ANZICS Clinical Trials Group
Activity Report
2016 - 2017

Promoting excellence in intensive care medicine through collaborative clinical research
SINCE 1994 CTG ENDORSED AND SUPPORTED STUDIES HAVE RANDOMISED OVER 47,000 PATIENTS INTO CLINICAL TRIALS INCLUDED MORE THAN 28,000 PATIENTS IN OBSERVATIONAL STUDIES RECEIVED OVER $110 MILLION IN TOTAL RESEARCH FUNDING PUBLISHED 166 PEER REVIEWED PUBLICATIONS, INCLUDING 12 PAPERS IN THE NEW ENGLAND JOURNAL OF MEDICINE WITH A $h$-INDEX of 45 IN 2016-2017 THERE WERE 76 ADULT AND PAEDIATRIC MEMBER INTENSIVE CARE UNITS ACROSS AUSTRALIA AND NEW ZEALAND WITH OVER 700 CLINICIANS & RESEARCHERS CURRENTLY SUBSCRIBED TO THE CTG MAILING LIST PARTICIPATING IN 39 ACTIVE STUDIES
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During my Presidency at ANZICS I have strongly advocated for Change across many facets of the Society.

The ANZICS Clinical Trials Group is a robust and reliable ANZICS entity that through its passionate engagement of contributors remains dynamic and cognisant for its need to embrace change and shape its Future, with indeed holds many challenges.

The continued success of the ANZICS CTG, to me, is primarily attributable to the CTG Community: the CTG Member Units, the Methods Centres (ANZiC RC, The George Institute, MRINZ), and the dedicated staff that work within these organisations. Ongoing support from ANZICS, via the CTG Committee and the CTG Office, is also crucial.

As this Report reflects, there is continued faith in the CTG by Funding and Grant bodies to support CTG governed or supported research, and deliver results that ultimately improve patient care. The continuing development, initiation, continuation and ultimately completion of multi-centre studies is evidence that this Group “has its act together”. Congratulations.

I invite you to read this report and reflect on your contribution to advancing research in the critical care arena. I congratulate and thank you for your contribution, and also I would like to challenge you to grow and change your contribution to engage with those critical care researchers that are less fortunate than us here in ANZ, and share your expertise and guide them on the path of establishing ‘Excellence in Critical Care Research’.

Dr Marc Ziegenfuss
President, ANZICS
The ANZICS Clinical Trials Group (CTG) is a network of intensive care units (ICUs), clinicians and researchers who collaborate to conduct multicentre research aimed at improving outcomes for people who require intensive care.

All of the research conducted by the CTG is investigator-initiated and funded through competitive public grants or unrestricted funding from other government or corporate sources. However, the true cost of conducting high-quality research is often not met by the funding awarded to individual studies and thus the work of the CTG is dependent on many thousands of hours of unpaid time contributed by research staff and individual clinicians in participating ICUs.

The dedication, shared expertise, cohesion and spirit of collegiality that are embodied by the CTG have been recognised globally as key features in our success.

The CTG provides world-leading evidence to intensive care clinicians to improve treatments in critical illness.

The group has published landmark studies investigating fluid resuscitation, medical emergency teams, nutrition, glycaemic control, renal replacement therapy, pandemic influenza, decompressive craniectomy and venous thromboembolism prophylaxis in critical care.

Currently underway are a number of important studies investigating treatments for sepsis, traumatic brain injury, acute respiratory illnesses, acute kidney injury, and those requiring fluids, nutrition, sedation, fever management or blood transfusions in the ICU.

The CTG continues to build strong cross-specialty partnerships to facilitate research which spans the care continuum before, during and after patients are treated in an intensive care unit, and increasingly studies have expanded to include international sites.

**MISSION**

To promote excellence in Intensive Care medicine through collaborative clinical research focused on improving patient centred outcomes.

**VISION**

To facilitate and promote investigator-initiated, collaborative clinical research in critical illness throughout Australia and New Zealand.

To foster and promote multi-disciplinary and international research collaboration.

To develop high-quality programs of research addressing clinically relevant questions.

To advance the education and understanding of research methodology and critical analysis.

**VALUES**

Innovation, creativity and intellectual development of scientific thought.

Respectful and collegiate relationships within our group, the intensive care community and with collaborators.

Integrity, responsibility and accountability to ourselves, our patients and the community.
The CTG has continued to flourish in 2016/17. Our incredible community across 76 sites can be immensely proud of its achievements since inception. We have received over 15 million in competitive grant funding and published seven articles including one in the New England Journal of Medicine.

Those who look only to the past or present are certain to miss future (John F Kennedy)

The Clinical Trials Group is a community of clinician researchers coordinated by a committee that exists as a subcommittee of the Australian and New Zealand Intensive Care Society. This structure has facilitated extraordinary success and we are recognised as one of the world’s leading clinical trial networks. However, the research landscape for clinical trials is changing: uncertainty exists following a structural review of the NHMRC grant program; the role of the Medical Research Future Fund is uncertain; and the increasing number of trial networks nationally and internationally across multiple disciplines increases competition for a finite pool of funding. I recognise change is unsettling – it is unwise to simply change for change’s sake. It is prudent, however, to critically evaluate our existing governance processes with other similar organisations. The committee has commenced this process. I am confident we will emerge with a structure that is consistent with our mission, vision, and values - and able to respond to future challenges.

Two large CTG endorsed studies finished recruitment this year: TRANSFUSE (freshest available versus standard issue red blood cells) and ADRENAL (hydrocortisone versus placebo in sepsis). Thank you to all participating sites who contributed. Results are planned for public release in the second half of 2017. These studies are the largest in the critically ill population addressing two important questions. The high quality evidence generated will influence practice globally. TARGET (augmented versus standard nutrition) has recruited at an extraordinary rate; it is likely to finish in November 2017. SPICE (targeted sedation using dexmedetomidine) continues to progress well and the end is in sight for POLAR (prophylactic hypothermia in TBI) and PHARLAP (open lung strategy in ARDS). Thank you to all. I particularly wish to acknowledge the resilience and commitment of the POLAR and PHARLAP teams: TBI and ARDS research is difficult to design conduct and recruit into.

Noosa remains a highly successful and engaging meeting. The committee acknowledge the community’s strong view that the meeting should remain at Noosa and remain a similar size. To manage demand it is planned in 2018 to have member units only registration period and restrict the number of “day only” delegates. Further the committee will develop the winter meeting into a genuine alternative to Noosa. In 2017 Queenstown is being evaluated as a long term venue. This will facilitate more members of the community to attend CTG meetings.

Our great work would not occur without three affiliated methods centres: the ANZIC RC, The George, and the MRINZ. Thank you. I also thank the extraordinary CTG office led by Donna Goldsmith who is ably assisted by Simone Rickerby. Their contribution is largely behind the scenes yet essential. We also thank our sponsors and supporters. And finally once again thank you to the CTG community; and to our generous patients and their families without them all this would not be possible.
GOVERNANCE & STRUCTURE
The Australian and New Zealand Intensive Care Society (ANZICS) Clinical Trials Group (CTG) Committee is a standing committee appointed by and accountable to the Board of ANZICS.

This Committee administers the CTG. In addition to a Chair, Vice-Chair, Secretary and Treasurer, this Committee consists of a representative from each ANZICS Region (nominated and elected by the ANZICS Regional Members), and representatives from the ANZICS Paediatric Study Group (PSG), ANZICS Centre for Outcomes and Resource Evaluation (CORE), and the Intensive Care Research Coordinators Interest Group (IRCIG). Other members include the Immediate Past Chair, the CTG Executive Officer, the CTG Executive Assistant, and co-opted research strategy leaders as required.

**OFFICE BEARERS**

**CHAIR:** Clin A/Prof Craig French, Director, Intensive Care, Western Health (1)

**VICE-CHAIR:** A/Prof Sandra Peake, Senior Staff Specialist, Intensive Care, The Queen Elizabeth Hospital (2)

**IMMEDIATE PAST CHAIR:** Dr Colin McArthur, Senior Staff Specialist, Critical Care Medicine, Auckland City Hospital (3)

**SECRETARY:** Dr Rachael Parke, Senior Research Fellow, Cardiothoracic and Vascular ICU, Auckland City Hospital (4)

**TREASURER:** (to May 2017) A/Prof David Gattas, Senior Staff Specialist, Intensive Care, Royal Prince Alfred Hospital (5) 
(from May 2017) Dr Manoj Saxena, Staff Specialist, Intensive Care, St George Hospital (6)

**CO-OPTED MEMBERS**

**IRCIG REPRESENTATIVE:** A/Prof Glenn Eastwood, Intensive Care Research Manager, Austin Hospital (14)

**ANZICS PSG REPRESENTATIVE:** Dr Marino Festa, Clinical Program Director for Critical Care Services, The Children’s Hospital at Westmead (15)

**ANZICS CORE REPRESENTATIVE:** A/Prof David Pilcher, Staff Specialist, Intensive Care, The Alfred (16)

**CO-OPTED:** Prof Imogen Mitchell, Senior Staff Specialist, Intensive Care, Canberra Hospital (17)

**Trainee Representative:** Dr Elissa Milford, Registrar, Sunshine Coast University Hospital / Australian Defence Force (18)

**REGIONAL REPRESENTATIVES**

**NEW SOUTH WALES:** Dr Manoj Saxena, Staff Specialist, Intensive Care, St George Hospital (6)

**QUEENSLAND:** A/Prof Jeremy Cohen, Senior Staff Specialist, Department of Intensive Care Medicine, Royal Brisbane and Women’s Hospital (7)

**SOUTH AUSTRALIA:** (to January 2017) A/Prof Adam Deane, Research Fellow, Intensive Care, Royal Adelaide Hospital (8)
(from January 2017) Dr Yasmine Ali Abdelhamid, Specialist Intensivist, Royal Adelaide Hospital & Alice Springs Hospital (9)

**TASMANIA:** Dr David Cooper, Staff Specialist, Intensive Care & Hyperbaric Medicine, Royal Hobart Hospital (10)

**VICTORIA:** A/Prof Andrew Udy, Intensivist, Intensive Care, The Alfred (11)

**WESTERN AUSTRALIA:** Dr Ed Litton, Staff Specialist, Intensive Care, Royal Perth Hospital (12)

**NEW ZEALAND:** Dr Paul Young, Intensive Care Specialist, Wellington Hospital (13)

The CTG Committee meets face-to-face three times a year and the involvement of committee members throughout the year is substantial. Representatives volunteer their time to facilitate the strategic development of the trials group, lead and contribute to special interest working groups, review study protocols and manuscripts for endorsement, plan scientific meetings and represent the CTG on external boards and committees. All members of the CTG Committee are gratefully acknowledged for their time, expertise and dedication to the CTG.
The operational activities of the ANZICS Clinical Trials Group are supported by membership subscriptions received from intensive care units. Membership is open to all ICUs, public and private, throughout Australia and New Zealand. The CTG also offers affiliate membership to international ICUs providing at least one clinician working in the unit is a financial member of ANZICS. Annual membership fees for July 2016 – June 2017 (AUD$2,500 for adult ICUs and AUD$1,200 for paediatric ICUs ex GST) remained static.

In the July 2016 – June 2017 period there were 76 adult and paediatric intensive care units who were members of the ANZICS Clinical Trials Group. The support received from these members was vital, both in terms of voluntary subscriptions and active participation in CTG research.

Income from CTG memberships is used to support the CTG Office which in turn coordinates CTG activities. Without this financial support it would be difficult to continue to maintain CTG activities such as the regular meetings for study presentation and critique, the scientific review of new projects and manuscripts for CTG endorsement, governance and policy implementation, research training and mentoring, and activities to preserve and build ICU research capacity.

Thank you to all our members.

CTG MEMBERS

NEW SOUTH WALES
Blacktown Hospital
Calvary Mater Hospital (Newcastle)
Concord Repatriation General Hospital
Gosford Hospital
Hornsby Ku-ring-gai Hospital & CHS
John Hunter Hospital
Liverpool Hospital
Nepean Hospital
Prince of Wales Hospital
Royal North Shore Hospital
Royal Prince Alfred Hospital
St George Hospital
St Vincent’s Hospital Sydney
St Vincent’s Private Hospital Sydney
Westmead Hospital
Wollongong Hospital

AUSTRALIAN CAPITAL TERRITORY
Canberra Hospital

NORTHERN TERRITORY
Alice Springs Hospital
Royal Darwin Hospital

QUEENSLAND
Cairns Hospital
Gold Coast University Hospital
Hervey Bay Hospital
Logan Hospital
Mater Health Services Brisbane
Nambour General Hospital
The Prince Charles Hospital
Princess Alexandra Hospital
The Queen Elizabeth II Jubilee Hospital
Royal Brisbane & Women’s Hospital
Toowoomba Hospital
Townsville Hospital
Wesley Hospital

SOUTH AUSTRALIA
Royal Hobart Hospital

TASMANIA

76 = number of CTG Members in FY2017
This includes 69 Adult and 7 Paediatric Members. Honorary CTG Members are not included in this total
MEMBERSHIP

VICTORIA

Alfred Hospital
Austin Hospital
Ballarat Health Services
Bendigo Health
Cabrini Hospital
Dandenong Hospital
Eastern Health
Epworth Richmond
Frankston Hospital
Knox Private Hospital
Monash Medical Centre
The Northern Hospital
Royal Melbourne Hospital
St John of God - Subiaco
St Vincent's Hospital Melbourne
University Hospital Geelong
Western Health

Fiona Stanley Hospital
Rockingham General Hospital
Royal Perth Hospital
Sir Charles Gairdner Hospital
St John of God - Subiaco

WESTERN AUSTRALIA

Auckland City Hospital (CVICU)
Auckland City Hospital (DCCM)
Christchurch Hospital
Dunedin Hospital
Hawke’s Bay Fallen Soldiers’ Memorial Hospital
Middlemore Hospital
Nelson Hospital
North Shore Hospital
Tauranga Hospital
Waikato Hospital
Wellington Regional Hospital

NEW ZEALAND

The Children’s Hospital at Westmead, NSW
Sydney Children's Hospital, NSW
Lady Cilento Children's Hospital, QLD
Women's and Children’s Hospital, SA
Royal Children's Hospital, VIC
Princess Margaret Hospital, WA
Starship Children’s Hospital, NZ

PAEDIATRIC

The Australian and New Zealand Intensive Care Research Centre
The George Institute Division Of Critical Care And Trauma
The Medical Research Institute of New Zealand

HONORARY

Number of CTG Member Units Per Jurisdiction
All grants listed were awarded to CTG Endorsed Studies in FY2017. All amounts in Australian dollars, unless otherwise specified.

ADRENAL
A CTG Endorsed Study
Adjunctive corticosteroid treatment in critically ill patients with septic shock
$317,997 National Health and Medical Research Council - Project Grant

BLING III
A CTG Endorsed Study
A phase III randomised controlled trial of continuous beta-lactam infusion compared with intermittent beta-lactam dosing in critically ill patients
$3,269,943 National Health and Medical Research Council - Project Grant

POLAR
A CTG Endorsed Study
Prophylactic hypothermia to lessen traumatic brain injury
$266,321 National Health and Medical Research Council - Project Grant (POLAR II)

REVISE
A CTG Endorsed Study
The re-evaluating the inhibition of stress erosions trial
$2,955,164 National Health and Medical Research Council - Project Grant

STARRT-AKI
A CTG Endorsed Study
Standard versus accelerated initiation of renal replacement therapy in acute kidney injury
$2,112,447 National Health and Medical Research Council - Project Grant
NZ$1,191,467 Health Research Council, New Zealand - Project Grant

TAME Cardiac Arrest
A CTG Endorsed Study
Targeted therapeutic mild hypercapnia after resuscitated cardiac arrest: A phase III multicentre randomised controlled trial
$2,069,878 National Health and Medical Research Council - Project Grant
€999,995 Irish Health Board (Irish HRB) - Project Grant

TEAM
A CTG Endorsed Study
Treatment of invasively ventilated adults with early activity and mobilisation
$1,467,137 National Health and Medical Research Council - Project Grant
A$15,033,333
= total amount of funding awarded to CTG Endorsed / Supported studies in FY2017.

Cumulative Total Research Funding

FY2017
$111,196,601

FY2015
$77,362,837

FY2013
$60,622,797

> 2011
$48,096,471
ENDORSEMENT PROCESS
The ANZICS Clinical Trials Group itself does not conduct studies; rather it provides endorsement or support for studies proposed to be conducted in its name. As such, the process by which studies are endorsed or supported is critical for the group's success.

The requirements for endorsement and support are set out in the CTG Terms of Reference which were last reviewed in February 2014, and include that studies must:

- accord with the CTG's mission, vision and values;
- attain the highest standards of scientific validity and feasibility;
- be presented at least one CTG meeting to provide an opportunity for input from the intensive care research community; and
- be managed by a group with appropriate skills and representation from investigators and research coordinators. Manuscripts arising from CTG studies must also undergo a process of rigorous peer review that is overseen by the CTG Committee prior to submission for publication.

