



Record amount funds anaesthesia and pain research projects

Project grant recipient Dr Rebecca Christensen from the Royal Brisbane and Women's Hospital, Qld. See page 45.

The ANZCA Research Committee has awarded funding of nearly \$A1.7 million through the ANZCA Research Foundation for research projects in 2017. The funding supports the:

- 2017 Douglas Joseph Professorship.
- The Academic Enhancement Grant.
- 22 new project grants.
- Eight continuing project grants.
- The Simulation/Education Grant.
- Three novice investigator grants.
- The pilot grant scheme.

These grants support important research initiatives in leading hospitals and universities in Australia, New Zealand and Hong Kong and are vital to ANZCA's continuing contribution to improvement in the safety and quality of patient care in anaesthesia, intensive care, perioperative medicine and pain medicine through high-quality medical research.

The foundation appreciates the supporters and sponsors who have provided the named research awards – the Cole family, the late Dr Robin Smallwood's family, the late Dr John Boyd Craig's family, Professor Barry Baker, Dr Peter Lowe and Australian Executors Trustees.

Douglas Joseph Professorship



Associate Professor Jennifer Weller

ANZCA congratulates Associate Professor Jennifer Weller for the award of the quadrennial Douglas Joseph Professorship for 2017. This prestigious award is open to Fellows of the College in Australia, New Zealand, Hong Kong, Malaysia or Singapore who are making an outstanding contribution to the advancement of the speciality to pursue scholarship and research in human anaesthesia. The tenure of the professorship is one year and Associate Professor Weller will hold the courtesy title "Douglas Joseph Professor of Anaesthesia".

Associate Professor Jennifer Weller is head of the Centre for Medical and Health Sciences Education at the University of Auckland, and a specialist anaesthetist at Auckland City Hospital. Associate Professor Weller is on the editorial board of the *British Journal of Anaesthesia*, and an editor of the new journal *BMJ Simulation and Technology*.

She is widely published in the areas of simulation-based learning, inter-professional teamwork, and patient safety and assessment, directs a masters program in clinical education, and is involved in inter-professional simulation-based initiatives in the medical and nursing undergraduate programs.

Associate Professor Weller will deliver the Australasian Visitor's Lecture at ANZCA's annual scientific meeting in Sydney in 2018 as part of the professorship.

The Douglas Joseph Professorship emolument will assist Associate Professor Weller in pursuing her study evaluating a national quality improvement initiative for safer surgery.

Evaluating a national quality improvement initiative: multidisciplinary operating room team simulation for safer surgery

Multidisciplinary Operating Room Simulation (MORSim) is a national simulation-based team-training program comprising realistic simulated surgical cases, which present communication challenges to all members of the operating room team. Each simulation is followed by a debrief to enable participants to reflect on the events, expose assumptions and explore issues with communication, as well as identify behaviours and strategies that improve the performance of the team. From this, participants identify new practices to apply in their workplace. The simulations are supported by presentations, videos and discussions on specific communication strategies.

The primary research aim is to demonstrate that a multidisciplinary simulation-based team training intervention for operating room staff (MORSim) improves outcomes for surgical patients. A second aim is to demonstrate improved processes in the operating room. Finally, the investigator will explore the implementation process itself, to identify factors that facilitate or limit the uptake of patient safety initiatives such as MORSim.

MORSim represents a major quality initiative to improve outcomes for our patients. The stepped rollout of the initiative across all 20 district health boards in New Zealand affords a limited time opportunity to produce evidence of the effectiveness of this innovative team-training initiative and inform implementation of future safety interventions. This anaesthetist-led national initiative is an international first and could lead the world in changing the way teams work together in operating rooms.

**Associate Professor Jennifer Weller,
University of Auckland, NZ.
\$A70,000**

Named research awards



Harry Daly Research Award – Professor Andrew Davidson

The Harry Daly Research Award was established by the Faculty of Anaesthetists, Royal Australasian College of Surgeons in 1981. The Harry Daly Research Award may be made in any of the categories of research award made by the College provided the project is judged to be of sufficient merit. The award is made each year to the grant ranked most highly by the ANZCA Research Committee.

