand Society for Blood Transfusion (ANZSBT) and Blood Synergy.

MASSIVE TRANSFUSION MANAGEMENT

Developing An International Consensus Definition

Massive transfusion (MT) is a term commonly used to refer to the transfusion of large volumes of blood products for patients with critical or major bleeding. The management of MT is an ongoing challenge for clinicians, hospitals and blood services, and accounts for around 10% of blood products used within hospitals. Yet, there is no universally accepted definition of MT, or even, what constitutes a 'major haemorrhage'. The result is the use of a variety of definitions between clinical settings, patient blood management guidelines, and research studies. The latter is particularly problematic in comparing clinical trials and patient outcomes between studies, and applying the findings to clinical practice. The benefit of standardising how MT is defined is the ability to capture its incidence across clinical settings and services, which will improve resource planning and monitoring of risk factors.

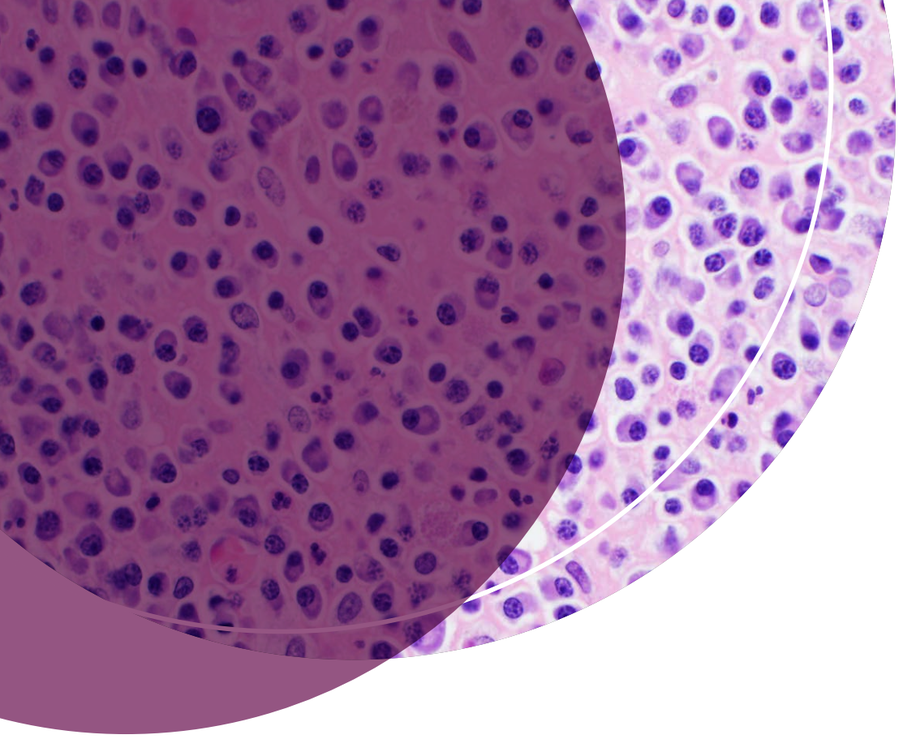
Prof Erica Wood, Prof Zoe McQuilten, and **Prof Simon Stanworth** in partnership with UK collaborator Dr Laura Green are working together to develop an international consensus definition. Supported by early-career investigators in Australia and the UK, the project commenced with a *Vox Sanguinis* International Forum on management of major haemorrhage (Green et al. 2022).

This was followed by a systematic review of international definitions of MT used in clinical trials (Lin et al. *Critical Care* 2023). The research was presented for discussion with the international community by Dr Victor Lin at the European Hematology Association 2023 Congress in Frankfurt, and by Dr Laura Green at the ISBT 2023 Congress in Gothenburg. Further work is underway with international partners.

Clinical Decision-Support Systems

Managing major haemorrhage is challenging and relies on the time-critical coordination of a multidisciplinary team to enact the massive transfusion protocol (MTP). Human factors can strongly influence the success of the process. One approach to address this issue is the development of computerised clinical decision-support systems (CDS), which assist by providing patient-specific recommendations and removing communication barriers between the team.

Dr Brenton Sanderson has led the design of an electronic CDS tool specific for MT. Informed by an initial survey of anaesthetists from across Australia and New Zealand (published in A*naestheisa & Intensive Care*, 2021), the prototype CDS tool was developed with a user-centred design approach. Testing in a simulated bleeding scenario by focus groups comprised of a laboratory haematologist, anaesthetist, trauma surgeon/emergency physician, blood bank scientist, and critical care nurse further refined the prototype (published in *Transfusion*, 2023). In the final evaluation phase (also published in *Transfusion)*, the developed CDS tool was shown to support more time-efficient decision-making compared to paper-based MT management.