A second category of ‘CTG Supported’ studies was developed to cover situations, particularly multinational investigator initiated studies, where the CTG might only be one of a number of collaborating trials groups, where it is not reasonable to hold the study to all the conditions of CTG endorsement. CTG supported studies undergo a similar process of peer review as Endorsed studies, to confirm that the supported studies accord with the CTG’s mission, vision and values and are of the highest standards of scientific validity and feasibility.

The CTG endorsement process is conducted by the CTG Committee. Peer review of study proposals and manuscripts arising from CTG studies is undertaken by members of the CTG Committee and invited reviewers and ICU Research Coordinators.

We thank all who contributed significant amounts of time and expertise to ensuring the highest scientific standards were maintained by the CTG for all of the 21 applications for endorsement in the past year.

Non-CTG Committee member reviewers who performed an endorsement review in the past 12 months.

Cecile Aubron
Adam Deane
Anthony Delaney
Carmel Delzoppo
Miranda Hardie
Peter Harrigan
Lisa Higgins
Belinda Howe
Daryl Jones
Peter Kruger
Jeffrey Lipman
Christopher MacIsaac
Johnny Millar
Elizabeth Moore
Lynne Murray
Alistair Nichol
Jeffrey Presneill
Dorrilyn Rajbhandari
Brigit Roberts
Yahya Shehabi
Mandy Tallott
Jane Thomas
Anna Tilsley
David Tuxen
Shirley Vallance
DICE II
Perioperative dexmedetomidine in high risk cardiac surgery evaluation

This is a multinational double blind randomised placebo controlled evaluation of peri-operative dexmedetomidine starting at induction of anaesthesia.

Population: Adults undergoing cardiac surgery with eGFR < 60 ml/min OR undergoing a combined or complex aortic surgery. Exclusion criteria include salvage surgery, eGFR < 15 ml/min, dialysis dependent, extracorporeal support

Sample size: 2600 patients. Stratified at randomisation according to eGFR lower or higher than 60 ml/min

Intervention: Dexmedetomidine 0.7 mcg/kg/hour starting at induction of anaesthesia. Continued at 0.35 mcg/kg/hr till 24 hours after surgery or as clinically desirable. Comparator: Placebo infusion.

Outcome: MAKE90 = death + dialysis + persistent AKI at day 90

Management Committee: Yahya Shehabi (Chair), Rinaldo Bellomo, Belinda Howe, Julian Smith, Z Endre and David Scott.

Administering Institution: ANZIC Research Centre, Monash University

Collaborators: Monash University; ANZCA Clinical Trials Network

Sample Size: 2600 patients

Project Status: An application for NHMRC funding has been submitted.

Contact: Yahya Shehabi (yshehabi@ozemail.com.au)

EPO TBI Long Term Follow Up
Long term effects of erythropoietin in patients with moderate to severe traumatic brain injury. A follow-up study of an international randomised controlled trial

Between 2010 and 2014 the EPO TBI study was conducted in Australia, New Zealand, Saudi Arabia, France, Finland, Germany and Ireland. A total of 606 patients with moderate to severe traumatic brain injury (TBI) treated in the intensive care unit were randomly given either subcutaneous erythropoietin (EPO) or placebo once a week for three weeks or until intensive care unit discharge. The study was published in October 2015 and showed no difference regarding neurological recovery, but with further analysis a possible difference in mortality at 6 months was noted.

In the current study we aim to study the long term outcome of the patients included in the EPO TBI study. We aim to check, at a variable time point 2 to 7 years from injury, the survival status of the included patients. Patients that are alive will be contacted and invited to participate in an interview in order to determine present neurological recovery and quality of life. If the patient is unable to take part in the interview we will, as in the primary study contact the person responsible. Written consent will be obtained in those participating. In the interview conducted by a trained assessor neurological function and quality of life using approved standardised methods.

The study will give important information on the long-term effects of EPO after TBI. Risks for participants can be considered to be low and participation in the neurological follow-up will be based on informed consent. By checking survival status of participants prior to contact, we can avoid contacting relatives of deceased patients.

Management Committee: Rinaldo Bellomo (Chair), Yaseen Arabi, Jamie Cooper, Craig French, Olivier Huet, Lorraine Little (Project Manager), Nora Luethi, Alistair Nichol, Jeffrey Presneill, Markus Skrifvars and Shirley Vallance.

Administering Institution: ANZIC Research Centre, Monash University

Sample Size: 278 patients (AU/NZ); 245 patients (Other)

Project Status: Study registration is being prepared at all sites. An application has been made for data linkage with the National Death Index (NDI) through AIHW for Australian sites.

Contact: Lorraine Little (lorraine.little@monash.edu)
Nora Luethi (Nora.Luethi@monash.edu)
EPO TRAUMA

A prospective, multicentre, randomised, double-blind placebo controlled, stratified phase III trial of epoetin alfa vs. placebo in critically ill trauma patients

Worldwide trauma is major cause of mortality and long term morbidity. The World Health Organization has forecast that, by 2030, trauma will become the third leading cause of disability and death globally. Erythropoietin is a glycoprotein hormone essential for erythropoiesis that was first purified in 1977. Its human recombinant analogues known as erythropoiesis stimulating agents (ESAs) are approved for human therapeutic use. However erythropoietin is also a pleiotropic cytokine with effects beyond erythropoiesis. Studies in animals have demonstrated its potential protective effects of erythropoietin to organs including the brain, kidney, liver and heart injury, and anti-inflammatory properties.

In two large multicentre, randomized, controlled trials Corwin and colleagues evaluated the use of the ESA epoetin alfa as a red blood cell transfusion sparing agent in critically ill patients. A post hoc pooled analysis of these two trials demonstrated lower mortality in the critically ill trauma patient.

The recent Erythropoietin in Traumatic Brain Injury Study (EPO TBI) was an international, multicentre, randomized, double blind, placebo controlled trial that compared the effect of epoetin alfa, administered within 24 hours of traumatic brain injury, with placebo on patient centred outcomes. This study demonstrated, following a pre-specified sensitivity analysis, a significant reduction in six month mortality. A meta-analysis with trial sequential analysis of all relevant randomised controlled trials evaluating ESAs critically ill trauma patients demonstrated they reduced mortality by at least 20%. This finding may have important implications for patient management.

We therefore plan to conduct a trial of the ESA epoetin alfa in critically ill trauma patients in The United States of America, United Kingdom, Canada, Australia and New Zealand.

Management Committee: Craig French (Chair), Rinaldo Bellomo, Jamie Cooper, Lorraine Little (Project Manager), Lena Napolitano, Alistair Nichol, Jeffrey Presnell and Michael Reade.

Administering Institution: ANZIC Research Centre, Monash University

Sample Size: 10000 patients

Project Status: An NHMRC grant application and a U.S. Department of Defense grant application have been submitted.

Contact: Craig French (Craig.French@wh.org.au)

HELP-ECMO

A randomised controlled trial of a heparin low dose protocol versus therapeutic dose heparin in patients on veno-venous extra corporeal membrane oxygenation

HELP-ECMO is an Australian-initiated, 230-patient, multicentre, randomised, controlled, parallel-group, assessor-blinded clinical trial designed to determine if low dose heparin during treatment with VV-ECMO when compared with standard care (therapeutic anticoagulation) reduces the proportion of patients experiencing major bleeding. The trial is a two-sided superiority trial that will randomly allocate VV-ECMO patients to low dose heparin or standard care in a 1:1 ratio.

Patients will be eligible if they fulfil all of the inclusion and none of the exclusion criteria:

Inclusion criteria: Intensive care patients who require VV-ECMO

Exclusions:

- Less than 16 years of age
- Contra-indication to heparin (e.g. heparin induced thrombocytopenia)
- Pre-existing indication for therapeutic anticoagulation (e.g. PE, intracardiac thrombus)
- Contra-indication to therapeutic anticoagulation at the time of randomisation (e.g. active bleeding)
- Greater than 48-hours ECMO support prior to enrolment
- Treating clinician deems the study is not in the patient's interest

The primary outcome is the proportion of patients who experience major bleeding. Secondary outcomes include thrombosis, mortality, blood product requirements, length of stay and health status using the EQ5D.

Management Committee: Zoe McQuilten (Chair), Cecile Aubron, Michael Bailey, Jamie Cooper, John Fraser, Carol Hodgson, Vincent Pellegrino, David Pilcher, Huyen Tran and Shirley Vallance.

Administering Institution: Monash University

Sample Size: 230 patients

Project Status: Currently awaiting outcome of project grant funding applications. The trial has not yet commenced.

Contact: Zoe McQuilten (zoe.mcquilten@monash.edu)
ICU ROX TRIPS inception cohort study

An inception cohort study comparing oxygen practices in mechanically ventilated patients in ANZ ICUs which participate in the ICU-ROX trial, with patients in ICUs which do not participate.

The ICU-ROX TRIPS inception cohort study is part of a programme of research assessing whether participating in the ICU-ROX trial changes attitudes and practices with regard to oxygen therapy, compared to the practices of ICUs which do not participate.

Our hypothesis is that for ICUs which participate in the ICU-ROX trial, the proportion of time patients who are mechanically ventilated spend breathing 21% oxygen (room air) will increase but that this practice change will not occur in ANZ ICUs which do not participate.

The study will be collected at three timepoints: (i) before ICU-ROX starts as baseline; (ii) after ICU-ROX is completed, but before it is published; and (iii) 6-12 months after the publication of the results of ICU-ROX.

Management Committee: Diane Mackle (Chair and Project Manager), Michael Bailey, Richard Beasley, Rinaldo Bellomo, Victoria Bennett, Adam Deane, Glenn Eastwood, Simon Finfer, Ross Freebairn, Ed Litton, Colin McArthur, Shay McGuinness, Kathy Nelson, Rakshit Panwar, Paul Young

Administering Institution: Medical Research Institute of New Zealand

Collaborators: ANZIC Research Centre

Sample Size: 642 (214 at 3 timepoints)

Project Status: Twelve ICU-ROX sites and 12 non-ICU-ROX sites have completed the first phase of the study (baseline data collection). The ICU-ROX trial will finish around March 2018, at which time all sites will conduct the inception cohort study again (2nd timepoint).

Contact: Diane Mackle (Diane.mackle@ccdhb.org.nz)

LUCID

Liberal glucose control in critically ill patient with pre-existing type 2 diabetes (LUCID): a phase II multicentre randomised controlled trial

Type 2 diabetes mellitus (T2DM) is a frequent pre-existing medical condition in critically ill patients. During critical illness patients with T2DM are often hyperglycaemic, which is treated with insulin infusions. Currently patients with T2DM are treated exactly like patients with previously ‘normal’ glucose tolerance, i.e. insulin is administered when blood glucose is ≥ 10 mmol/L and titrated to target < 10 mmol/L, regardless of T2DM.

Observational data consistently show that increases in blood glucose concentrations that are associated with harm in patients with pre-existing ‘normal’ glucose tolerance have no impact on mortality or morbidity in patients with T2DM. However, both hypoglycaemia (both absolute and relative) and glycaemic variability, which are inevitable outcomes from the administration of insulin, occur frequently and are strongly associated with adverse outcomes: specifically, there are strong associations between all of these glycaemic metrics and increased mortality. We have conducted two preliminary studies that show non-significant trends to reduce incident hypoglycaemia and attenuate glycaemic variability with a more liberal approach. Accordingly, we believe that patients with T2DM have the potential to benefit from a more liberal approach to blood glucose control when compared to current standard care.

Management Committee: Adam Deane (Chair), James Anstey, Rinaldo Bellomo, Vishwanath Biradar, Glenn Eastwood, Simon Finfer, Mark Finnis, Craig French, Simon Heller, Michael Horowitz, Palash Kar, Peter Kruger, Colin McArthur, Shay McGuinness, Johan Martensson, Matthew Maiden, Alexis Poole (Project Manager), Paul Secombe, Antony Tobin, Andrew Udy and Sophia Zoungas.

Administering Institution: Royal Adelaide Hospital

Sample Size: 450 patients

Project Status: We have developed and tested the eCRF and Web based randomisation using RedCaps.

Recruitment has commenced at three sites.

We have submitted additional project grant funding to Diabetes Australia and the Intensive Care Foundation. If successful this would support central organisation and allow us to increase the modest per-patient payment.

Governance applications are in progress for another eight sites, with many of these expected to commence recruitment around September 2017. HREC application for New Zealand is in progress.

Contact: Adam Deane (adam.deane@mh.org.au)
Alex Poole (Alex.Poole@sa.gov.au)

Clinical Trial Registration No: ACTRN12616001135404
NO in CPB (Paediatric)
Nitric oxide on cardio pulmonary bypass in congenital heart disease

Congenital heart disease occurs in about 1% of all children and the majority of these children will require corrective or palliative cardiac surgery at some stage during childhood. In Australia and New Zealand the cardiac surgical and intensive care mortality of children is low with an estimated 2-5% death rate dependent on the complexity of the procedure and represents worldwide one of the highest standards. However, morbidity and long term outcomes are still a concern in these children. In the hours immediately following heart surgery on cardiopulmonary bypass (CPB), children frequently suffer from low cardiac output syndrome (LCOS). Low cardiac output may result in a fall in blood pressure (hypotension) causing inadequate organ blood flow (hypoperfusion) resulting in organ dysfunction and injury. The most common complications are renal failure, liver failure and most importantly potential neurological injury.

A recent randomised controlled pilot study from our group showed that the delivery of gaseous nitric oxide (NO) to the CPB circuit for children undergoing cardiac surgery for a specific subgroup of congenital heart defects resulted in myocardial protection, improved fluid balance, and an improved postoperative intensive care course. In order to confirm these preliminary findings we aim to investigate, in a multicentre randomised controlled trial, if NO reduces mortality and the need for ECLS postoperatively.

This study is supported by a well-experienced paediatric intensive care research and cardiac surgical network across Australia and New Zealand. The investigators have substantial track record in multi-centre trials and this study would represent the first population based interventional trial in cardiac surgical and paediatric intensive care patients.

Management Committee: Andreas Schibler (Chair), Debbie Long (Project Manager), John Beca, Warwick Butt, Simon Erickson, Marino Festa, Steve Horton, Mark Jones and Luregn Schapbach.

Administering Institution: Lady Cilento Children’s Hospital, Queensland

Sample Size: 1470 patients

Funding:

- Children’s Health Foundation QLD $274,000
- HeartKids $50,000

Project Status: NHMRC Grant Application in progress.

REACTOR
Randomised evaluation of active control of temperature vs. ordinary temperature management

The REACTOR trial is a multi-centre, open label, parallel groups, phase II feasibility trial in invasively mechanically ventilated adults without acute brain pathologies. This trial is principally being conducted to assess the feasibility of a subsequent phase 3 clinical trial. The proposed phase 3 trial will answer the following PICO question:

Among adults in ICU without acute brain pathologies who are expected to be ventilated beyond the day after randomisation, does systematic control of body temperature using regular IV paracetamol combined with physical cooling to treat fever, compared to standard temperature management, alter day 90 mortality?

The primary aim of this current trial is to establish the feasibility of the temperature control strategy being assessed in the intervention arm by determining whether or not it reduces mean body temperature compared to standard temperature management.

Management Committee: Paul Young (Chair), Michael Bailey, Frances Bass (Project Manager), Richard Beasley, Rinaldo Bellomo, Ross Freebairn, Naomi Hammond, Frank van Haren, Meg Harward (Project Manager), Seton Henderson, Diane Mackle, Colin McArthur, Shay McGuinness, John Myburgh, Manoj Saxena, Anne Turner (Project Manager) and Steve Webb.

Administering Institution: Medical Research Institute of New Zealand

Collaborators: The George Institute of Global Health

Sample Size: 184 patients

Funding:

- Health Research Council of New Zealand Feasibility Grant NZ$149,799

Project Status: Five sites in New Zealand and three sites in Australia are initiated to recruit participants. Canberra Hospital are awaiting governance approval.

There are 36 participants enrolled to date.

Clinical Trials Registration No: ACTRN12616001285448 & U1111-1182-7938

Contact: Paul Young (Paul.Young@ccdhb.org.nz)
The re-evaluating the inhibition of stress erosions trial

There is currently inadequate evidence to support the widespread current practice of stress ulcer prophylaxis through the daily administration of pantoprazole. Current data indicate that despite the increase in proton pump inhibitor administration the prevalence of clinically important gastrointestinal bleeding is unaffected. There are theoretical reasons and existing data which suggest that current practice may harm. It is likely that use of proton pump inhibitors increase the risk of ventilator-associated pneumonia, which is estimated to carry an attributable mortality of at least 6% and to increase hospital length of stay by approximately 6 days, and *Clostridium difficile* infection. Accordingly, a definitive methodologically rigorous study is needed to establish whether routine proton pump inhibitor administration results in net benefit or harm.