Neurodevelopmental outcome after sevoflurane versus dexmedetomidine/remifentanyl anaesthesia in infancy: a randomised controlled trial

There is strong evidence that commonly used general anaesthetics, such as sevoflurane, have a profound effect on the developing brain in the animal model, especially with prolonged exposure. In contrast, there is evidence that dexmedetomidine does not produce these effects. There is also mixed human cohort evidence that surgery in early childhood may be associated with an increased risk of later poorer performance in language and cognition. The role, if any, of anaesthesia in this association is unknown.

In the proposed study, the investigators plan to randomise 440 infants, aged less than one year, having more than two hours of surgery to either a standard general anaesthetic with sevoflurane or a new anaesthetic regimen using dexmedetomidine and remifentanyl. Dexmedetomidine and remifentanyl have so far appeared to cause little, if any, of the changes that are seen in animals with the other anaesthetic agents.

The trial will be led from Melbourne and will recruit children in Sydney, Perth, the US, Switzerland and Italy. It will be based on the successful network established through the GAS trial. They will then have a battery of standard neuropsychological tests, known as the Bayley-III. This tests their cognitive, language, motor and emotional and behavioural development.

Millions of infants have anaesthetics around the world. In Australia alone, more than 70,000 children under four years of age have an anaesthetic every year. Over 80 per cent of infant anaesthesia administrations are of less than two hours duration. If the dexmedetomidine/remifentanyl technique proves to have superior outcomes compared to volatile anaesthesia, this will provide significant opportunities to improve neurodevelopmental outcomes after surgery in infants. It also will provide the strongest evidence to date that neurotoxicity is indeed a significant issue for paediatric anaesthesia, which will prompt clinicians to consider delaying lengthy surgery if safe to do so, and provide further impetus to the development of other less toxic regimens.

However, if this study finds little evidence of difference in outcomes the results from this study, along with the GAS trial results, would provide the strongest evidence to date that neurotoxicity seen in the preclinical studies is not likely to be a significant clinical issue for the majority of paediatric cases. This would provide strong evidence that clinicians do not have to change their current standard of practice.

Professor Andrew Davidson, Royal Children's Hospital, Melbourne, Vic; Dr Justin Skowno, The Children's Hospital at Westmead, NSW.

\$A66,019



The Russell Cole Memorial ANZCA Research Award – Dr Paul Wrigley

The Russell Cole Memorial ANZCA Research Award was established following a generous ongoing commitment to the ANZCA Research Foundation from the family of the late Dr Russell Cole to support a highly ranked pain-related research grant.

The long-term effects of spinal cord stimulation on neural function in chronic low back pain – a pilot study

The Global Burden of Disease study now ranks chronic low back pain as the number one cause of disability in Australasia affecting three million Australians and costing more than \$A14 billion a year. Despite extensive efforts, sustained pain relief for people with chronic low back pain has been difficult to achieve using conventional medical treatments.

Spinal cord stimulation (SCS) has been employed for the management of chronic pain for over 50 years. Over this time, SCS has become a well-established mode of treatment for neuropathic pain. Until recently most success with SCS has been obtained with pain involving the limbs with relief of chronic low back pain more difficult to achieve.

Dr Paul Wrigley will lead a study examining the long-term effects of SCS on nerve function. While SCS has been used for many years, the way it works remains poorly understood. Even less is known about the newer forms of stimulation, including the introduction of high frequency SCS (500Hz to 10,000Hz), raising concerns about the potential for effects on spinal cord function over time.

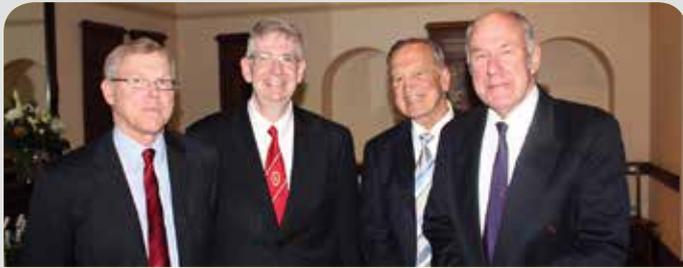
This pilot study will monitor changes in neural function associated with propriety low (<100Hz) and high frequency (10kHz) SCS in 30 people with chronic low back pain over 12 months. The project will inform the development of a full-scale trial.