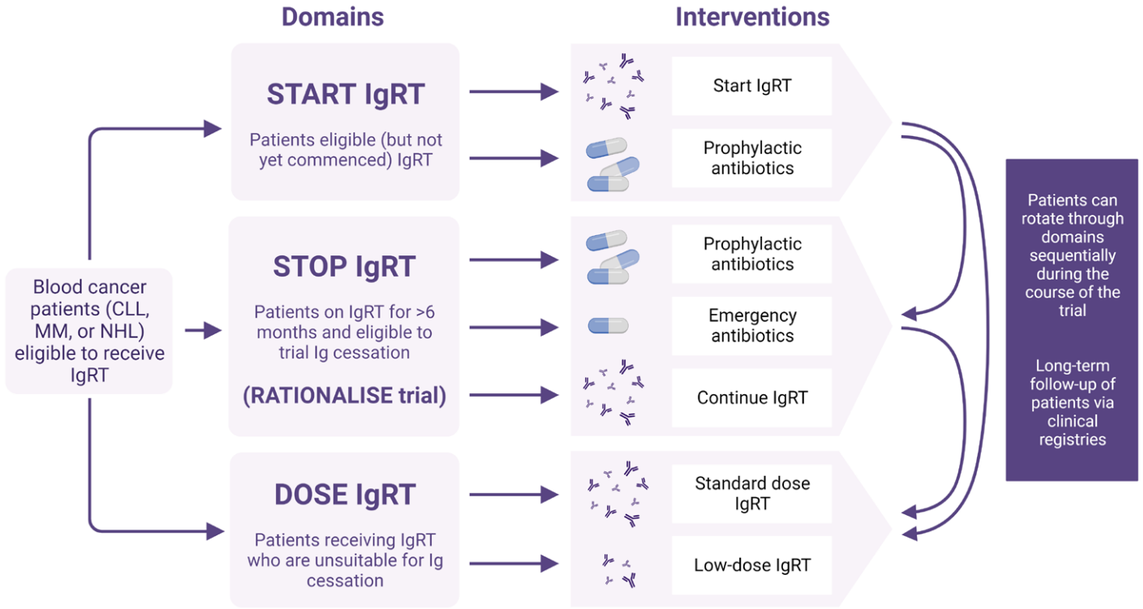
RATIONALISE AND THE RATIONAL PLATFORM

Infection Prevention In Patients With Blood Cancers

Serious infection is a common occurrence in people with blood cancers such as chronic lymphocytic leukaemia (CLL), multiple myeloma (MM) and non-Hodgkin lymphoma (NHL), and a major cause of mortality and morbidity. As a result, immunoglobulin (Ig), made from donated plasma, is routinely used for infection prevention in these patients. However, evidence to support this approach is limited, and clinical management of these conditions has changed greatly in recent decades since the original trials were conducted. The RATIONAL pilot trial also highlighted the need to optimise our use of this scarce resource and revisit our approach to reduce infections in individuals with blood cancer.

The **RATIONAL platform trial** focuses on strengthening the evidence in infection prevention, and builds upon our previous RATIONAL feasibility trial of prophylactic oral antibiotics as an alternative to Ig replacement therapy (IgRT). The RATIONAL platform is an adaptive platform trial with three domains. This approach provides an opportunity to examine the key questions in parallel: 1) Are prophylactic antibiotics a safe, efficient and cost-effective alternative to IgRT, 2) Is it safe to stop IgRT if patients are free of serious infection, and 3) Does a lower dose IgRT offer suitable protection against infection. Individuals with CLL, MM or NHL who are eligible for IgRT enter the trial through the domain that suits their current circumstances, and can then rotate into other domains as appropriate. Data are collected on mortality, infection, microbiome and immune function. Patient preferences, and quality of life measures are also being examined alongside a health economic analysis to evaluate the true cost-effectiveness of treatment.

The MRFF-funded RATIONAL platform trial is led by **Prof Zoe McQuilten** and **Prof Erica Wood**. The STOP IgRT domain, which is also known as the **RATIONALISE** trial, is funded by an NHMRC Clinical Trials and Cohort Studies grant and commenced patient recruitment at the first participating Australian sites in 2023.



USING BLOOD PRODUCTS WISELY

Health Economics Program

Alongside our trials and studies, a core component of the Blood Synergy is the analysis of the costs and cost-effectiveness of delivering transfusion support. The health economics program is led by **Dr Lisa Higgins**, with support from **Prof Anthony Harris**, **Dr Adam Irving** and colleagues at the Monash Centre for Health Economics. The program's focus is to identify the true costs of transfusion to health services - from delivery through to the ongoing healthcare costs after transfusion. There is also an emphasis on incorporating patient outcomes and preferences, along with identifying the cost-effectiveness of different transfusion strategies and interventions through the conduct of health economic evaluations alongside clinical trials. With this knowledge we can provide evidence-based guidance to optimise blood use and patient care.

Biostatistics

Statistical and methodological support for our trials and studies teams is critical to ensure that we are designing and conducting research that is robust, and can effectively (and efficiently) answer the questions being asked. Our biostatistical leads **A/Prof John Reynolds** and **Dr Thao Le** work closely with each investigator team in the project planning and development phases, through to implementation, analysis and publication.