Management Committee: Adam Deane (Co-Chair), Simon Finfer (Co-Chair), Waleed Alhazzani, Frances Bass, Marianne Chapman, Deborah Cook, Parisa Glass, Serena Knowles, John Myburgh, Alexis Poole, Kelly Thompson, Bala Venkatesh and Paul Young.

Administering Institution: The George Institute for Global Health

Collaborators: Canadian Critical Care Trials Group (McMaster University)

Sample Size: 4800 patients

Funding:

| National Health and Medical Research Council Project Grant | $2,955,000 |

Project Status: Start-up activities for REVISE are progressing well.

The protocol, Version 1.0 has been finalised. An NMA application has been submitted to Northern Sydney Local Health District Human Research Ethics Committee (NSLHD) for QLD, NSW, VIC and SA sites. We are currently awaiting acknowledgment of approval.

Our collaborators (Canadian Critical Care Trials Group) led by Deborah Cook and Gordon Guyatt have been successful in obtaining a CIHR project grant, ensuring both regions will be able to recruit into the trial. The George Institute for Global Health will be the Australian and New Zealand coordinating centre and the Canadian group (McMaster University) will coordinate Canadian sites.

The management committee has been meeting regularly. There will be a restructure of the committee to reflect the international collaboration and region specific MCs will be established.

Australia and New Zealand will contribute 2800 patients from approximately 20-25 sites to the study. The remaining 2000 patients will come from Canada, or other regions if required.

We are currently investigating options for study drug procurement.

The CRF development and database management will be coordinated by McMaster University, and the first draft version of the CRF have been reviewed by the MC.

Australian and New Zealand site EOI are currently being reviewed and site feasibilities will be sent shortly. We welcome further EOI's from interested sites.

Contact: Adam Deane (adam.m.deane@gmail.com)

TAME Cardiac Arrest Trial

Targeted therapeutic mild hypercapnia after resuscitated cardiac arrest: A phase III multi-centre randomised controlled trial

The TAME Cardiac Arrest trial will study the ability of higher carbon dioxide (CO2) levels to reduce brain damage, comparing giving patients ‘normal’ to ‘slightly higher than normal’ blood CO2 levels and assessing their ability to return to normal life-tasks. It will be the largest trial ever conducted in heart attack patients in the ICU. This therapy is cost free and, if shown to be effective, will improve thousands of Australian lives, transform clinical practice, and yield major savings.

Management Committee: Glenn Eastwood (Chair), John Archer, Rinaldo Bellomo, Stephen Bernard, Carol Hodgson, Shay McGuinness, Alistair Nichol, Niklas Nielsen, Rachael Parke and Dion Stub.

Administering Institution: ANZIC Research Centre, Monash University

Collaborators: Irish Critical Care – Clinical Trials Group

Sample Size: 1700 patients

Funding:

| National Health and Medical Research Council Project Grant |
| Irish Health Research Board |

Project Status: Protocol: Ethics approval has been received for Australia. Provisional ethics approval has been received for the United Kingdom. Other ethics reviews are occurring in Ireland and Italy. Work-up phase – Italy, Sweden, the Netherlands & Saudi Arabia.

Harmonisation with TTM2 (NCT02908308) continues.

Clinical Trial Registration No: ACTRN12617000036314 & NCT03114033

Contact: Glenn Eastwood (glenn.eastwood@austin.org.au)
TTM2
Targeted hypothermia versus targeted normothermia after out-of-hospital cardiac arrest 2, a randomised clinical trial

TTM2 is an international, multicentre, parallel group, non-commercial, randomised, superiority trial in which a target temperature of 33°C after cardiac arrest will be compared to normothermia with early treatment of fever.

Management Committee: Manoj Saxena (Chair), Anders Åneman, Frances Bass (Project Manager), Rinaldo Bellomo, Stephen Bernard, Glenn Eastwood, Naomi Hammond, John Myburgh, Niklas Nielsen and Paul Young.

Administering Institution: The George Institute

Collaborators: Lund University

Sample Size: 1900

Funding: The Swedish Research Council

Project Status: Ethics applications in Australia and New Zealand are in progress.

NHMRC Project Grant under review. Additional grants from Ian Potter Foundation and Intensive Care Foundation also under review.

EOI from sites in progress.

Collaboration and Coenrolment with the TAME Cardiac Arrest Trial is being explored to harmonise elements including eligibility criteria, Case Report Forms, Database.

Contact: Manoj Saxena (msaxena@georgeinstitute.org.au) Frances Bass (fbass@georgeinstitute.org.au)


166
= total number of publications 1998 - FY2017

$h$-index = 45
ENDORSED STUDIES
COMPLETED FY2017

EGDT IPDMA (PRISM)
Protocolised resuscitation in sepsis meta-analysis
Management Committee: Derek Angus, Michael Bailey, Rinaldo Bellomo, Anthony Delaney, Anna Holdgate, Belinda Howe, Sandra Peake, Michael Reade, Kathryn Rowan and Steve Webb, in collaboration with Derek Angus and the ProCESS investigators from the University of Pittsburgh and Kathryn Rowan and the ProMISe investigators from the UK Intensive Care National Audit and Research Centre.

Several ANZICS studies have spent long in gestation but few rival the PRISM individual patient data meta-analysis, published in the NEJM in March 2017 on the day of its presentation in the opening session of the Brussels ISICEM conference. Recognising that country-specific elements of protocol implementation and intercurrent care might affect the effectiveness of “Early Goal Directed Therapy” (EGDT) for septic shock, in 2006 the ARISE, ProCESS and ProMISE investigators agreed to harmonise, to the degree possible, trial entry criteria, intervention protocols, outcomes, major resource-use measures, and data collection across the three trials. The three trials were published individually in the NEJM, 2014-2015, with none identifying any benefit of EGDT – in contrast to the results of the original single-centre trial published by Rivers et al. in 2001. However, after the publication of these three larger trials, concern was expressed that treatment effects might have been obscured because patients were, on average, not as unwell as those in the Rivers study, or because of differences in intercurrent and baseline care. A trial-level meta-analysis was published by our group that, not surprisingly, found no benefit with EGDT (Angus DC et al. Intensive Care Med 2015; 41: 1549-60). However, due to a phenomenon known as the “ecological fallacy”, in which spurious inferences about individual characteristics are made based upon aggregate statistics for the group to which those individuals belong, trial-level meta-analysis cannot properly identify or adjust for differences in patient- or hospital-level subgroups. PRISM allowed exploration of differences in EGDT effect in prespecified subgroups defined by age, sex, comorbidity, site of infection, and severity of illness. PRISM was prospectively registered as an independent study (NCT02030158). We found no evidence of treatment benefit with EGDT in patients with greater severity of illness, and despite wide variation in practice, even in those emergency departments with the least aggressive approach to resuscitation, there was no evidence of benefit with EGDT.

Significance of these results
There are two important implications of the PRISM results. First, in contemporary emergency department and intensive care practice and in subgroups defined by various patient and hospital criteria, EGDT is not associated with improved 90-day mortality, and the probability that EGDT is cost-effective was less than 0.25. Secondly, we have demonstrated the feasibility and success of prospective individual patient data meta-analysis applied to large critical care effectiveness trials. Individual patient data meta-analysis is potentially more relevant to intensive care research than in other fields, given the typical heterogeneity of patients and intercurrent treatments within each trial. PRISM will hopefully become a template upon which other trials will build.

Administering Institution: ANZIC Research Centre, Monash University


Fluid TRIPS
The fluid translation of research into practice study (Fluid-TRIPS): an international cross sectional survey of fluid resuscitation practice
Management Committee: Naomi Hammond (Co-Chair), Colman Taylor (Co-Chair), Laurent Billot, Maryam Correa (Project Manager), Simon Finfer, Parisa Glass, Bette Liu, John Myburgh, Anders Perner, Manoj Saxena and Nicola Watts.

The Fluid – Translation of Research Into Practice Study (Fluid-TRIPS) was an international cross-sectional study of fluid resuscitation practices conducted in 426 ICUs in 27 countries in 2014. The aim of this study was to document the type of fluid resuscitation used in international clinical practice, determine the predictors of fluid choice, and whether these have changed since the conduct of SAFE-TRIPS in 2007. The results of this study have been published in PLoS ONE, May 2017.

Over the 24-hour study day, 21.7% (1456/6707) of patients received fluid resuscitation during 2716 resuscitation episodes. Crystalloids were administered to 84.3% (1227/1456) of patients during 81.3% (2208/2716) episodes and colloids to 27.1% (394/1456) patients during 21.4% (581/2716) episodes. In multivariate analyses, practice significantly varied between geographical regions.

To determine if resuscitation practices had changed between 2007 and 2014, we analysed data from a cohort of ICUs that participated in both SAFE-TRIPS and Fluid-TRIPS. A total of 84 ICUs from 17 countries contributed...
Based on these data, fluid resuscitation practices have changed between 2007 and 2014. Geographical location continued to be a strong predictor for the type of fluid that is administered for fluid resuscitation. Overall, there has been a switch to the preferential use of crystalloids, specifically balanced salt solutions, over colloids. When colloids are administered, albumin is the preferred choice. The results of this study have highlighted an evidence practice gap in respects to the use of balanced salt solutions over 0.9% saline where there is limited robust evidence to support the use of balanced salt solutions. As such we are conducting the NHMRC funded Plasma-Lyte® v Saline (PLUS) study to provide reliable estimates of the risks and benefits of the use of a balanced salt solution compared to 0.9% saline (ClinicalTrials.gov: NCT02721654).

Administering Institution: The George Institute for Global Health


IRONMAN
Intravenous iron or placebo for anaemia in intensive care: the IRONMAN randomised controlled trial

Management Committee: Edward Litton (Chair), Stuart Baker, Wendy Erber, Shannon Farmer, Janet Ferrier (Project Manager), Craig French, Joel Guummer, David Hawkins, Alisa Higgins, Axel Hofmann, Bart De Keulenaer, Julie McMorrow, John K. Olynyk, Toby Richards, Simon Towler, Robert Trengove and Steve Web.

Both anaemia and allogenic red blood cell transfusion are common and potentially harmful in patients admitted to the intensive care unit. The In Intravenous Iron or Placebo for Anaemia in Intensive Care (IRONMAN) multicentre randomised placebo-controlled, blinded trial was designed to test the hypothesis that, in anaemic, critically ill patients admitted to the intensive care unit, early administration of intravenous iron, compared with placebo, reduces allogenic red blood cell transfusion and increases haemoglobin to hospital discharge.

The study enrolled 140 participants and found that IV iron resulted in a significant increase in median haemoglobin at hospital discharge (107 (IQR 97-115) vs. 100 g/L (IQR 99-111), P=0.02). The iron group received 97 red blood cell units versus 136 red blood cell unit in the placebo group, but this decrease did not reach statistical significance [incidence rate ratio 0.71, 95% confidence interval (0.43-1.18) P=0.19]. Follow up work is ongoing investigating the role of hepcidin in predicting progressive anaemia and response to IV iron, as well as the medium-term effects of IV iron on recovery from critical illness and quality of life.

Administering Institution: Royal Perth Hospital, WA


ENDORSED STUDIES
BLING III
A phase III randomised controlled trial of continuous beta-lactam infusion compared with intermittent beta-lactam dosing in critically ill patients

A phase III randomised controlled trial of continuous beta-lactam infusion compared with intermittent beta-lactam dosing in critically ill patients. This is a prospective, multicentre study with 7000 patients recruited from 100 sites worldwide, open label randomised controlled trial with blinded outcome assessment.

Management Committee: Jeffrey Lipman (Chair), Menino Cotta, Joshua Davis, Jan De Waele, Joel Dulhunty, Simon Finfer, Parisa Glass, Shay McGuinness, John Myburgh, David Paterson, Dorrilyn Rajbhandari (Project Manager), Sandra Peake, Andrew Rhodes, Jason Roberts, Charudatt Shirwadkar, Therese Starr, Colman Taylor.

Administering Institution: The George Institute for Global Health

Collaborators: University of Queensland

Sample Size: 7000

Funding: National Health and Medical Research Council Project Grant $3,269,942

Project Status: The Trial is in the set up phase. Ethics approval has been gained for eastern seaboard states. Overseas collaboration is being finalized with funding grants submitted in NZ, Belgium, UK collaboration in process.

Usual trial set processes in different stages of completion.

Contact: Dorrilyn Rajbhandari (drajbhandari@georgeinstitute.org.au)
Jeff Lipman (jlipman@uq.edu.au)
Joel Dulhunty (joel.dulhunty@health.qld.gov.au)

PLUS
The Plasma-Lyte 148® versus saline study

PLUS is a multi-centre, blinded, randomised, controlled trial (RCT) to determine whether fluid resuscitation and therapy with a “balanced” crystalloid solution (Plasma-Lyte 148®) decreases 90-day mortality in critically ill patients requiring fluid resuscitation when compared with the same treatment using 0.9% sodium chloride (saline). This study will enrol 8,800 patients in approximately 40 study sites in Australia and New Zealand.

Participants will be patients expected to be treated in the Intensive Care Unit (ICU) for three days or more. They will be randomly assigned to receive either Plasma-Lyte 148® or saline for all resuscitation episodes and for all compatible crystalloid therapy while in ICU for up to 90 days after the first episode of fluid resuscitation.

PLUS is a pivotal trial that will provide an accurate and reliable estimate of the comparative risks versus benefit of Plasma-Lyte 148® versus 0.9% sodium chloride. As the only definitive trial comparing normal saline with a balanced solution, PLUS will influence clinical practice guidelines and clinical practice worldwide and will affect the health of millions of acute and critically ill people.

Management Committee: Simon Finfer (Chair), Rinaldo Bellomo, Naomi Hammond, Martin Gallagher, David Gattas, John Myburgh, Diane Mackle, Sharon Micallef (Project Manager), Manoj Saxena, Colman Taylor and Paul Young.

Administering Institution: The George Institute for Global Health / University of NSW, Sydney

Collaborators: Baxter Healthcare (provision of fluids)

Sample Size: 8800 patients

Funding: National Health and Medical Research Council Project Grant $5,984,818
Health Research Council of New Zealand - Project Grant NZ$1,385,250

Project Status: Protocol finalised and study registered at ClinicalTrials.gov. NMA Ethics submission to Royal North Shore Hospital HREC in April for sites in NSW, QLD, SA and VIC – response to HREC questions submitted in May. 44 sites in ANZ completed EOI and majority of Site Feasibility Questionnaires completed. Ethics approval granted in NZ.

Clinical Trial Registration No: NCT02721654

Contact: Sharon Micallef (smicallef@georgeinstitute.org.au)
Simon Finfer (sfinfer@georgeinstitute.org.au)
TEAM RCT
Treatment of invasively ventilated adults with early activity and mobilisation

TEAM is a program of research to evaluate the effect of early mobilisation to assess functional recovery and patient-centred outcomes of ICU survivors.

Rationale: Patients in intensive care (ICU) traditionally receive bed rest as part of the management of their critical illness. It is possible that patients develop muscle weakness even after only a few days of mechanical ventilation that may prolong their time in ICU and in hospital and delay functional recovery resulting in slower return home and to work. Moreover, it is plausible that failure of recovery of physical performance is a contributing factor to late mortality after critical illness. Weakness may be avoided with simple strategies of early exercise in ICU.

Goal: This program of research has included (1) reviews and systematic reviews of early mobilisation in ICU, (2) a multi-centre observational study to define standard care funded by the Intensive Care Foundation and endorsed by the ANZICS Clinical Trials Group, (3) a pilot RCT to determine if a phase III RCT of early mobilisation was feasible in ICUs in Australia and New Zealand. Results were published in 2016 (Crit Care Med) and we successfully received NHMRC funds to conduct a Phase III trial in 2016.

Management Committee: Carol Hodgson (Chair), Rinaldo Bellomo, Heidi Buhr, Belinda Gabbe, Meg Harrold, Alisa Higgins, Theodore Iwashyna, Jeffrey Presneill, Manoj Saxena, Janani Sivasuthan (Project Manager), Lizzie Skinner, Claire Tipping, Steve Webb, Nia Wyn Davies and Paul Young.

Administering Institution: ANZIC Research Centre, Monash University

Collaborators: Medical Research Institute of New Zealand

Sample Size: 750 patients

Funding:

| National Health and Medical Research Council Project Grant | $1,467,137 |

Project Status: TEAM study was submitted to Alfred Ethics Committee in May 2017 under the National Mutual Acceptance Scheme and it will cover VIC, NSW, QLD and SA sites.

Expression of interest form was circulated to all the sites under CTG and thus far 31 sites from Australia and New Zealand have expressed interest in the study. Site survey has been sent out to all 31 sites.

Research Path has been chosen to provide database services and contract has been signed and project kick-off meeting was held in May 2017. CRFs for the study are nearing final stages of TEAM Management Committee approval before commencing eCRF development.