While no definitive evidence of neural damage has been found to date using physical examination, it is crucial to obtain long-term safety data using more sensitive assessments. This information will better inform patient selection and cost benefit analyses. With this in mind, a one-year follow-up study will be undertaken using sensitive measures of spinal cord nerve function to track patients following spinal cord stimulator implantation.

This research will provide essential information to determine the safety of spinal cord stimulation in the long-term management of chronic low back pain.

Dr Paul Wrigley, Pain Management Research Institute, Royal North Shore Hospital, Sydney, NSW.

\$A70,000



The Elaine Lillian Kluver ANZCA Research Award – Professor Eric Visser for his Academic Enhancement Grant

The Elaine Lillian Kluver ANZCA Research Award was established following a generous gift to the ANZCA Research Foundation from the estate of the late Dr Elaine Kluver to support a highly ranked pain-related research grant.

Sympathetically maintained pain in complex regional pain syndrome

In 2015, the University of Notre Dame Australia (UNDA) in Fremantle, WA, appointed Professor Eric Visser to the inaugural Churack Chair of Chronic Pain Education and Research in the School of Medicine. This new academic chair was tasked with reducing the impact of chronic pain, one of the biggest unrecognised health problems in the community, by furthering research and the education of medical students in chronic pain management.

Specifically, Professor Visser was charged with developing a pain education curriculum and research program at UNDA, and to establish a strong collaborative pain research program with Murdoch University's Centre for Research on Chronic Pain and Inflammatory Diseases, under the direction of Professor Peter Drummond and Professor Philip Finch. They have collaborated on pain research for many years at Murdoch University, and have published a large number of scientific papers on complex regional pain syndrome and other forms of pain.

The vision is to develop the Churack chair as a co-operative academic organisation (UNDA and Murdoch University) to foster much needed expansion in pain science research.

To achieve this goal, UNDA will establish a "flagship" post-doctoral research position at Murdoch University's pain research centre, known as the Churack Post-Doctoral Pain Research Fellowship. This position will not only contribute to the advanced pain research program at Murdoch University, it will also underpin the new research/education programs of the Churack chair (particularly in basic pain neurosciences), thus laying the groundwork for collaboration between the two universities.

By providing access to technical expertise, research facilities and equipment at Murdoch University, there will be opportunities for medical, health and science graduates and, specifically, ANZCA and Faculty of Pain Medicine trainees and Fellows, to complete a masters or doctor of philosophy in pain research at UNDA/Murdoch University under the direction of staff from both universities.

A major research focus of Murdoch University's pain research centre has been to clarify the involvement of the sympathetic nervous system in complex regional pain syndrome. The specific aim of this application is to build on this research through the use of several complementary approaches: (i) looking for "pain targets" in tissue samples taken from the site of chronic pain; (ii) clarifying the role of these "pain targets" under tightly controlled cell culture conditions in terms of inflammatory processes that might contribute to pain; and (iii) determining whether similar processes can be identified in healthy human participants.

Chronic pain is a major cause of worldwide suffering and for many patients the mechanisms that drive their pain are poorly understood and effective therapies are therefore often lacking. Identifying these mechanisms is crucial for the advancement of pain management and the development of new treatments for certain forms of intractable pain. With the involvement of the Churack chair, these studies will establish a strong base upon which to build a distinctive and clinically relevant research program across the two universities and links with ANZCA and the Faculty of Pain Medicine.

Professor Eric Visser, University of Notre Dame Australia, WA, Professor Peter Drummond, Associate Professor Philip Finch, Murdoch University, WA.

\$A99,788

Named research awards (continued)



John Boyd Craig Research Award – Professor Britta Regli-von Ungern-Sternberg

The John Boyd Craig Research Award was established following generous donations from Dr John Boyd Craig to the ANZCA Research Foundation to support pain-related research by Fellows, particularly Western Australians.