Embedding the expertise of health economics and biostatistics in each project ensures that research outcomes are relevant and have greatest impact

NATIONAL TRANSFUSION DATASET

Linking Australian Transfusion Data

Blood transfusions are administered in ambulances, hospitals, community facilities and increasingly, within people's homes. Now, for the first time, data on how, where and when the various blood products are used is being aggregated nationally and linked to patient outcomes. The **National Transfusion Dataset** (NTD), led by **Prof Erica Wood**, builds upon the well-established Australian and New Zealand Massive Transfusion Registry (ANZ MTR), to collate data on all blood products across all clinical settings. In an important step forward, the data are now also being linked with existing clinical registries for a range of situations, including intensive care, and blood disorders and cancers. Initially developed with co-investment from the Australian Research Data Commons (ARDC) Data Partnerships Program, from 2023 the NTD is also supported by an MRFF Research Data Infrastructure Initiative grant.

In its initial pilot phase the NTD made the first linkages between transfusion data and national clinical registry data. Participants in the pilot included Ambulance Victoria, the South Australian Ambulance Service, and pilot hospitals Alfred Health and Flinders Medical Centre, as well as registries for Aplastic Anaemia and other bone marrow failure syndromes (AAR), Myeloma and Related Diseases (MRDR), and the Australian and New Zealand Intensive Care Society's Adult Patient Database (ANZICS APD).

With support from the MRFF the NTD has expanded to incorporate data from more prehospital services and hospitals across the country, and link with additional clinical datasets, which will include data from Australian Red Cross Lifeblood. The team has also commenced a project using machine learning to analyse hospital electronic medical records, and joined as a key partner in Australia's first registry-based clinical trial which will investigate blood transfusion in critically ill patients on extra-corporeal membrane oxygenation (ECMO).

The end-goal of the NTD is to provide data reports to hospitals and policymakers to improve practice, and to facilitate research into national priority areas, including health economic analyses relevant to the Australian setting and areas of high use of blood products, such as the support of critically ill patients and those with major haemorrhage or bone marrow failure.

PREHOSPITAL PLASMA TRIAL

Patients treated in hospital for severe bleeding after trauma have improved survival when plasma is transfused alongside red blood cells. The use of plasma in prehospital settings may offer similar benefit, particularly where lengthy transport times to hospital are involved.

Plasma in Australia is currently only available as a frozen product - to be thawed and warmed prior to infusion. Freeze-dried plasma provides an attractive alternative for prehospital use due to ease of storage and reconstitution, and longer shelf-life.

Aeromedical emergency services in rural and remote areas of Australia can face longer transport times than their overseas counterparts. As a result, international trials assessing time-critical prehospital treatments may not always translate to our setting. One likely example is the early use of plasma transfusion for critical bleeding, which has been found beneficial only when patients are faced with longer prehospital transport times.

Prof Biswadev Mitra recently led the first pilot trial of freeze-dried plasma in an Australian prehospital setting. Supported by the Blood Synergy and a National Blood Authority seed grant and published in *Academic Emergency Medicine*, the trial demonstrated the feasibility of transfusing freeze-dried plasma with red blood cells by aeromedical services, and set the scene for a definitive trial in patients who have critical bleeding after trauma.

TRANSFUSION PRACTICE IN CRITICAL CARE

To identify how blood products are currently used in the care of critically ill patients, **Prof Zoe McQuilten** and **Dr Andrew Flint** have led two observational studies of transfusion practice in critical care in Australia and New Zealand. Commencing with a one-day point prevalence study (conducted with The George Institute for Global Health and ANZICS Clinical Trials Group) the team collated data on all transfusions in 51 intensive care units within a single 24-hour period. Study outcomes accepted for publication in *Critical Care and Resuscitation*, revealed that 10% of patients treated in intensive care received a blood transfusion. While the majority of red blood cell (RBC) transfusions were administered according to the national patient blood management guidelines, non-RBC transfusions often were not.

A second, larger point prevalence study was then undertaken in collaboration with international partners at the University of Amsterdam, Netherlands. The Australian and New Zealand arm of the **InPUT** study captured information on blood product use over a one-week period in 40 intensive care units, from over 900 participating patients, and contributed a quarter of the data collated by the international study. International data on RBC transfusions was published in *JAMA* (2023). Together with the Australian and New Zealand outcomes (to be published 2024), these studies provide a comprehensive up-to-date snapshot of transfusion practice in critical care locally and globally.

Observational point prevalence studies provide a crucial insight to current transfusion practices in intensive care, and the first since introduction of the national patient blood management guidelines in 2013

BUILDING CAPACITY

Home Transfusion

Many aspects of haematology supportive care, including antibiotics and chemotherapy, are now routinely delivered outside the hospital setting. A potentially unmet clinical need is the transfusion of red blood cells and platelets at home. However, there are concerns about cost-effectiveness and safety. Haematologist **Dr Briony Shaw** is conducting a pilot feasibility study of home-based blood transfusion in patients with haematological malignancy as part of her PhD studies. Incorporating health economic analyses and patient-reported clinical outcomes, the study will provide a framework which can be used by other health services around Australia.