TEAM DSMC members have been chosen and the DSMC charter has been finalised.

TEAM project manager, Janani Sivasuthan, was appointed in March 2017.

Contact: Carol Hodgson (carol.hodgson@monash.edu)
ICU-ROX
A phase 2b, multi-centre, randomised, single blinded clinical trial parallel groups comparing liberal vs. conservative oxygen therapy in mechanically ventilated adults in the Intensive Care Unit (ICU).

ICU-ROX is a phase 2b, multi-centre, randomised, single blinded clinical trial parallel groups comparing liberal vs. conservative oxygen therapy in mechanically ventilated adults in the Intensive Care Unit (ICU).

Our study hypothesis is that a conservative approach to oxygen therapy, which minimises unnecessary exposure to hyperoxaemia, will increase ventilator-free days compared to a more liberal approach to oxygen therapy which does not specifically aim to avoid exposure to hyperoxaemia.

Management Committee: Paul Young (Chair), Michael Bailey, Richard Beasley, Rinaldo Bellomo, Victoria Bennett, Adam Deane, Glenn Eastwood, Simon Finfer, Ross Freebairn, Natalie Linke (Project Manager) Ed Litton, Colin McArthur, Shay McGuinness, Diane Mackle (Project manager) and Rakshit Panwar.

Administering Institution: Medical Research Institute of New Zealand

Collaborators: ANZIC Research Centre, Monash University

Sample Size: 1000 patients

Funding: Health Research Council of New Zealand - Project Grant NZ$1,404,525

Project Status: The pilot study of 100 patients has been completed and analysed. No significant changes to the protocol were necessary, and the main study (900 patients) re-started on Monday 13th March 2017. All 10 NZ sites and two Australian sites are actively recruiting, with the remaining nine Australian sites due to start in August. Recruitment has been going very well, and is anticipated to finish in early 2018. No significant problems with the protocol have been reported by sites.

Clinical Trial Registration No: ACTRN12615000957594

Contact: Paul Young (paul.young@ccdhb.org.nz)

The PATCH Study
Pre-hospital anti-fibrinolytics for traumatic coagulopathy and haemorrhage

The PATCH Trauma study aims to address whether early administration of tranexamic acid (TXA), compared to placebo, reduces mortality and improves recovery at six months in severely injured adults at risk of acute traumatic coagulopathy (ATC) who are treated in advanced trauma systems.

In 10-25% of severely injured patients, bleeding is exacerbated by ATC characterized by hyperfibrinolysis detectable on hospital arrival. Patients with ATC are 3-4 times more likely to die and develop multiple organ failure, and have longer intensive care and hospital stays. A large international study (CRASH-2) showed TXA reduced all-cause mortality in adult trauma patients with, or at risk of, significant haemorrhage. Almost all of the patients enrolled in CRASH-2 were treated in hospitals in low and middle income countries that have markedly different standards of care for the management of ATC, higher baseline mortality rates, and a younger patient population than trauma centres in Australia and New Zealand. A post-hoc analysis of the CRASH-2 trial results found there was an unexpected increase in the risk of death due to bleeding when TXA was given beyond three hours from injury.

The PATCH Trauma study is a multi-centre randomised, placebo-controlled and blinded study that will enroll 1200 severely injured patients at risk of ATC in the prehospital setting. Emergency medical services clinicians will assess patient eligibility using the coagulopathy of severe trauma (COAST) score. TXA or placebo will be administered in the prehospital and a second dose given soon after hospital arrival. The primary outcome of the study is the proportion of patients with a favourable outcome at six months (moderate disability to good recovery, GOSE scores 5-8) compared to those who have died (GOSE 1), or have severe disability (GOSE 2-4). Secondary outcomes include vascular occlusive events (AMI, stroke, DVT, PE), blood product use, 24 hour and 28 day mortality, and the effects of TXA on coagulation, fibrinolysis and inflammatory mediators.


Administering Institution: ANZIC Research Centre, Monash University

Sample Size: 1184 Patients

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**Funding:**

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<th>Source</th>
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<td>Health Research Council of New Zealand</td>
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**Project Status:** The PATCH study has enrolled 370 participants to date. A planned interim safety analysis is in progress (25% enrolment, 296 participants). The first sites will commence in NSW in July 2017. It is expected that four prehospital retrieval services and 5 major trauma centers across NSW will be participating by the end of 2017. Addition of these sites is expected to increase the current rate of enrolment across 14 other participating sites in Victoria, South Australia, Queensland, and New Zealand.

Clinical Trial Registration No: NCT02187120

Contact: Stephen Bernard (s.bernard@alfred.org.au)  
Veronica Pitt (veronica.pitt@monash.edu)

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**PEPTIC**

A multi-centre, cluster cross over, randomised registry trial comparing the safety and efficacy of proton pump inhibitors with histamine-2 receptor blockers for ulcer prophylaxis in intensive care patients

The PEPTIC Study will use a cluster crossover registry design to compare proton pump inhibitors (PPI) and histamine-2 receptor blockers as the default therapy for ulcer prophylaxis in mechanically ventilated patients in ICU. The study will provide robust estimates of the relative risk of stress-related upper gastrointestinal (GI) bleeding and complications that are potentially related to using PPIs vs H2RBs for stress ulcer prophylaxis. During the first treatment period, half of the participating ICUs will be randomly assigned to use PPIs for stress ulcer prophylaxis in patients who require life-support while the other half will use H2RBs. During the second treatment period each ICU will swap to using the opposite treatment. Data will be collected primarily from existing data sources rather than the medical records of individual patients. There will be two study treatment periods. The primary endpoint is in hospital mortality (censored at 90 days).

Management Committee: Paul Young (Chair), Michael Bailey, Richard Beasley, Rinaldo Bellomo, Glenn Eastwood, Marino Festa, Andrew Forbes, David Gattas, Frank van Haren, Ed Litton, David Pilcher, Diane Mackle (Project Manager), Shay McGuinness, Alistair Nichol, Manoj Saxena, Steve Webb, Sean Bagshaw, Paul Mouncey and Stephen Wright.

Administering Institution: Medical Research Institute of New Zealand

Project Managers: Leanlove Navarra and Diane Mackle

Collaborators: Austin Hospital; Irish Health Research Board; Intensive Care National Audit & Research Centre (ICNARC)

**Funding:**

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<td>Health Research Council of New Zealand, Research Partnerships for New Zealand Health Delivery</td>
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**Project Status:** 20 sites from Australia, 7 sites from New Zealand and 1 site from Ireland have started the PEPTIC Study beginning in August last year. Sites complete a monthly audit form to capture patients who are mechanically ventilated receiving or not receiving stress ulcer prophylaxis as outlined in their 'pre-study forms'. The first batch of sites who started August last year are expected to finish the PEPTIC study next month. In addition to this, a collaboration with UK (ICNARC) to start PEPTIC Study has been initiated and we are expecting to have at least 12 sites participating from UK and hoping to commence late this year.
We have designed a ventilation strategy (PHARLAP) combining tidal volume and plateau pressure limitation with a comprehensive open lung strategy. In a pilot study we demonstrated that this strategy was safe and improved a range of physiological and inflammatory markers in patients with ARDS. We aim to investigate the clinical efficacy of PHARLAP strategy compared to standard mechanical ventilation in ARDS patients. The primary outcome is ventilator free days at day 28. In addition, physiological, inflammatory, clinical and safety economic outcomes variables will be compared between both groups. In a prospective, multi-centre, randomised controlled trial we will enrol 340 adult patients who have developed ARDS within the last 72 hours and randomly allocate them to either the PHARLAP or a control ventilation strategy. PHARLAP strategy: pressure control ventilation to maintain a Pplat ≤ 30 cmH2O and a Vt at 4-6 ml/kg while tolerating respiratory acidosis as long as pH is above 7.15, daily staircase recruitment manoeuvre and individual PEEP titration. Control strategy: low tidal volume based on ARDSnet protocol using volume control ventilation with Vt = 6 ml/kg, Pplat ≤ 30 cmH2O and a FiO2/PEEP titration according to a FiO2/PEEP/oxygen saturation chart. Sedation and weaning from mechanical ventilation and follow-up at 6 months will be the same for both groups.

Management Committee: Carol Hodgson (Co-Chair), Alistair Nichol (Co-Chair), Victoria Bennett (Project Manager - leave), Yaseen Arabi, Andrew Bersten, Kathy Brickell, Jamie Cooper, John Fraser, Shay McGuinness, Lynne Murray, Rachael Parke, David Tuxen, Shirley Vaillance and Meredith Young (Project Manager – acting).

Administering Institution: ANZIC Research Centre, Monash University

Sample Size: 340 patients

Funding:

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Project Status: The PHARLAP Study has twenty three active sites in five countries - Australia, New Zealand, Saudi Arabia, Ireland and the United Kingdom. There are one hundred and ten patients enrolled to date. We are continuing to make progress with recruitment since the addition of sites in the UK and Ireland. There are eight live sites in the UK with one additional UK site to commence next month. Three sites are now live in Ireland, with a further four scheduled to commence in 2017.

We are also collaborating with San Raffaele Hospital, Milan and anticipate initiating activity here in the second half of 2017.

In 2017, we have focused on early monitoring visits for our international sites and ongoing site education and support.

Clinical Trial Registration No: NCT01667146

Contact: Meredith Young (Meredith.young@monash.edu)
POLAR
Prophylactic hypothermia to lessen traumatic brain injury

The POLAR trial is a multicenter, randomised controlled trial of early and sustained prophylactic hypothermia in patients with severe traumatic brain injury. The primary aim of the study is to determine whether early and sustained prophylactic hypothermia, compared to standard normothermic care, is associated with an increased proportion of favourable neurological outcomes for patients six months after severe traumatic brain injury.

Management Committee: Jamie Cooper (Chair), Peter Cameron, Gilles Capellier, Andrew Forbes, Colin McArthur, Lynne Murray, Lynette Newby, Alistair Nichol, Jeff Presneill, Stephen Rashford, Jeffrey Rosenfeld, Tony Smith, Michael Stephenson, Shirley Vallance, Dinesh Varma, Tony Walker and Steve Webb.

Administering Institution: ANZIC Research Centre, Monash University

Project Manager: Tony Trapani

Sample Size: 500 patients

Funding:

- National Health and Medical Research Council Project Grant $1,958,075
- National Health and Medical Research Council Project Grant (POLAR II) $266,321
- Transport Accident Commission (formerly Victorian Neurotrauma Initiative) $669,970

Project Status: The study has continued to progress - recruiting at 7-8 patients / month. Recruited 478 patients (n=500). It is anticipated that recruitment will be completed in October 2017 and 6 month follow up in April 2018.

A Statistical Plan Manuscript was submitted to TRIALS in May – waiting for response from editor.

The lead site is The Alfred Hospital and the lead pre hospital organisation is Ambulance Victoria. 100 Patients have also been recruited in France + 1 other site in Europe (Switzerland) and at 2 sites in Middle East (Saudi Arabia and Qatar).

DSMC
Post review for safety @ 400 Patient + 6-month follow-up, DSMC Chair has supported the continuation of the study to completion without further reviews.

Clinical Trial Registration No: NCT 00987688 & ACTRN12609000764235

Contact: Tony Trapani (Tony.Trapani@monash.edu)

REACT Shock Study
Relative hypotension and acute kidney injury in patients with shock: a prospective multicentre cohort study

We aim to investigate the degree of relative hypotension that is inadvertent accepted in routine clinical care and assess its relationship with mortality and morbidity among patients who are managed for shock. The rationale for this study is that targetting a standard BP level for all ICU patients with shock may leave a degree of untreated relative hypotension during vasopressor therapy particularly among those with higher pre-morbid BP. This may potentially be suboptimal for the organs, and either delaying recovery or causing new onset organ dysfunction among shocked ICU patients. Determining the patients’ basal BP, then comparing it to what is achieved during ICU management of shock, and quantifying the BP-deficit between the two as a measure of relative hypotension are the core elements of this proposed study. We aim to assess BP-deficit in patients with shock in routine care across several ICUs in Australia and New Zealand; and determine if it is associated with a higher rate of subsequent acute kidney injury or death. To achieve this, we are prospectively enrolling 300 consecutive eligible patients across seven participating centres, and assess the degree of untreated relative hypotension during the initial 120 hours of treatment of shock in ICU. We will then assess its relationship with the incidence of significant progression of acute kidney injury, incidence of de novo chronic kidney disease and mortality.

Management Committee: Rakshit Panwar (Chair / Project Manager), Rinaldo Bellomo, Frank van Haren, Nicholas Lanyon, John Myburgh, Manoj Saxena and Miranda Hardie.

Administering Institution: John Hunter Hospital, NSW

Sample Size: 300 patients

Funding:

- John Hunter Hospital Charitable Trust $23,809
- Royal Brisbane Hospital Research Trust $20,500

Project Status: 247 patients are enrolled so far. We are 53 short of the originally planned sample size. We will endeavour to enrol these remaining 53 patients over the next 2-3 months.

Clinical Trial Registration No: ACTRN12613001368729

Contact: Rakshit Panwar (rakshitpanwar@hotmail.com)
SPICE RCT
Sedation practice in intensive care evaluation randomised controlled trial

Each year, more than 3 million patients in intensive care worldwide receive sedative drugs to facilitate mechanical ventilation and life-saving therapies, however, they are also associated with significant harm. Unfortunately, despite their widespread use, there is no high quality evidence to guide clinical practice. In a recent multicentre observational study, we found that current practice is commonly associated with deep sedation and a high incidence of delirium. Both are modifiable and can be targeted to improve outcomes. Currently used sedative drugs have many side-effects that may be attenuated by use of a new approach to sedation that uses the alpha-2 agonist dexmedetomidine (DXMD) instead. DXMD has been shown in multiple phase II trials to shorten ventilation time, reduce delirium, provide analgesia and deliver lighter sedation with minimal respiratory depression. We believe that, in mechanically ventilated patients, early use of a sedative algorithm based on DXMD will result in safe but lighter sedation, higher delirium free days, less time on mechanical ventilation, in ICU and in hospital, and increased survival. Accordingly, we have designed a multicentre randomised controlled trial of 4000 patients. This study will compare Early Goal-Directed Sedation delivered within hours of initiation of ventilation, using DXMD as a primary sedative drug, targeting light sedation and minimising use of other sedative drugs, with best current care. The primary outcome will be 90 day all-cause mortality. Other outcomes include institutional dependency at 90 days, cognitive function at 6 months, ventilation time, incidence and duration of delirium.

Management Committee: Yahya Shehabi (Chair), Frances Bass, Rinaldo Bellomo, Simon Erickson, Belinda Howe (Project Manager), Suhaini Kadiman, Colin McArthur, Lynne Murray, Michael Reade, Ian Seppelt, Jukka Takala, Steve Webb and Matthew Wise.

Administering Institution: ANZIC Research Centre, Monash University

Collaborators: Pfizer; Orion Pharma

Sample Size: 4000 patients

Funding:

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<td>National Heart Institute of Malaysia, Institut Jantung Negara</td>
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Project Status: The SPICE study is the largest study of ICU sedation ever conducted in the world. The study has currently recruited 3261 patients across 70 sites internationally. The study is recruiting approx. 100 patients per month which should have the study completed on time and on budget.

The study has formed important relationships with investigators at international sites in Malaysia, UK, Ireland, Switzerland, Italy and Saudi Arabia. Most importantly this study will provide evidence to guide sedation practice internationally in order to improve patient centred outcomes of mortality, delirium and cognitive function.

Clinical Trial Registration No: NCT01728558

Contact: Belinda Howe (belinda.howe@monash.edu)

STARRT-AKI
Standard versus accelerated initiation of renal replacement therapy in acute kidney injury

To determine whether immediate initiation of renal replacement therapy (RRT), compared to delayed approach to RRT initiation, improves survival and renal recovery (RRT independence) at 90 days in critically ill patients with severe AKI.

Management Committee: Martin Gallagher (Chair), Sean Bagshaw, Rinaldo Bellomo, Heidi Buhr, Erika Dempsey (Project Manager), Glenn Eastwood, David Gattas, Shay McGuinness, Rachael Parke, Andrew Udy, Ron Wald and Amanda Wang.

Administering Institution: The George Institute for Global Health, Australia (Renal and Metabolic Division)

Collaborators: St Michael's Hospital, Canadian Critical Care Trials Group

Sample Size: 2866 patients

Funding:

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Project Status: STARRT-AKI has a global recruitment target of 2866 participants. As of June 2017, the study has recruited more than 28% of the target recruitment with more than 85 active sites throughout Europe, North America and the ANZ region, with plans to expand to more than 100 sites over the next 6 months.

STARRT-AKI is recruiting well in the ANZ region, with 25% of the target 700 patients recruited thus far. The study is expanding to more than 20 sites in Australia and New Zealand over the next 6 months.