Palatable and chewable tramadol chocolate-based tablets for effective pain management in young paediatric patients

Medical specialists now have a limited list of approved potent analgesics to prescribe to children undergoing surgery and cancer therapy. Tramadol is used widely in adults and clinical trials have shown it to be effective and safe in children in acute, subacute and chronic pain settings. It provides effective analgesia with low risk compared to other opioids and thus is suited for inpatient use and in the home setting. It is particularly useful for short periods in those experiencing moderate pain following procedures, where nonsteroidal anti-inflammatories (NSAIDs) are insufficient or contraindicated.

However, none of the 82 registered tramadol products in Australia are recommended or appropriate for young children, and caregivers have to perform a multi-step manipulation to transform the tramadol capsule into a liquid for young children. This practice is tedious, potentially risky, and yields a gritty suspension with no mechanism to mask the bitter taste.

A multi-disciplinary study team has designed a tramadol tablet based on a chocolate-flavoured platform. This platform has been successfully applied to midazolam, another bitter drug, and is now in trial at the Princess Margaret Hospital in Perth. The tramadol tablet will be optimised to conform to compendia specifications prior to the conduct of a pilot randomised clinical study in children.

The investigators plan to test the chocolate tramadol tablet against the current broken-open capsule method of delivering tramadol following minor to moderate operations at Princess Margaret Hospital. They aim to determine whether a novel tramadol oral tablet will contribute towards a seamless continuum of care for paediatric patients by providing a palatable, safe and effective product for managing moderate to severe pain. This system will also allow the delivery of a smaller defined dose, not previously available in Australia, which will allow easier and more reliable dosing in smaller children.

The expected outcome is a cost-effective, palatable, safe and effective tramadol oral tablet for managing moderate to severe paediatric pain, and a convenient product to administer in homes and hospitals. The data will confirm the versatility of the chocolate-flavoured delivery platform for the formulation of bitter drugs poorly tolerated by young patients.

Professor Britta Regli-von Ungern-Sternberg, Dr Laurence Cheung, Dr David Sommerfield, Princess Margaret Hospital, Perth, WA; Professor Lee Yong Lim, Dr Sam Salman, University of Western Australia, WA.

\$A56,000



The Robin Smallwood Bequest – Associate Professor Philip Peyton

The Robin Smallwood Bequest was established following a generous bequest from the late Dr Robin Smallwood to support a highly ranked grant in anaesthesia, intensive care or pain medicine.

Redefining pulmonary uptake of anaesthetic agents

Thorough understanding of the way anaesthetic agents are taken up by the lung is essential to their proper clinical use by anaesthetists to achieve optimal and safe depth of anaesthesia. However, most teaching in this field is simplistic, and sometimes misleading.

Anaesthetic depth is determined most directly by the concentration of the agent in blood to the brain, but this is not readily measurable in routine clinical practice. Instead, concentrations in the gas we breathe are monitored, which are quite different.

This “A-a” difference arises in large part from mismatch of ventilation and blood flow throughout the lungs, which is significant in all patients under anaesthesia. The traditional way this “V/Q” mismatch is conceived and taught is the three-compartment or “Riley” model, which estimates shunt and dead space in the lung using blood gas measurements.

However, this model does not properly explain the way that anaesthetics are taken up by the lung, and the concentrations achieved in blood. This has led to much confusion and misunderstanding over the years about the behaviour of anaesthetic gases in the lung.

Associate Professor Philip Peyton has previously developed and used sophisticated computer models, which have better explained the way anaesthetic gases are taken up by the lungs, but these are too complex for routine clinical use.

What is needed is a simple model of lung gas exchange during anaesthesia, which still retains accuracy in predicting the behaviour of a range of gases used in anaesthesia. Such a model needs to then be validated using data generated from samples collected from patients under inhalational anaesthesia, and against a state-of-the-art lung model, which incorporates realistic distributions of ventilation and blood flow, as well as lung tissue, blood and alveolar volumes and longitudinal gas diffusion limitation. This will allow it to accurately simulate the behaviour of a range of gas species relevant to inhalational anaesthesia.