Cost Of Transfusion Support

TRUST-MDS (True cost of transfusion support in MDS) is an observational study examining the cost of red cell transfusion in patients with myelodysplastic syndromes (MDS), a type of blood cancer. Currently, there are few data on the total cost of transfusion in MDS, despite the high transfusion burden. Led by **Dr Allison Mo** as part of her PhD studies, the project calculates both the direct costs (salaries, products, and consumables) and indirect costs (management, administration, and overheads) at hospital sites in Australia and the UK. The data are expected to guide future policy development and ultimately, improve health outcomes for patients with MDS.

Costs Of Immunoglobulin Therapy

Australian patients are among the highest per capita users of immunoglobulin (Ig) products, costing the community >$800 million per year (2021-22) - over half the total national blood product budget. Yet, the product costs of Ig do not encompass the full cost of treatment. **Ms Sara Carrillo de Albornoz** is an experienced health economist. Her PhD research, supported by a Blood Synergy scholarship, is examining the treatment pathway of patients with blood cancers receiving Ig to identify the true economic costs, the benefit of Ig on infection prevention, and opportunities to improve the use of Ig therapy and clinical outcomes.

Immunglobulin Use In alloSCT

One of the treatment options for some people with blood and bone marrow diseases is allogeneic haematopoietic stem cell transplantation (alloSCT). After alloSCT, patients often have low levels of antibodies which can increase the risk of serious infection. Immunoglobulin replacement (IgRT) may be given to increase a patient's antibody levels. However, previous studies have not consistently shown that patients benefit from this treatment. It is not clear how IgRT can best be used to help prevent infection, which patients should be given IgRT, or what the best dose is to use. For this reason, there is much variation in practice.

The Post-Allograft Immunoglobulin Study (**PAIRS**) is being led by infectious diseases specialist and PhD candidate **Dr Aleece MacPhail** and examines these questions through the collection of observational data on patients who received alloSCT in Australia and New Zealand. The study will gather information on patient antibody levels, whether they received IgRT, whether their antibody levels increased after IgRT, and whether they experienced any serious infections or died. The results will identify current practice, and help to improve our understanding of how to administer immunoglobulin replacement therapy to patients following alloSCT.

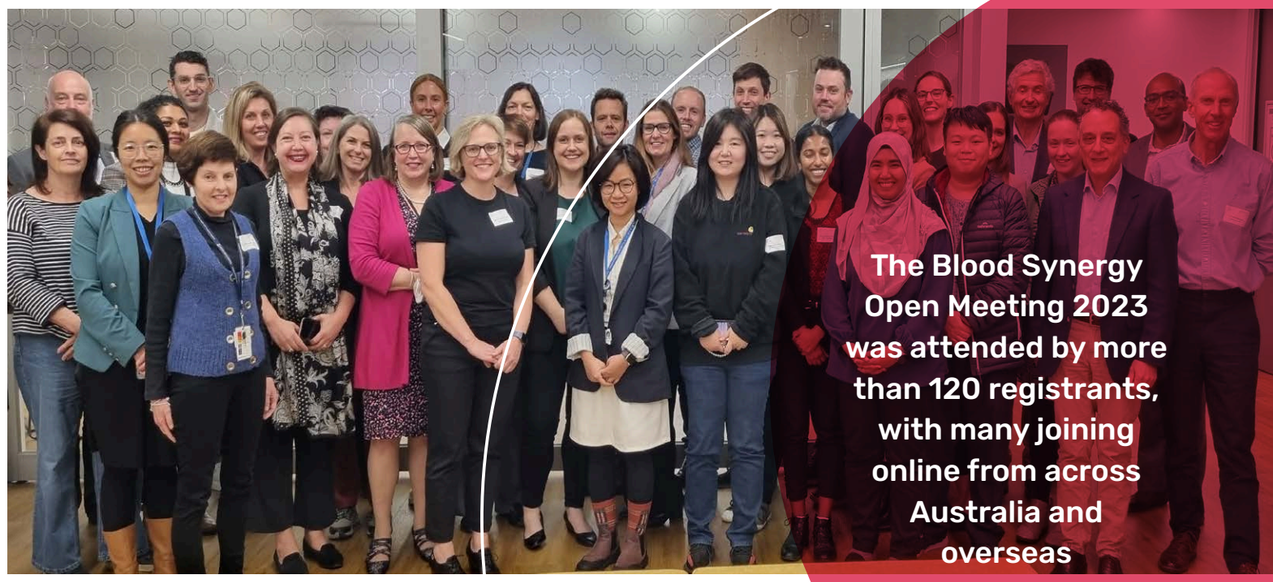
OPEN MEETINGS 2022 & 2023

The Blood Synergy team was delighted to welcome our research partners, Advisory Committee and members of the public to join us for the Blood Synergy Open Meetings 2022 and 2023. The meetings provided a forum to present the latest research, hear about new projects commencing, and discuss evidence gaps and future research needs. The hybrid format also enabled colleagues from far and wide to join the conversation.