Clinical Trial Registration No: NCT02568722

Contact: Rinaldo Bellomo (rinaldo.bellomo@austin.org.au)
Erika Dempsey (edempsey@georgeinstitute.org.au)
TARGET: The augmented versus routine approach to giving energy trial

The Augmented versus Routine approach to Giving Energy Trial (TARGET).

Although the importance of nutrition in critical illness is widely recognized, there remains uncertainty about the optimal target for caloric requirements. We plan to conduct a pivotal, 4000-patient, multicentre, double-blinded, randomised, controlled, parallel-group, phase III clinical trial to determine if the delivery of more calories improves survival following critical illness.

Aim: The primary aim of the study is to determine if augmentation of calorie delivery using energy dense enteral nutrition in mechanically ventilated patients improves 90 day survival when compared to routine care. A secondary aim is to determine if augmentation of calorie delivery using energy dense enteral nutrition in mechanically ventilated patients improves functional outcomes when compared to routine care. Primary Study Hypothesis: We hypothesise that, in mechanically ventilated patients, the enteral delivery of energy dense nutrition improves 90 day survival when compared to standard enteral care (which usually results in under-nutrition). Our secondary hypothesis is that enteral delivery of energy dense nutrition will also improve functional outcomes.

We have developed a simple & inexpensive strategy to deliver more calories safely & effectively via the enteral route. The strategy is to substitute standard formula (1.0 kcal/ml) with energy dense formula (1.5 kcal/ml) & deliver it at the same rate. This is a novel concept. Concentrated feed formulae are used in ICU feeding practice but are usually given at a reduced rate to patients who require fluid restriction. This is the first time that a concentrated formula has intentionally been given at full rate with the aim of increasing calorie delivery in the knowledge that over a 24 hour period the full target volume of feed is rarely given. We confirmed the safety & efficacy of this in a phase II multicentre, double-blind, randomised controlled trial, which has shown promising beneficial results. It is now logical, opportune & important to determine if this strategy can improve clinical outcomes including survival in a pivotal phase III double-blind, multicentre, randomised controlled trial.

The primary endpoint is survival at 90 days.

Secondary endpoints include: Death at ICU discharge, hospital discharge, 28 days, and 180 days; length of stay in ICU and hospital; ventilator free days, dialysis free days and inotrope free days, all to day 28; functional outcomes at, 180 day (EQ-5D-5L; Australian Work Force Survey; or WHODAS2.0 or Adelaide Activities Profile). All data will be analysed using the intention-to-treat principle.

Management Committee: Marianne Chapman (Co-Chair), Sandra Peake (Co-Chair), Rinaldo Bellomo, Andrew Davies, Adam Deane, Suzie Ferrie, Frank van Haren, Michael Horowitz, Sally Hurford (Project Manager), Theodore Iwashyna, Kylie Lange, Lorraine Little (Project Manager), Edward Litton, Diane Mackle (Project Manager), Stephanie O’Connor, Jeffrey Presneill, Emma Ridley, Vanessa Singh, Patricia Williams and Paul Young.

Administering Institution: ANZIC Research Centre, Monash University

Collaborators: The National Health & Medical Research Council - Centre of Research Excellence for the Translation of Nutritional Science into Good Health (NHMRC CREnutrition)

Sample Size: 4000 patients

Funding:

| National Health and Medical Research Council | A$3,534,236 |
| Health Research Council of New Zealand - Project Grant | NZ$1,200,000 |

Project Status: TARGET’s rapid recruitment continues, over 1,000 patients were enrolled in the past 3 months. Total recruitment stands at 2500 out of the planned 4000. There have been no major issues with the conduct of the trial. There has not been an untoward number of SAEs reported. At the current recruitment rate (2.60 patients per week / 334 patients per month) recruitment will be completed in December 2017.

Interim analysis for 1,500 patients to Day 90 is due in August 2017; the DSMC meeting will be held in September 2017.

The third and final shipment of TARGET EN arrived at Sydney from Fresenius Kabi Deutschland GmbH in July 2017.

Approval was granted by the manufacturer for a three month extension on the shelf life for TARGET EN that expires 31 July 2017. The extension ensures that we will use all of the second production products.

Jane Parker and Alex Poole were employed in March and July respectively to support the management of TARGET at ANZIC-RC.

Clinical Trial Registration No: NCT02306746

Contact: Marianne Chapman
(marianne.chapman@sa.gov.au)
ADRENAL Adjunctive corticosteroid treatment in critically ill patients with septic shock

Septic shock is the result of an infection, which triggers an inflammatory response that causes a decrease in blood pressure and subsequently one or more organ failures. About a quarter of the people who suffer septic shock that is not rapidly reversed, will die.

Whether steroids are useful or not in the treatment of septic shock has been studied for more than 50 years. Previous research has suggested that the use of low dose steroid may have short term benefits in improving the circulation. However, there is no agreement amongst doctors around the world about whether treatment with or without low dose steroids improves the overall recovery and survival in patients with septic shock.

The purpose of this study is to find out whether adult patients admitted to the Intensive Care Unit with septic shock who are given hydrocortisone 200mg compared to placebo daily for 7 days continuous intravenous infusion while in intensive care, will have an improved rate of survival 90 days later. The study will include 3800 adult intensive care patients who have septic shock. The primary outcome is all cause mortality at 90 days after randomisation. Secondary endpoints include shock resolution, organ failure scores, 28 day mortality and Quality Adjusted Life Years (QALY).

Management Committee: Bala Venkatesh (Chair), Yaseen Arabi, Rinaldo Bellomo, Jeremy Cohen, Maryam Correa, Simon Finfer, Parisa Glass, Meg Harward, Chris Joyce, Colin McArthur, John Myburgh, Anders Perner, Dorrilyn Rajbhandari (Project Manager), Andrew Rhodes and Steve Webb.

Administering Institution: The George Institute for Global Health

Sample Size: 3800 patients

Funding:

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<td>Health Research Council of New Zealand - Project Grant</td>
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Project Status: Study Recruitment of the 3800th patient was completed on 21st April 2017. Study follow up continues and in combination with data cleaning. We expect a database soft lock for the primary out in the next month. The data will be pulled and analysed as per the published Statistical analysis plan.

The last patient follow up at six months is due on the 21st October 2017. A Health Economic Analysis will be completed including the quality of life information.

ADRENAL Consent Substudy

A multicentre, prospective, observational study of the process of obtaining consent from potential participants or their substitute decision-makers in the adjunctive corticosteroid treatment in critically ill patients with septic shock (ADRENAL) Study

The ADRENAL Consent Study is a multicentre, prospective, observational study which aims to describe the process through which written informed consent is sought from potential participants or their substitute decision-makers for the adjunctive corticosteroid treatment in critically ill patients with septic shock (ADRENAL) Study. The ADRENAL study is a randomised controlled trial of the effect of hydrocortisone on mortality in critically ill patients with septic shock.

Aims: 1. To describe the rates of consent for enrolment and continued participation in the ADRENAL Study. 2. To describe professional characteristics of the person seeking consent and the contextual features of the consent encounter, including coenrolment and readability of the information and consent form. 3. To determine the time required by research coordinators to obtain a consent decision from potential ADRENAL participants or their substitute decision-makers.

Management Committee: Heidi Buhr (Chair), Deborah Cook, David Gattas, Julie Potter, Dorrilyn Rajbhandari, Kelly Thompson, Bala Venkatesh and Leonie Weisbrodt.

Funding:

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<tr>
<td>Intensive Care Foundation</td>
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Project Status: The parent trial, ADRENAL, completed patient recruitment on 21 April 2017. To date 1940 ADRENAL Consent Study CRFs have been entered in the database; data entry at sites is not yet complete. Data analysis will commence once data entry is complete.

Contact: Heidi Buhr (heidi.buhr@sswahs.nsw.gov.au)
ARISE Economic Evaluation  
Economic evaluation of resuscitation in sepsis

Resources in the healthcare system are scarce and there is a constant challenge to maximise health benefits to patients within the available resources. This is particularly relevant in the intensive care setting where there is an increasing demand for services coupled with newer and more expensive technologies. Economic evaluations enable the clinical and resource effects of healthcare interventions to be estimated, aiding decisions about which therapies to implement in an environment of heightened cost-consciousness and where there are competing demands for limited health care resources. The conduct of economic evaluations alongside clinical trials produces high quality evidence on comparative outcomes and costs of new therapies prior to their introduction. In the critical care setting, parallel studies with economic and clinical endpoints provide an accurate estimate of the cost-effectiveness of new therapies in this area before their widespread introduction. The aim of this study is to determine the cost-effectiveness and cost-utility of protocolised resuscitation compared to usual care in patients presenting to Emergency Departments with severe sepsis. The study is conducted alongside the ARISE RCT and will use an analytic timeframe of one year to compare the cost per life year gained and the cost per quality adjusted life year (QALY) gained from the alternative treatments. A representative subgroup of 200 patients (100 EGDT®, 100 standard care) from the ARISE-RCT form the group of patients who contribute both cost and quality of life (QoL) data for the economic evaluation.

Management Committee: Alisa Higgins (Chair and Project Manager), Rinaldo Bellomo, Jamie Cooper, Anthony Delaney, Anthony Harris, Belinda Howe, Alistair Nichol, Sandy Peake and Tricia Williams

Administering Institution: ANZIC Research Centre, Monash University

Collaborators: Centre for Health Economics, Monash University

Sample Size: 1540 patients

Funding:

| Intensive Care Foundation | $100,000
| Public Health PhD Scholarship | $85,827 |

Project Status: Quality of life data collection and costing data collection has been completed. Quality of life data has been analysed and costing data is currently being analysed.

Clinical Trials Registration No: ACTRN1260800053325 & NCT00975793 (as per ARISE)

Contact: Lisa Higgins (lisa.higgins@monash.edu)

Baby SPICE Pilot Study  
Sedation practice in paediatric intensive care in Australia and New Zealand

Intravenous sedatives and analgesics are commonly administered to mechanically ventilated children, however there is substantial variability in sedation practices in different intensive care units and in different countries around the world. The BabySPICE pilot study will evaluate the hypothesis that a sedation regimen based on safe, light sedation with dexmedetomidine as the primary sedative agent and in which benzodiazepine use is minimised, will lead to improved patient centred outcomes. The purpose of the BabySPICE Pilot RCT is to obtain preliminary data on the feasibility and safety of conducting a study that tests this hypothesis.

This is a pilot prospective randomised controlled trial that will be conducted in six tertiary paediatric intensive care units in Australia and New Zealand and will recruit 60 patients with a maximum of 15 patients from each participating site. The study will recruit patients ventilated for less than 12 hours, who are expected to remain ventilated at least 24 hours after enrolment AND need immediate and ongoing sedation. Patients will be recruited into one of two study groups. The intervention arm will receive dexmedetomidine as the primary agent, with the addition of second line sedatives as required. The use of benzodiazepines in this arm will be minimized and clonidine will not be used concurrently with dexmedetomidine. The control arm will have sedation according to usual practice as chosen by the treating clinician. This may include the use of clonidine according to standard unit practice but can only include dexmedetomidine as a last resort if all other agents have failed. In both groups, the default sedation level is light sedation, as defined by a target State Behaviour Scale (SBS) of -1 to +1, unless otherwise specified by the treating clinician. The primary outcome measure for the pilot study is to demonstrate separation between the intervention group (GpDex) and a ‘wildtype’ (usual practice) control group (GpStd) with respect to the proportion of patients achieving light sedation (SBS -1 to +1) in the first 48 hours of sedation in intensive care. Information from the Pilot RCT will be used to design a subsequent phase III trial.

Management Committee: Simon Erickson (Chair / Project Manager), Brian Anderson, John Awad, John Beca, Carmel Delzoppo, Marino Festa, Debbie Long, Mary Lou Morritt, Johnny Millar, Yahya Shehabi, Claire Sherring and Tony Slater.

Administering Institution: Princess Margaret Hospital, Perth

Collaborators: Hospira Ltd (Melbourne, Australia)

Sample Size: 60 patients

Funding:

| Hospira Ltd. Unrestricted Grant | $15,000
| Princess Margaret Hospital for Children Research Foundation Seeding Grant | $20,000 |
Project Status: Recruitment and data cleaning has been completed

Data is currently being analysed and manuscript is in preparation.

Clinical Trials Registration No: ACTRN12614000225617

Contact: Simon Erickson
(Simon.Erickson@health.wa.gov.au)
Debbie Long (DebbieA_Long@health.qld.gov.au)

Baby SPICE Pilot Study continued

BLISS
Bacteraemic load and survival in septic patients

It is established that earlier and correct antibiotic therapy improves survival for patients with septic shock. This study will evaluate a new technique, in which a molecular diagnostic method, termed PCR, is used to measure the amount of DNA from bacteria in the bloodstream of patients with septic shock. Different pathogenic bacteria have different sequences of DNA, and these differences are utilised to identify the type of bacteria that are present. It is known that the body’s immune response (mediated by proteins called cytokines) is the process by which recognition of infection by the body leads to the organ damage that characterises the process of sepsis. It is also known that patients’ genes influence their immune response to infection, the severity of septic shock, and a patient’s susceptibility to septic shock. BLISS aims to measure the bacterial DNA load and cytokine response over time in the first 72 hours and determine the diagnostic utility of this approach and the relationship/s between these parameters and the risk of death.

Management Committee: Jon Iredell (Chair), Michael Bailey, Simon Brown, Miranda Hardie, Masrura Kabir (Project Manager), Vineet Nayar, Alistair Nichol, Ian Seppelt, Keith Stanley and Steve Webb.

Administering Institution: infectious Disease and Microbiology, Westmead Hospital, University of Sydney

Collaborators: University of Sydney; University of Western Sydney; Monash University

Sample Size: 200

Funding:

National Health and Medical Research Council Project Grant $647,738

Project Status: Repeat analysis of the data is underway.

Clinical Trials Registration No: ACTRN12611000637943

Contact: Jon Iredell (jon.iredell@sydney.edu.au)

Delayed Discharge Study
Evaluation of clinical outcomes and cost consequences of delayed discharge from intensive care: A multicentre prospective observational study

A significant minority (18 - 28% during 2012) of patients in Australian intensive care units experience delays in their discharge from the ICU to the general ward. The effects of delayed discharge from the intensive care unit are not known but may be associated with disturbances in sleep, delirium, nosocomial infections and prolonged length of hospital stay. In addition, delayed ICU discharge is a significant contributor to waste in the health care system.

Given these concerns, it is important to assess the exact incidence, duration and the impact of delayed discharge on clinical and economical outcomes. This will aid in improving not only the clinical outcomes but also efficient use of critical care resources. In this 3-month prospective observational study involving five ICUs in Victoria, we aim to assess the clinical and economic effects of delayed discharge from ICU.

Management Committee: Ravi Tiruvoipati (Chair), John Botha and David Lewis.

Administering Institution: Frankston Hospital, Peninsula Health

Project Manager: Sharon Allsop

Sample Size: 1000 patients

Funding:

Australian and New Zealand Intensive Care Society Safety, Quality Audit & Outcomes Grant $15,000

Project Status: Publication of the study results will occur in July 2017.

Contact: Ravi Tiruvoipati (travindranath@hotmail.com)
iPIT3 and iPIT3 NZ – The Influenza Pandemic Survey
A survey of Australian and New Zealand public opinion on methods to triage intensive care patients in an influenza pandemic

This study is a voluntary survey using a written questionnaire posted to a random sample of 2000 registered voters listed on the Australian Electoral Commission (AEC) electoral roll, and 2000 registered voters listed on the New Zealand Electoral Commission (NZEC) electoral roll.

The questionnaire will ask participants about their views on the use of six different methods to decide which patients should be allowed access to intensive care resources during a major influenza pandemic, where demand for these resources significantly exceeds supply.

The primary outcome measure will be which of six methods do respondents most prefer to use to allocate intensive care resources during a major influenza pandemic. The secondary outcome measures will be the respondent’s measure of fairness for each of the six methods.

Management Committee: Winston Cheung (Chair / Project Manager), Nikki Blackwell, Fiona Blythe, Debra Chalmers, Shannon DeMonte, Kalpesh Gandhi, Claire Hooker, Ian Kerridge, Mark Kol, Shay McGuinness, John Myburgh, Vasi Naganathan, Priya Nair, Rachael Parke, Michael Parr, Nicholas M Saunders, Manoj Saxena, Ian Seppelt, and Govindasamy Thanakrishnan.

Administering Institution: Concord Repatriation General Hospital

Collaborators: Centre for Values, Ethics and the Law in Medicine, School of Public Health, Sydney Medical School, University of Sydney; Centre for Education and Research on Aging, Concord Repatriation General Hospital; Division of Critical Care and Trauma, The George Institute for International Health

Sample Size: 2000 questionnaires distributed in Australia 2000 questionnaires distributed in New Zealand

Project Status: Study was finished in March 2016. Manuscript currently in press – Critical Care and Resuscitation (September 2017).