The 2022 meeting commenced with an overview of evidence gaps and research priorities, with presentations delivered by members of the National Blood Authority, Australian Red Cross Lifeblood, and the Victorian Blood Matters program. Prof Craig French provided an update on the latest patient blood management guidelines, whilst Prof Michael Reade gave a summary of evidence gaps in critical bleeding and critical care. Dr Lisa Higgins highlighted the need for an economic analysis of immunoglobulin use, and Dr Brenton Sanderson introduced us to machine learning possibilities in haematology. We were also treated to study updates on the National Transfusion Dataset, observational studies in intensive care blood practice, as well as the FEISTY II, REDDS-2 and RATIONALISE trials. The day was rounded out by a presentation from our UK-based investigator Prof Simon Stanworth on international collaborations in transfusion medicine.

Our 2023 meeting was opened by a keynote presentation from Prof Michael Murphy, the Blood Synergy Advisory Committee Chair. Prof Murphy spoke on progress in transfusion practice and research in England and collaborations with similar international initiatives. We heard updates on the ROSETTA pilot trial, RATIONAL platform trial, and the pilot trial on prehospital use of lyophilised plasma. The cost of transfusion session provided an opportunity to hear from colleagues at the Monash Centre for Health Economics, while the final session covered opportunities to integrate and apply clinical datasets. Topics ranged from measuring patient preferences in infection-prevention strategies, to artificial intelligence tools, and haemovigilance. The meeting concluded with a presentation from Prof Susannah Ahern on the 'big picture' in clinical registries.

We extend our most sincere thanks to the presenters and keynote speakers, panel members and those chairing the meeting sessions, as well as the audience participants.



HIGHLIGHTS 2022 & 2023

The Blood Synergy team's ongoing commitment to excellence in clinical research was recognised by a number of grants to expand and support the current program of work. This included funding to extend upon the development of a National Transfusion Dataset and grants to enable critical work in the optimisation of immunoglobulin use. Recognition of research expertise and excellence was also received through a number of awards, as well as invitations to present the work of the Blood Synergy team at key national and international meetings and conferences. Likewise, study outcomes were published in the leading peer-reviewed journals to ensure that our research is disseminated widely and makes a meaningful and lasting contribution to the clinical research landscape.

Awarded grants reflect the success of investment in infrastructure and partnerships funded by the NHMRC Synergy grant

Grants

2022 MRFF Research Data Infrastructure initiative grant:
National Transfusion Research Data Infrastructure Initiative (*Investigators: Erica Wood, Zoe McQuilten, Carol Hodgson, Lisa Higgins, Shelley Cox, James Daly, David Roxby, Adam Irving, Susan Morgan, Simon Benson, Christopher Berry, Linley Bielby, Karina Brady, Fiona Chen, Kim Huynh, Neil Waters, Cameron Wellard, Shannah Anderson*)

2022 MRFF Optimising the Clinical Use of Immunoglobulins:
Generating evidence to improve use of immunoglobulin replacement to reduce infections in blood cancers: the RATIONAL Platform Trial (*Investigators: Zoe McQuilten, Dennis Petrie, Eliza Hawkes, John Reynolds, Philip Crispin, Laura Fanning, Robert Weinkove, Andrew Spencer, Orla Morrissey, David Paterson, Erica Wood, Jason Roberts, Simon Stanworth, Stephen Mulligan, Stephen Opat*)

eVidence synthesis to inform the optimAL UsE of Immunoglobulin (The VALUE-Ig Study) (*Investigators: Dennis Petrie, Zoe McQuilten, Anthony Harris, Erica Wood, Adam Irving, Anneke van der Walt, Stephen Reddel, Laura Fanning, Andrew Spencer, Eliza Hawkes, Philip Crispin*)

2023 NHMRC Centres of Research Excellence:
OPTIMAL: OPTimising Immunoglobulin Management in Australia (*Investigators: Erica Wood, Zoe McQuilten, Dennis Petrie, Linley Bielby, Laura Fanning, David Burgner, Jason Roberts, Anneke van der Walt, Leah Heiss, James Daly*)

2022 ANZSBT Research Fund:
Red BlOod Cell TranSfusion in ECMO – a feasibiliTy TriAl (the ROSETTA trial) (*Investigators: Hergen Buscher, Zoe McQuilten, Tim Southwood, Aiden Burrell, Carol Hodgson, Alistair Nichol, Mark Dennis, Lisa Higgins)*