Contact: Winston Cheung (Winston.Cheung@sswhs.nsw.gov.au)

PINBALL Inception Cohort Study
Prophylactic intra-aortic balloon counterpulsation in high-risk cardiac surgery: an inception cohort study

PINBALL is a prospective observational study investigating current management strategies and outcomes of high risk patients undergoing CABG surgery. It is part of a program of research ultimately designed to determine the feasibility of an RCT of prophylactic IABP for high risk patients undergoing CABG surgery.

Management Committee: Ed Litton (Chair), Frances Bass, Anthony Delaney, Mark Edwards, Graham Hillis, Silvana Marasco, Dan Mullany, Paul Myles, Chris Reid and Julian Smith.

Project Manager: Nicole Marrow

Collaborators: Australian and New Zealand Cardiac and Thoracic Surgeons Database Program

Sample Size: 135 patients

Funding:

Cardiothoracic Surgery Research Grant Scheme, Sydney Medical School, The University of Sydney, NSW $50,000

Intensive Care Foundation $34,000

Heart Foundation Vanguard Grant $72,000

Project Status: 247 patients are enrolled so far. We are 53 short of the originally planned sample size. We will endeavour to enrol these remaining 53 patients over the next 2-3 months.

Project Status: The study has been completed and the results manuscript is being prepared.

Contact: Ed Litton (ed_litton@hotmail.com)
PINBALL Pilot
Prophylactic intra-aortic balloon counterpulsation in high-risk cardiac surgery: A pilot randomised controlled trial

The PINBALL Pilot RCT is a multicentre trial that will assess the feasibility of conducting a definitive phase III RCT of prophylactic IABC in addition to standard care, versus standard care without prophylactic IABC for high-risk patients undergoing cardiac surgery. We propose to conduct a prospective multicentre pilot study of high-risk patients undergoing cardiac surgery in order to assess the feasibility of a phase III RCT. The primary hypothesis is that a phase III RCT of prophylactic IABC in high-risk patients undergoing cardiac surgery is feasible on the basis of achieving threshold criteria for recruitment rates, delivery of the assigned intervention and study follow up.

The primary outcome will be study feasibility. A phase III RCT of prophylactic IABC in high-risk patients undergoing cardiac surgery will be deemed feasible if all three of the following criteria are met:
- ≥ 2 participants recruited per site per month
- ≥ 90% of participants receiving the assigned intervention preoperatively
- ≥ 90% of participants with complete follow up

Management Committee: Ed Litton (Chair), Frances Bass, Anthony Delaney, Graham Hillis, Nicole Marrow (Project Manager), David McGiffin, Shay McGuinness, Chris Reid, Julian Smith and Liz Yarad.

Collaborators: Australian and New Zealand Society of Cardiac and Thoracic Surgeons Database Program; MAQUET; Teleflex.

Sample Size: 40 patients

Funding:

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Project Status: Follow up complete and data being analysed with view to preparing manuscript for publication. Plan for provisional results to be presented at the CTG Winter Research Forum 2017.

Contact: Ed Litton (ed_litton@hotmail.com)

Clinical Trial Registration No: ACTRN 12614000712606

POLAR-BEAR
The prophylactic hypothermia trial to lessen traumatic brain injury basal energy assessment research

POLAR BEAR is a sub-study of the POLAR trial. POLAR BEAR will investigate the effect of prophylactic hypothermia on metabolic rate and the provision of nutrition to patients with traumatic brain injury. Those with hypothermia will be compared to those who are normothermic to see if there is any difference in metabolic rate or feeding outcomes. The primary outcome is the average energy expenditure over the first 72 hours post enrolment with other areas of interest being nutrition provision in these patients. The results will inform the intensive care community of the metabolic process and feeding challenges in this group. This will be particularly important if prophylactic hypothermia becomes routine practice in the management of patients with traumatic brain injury.

Management Committee: Emma Ridley (Chair / Project Manager), Michael Bailey, Stephen Bernard, Jamie Cooper, Andrew Davies, Lyn Gillanders, Colin McArthur, Lynette Newby and Tony Trapani.

Funding:

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<td>Alfred Foundation</td>
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Project Status: The study is complete but is awaiting the completion of the parent study (POLAR).

Contact: Emma Ridley (emma.ridley@monash.edu)
The optimal fluid regimen, haemodynamic (or other) targets and fluid choice (colloid or crystalloid) for patients undergoing major surgery are based on rationales that are not supported by strong evidence. Practices vary substantially; guidelines are vague, small trials and meta-analyses are contradictory. The strongest and most consistent evidence, and biological plausibility regarding tissue oedema, supports a restrictive fluid strategy. There is less (and more contradictory) evidence supporting goal-directed therapy using a flow-directed device and/or dopexamine, and use and choice of colloids. A large, definitive clinical trial evaluating perioperative fluid replacement in major surgery is required.

We are thus proposing to study the effects of fluid restriction (vs. liberal), and the possible effect-modification of goal-directed therapy using either oesophageal Doppler or Flotrac® and colloid replacement. The first will be randomly assigned; the latter will be measured covariates according to local practices (and beliefs).

Management Committee: Paul Myles (Chair), Rinaldo Bellomo, Thomas Corcoran, Chris Christophi, Andrew Forbes, Philip Peyton, David Story and Sophie Wallace (Project Manager).

Administering Institution: Monash University

Sample Size: 2800 patients

Funding:

- National Health and Medical Research Council Project Grant $2,384,173
- Health Research Council of New Zealand Project Grant NZ$770,668

Project Status: Trial recruitment of 300 participants is complete and awaiting the completion of the 12 month follow up on 6th September 2017.

Clinical Trial Registration No: NCT01424150

Contact: Paul Myles (P.Myles@alfred.org.au)
The RENAL substudy of POLAR

Hypothermia has been shown to provide a protective effect after renal injury in animal models. However, there has been little clinical investigation of the renal effects of hypothermia. Taking advantage of the opportunity offered by the POLAR multicentre randomised controlled trial of hypothermia in traumatic brain injury (TBI), this substudy will investigate whether in patients with TBI: a) early and sustained hypothermia reduces the severity, incidence and duration of Acute Kidney Injury (AKI); b) the release of biomarkers of kidney injury including NGAL is reduced by cooling compared to maintenance of normothermia; c) the release of biomarkers of kidney injury including NGAL will predict the severity, occurrence and duration of AKI in patients with TBI.

This study provides a unique opportunity to evaluate the benefit of early and sustained hypothermia as a treatment for AKI and may provide insight into the mechanisms of action of hypothermia in AKI. Study of the biomarkers will provide unprecedented insight into their release and performance as markers of AKI and their response to therapy.

Management Committee: Edward Litton (Chair), Stuart Baker, Wendy Erber, Shannon Farmer, Janet Ferrier, Craig French, David Hawkins, Alisa Higgins, Axel Hofmann, Bart De Keulenaer, Julie McMorrow, John Olynyk, Toby Richards, Simon Towlar and Steve Webb.

Management Committee: Elizabeth Moore (Chair / Project Manager), Michael Bailey, Rinaldo Bellomo and Alistair Nichol.

Administering Institution: ANZIC Research Centre, Monash University

Collaborators: Robert Atkins

Sample Size: 500 patients – POLAR-AKI; 53 patients – POLAR-Biomarkers

Funding:

<table>
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<tr>
<th>Funding Source</th>
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<tr>
<td>Intensive Care Foundation (joint funding for EPO-TBI and POLAR renal substudies)</td>
<td>$13,553</td>
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</tbody>
</table>

Project Status: Results are embargoed and the substudy cannot be completed until the POLAR parent study is published.

Contact: Elizabeth Moore (elizabeth.moore@monash.edu)

Clinical Trial Registration No: ACTRN12609000764235 (POLAR Study)

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SMARRT

Sampling antibiotics in renal replacement therapy

Inadequate antibiotic therapy is a critical determinant of survival in patients admitted to an Intensive Care Unit (ICU) with overwhelming infection requiring renal replacement therapy (RRT). Guidelines for effective dosing are not available because RRT can be vastly different between ICUs, resulting in significantly different antibiotic pharmacokinetics. Developing an evidence-based antibiotic dosing guideline is of global significance and should be considered a priority to improving clinical outcomes for patients requiring RRT that have infections.

The aim of the SMARRT Study is to develop optimised antibiotic dosing guidelines for ICU patients with life-threatening infections that account for patient characteristics and the type of RRT they are prescribed. This will be achieved through completion of the following aims:

1. Describe detailed demographic, clinical, RRT and plasma antibiotic concentration-time data in a large ICU patient cohort.
2. Perform a robust pharmacokinetic and statistical analysis of the data collected in Aim 1 to develop an enhanced preliminary prediction algorithm for antibiotic dosing.

Management Committee: Jason Roberts (Chair), Rinaldo Bellomo, Gordon Choi, Louise Cole, Renae Deans (Project Manager), Melissa Lassig-Smith, Jeffrey Lipman, Sanjoy Paul, Sandra Peake, Michael Roberts, Therese Starr, Dianne Stephens and John Turnidge.

Administering Institution: The University of Queensland

Sample Size: >450 patients

| National Health and Medical Research Council | $1,034,979 |

Project Status: Official sign off by all sites that successfully recruited patient and entered data occurred in June 2017. Data analysis continues at this time.

Clinical Trial Registration No: ACTRN12613000241730

Contact: Jason Roberts (j.roberts2@uq.edu.au)
TRANSFUSE
Standard issue transfusion versus fresher red blood cell use in intensive care - a randomised controlled trial

Randomised controlled trial of 5000 critically ill patients who will be given either the freshest available red blood cells or standard issue red blood cells when they require a blood transfusion in the ICU. The study aim is to determine whether, compared to standard care, transfusion of the freshest available allogenic red blood cells decreases patient mortality.

Patients will be screened in the ICU and randomized using a web based system when they first need a blood transfusion. The blood service will then deliver RBC according to the randomization as either freshest available (“back of the fridge”) or standard care (“front of the fridge”). The primary endpoint is 90 day mortality; secondary endpoints are ICU, hospital and day 28 mortality, ventilation free days by day 90, ICU free days by day 90, duration of renal replacement therapy and haemodynamic support.

Management Committee: Jamie Cooper (Chair), Bridget Ady (Project Manager), Cecile Aubron, Michael Bailey, Rinaldo Bellomo, Craig French, Dash Gantner, David Irving, Maija Kaukonen, Colin McArthur, Zoe McQuilten, Phillip Mondy, Lynne Murray, Alistair Nichol, Neil Orford, Ville Pettila, Louise Phillips (retired), Jeff Presneill, Michael Reade, Alison Street (retired), Shirley Vallance and Andrew Webb.

Administering Institution: ANZIC-RC, Monash University

Collaborators: Health Research Council of New Zealand; National Blood Authority; Australian Red Cross Blood Service; Transfusion Outcomes Research Collaborative

Sample Size: 5000 patients

Funding:

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<th>Source</th>
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<td>National Health and Medical Research Council</td>
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<td>Health Research Council of New Zealand</td>
<td>NZ$775,723</td>
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<td>Australian Red Cross Blood Service</td>
<td>$300,000</td>
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<td>Health Research Board Ireland (Definitive Intervention Award)</td>
<td>€799,999</td>
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<tr>
<td>Health Research Board Ireland (Clinical Trial Network Award)</td>
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Project Status: TRANSFUSE data collection, cleaning, database lock and statistical analysis is complete.

The TRANSFUSE study manuscript will be progressed over the coming period with presentation of results to the intensive care community and the public at the ANZICS CTG Winter Research Forum, Queenstown on 23 August 2017, as well as journal publication to be released simultaneously with results presentation at the European Society of Intensive Care Medicine Conference in Vienna from 23 - 27 September 2017.

Contact: Bridget Ady (bridget.ady@monash.edu)
Vanessa Singh (vanessa.singh@monash.edu)

Clinical Trial Registration No: ACTRN12612000453886
SUPPORTED STUDIES
Severe Community Acquired Pneumonia (severe CAP) is a major cause of mortality. In Australia, CAP is responsible for more than 7000 ICU admissions and 1400 deaths each year. The annual direct cost of ICU care of these patients is in the order of $200 million. The existing evidence-base, for treatment of patients with Severe CAP is limited, reflected in variation in Australian and international guidelines as well as variation in practices including choice of antibiotic, choice of ventilator strategy, and use of immune modulating agents. Accordingly, we have designed a multi-centre randomised controlled platform trial utilising Bayesian adaptive methods for 2800 Australian and New Zealand ICU patients with severe CAP to be analysed in conjunction with patients enrolled in other locations. Making it the largest study on severe CAP ever conducted.

The primary objective is to determine the impact on 90 day mortality of: 1) Alternative antibacterial strategies; 2) Administration of azithromycin, acting as an immunomodulatory agent; 3) Administration of a Corticosteroid; & 4) Following on from these 3 initial research questions to evaluate additional interventions over the life-time of the platform.

The secondary objective is to provide Australia and New Zealand's contribution to the pre-prepared global research response to future pandemics of Severe Acute Respiratory Illness (SARI) by seamlessly and rapidly (within days) adapting the platform to test the most promising interventions for pandemic infection and providing trial results during the first wave of a pandemic.

The primary outcome measure is 60 day all-cause mortality. Other outcome measures include the development and resolution of organ failures; Acquisition of resistant organisms including C. difficile; ICU and hospital length of stay; and Post-Hospital outcomes Quality of life using the EQSD and Disability status using the WHO-DAS assessed at 1 year. Once completed this landmark trial will provide definitive evidence to change clinical practice in Australia and worldwide. This trial will also introduce platform trials to the Australian and international research community.

Management Committee: Steve Webb (Chair), Allen Cheng, Lennie Derde, Andrew Forbes, David Gattas, Stephane Heritier, Lisa Higgins, Peter Kruger, Ed Litton, Colin McArthur, Shay McGuinness, Lynnette Murray, Alistair Nichol, Genevieve O'Neill (Project Manager - Australia), Rachael Parke, Jeff Presneill, Anne Turner (Project Manager - New Zealand) and Paul Young comprise the ANZ Regional Management Committee.

Administering Institutions: ANZIC Research Centre, Monash University and the Medical Research Institute of New Zealand

Funding:

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<tr>
<td>National Health and Medical Research Council Project Grant</td>
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<td>Health Research Council of New Zealand - Programme Grant</td>
<td>NZ$34,800,000</td>
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<tr>
<td>European Union FP7-HEALTH-2013-INNOVATION</td>
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Project Status: REMAP-CAP has HREC approval in New Zealand with sites currently in discussion to participate. An NMA HREC application has been submitted in Australia and sites expected to be confirmed in the near future. CRFs and database development are in progress.

It is anticipated that vanguard sites in Australia and New Zealand will be ready to begin participant recruitment in late 2017.

Study tools and educational material are in development.

Clinical Trial Registration No: NCT02735707

Contact: Steve Webb (steve.webb@uwa.edu.au)

SuDDICU study

A cluster randomised controlled trial of the clinical effectiveness and cost-effectiveness with a contemporaneous study of the ecological impact of selective decontamination of the digestive tract in critically ill patients treated in intensive care units

Selective Decontamination of the Digestive Tract (SDD) is a treatment designed to reduce the risk of infection and improve survival for critically ill patients, involving the deliberate application of antibiotics and antifungal drugs to the throat and their instillation into the stomach, combined with a short course of intravenous antibiotics. Although many trials suggest that SDD works, the research results have not been convincing enough to lead to the widespread uptake of SDD. Clinicians are concerned that SDD will increase antibiotic resistance amongst endemic bacteria, despite evidence that this does not happen. As a result, SDD is not currently widely practiced.

This study will be the definitive trial to resolve this uncertainty. We will conduct a cluster randomised controlled trial (cRCT) for 12 months in 100 ICUs in Australia, NZ, Canada, Germany, Brazil and the UK, recruiting 23,600 critically ill mechanically ventilated patients. Mortality rates will be compared between the two groups and antibiotic resistance levels will be evaluated in samples from all patients prior to, during and after the trial. In addition we will conduct a simultaneous ecology study of all ICU patients (whether or not enrolled in the SuDDICU cRCT), examining about 70,000 patients.

This trial will provide a definitive answer to a fundamental question in intensive care medicine - does SDD reduce critically ill patients’ risk of dying without increasing antibiotic resistance rates? If SDD is found to be effective
without increasing antibiotic resistance, the study will have a global impact, leading to improved survival and reduced infection rates in critically ill patients. The results of this study will change practice and be of immense value to clinicians, policy makers and regulators.

ANZ Management Committee: John Myburgh (Co-Chair), Ian Seppelt (Co-Chair), Farah Al-Beidh, Laurent Billot, Maryam Correa (Project Manager), Brian Cuthbertson, Joshua Davis, Simon Finfer, Parisa Glass, Anthony Gordon, Jon Iredell, Stephen Jan, Jennene Miller, Coleman Taylor and Paul Young.