2022 NHMRC Investigator Grants:
Prof Jamie Cooper

2022 NHMRC Postgraduate Scholarships:
Dr Aleece MacPhail
Dr Briony Shaw

2023 HSANZ Leukemia Foundation New Investigator PhD Scholarship:
Dr Briony Shaw

Awards

- Prof Erica Wood received recognition of her distinguished service to transfusion medicine, haemovigilance, haematology, and national and international organisations with an award of Officer of the Order of Australia (AO) in the King's Birthday Honours list 2023
- Prof Jamie Cooper and the team of the Australian and New Zealand Massive Transfusion Registry were featured in the NHMRC '10 of the Best' (13th edition) for their work on "Improving outcomes for patients with critical bleeding requiring massive transfusion"
- Dr Allison Mo once again received the award for the best presentation on patient blood management at the Blood2022 conference
- Prof Erica Wood was awarded the International Haemovigilance Medal at the IHN-SHOT Symposium 2022 in recognition of her extraordinary contribution to the work of the International Haemovigilance Network
- Prof Erica Wood was inducted as a 2023 Fellow of the Australian Academy of Health and Medical Sciences
- Prof Judith Trotman was appointed Chair of the Scientific Advisory Committee of the Australasian Leukemia and Lymphoma Group (ALLG)

Presentations

Invited plenary and conference presentations by the investigator group in 2022 and 2023 include:

- Prof Erica Wood talked about outcomes from the Massive Transfusion Registry and National Transfusion Dataset at the Australian & New Zealand Trauma Society conference, Trauma 2022
- Prof Michael Reade shared an update on CLIP II at the ANZCA Clinical Trials Network meeting 2022
- Presentations at Blood2022 included
  - Outcomes of the point prevalence study of transfusion practices in ICU (Dr Andrew Flint)
  - Interventions to reduce infections in patients with haematological malignancies (Dr Khai Li Chai)
  - Immunoglobulin use and Outcomes in CLL and NHL (ICAN) study (Dr Khai Li Chai)
  - Platelet transfusions in myelodysplastic syndromes (Dr Allison Mo)
  - An overview of transfusion clinical research in Australia and New Zealand (Prof Erica Wood)
  - The FEISTY II trial (Dr James Winearls)
- Dr Andrew Flint delivered an update on the InPUT study outcomes at the ANZICS Clinical Trials Group meeting Noosa 2023
- Prof Erica Wood presented the National Transfusion Dataset at the ISBT Congress Gothenburg 2023 in a session on precision transfusion medicine and big data
- Prof Zoe McQuilten provided an introduction to the RATIONAL platform trial and RATIONALISE trial at the May 2023 Scientific Meeting of the Australasian Leukaemia & Lymphoma Group (ALLG)
- Dr Allison Mo spoke at ISBT Congress Gothenburg 2023 on personalising the transfusion pathway for MDS patients via the REDDS-2 trial, as well as a systematic review of quality of life in MDS
- Mrs Helen Haysom presented the ANZ-MTR findings on the use of RhD negative RBCs for critically bleeding patients at the ISBT Congress Gothenburg 2023
- Ms Sara Carrillo de Albornoz delivered a presentation on her economic analysis of immunoglobulin at the Health Technology Assessment International (HTAi) Annual Meeting 2023
- Dr Aleece MacPhail gave a presentation on the PAIRS observational cohort protocol at the Australia New Zealand Transplant and Cellular Therapies Annual Scientific Meeting 2023
- Dr Andrew Flint reported on studies of blood transfusion practices in ICU and their implications for ADF ICUs at the Australasian Military Medicine Association conference in Perth 2023

Publications

- Irving, et al. Economic Evaluation of National Patient Blood Management Clinical Guidelines in Cardiac Surgery. *Value in Health* 2022 (doi: 10.1016/j.jval.2021.07.014)
- Mitra, Wood, & Reade. Whole blood for trauma resuscitation? *Injury* 2022 (doi: 10.1016/j.injury.2022.04.001)
- Shaw, Wood, Callum, & McQuilten. Home Delivery: Transfusion Services When and Where They Are Needed. *Transfusion Medicine Reviews* 2022 (doi: 10.1016/j.tmrv.2022.06.003)
- Al-Riyani, et al. Early and out-of-hospital use of COVID-19 convalescent plasma: An international assessment of utilization and feasibility. *Vox Sanguinis* 2022 (doi: 10.1111/vox.13347)
- Green, et al. International Forum on the Management of Major Haemorrhage. *Vox Sanguinis* 2022 (responses doi: 10.1111/vox.13243, summary doi: 10.1111/vox.13244)
- Denholm, et al. ASCOT ADAPT study of COVID-19 therapeutics in hospitalised patients: an international multicentre adaptive platform trial. *Trials* 2022 (doi: 10.1186/s13063-022-06929-y)
- Badami, et al. Red blood cell alloantibodies in the context of critical bleeding and massive transfusion. *Blood Transfusion* 2022 (doi: 10.2450/2022.0131-22)
- Mo, & Higgins. Restrictive transfusion thresholds: Have we left patient-centered outcomes behind? *Transfusion* 2022 (doi: 10.1111/trf.17105)
- Reade, et al. Cryopreserved platelets compared with liquid-stored platelets for the treatment of surgical bleeding: protocol for two multicentre randomised controlled blinded non-inferiority trials (the CLIP-II and CLIPNZ-II trials). *BMJ Open* 2022 (doi: 10.1136/bmjopen-2022-068933)
- Kimber, et al. Hyperimmune immunoglobulin for people with COVID-19. *Cochrane Database Systematic Reviews* 2023 (doi: 10.1002/14651858.CD015167.pub2)
- Iannizzi, et al. Convalescent plasma for people with COVID-19: a living systematic review. *Cochrane Database Systematic Reviews* 2023 (doi: 10.1002/14651858.CD013600.pub5)
- REMAP-CAP Investigators. Long-term (180-Day) Outcomes in Critically Ill Patients With COVID-19 in the REMAP-CAP Randomized Clinical Trial. *JAMA* 2023 (doi: 10.1001/jama.2022.23257)
- Chai, et al. Interventions to reduce infections in patients with hematological malignancies: a systematic review and meta-analysis. *Blood Advances* 2023 (doi: 10.1182/bloodadvances.2022008073)
- Zeibi Shirejini, et al. Current and future strategies to monitor and manage coagulation in ECMO patients. *Thrombosis Journal* 2023 (doi: 10.1186/s12959-023-00452-z)
- Sanderson, et al. Multicenter, multidisciplinary user-centered design of a clinical decision-support and simulation system for massive transfusion. *Transfusion* 2023 (doi: 10.1111/trf.17315)
- Wood, Whitaker, & Townsend. Haemovigilance: Giving it our best SHOT! *Vox Sanguinis* 2023 (doi: 10.1111/vox.13411)
- Mitra, et al. Pre-hospital freeze-dried plasma for critical bleeding after trauma: A pilot randomized controlled trial. *Academic Emergency Medicine* 2023 (doi: 10.1111/acem.14745)
- Lin, et al. Definitions of massive transfusion in adults with critical bleeding - a systematic review. *Critical Care* 2023 (doi: 10.1186/s13054-023-04537-z)
- Mo, et al. Platelet transfusions and predictors of bleeding in patients with myelodysplastic syndromes. *European Journal of Haematology* 2023 (doi: 10.1111/ejh.14049)
- Mo, et al. Do anemia treatments improve quality of life and physical function in patients with myelodysplastic syndromes (MDS)? A systematic review. *Blood Reviews* 2023 (doi: 10.1016/j.blre.2023.101114)
- Raasveld, et al. Red Blood Cell Transfusion in the Intensive Care Unit. *JAMA* 2023 (doi: 10.1001/jama.2023.20737)
- Flint, et al. Transfusion practices in intensive care units: an Australian and New Zealand point prevalence study. *Critical Care & Resuscitation* 2023 (Dec)
- Sanderson, et al. Clinical decision support versus a paper-based protocol for massive transfusion: impact on decision outcomes in a simulation study. *Transfusion* (in press)

GOVERNANCE

Steering Committee Members

- Prof Erica Wood (Chair)
- Ms Linley Bielby
- Dr Karina Brady
- Ms Kirsten Caithness
- Prof Peter Cameron
- Dr Khai Li Chai
- Prof Enrico Coiera
- Prof Jamie Cooper
- Prof Craig French
- Dr Andrew Flint
- Prof Anthony Harris
- Dr Lisa Higgins
- Dr Adam Irving
- Dr Thao Le
- Prof Zoe McQuilten
- Prof Biswadev Mitra
- Dr Allison Mo
- Prof Michael Reade
- A/Prof John Reynolds
- Dr Brenton Sanderson
- A/Prof Rosemary Sparrow
- Prof Simon Stanworth
- Prof Judith Trotman
- Ms Tina van Tonder
- Mr Neil Waters
- Dr Cameron Wellard
- Dr James Winearls

Working Group Members

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- Dr Brendon Beaton
- Dr Karina Brady
- Ms Kirsten Caithness
- Dr Edward Chew
- Dr Andrew Flint
- Dr Lisa Higgins
- Dr Chris Hogan
- Dr Adam Irving
- Dr Giles Kelsey
- Prof Zoe McQuilten
- Prof Biswadev Mitra
- A/Prof Tina Noutsos
- Dr David Read
- Dr Brenton Sanderson
- A/Prof Rosemary Sparrow
- Ms Tina van Tonder
- Mr Neil Waters
- Dr James Winearls
- Prof Erica Wood

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- Ms Kirsten Caithness
- Prof Jamie Cooper
- Prof Craig French
- Dr Lisa Higgins
- Dr Adam Irving
- Prof Zoe McQuilten
- A/Prof Tina Noutsos
- Mr Alex Poole
- Prof Michael Reade
- Mr Neil Waters
- Dr James Winearls
- Prof Erica Wood

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- Dr Allison Mo (Chair)
- Dr Brendon Beaton
- Ms Linley Bielby
- Dr Karina Brady
- Ms Kirsten Caithness
- Ms Sara Carrillo de Albornoz
- Dr Philip Crispin
- Dr Lisa Higgins
- Dr Adam Irving
- Dr Thao Le
- Dr Aleece MacPhail
- Prof Zoe McQuilten
- A/Prof Tina Noutsos
- Dr Briony Shaw
- Prof Judith Trotman
- Mr Neil Waters
- Dr Robert Weinkove
- Prof Erica Wood