Administering Institution: The George Institute for Global Health

Sample Size: 6,900 in x-cRCT

Funding:

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<td>National Health and Medical Research Council</td>
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<tr>
<td>National Health and Medical Research Council [metagenomic and resistance substudy]</td>
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<tr>
<td>Canadian Institutes of Health Research</td>
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Project Status: Australian sites commencing pretrial ecology data collection phase. Main trial commencement delayed three months because of issues with colistin stability and need to confirm a reliable 28 day shelf life of the suspension.

SuDDICU is again a multinational x-cRCT. UK sites will be joining as part of the Australian funded trial. In parallel Canadian sites will be participating as part of a Canadian funded arm of the trial. The Canadian sponsor is the Sunnybrook Health Sciences Centre, the Australian and UK sponsor is the George Institute for Global Health.

Barring any further delays with drug preparation the trial will finally be underway in December 2017

Clinical Trial Registration No: ACTRN12615000411549 & NCT02389036

Contact: Ian Seppelt (ian.seppelt@sydney.edu.au)
The BALANCE Study

Bacteremia antibiotic length actually needed for clinical effectiveness: a pilot rct

Bloodstream infections are a common and serious problem, affecting 15% of critically ill patients and resulting in increased mortality. Optimal antibiotic treatment duration for these patients has not been studied. The aim of this study is to determine optimal treatment duration for bloodstream infections; maximizing clinical cure while minimizing antimicrobial treatment harms.

The BALANCE pilot RCT is to determine if it feasible to perform the main BALANCE RCT among critically ill patients with bloodstream infection to determine whether shorter duration antibiotic therapy (7 days) is as effective as longer duration antibiotic therapy (14 days)?

We hypothesize that the RCT will be feasible, as determined by 1) Adherence to antibiotic treatment protocols, and 2) Timely recruitment.

Management Committee: Nick Daneman (Co-Chair), Rob Fowler (Co-Chair), Deborah Cook, Rick Hall, John Musceder, Ruxandra Pinto, Steven Reynolds and Asgar Rishu (Project Manager).

Administering Institution: Sunnybrook Research Institute

Collaborators: Canadian Critical Care Trials Group; ANZICS Clinical Trials Group; Centre hospitalier universitaire vaudois, Lausanne, Switzerland; King Abdulaziz Medical City Riyadh, KSA

Sample Size: 115

Funding:

- Canadian Institute of Health Research (CIHR) $100,000
- Ministry of Health and Long-Term Care Alternate Funding Plan (AFPI), Sunnybrook Hospital, Ontario, Canada $81,894
- Ministry of Health and Long-Term Care Alternate Funding Plan (AFPI), Kingston Hospital, Ontario, Canada $65,000
- Ministry of Health and Long-Term Care Alternate Funding Plan (AFPI), London Health Sciences, Ontario, Canada $69,800
- Health Research Council New Zealand Project Grant NZ $1,190,000

Project Status: Recruitment for BALANCE is ongoing.

Clinical Trial Registration No: NCT02261506

Contact: Rachael Parke (RParke@adhb.govt.nz)

SPRINT-SARI

Short Period Incidence Study of Severe Acute Respiratory Infection

Severe acute respiratory infection (SARI) continues to be of major relevance to public health worldwide. In the last 10 years there have been multiple SARI outbreaks around the world. The 2009 H1N1 pandemic was estimated to result in more than 200,000 respiratory deaths globally (1-3). The World Health Organization (WHO) defines SARI as an acute respiratory infection of recent onset (within 10 days) requiring hospitalisation, manifested by fever (≥38°C) or a history of fever and cough (4-7). There is international consensus that it is important to undertake observational studies of patients with SARI as an essential component of pandemic and epidemic research preparedness (8, 9).

Due to the severity and communicable nature of SARI - as demonstrated though the 2009 H1N1 pandemic, compounded with annual incidence of SARI during seasonal influenza epidemics - it is clear that investigation of SARI can provide large scale benefits to improve public health. Rapidly obtaining accurate information on the epidemiology of SARI and providing information on how these patients are currently diagnosed and treated is essential.

The primary aim of this study is to establish a research response capability for a future epidemic / pandemic through a global SARI observational study. The secondary aim of this study is to investigate the descriptive epidemiology and microbiology profiles of patients with SARI. The tertiary aim of this study is to assess the Ethic, Administrative, Regulatory and Logistic (EARL) barriers to conducting pandemic research on a global level.


Administering Institution: ANZIC Research Centre, Monash University

Project Manager: Maya George
Collaborators: International Severe Acute Respiratory and Emerging Infection Consortium (ISARIC)
The Platform for European Preparedness Against (Re-)emerging Epidemics (PREPARE)
The International Forum for Acute Care Trialists (InFACT)
European Society of Intensive Care Medicine (ESICM)

Participating Research Networks: Asian Critical Care Trials Group; Australian and New Zealand Intensive Care Society Critical Trials Group; Australian Society for Infectious Diseases Clinical Research Network; Brazilian Research in Intensive Care Network; Centers for Disease Control and prevention; the Community-Acquired Pneumonia in Unidad de Cuidados Intensivos 3; Canadian Critical Care Trials Group; European Society of Intensive Care Medicine; The Influenza Complications Alert Network (FluCAN); Global Approach to Biology in Response to Infectious Epidemics in Low-income Countries; Gruppo italiano per la Valutazione degli interventi in Terapia; Hellenic Sepsis Study Group; Irish Critical Care Trials Group; Intensive Care National Audit and Research Centre; Intensive Care Society; Institut Pasteur; KEMRI Clinical Trials Facility/Emergency Care Research Group; The Mexican Emerging Infectious Diseases Clinical Research Network; Latin American Critical Care Trials Investigators’ Network; North African Network for ICM Research; Oxford University Clinical Research Unit; Research Network on Respiratory Failure and Artificial Ventilation; Scandinavian Critical Care Trials Group; Sino-International Severe Community-Acquired Pneumonia Consortium; Singapore Infectious Diseases Network; The Toronto Invasive Bacterial Diseases Network; Trial Group for Global Evaluation and Research in Sepsis uk; United States Critical Illness and Injury Trials Group Program for Emergency Preparedness; and World Health Organisation

Project Status: Recruitment is ongoing.

Contact: Steve Webb (steve.webb@uwa.edu.au)
The CTG Point Prevalence Program (PPP) has been running now for nine years and the tenth point prevalence study day was held in August 2016, with nested studies examining pain and pain management in ICU, the prevalence of smoking in patients admitted to ANZ ICUs, pressure injuries and the use of support mattresses in ICU, as well as a repeat of the ongoing fluid resuscitation time series data collection. Data from these study days were presented in Noosa in March 2017 and publications are in progress.

The program continues to be a unique resource allowing investigators to collect prevalence data using single day ‘snapshot’ studies. The value and research output of this program have been recognized and appraised by the CTG research community. A manuscript describing the methodological principles of the PPP has been published and this will be a valuable source of information for future researchers:


Other papers arising from the program have also been published in 2016/2017, and further manuscripts are in preparation:


No PP study day has been held in 2017. This has been a particularly busy year for the ANZICS CTG with many major trials recruiting and for logistic and workload reasons a decision was made to suspend the PPP for a year. There is an intention to continue the PPP with a study day later in 2018 and plans for this will be presented in Noosa in 2018.

The Point Prevalence Management Committee thanks the wonderful sites who have supported the Point Prevalence Program for the past nine years. We couldn’t do it without you.
On behalf of the Intensive Care Research Coordinators Group (IRCIG) members it is with great pleasure that I contribute to the 2016-2017 ANZICS CTG Annual Activity report.

Into our 17th year, the maturity and professionalism of all IRCIG members is to be acknowledged and applauded. With enthusiasm and an eye on safety, our research coordinators play an integral role for the ANZICS CTG. Each research coordinator applies his/her skills at the clinical interface in order to maintain the highest standards of clinical research coordination in our two countries.

This year the Research Coordinators workshop in Noosa was attended by >100 research coordinators and representatives from the three methods centres. I extend, once more, my thanks to Prof Anthony Gordon (Anaesthesia and Critical care, Imperial College, London) and Prof Tracey Bucknall (Professor and Foundational Chair in Nursing, Alfred Health) who both provided valued insights and perspectives in relation to trial management. To all other presenters, well done you did a wonderful job. To all those who would like to present please be in touch as next year’s workshop is fast approaching. For all IRCIG regional representatives I strongly encourage the conduct of region based days/workshops as a valuable means to forge professional and personal friendships with those close at hand.

We are also grateful to the project managers and administrative staff working in the ANZIC RC, The George Institute for Global Health and the Medical Research Institute of New Zealand. The seen and unseen support provided by these methods centres cannot be underestimated. In addition, we acknowledge the financial and administrative support provided to IRCIG by the ANZICS CTG, the CTG Committee, the Executive Officer and Executive Assistant. It really is a team effort.

Finally, I remain extremely grateful for the personal and professional support afforded to me by IRCIG the Executive Committee and the IRCIG Regional Representatives. Each of you does a remarkable job, give generously of your time and provide valued insights; well done.

Office Bearers
Chair: A/Prof Glenn Eastwood, Intensive Care Research Manager, Austin Hospital, VIC
Vice Chair: (to October 2016) Ms Helen Rodgers, Research Coordinator ICU, The Canberra Hospital, ACT
(from March 2017) Ms Naomi Hammond, Research Coordinator, Intensive Care Clinical Research Unit, Royal North Shore Hospital, NSW
Immediate Past Chair: Dr Rachael Parke, Nurse Senior Research Fellow, Cardiothoracic and Vascular ICU/HDU, Auckland City Hospital, NZ
Secretary: Ms Elizabeth Yarad, Research Coordinator, Intensive Care Clinical Research Unit, Royal North Shore Hospital, NSW
IRCIG Email List Moderator: (From July 2016) Mr Jason Meyer, Research Coordinator ICU, Princess Alexandra Hospital ICU, QLD.
(from January 2017) Christina Whitehead Paediatric Study Group Representative: Ms Claire Sherring, Research Coordinator, ICU, Starship Hospital, NZ

Regional Representatives
New South Wales & Australian Capital Territory: (Acting) Ms Heidi Buhr, Research Manager, Intensive Care Service, Royal Prince Alfred Hospital
Queensland: Mr Paul Jarret, Research Coordinator ICU, The Prince Charles Hospital
South Australia: Ms Patricia Williams, Research Coordinator, Critical Care Services, The Queen Elizabeth Hospital
Tasmania: Mr Rick McAllister, Research Coordinator ICU, Royal Hobart Hospital
Victoria: Mrs Samantha Bates, Research Manager, Western Health
Western Australia: Annemarie Palermo, Research Coordinator ICU, Fiona Stanley Hospital
New Zealand: Mrs Eileen Gilder, Specialty Clinical Nurse - Research, Cardiothoracic and Vascular ICU, Auckland City Hospital
In 2016 the ANZICS board decided to create a trainee representative role on all ANZICS committees in an effort to embrace trainees within the intensive care profession. I was thrilled to be selected as the trainee representative on the CTG committee and commenced my two-year term in this role at the start of 2017. I hope to use my time in the position to advocate for and support trainee members with an interest in clinical trials.

While the ANZICS CTG has a well-earned reputation as one of the leading clinical trials groups in the world, there is a relatively poor level of understanding amongst trainees about the CTG. From my discussions with other trainees I have been surprised by how many don’t even know the CTG exists! Engaging with and educating trainees as they progress through training and become early career Intensivists is important for the ongoing success of the CTG. Not only because some of these doctors will form the next generation of critical care researchers, but also because nearly all Intensivists working in Australian and New Zealand units are involved in facilitating the conduct of clinical trials and translating research outcomes into practice. The intensive care research community of course is not limited to doctors, so the same can be said about encouraging and engaging with all clinicians, including nursing and allied health novice researchers.

In 2017 the committee continues to support and encourage novice researchers by requiring at least one early career investigator on the management committee of endorsed studies, by supporting the BASIC Clinical Research course and by introducing a dedicated trainee presentation session at the Winter Research Forum in 2018.

I look forward to working with the CTG in 2018 and would encourage any interested trainees to nominate for the position when I finish my term. I would also encourage any novice researchers with an interest in intensive care clinical research to attend either the annual meeting in Noosa or the winter research forum – novice researchers are most welcome and I believe will greatly benefit from attending these meetings.

Dr Elissa Milford
ANZICS CTG Trainee Representative
This year the Paediatric Study Group (PSG) welcomed Monash PICU (Victoria) as its latest member unit. The PSG continues to exist as a strong advocate for paediatric research within the ANZICS CTG. An excellent and productive relationship continues between the PSG and the ANZPIC Registry. The strength of the collaboration between PSG and ANZPIC will be developed further by current pilot studies of data linkage in NSW and Queensland, which seek to link Registry data with long-term patient outcomes.

The PSG also maintains excellent working relationships with national and international research groups. The THRIVE study is being conducted in collaboration with PREDICT, the Australasian paediatric emergency department research collaborative. International linkages and collaborations with paediatric critical care research groups have included the PALISI network (North America), Canadian Critical Care Trials Group (CCCTG), PICS(UK) Study Group and several other European paediatric intensive care research groups. The PSG is internationally recognised and was invited to contribute to an opinion piece summarising current and future paediatric intensive care international research priorities:


Overall, 2016/17 was another busy and productive year with publication of four PSG/ANZPIC Registry studies, and the CTG Committee endorsement of the "Nitric Oxide on Cardiopulmonary Bypass in Congenital Heart Disease" study for which we currently await the outcome of a national (NHMRC) funding application. In addition, the PSG has taken an important step in closer collaboration with the adult intensive care researcher community by development of a joint study proposal which aims to recruit patients aged 12 years and above in an RCT of buffered salt solutions in severe diabetic ketoacidosis.

Data collection was completed for a multicentre pilot study which sought to randomise sedation practice bundles in ventilated children in intensive care (Baby SPICE, CI D Long, S Erickson), and publication of results is anticipated this year.

The PSG worked together on a number of other studies in 2016/7:

- Moral Distress in PICU: CI C Larsen, J Millar.
- Dexamethasone in Bronchiolitis study: CI B Gelbart
- KIDS THRIVE: randomised controlled study of Transnasal Humidified Rapid-Insufflation Ventilatory Exchange on oxygenation during emergent intubation in children: CI S George, A Schibler

In addition to continuing to progress these studies, the PSG is planning new research studies in 2017/8:

- Nitric oxide on cardiopulmonary bypass. CI A Schibler, W Butt, L Schlapbach
- Paediatric sepsis definitions and outcomes. CI L Schlapbach, M Festa, J Millar
- Malignant Pertussis Prediction Model Validation Study. CI A Ganeshalingam
- Impact of Gestational Age on PICU Outcome. CI S Namachivayam
- Effectiveness of ECMO in Sepsis Management. CI L Schlapbach, G McLaren
- Epidemiology of Paediatric Death in Australasian ICUs. CI K Moynihan, B Gelbart, S Jacobe, J Millar

This year's PSG meetings undertook a new format in order to improve interaction with the wider CTG meeting and to enable opportunities for PSG researchers to work collaboratively in break-out sessions to drive key projects forward. Together with the achievements and work of the group this year, this ongoing collaboration and group cohesion will allow us to build on our recent successes and to enhance the capability of the PSG to meet the future research agenda in critically ill children.

The next meeting of the PSG is planned for Sunday 4th March 2018, immediately preceding the wider ANZICS Clinical Trials Group and IRCIG meetings. All researchers in the CTG interested in contributing to paediatric intensive care research are welcome!
Office Bearers
Chair: Marino Festa (NSW)

Regional Representatives
New South Wales: Gary Williams, Mary-Lou Morriss, Jonathan Egan, Brad Ceely
Queensland: Luregn Schlapbach, Debbie Long
South Australia: Subodh Ganu, Georgia Letton
Victoria: Warwick Butt, Carmel Delzoppo, Felix Oberender, Kellie Fenwick
Western Australia: Simon Erickson, Samantha Barr
New Zealand: Anusha Ganeshalingam, Claire Sherring
Co-opted ANZICS Paediatric Representative: Johnny Millar
Co-opted ANZPIC Registry: Jan Alexandra
Co-opted CTG Representative: Neil Orford

PSG Publications 2016/17


Media coverage:


• ABC (http://www.abc.net.au/news/2017-01-30/indigenous-child-health-icu-research-uq/8218928)


The Winter Research forum returned to Coogee in August 2016 and had over 70 delegates from the CTG Community.

An early theme of the meeting was the continued exploration of neurocritical care research with Andrew Cheng describing a potential point prevalence study to describe current neuromonitoring practice and the use of interventions in neurocritical care across Australia and New Zealand. Andrew Udy described a prospective program of research to investigate intracranial pressure management for traumatic brain injury and updated on the prospective observational study of subarachnoid haemorrhage. Dashiell Gantner described a series of sub studies following the EPO-TBI study.