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- Ms Kirsten Caithness (2023 -)
- Dr Kim Huynh (2020 - 2022)
- Prof Zoe McQuilten
- Ms Tina van Tonder (2022 -)
- Mr Neil Waters
- Prof Erica Wood

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Independent Chair

- Prof Michael Murphy (2022 -)
- Mrs Jennifer Roberts (2021 - 2022)

Consumer Respresentatives

- Ms Kate Wilson
- Ms Vera Thomas (2021)

Independent experts in blood transfusion and clinical sciences

- A/Prof James Daly (Australian Red Cross Lifeblood)
- Prof Sant-Rayn Pasricha (WEHI)
- Prof Mark Polizzotto (Australian National University)

ANZSBT Representative

- Prof Wendy Erber (University of Western Australia)

National Blood Authority Representative

- Ms Sarah Jones (2022 - 2023)
- Ms Claire Bramwell (2021 - 2022)

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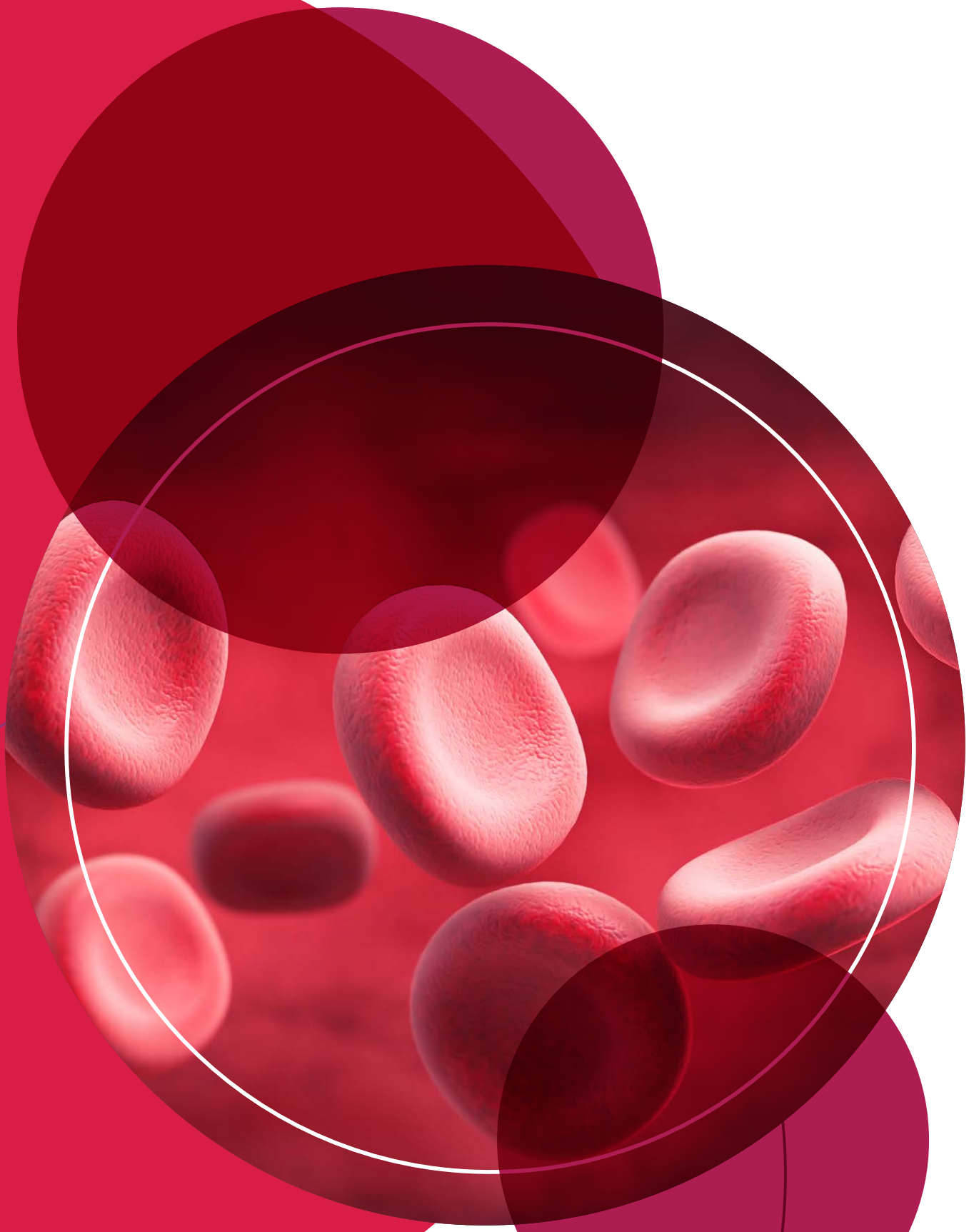
We acknowledge the traditional owners of the lands on which our research is conducted. We pay our respects to their Elders, past and present, and extend that respect to all Aboriginal and Torres Strait Islander peoples.



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