Interest in measuring long-term outcomes and health economic analyses continues with Lisa Higgins (ARISE long-term outcomes) and Carol Hodgson (ICU Recovery) generating a lot of important discussion and Colman Taylor discussing the challenges of undertaking Health Economic Analyses.

Several study updates were given including clinical trials on nutrition dose (TARGET), oxygen targets (ICU ROX and ICU ROX TRIPS), selective digestive decontamination (SuDDICU), stress ulcer prophylaxis (PEPTIC) and the timing of renal replacement therapy (STAART AKI). New research ideas were also discussed and these included a program of work on analgesia use (Ben Moran), acute kidney injury after cardiac surgery (Yahya Shehabi), high flow nasal CPAP for hypoxic respiratory failure (Rachael Parke) and a feasibility study of remote ischaemic preconditioning after liver transplantation (Samiul Islam).

The meeting continues to be successful, generating lively debate and allowing the collaborative development of important programs of clinical relevant research.

Winter Research Forum 2016 Convenors: Dr Manoj Saxena, Dr Marino Festa
CTG Update
Craig French

A prospective, multicentre, randomised, double-blind placebo controlled, stratified phase III trial of epoetin alfa vs. placebo in critically ill trauma patients (EPO Trauma)
Craig French

Erythropoietin in traumatic brain injury (EPO TBI)
- Substudies
Dashiel Gantner

A point prevalence study of intervention use in neurocritical care
Andrew Cheng

Liberal versus Conservative ICP Management in Traumatic Brain Injury: A proposal for a prospective program of research (LIBERTY TRIAL)
Andrew Udy

Prospective multicentre observational study of aneurysmal subarachnoid haemorrhage in Australasian intensive care (PROMOTE-SAH)
Andrew Udy

Paediatric Study Group (PSG) Update
Marino Festa

The efficacy, cost-effectiveness and ecological impact of selective decontamination of the digestive tract in critically ill patients treated in the ICU (SuDDICU) - Update
Ian Seppelt

The augmented vs. reduced goal for energy delivery in ICU trial (TARGET) - Update
Sandra Peake

Proton pump inhibitors vs. histamine receptor blockers for ulcer prophylaxis therapy in the ICU (PEPTIC) - Update
Di Mackle

Outcome of the SPICE (Early goal directed sedation vs standard care in mechanically ventilated critically ill adults) Appeal
Yahya Shehabi

Remote ischaemic preconditioning for liver transplant (RIPC) feasibility study
Samiul Islam

Acute Kidney Injury in High Risk Cardiac Surgery Patient
Yahya Shehabi

Australasian resuscitation in sepsis evaluation (ARISE) - long term outcomes and quality of life
Lisa Higgins

Recovery at 6 months following critical illness: a multicentre cohort study (ICU-Recovery)
Carol Hodgson

ANZICS Centre for Outcome and Resource Evaluation (CORE) Update
David Pilcher

There is no such thing as a negative trial / Data Sharing Update
John Myburgh

Fluid translating research into practice study (Fluid TRIPS) - DCE Results
Colman Taylor

Lessons learned from undertaking the Crystalloid hydroxyethyl starch trial (CHEST) health economic evaluation
Colman Taylor

An example using Self Controlled Case Series on fluid boluses
Lewis Campbell

Pain Management in ICU Point Prevalence Study
Benjamin Moran

Standard versus accelerated initiation of renal replacement therapy in acute kidney injury (STARRT AKI) - Update (including NEJM & JAMA Papers)
Martin Gallagher

Research Foundations Workshops
Rachael Parke

Randomised evaluation of active control of temperature vs. ordinary temperature management (REACTOR) trial
Paul Young

Intensive Care Research Coordinators Interest Group (IRCiG) Update
A/Prof Glenn Eastwood

adaptive platform trial for severe community acquired pneumonia (AD-SCAP)
Colin McArthur

High Flow Nasal Oxygen Therapy for Acute Hypoxaemic Respiratory Failure
Rachael Parke

A multi-centre, randomised, single blinded clinical trial comparing liberal vs. conservative oxygen therapy in mechanically ventilated adults in the ICU (ICU-ROX) - Update
Di Mackle

ICU-ROX TRIPS study
Di Mackle
The 19th Annual Meeting of the Clinical Trials Group (CTG) was attended by a record number of delegates this year (268 delegates). The meeting included many visiting international as well as local speakers and delegates. Our invited speakers were Professor Anthony Gordon, Chair in Anaesthesia and Critical Care at Imperial College (UK) and Dr Howard Bauchner, the editor of the Journal of the American Medical Association; both made an outstanding contribution to the program. Professor Anthony Gordon gave talks on conducting clinical trials in Europe and phase II outcome measures in clinical trials giving some valuable insights from trials evaluating vasopressin and levosimendan for septic shock. Howard Bauchner discussed the future of Medical publishing including insights into the peer review process, data sharing and open access.

Several new projects that are currently under review for major funding were presented and debated. These included evaluating fluid resuscitation and management with a buffered solution vs. 0.9% saline in diabetic ketoacidosis (Bala Venkatesh), heparin dosing during ECMO (Jamie Cooper) and hypothermia vs. normothermia after cardiac arrest (the TTM2 study: Manoj Saxena). The last presentation re-opened an excellent ongoing discussion on co-enrolment, provoked by the intended harmonisation of the TTM2 and TAME studies being planned.

An important discussion that occurred during the meeting was around the issue of the research capacity of the CTG community in the context of our increasing success as a collaborative group, with several important clinical trials planned for the near future. Paul Young presented some survey data on capacity and recruitment rates across Australia and New Zealand (ANZ) and John Myburgh gave an overview of the history of the CTG from inception, through expansion and consolidation, noting the increased activity that will be needed over the next 5 years. Although it was noted that recruitment rates and capacity at ANZ sites vary considerably, the reasons for the differences are complex and difficult to disentangle. Similar challenges were noted in several other international jurisdictions in which international speakers shared their experiences of conducting clinical research in Canada, several countries in Europe and Scandinavia. Diversity, in particular gender diversity in Management Committees as an example, was also discussed in a presentation reviewing previous CTG publications (Naomi Yarwood). It is also a contemporary issue that, like the capacity issue, needs an active approach both at site level and through the CTG Committee, the Research Methods Centres and Management Committees. These issues will be considered further at the strategic planning day this year by the CTG Committee.

New ideas that were presented included a program of work to develop a core outcome set for aneurysmal subarachnoid haemorrhage (Chris Anderson), proposals for a feasibility study of nicotine replacement and an adaptive trial for traumatic brain injury management (both by Andrew Udy) and projects on central line and cardiopulmonary resuscitation accreditation (Winston Cheung). Ianthe Boden presented a proposal for an observational study of post-operative pulmonary complications and Dr Lisa Smart presented a phase II study of Gelofusin vs. balanced crystalloid, having conducted prior basic science studies in a canine model. Congratulations to Dr Carol Hodgson for winning the inaugural Best New Project presentation for the PREDICT study, a proposal for a registry of critically ill patients to predict disability free survival.

The meeting continues to be a highlight in the Australia and New Zealand Calendar providing a beautiful venue and a broad mix of international and local academics to interact with the CTG community, discussing cutting edge clinical research and providing opportunities for new projects and researchers. The project presentations and several podcast interviews with investigators (conducted by Dr Todd Fraser) are all available for free download from the CTG Member area (http://www.anzics.com.au/clinical-trials-group).

19th Annual Meeting on Clinical Trials in Intensive Care
Convenor: A/Prof Sandra Peake
Randomized, embedded, multifactorial adaptive platform trial for community-acquired pneumonia (REMAP-CAP)
Prof Steve Webb

A multi-centre RCT of an open lung strategy including permissive hypercapnia, alveolar recruitment, and low airway pressure in patients with ARDS (PHARLAP) - Update
A/Prof Carol Hodgson / Prof Alistair Nichol

A multi-centre, randomised, single blinded clinical trial comparing liberal vs. conservative oxygen therapy in mechanically ventilated adults in the ICU (ICU-ROX) Pilot - Results
Ms Diane Mackle

Nicotine Replacement Therapy in ICU
A/Prof Andrew Udy

Ketamine Phase 1 Study
Prof Yahya Shehabi

Randomised evaluation of active control of temperature vs. ordinary temperature management (REACTOR) - Update
Dr Paul Young

Intensive Care Research Coordinators Interest Group (IRCGIG) Update
A/Prof Glenn Eastwood

Conducting a Critical Care Drug Trial in the UK/EU
A/Prof Anthony Gordon

Research Around the Globe
- A/Prof Sean Bagshaw - Canada
- Prof Jan De Waele - Belgium
- Prof Jukka Takala - Switzerland
- Prof Alistair Nichol - Ireland
- Dr Maria Cronhjort - Sweden

20 Years of CTG Publications
Dr Naomi Yarwood

Variability in Recruitment Rates and Research Funding Among ANZ ICUs
Dr Paul Young

CTG Capacity for the Next Five Years
Prof John Myburgh

Panel Discussion
Moderator: A/Prof Craig French
- Prof John Myburgh - The George Institute
- Prof Rinaldo Bellomo - ANZIC-RC
- Dr Paul Young - MRINZ
- A/Prof Sandra Peake - ANZICS CTG
- A/Prof Glenn Eastwood - IRCIG
- Dr Marino Festa - ANZICS PSG

Crystalloid hydroxyethyl starch trial (CHEST) reanalysis
Prof John Myburgh

A pivotal, multicenter, parallel-group, double-blind randomised controlled trial of plasmalyte use vs. saline in adult patients critically ill patients deemed to require fluid resuscitation (PLUS)
Prof Simon Finfer

A Randomised Controlled Trial of Plasmalyte Versus Normal Saline as Resuscitation and Maintenance Fluid Therapy for Patients Presenting with Diabetic Ketoacidosis
Prof Bala Venkatesh

Adjunctive corticosteroid treatment in critically ill patients with septic shock (ADRENAL) - Update
Prof Bala Venkatesh

Early goal directed sedation vs standard care in mechanically ventilated critically ill adults (SPICE) - Update
Dr Yahya Shehabi

Allostasis, the stress response and the SPICE study (ALL-SPICE) - Update
Dr John Moore

Outcome Measures for Phase II Sepsis Trials
A/Prof Anthony Gordon

A registry in critically ill patients to determine predictors of disability-free survival (The PREDICT Study)
A/Prof Carol Hodgson

Inaugural Winner of the Best New Project Presentation

Development of Core Outcome Sets in Critical Care
Dr Chris Andersen

Core Outcome Sets for Critical Care
Dr Bronwen Connolly

How Well Do We Do Dying in Acute Hospitals?
Prof Imogen Mitchell

Treatment of invasively ventilated adults with early activity and mobilisation (TEAM) - Phase III
Prof Carol Hodgson

ANZICS Centre for Outcome and Resource Evaluation (CORE) Update
Ms Sue Huckson / Prof Dave Pilcher

Perioperative Dexmedetomidine in high risk cardiac surgery evaluation (DiCE) Pilot Results & DiCE II Update
Prof Yahya Shehabi

Sedation practice in paediatric intensive care in Australia and New Zealand (BabySPICE) - Update
Ms Debbie Long

Standard issue transfusion versus fresher red blood cell use in intensive care – An RCT (TRANSFUSE) Update
Prof Jamie Cooper
Prospective multicentre observational study of aneurysmal subarachnoid haemorrhage in Australasian intensive care (PROMOTE-SAH) - Update
A/Prof Andrew Udy

TBI REMAP
A/Prof Andrew Udy

Prophylactic hypothermia to lessen traumatic brain injury (POLAR) - Update
Mr Tony Trapani

A randomised, placebo-controlled trial of erythropoietin in ICU patients with traumatic brain injury health economic evaluation (EPO TBI HEE) - Results
Ms Lisa Higgins

Central Venous Catheterisation Insertion Accreditation (CVC Accred) Study
A/Prof Winston Cheung

A multicentre observational study to determine the adverse event rate of a new CVC insertion accreditation program (CHESTY)
Ms Ianthe Boden

Point Prevalence Program (PPP) - Update
A/Prof Ian Seppelt

The Future of Medical Journalism
Dr Howard Bauchner

Paediatric Study Group (PSG) - Update
Dr Marino Festa

Targeted Hypothermia vs. Targeted Normothermia after Out-of-hospital Cardiac Arrest (TTM2) Trial
Dr Manoj Saxena
Honourable Mention - Best New Project Presentation

Targeted therapeutic mild hypercapnia after resuscitated cardiac arrest: A phase III multi-centre randomised controlled trial (TAME Cardiac Arrest Trial)
A/Prof Glenn Eastwood

Australia and New Zealand Cardiac arrest Outcome Determinants, and ECMO Suitability Study
A/Prof Daryl Jones

A randomised controlled trial of a heparin low dose protocol versus therapeutic dose heparin in patients on veno-venous extra corporeal membrane oxygenation (HELP-ECMO)
Dr Zoe McQuilten

Timing of Cardiopulmonary Resuscitation Accreditation (CPR Accred) Study
A/Prof Winston Cheung

The augmented vs. reduced goal for energy delivery in ICU trial (TARGET) - Update
A/Prof Sandra Peake

Embedding Clinical Trials using a Clinical Information System
A/Prof Peter Kruger

Proton pump inhibitors vs. histamine receptor blockers for ulcer prophylaxis therapy in the ICU (PEPTIC) - Update
Dr Paul Young

Metagenomic Sub Study of SuDDICU (The efficacy, cost-effectiveness and ecological impact of selective decontamination of the digestive tract in critically ill patients treated in the ICU)
A/Prof Ian Seppelt

Re-evaluating the inhibition of stress erosions: gastrointestinal bleeding prophylaxis in ICU (REVISE)
A/Prof Adam Deane

ANZICS CTG Update
A/Prof Craig French

A phase III randomised controlled trial of continuous beta-lactam infusion compared with intermittent beta-lactam dosing in critically ill patients (BLING III)
Prof Jeffrey Lipman

Bacteremia antibiotic length actually needed for clinical effectiveness: a phase III RCT (BALANCE)
Dr Shay McGuinness

Standard versus accelerated initiation of renal replacement therapy in acute kidney injury (STARRT-AKI) - Update
A/Prof Sean Bagshaw

The effect of 4% succinylated gelatine on acute kidney injury in patients with critical illness: the GELATI Trial
Dr Lisa Smart
Honourable Mention - Best New Project Presentation

Determinants of antimicrobial use and de-escalation in critical care (DIANA)
Prof Jan de Waele

Meeting Summation
A/Prof Craig French
MAJOR COLLABORATORS

Ambulance Victoria (AV)
www.ambulance.vic.gov.au
Australian Red Cross Blood Service (ARCBS)
www.donateblood.com.au
Australasian College of Emergency Medicine
Clinical Trials Group (ACEM CTG)
www.acem.org.au
Australasian Society for Infectious Diseases (ASID)
www.asid.net.au
Australian Clinical Trials Alliance (ACTA)
www.clinicaltrialsalliance.org.au
Australasian Society for Parenteral and Enteral Nutrition (AuSPEN)
www.auspen.org.au
Australian and New Zealand College of Anaesthetists Trials Group (ANZCA TG)
www.anzca.edu.au
Australian and New Zealand Intensive Care Research Centre (ANZIC RC)
www.anzicrc.monash.org
Australian and New Zealand Intensive Care Society Centre for Outcome and Resource Evaluation (ANZICS CORE)
Australian and New Zealand Society of Cardiac and Thoracic Surgeons Database Program
http://dev.anzscts-database.org/
Canadian Critical Care Trials Group (CCCTG)
http://www.ccctg.ca/
Clinical Research Network (ASID CRN)
www.asid.net.au/CRN
Centre for Health Economics,
Monash University
http://business.monash.edu/centre-for-health-economics
Centre for Education and Research on Aging

Centre for Values, Ethics and the Law in Medicine, School of Public Health,
Sydney Medical School, University of Sydney
www.sydney.edu.au/medicine/velim/
European Society of Intensive Care Medicine
http://www.esicm.org/
The George Institute for Global Health
www.georgeinstitute.org.au
Intensive Care Foundation (ICF)
www.intensivecarefoundation.org.au
International Forum of Acute Care Trialists (InFACT)
www.infactglobal.org
International Severe Acute Respiratory and Emerging Infection Consortium (ISARIC)
www.isaric.tghn.org
Medical Research Institute of New Zealand (MRINZ)
www.mrinz.ac.nz
Monash University Department of Epidemiology and Preventive Medicine
www.med.monash.edu.au/epidemiology
National Trauma Research Institute (NTRI)
www.ntri.org.au
National Blood Authority (NBA)
www.blood.gov.au
NZ Blood Service
www.nzblood.co.nz
Queensland Ambulance Service
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St John Ambulance New Zealand
www.stjohn.org.nz
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Transfusion Outcomes Research Collaborative
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