The aim is to ultimately provide a more accurate and accessible tool for teaching and research in the field of lung gas exchange physiology and the pharmacokinetics of inhalational anaesthetics.

Associate Professor Philip Peyton, Austin Health, Melbourne, Vic.

\$A62,560



Australian Executor Trustees ANZCA Research Award – Dr Thomas Painter

The Australian Executor Trustees ANZCA Research Award was established to encourage excellence in South Australian medical research in the field of anaesthesia, perioperative and pain medicine by supporting a highly ranked project grant from a South Australian ANZCA Fellow anaesthetist or pain medicine specialist.

Do bolus intravenous fluids cause lung injury: Role of TRPV4 channels

Administration of intravenous fluid boluses is one of the most common hospital interventions for patients who are thought to be dehydrated due to illness or after surgery.

However, recent evidence suggests that these large amounts of fluid may, at best, have no effect or, at worst, exacerbate illness possibly increasing the rate of death in some patients. These negative effects are particularly manifest in the lung.

In our preliminary studies, the mechanism by which large doses of intravenous fluids may adversely affect the lung showed the importance of a particular type of channel that is found on the surface of cells lining the circulatory system and which controls the movement of water into and out of the lung, transient receptor potential vanilloid (TRPV4).

These channels also have been associated with other subsequent actions, which control inflammation and the movement of inflammatory immune system cells into the lung. The accumulation of both water and cells in the lung leads to a condition called acute lung injury, or acute respiratory distress syndrome (ARDS). ARDS remains a common problem in intensive care units and retains a 30 per cent mortality rate worldwide.

The aim of this study is to examine further the mechanisms by which administration of large volumes of intravenous fluid can lead to lung injury, by examining the health outcomes and blood of hospital patients.

The investigators will use samples already collected from the REstrictive Versus LIbEral Fluid Therapy in Major Abdominal Surgery (RELIEF) clinical trial whereby patients were randomly assigned to receive either the standard or a restricted amount of fluid after surgery. The effects of each fluid regime on factors in the blood, which either affect the function of TRPV4, or which are affected by the activation of TRPV4, will be determined.

As high-volume bolus fluid resuscitation remains clinically necessary in various cohorts of critically ill patients, this project will extend our knowledge of the involvement of the TRPV4 channel in the patient population and the mechanistic pathway involved in fluid-induced lung injury. Understanding this pathway will assist the development of targeted interventions with potential improved patient safety.

Dr Thomas Painter, Royal Adelaide Hospital, SA; Professor Paul Myles, The Alfred, Melbourne, Vic; Professor Andrew Bersten, Dr Shailesh Bihari, Flinders Medical Centre, SA; Dr Dani-Louise Dixon, Flinders University, SA.

\$A65,869



Provisional New Fellow ANZCA Research Award – Dr Matthew Doane

Professor Barry Baker, retired anaesthetist and ANZCA Executive Director of Professional Affairs, and former Nuffield Professor of Anaesthetics, University of Sydney, made a generous donation to the foundation in 2014 to support its ability to provide novice investigator grants. This award is to support a highly ranked novice investigator, who is either a provisional year trainee or a new Fellow within five years of first specialist qualification.

The efficacy of an anaesthetic record in transferring information across hospital settings

In medical practice, communication is an essential component throughout all aspects of patient care. Communication between healthcare providers, when transferring patient information and care, is a varied process.

Over the past 10 years, an extensive amount of work has been published regarding the importance of "handover" in medical care; the act of transferring care and information regarding a patient from one team or team member to another. After handover, when further questions arise, the medical record serves as an essential source of information. However, adverse events related to poor handover of patient information and care is well documented in the perioperative setting. Even with facilitated communication tools, details can be lost in this process.

The aim of this study is to investigate whether anaesthetic records are regularly reviewed by other medical personnel and, if so, whether they are able to identify clinically pertinent information.

Sample charts will be constructed, each based on a fictitious patient, and anonymously administered to medical staff. The charts will contain an arrangement of paperwork identical to what would be expected for a simple operative hospital stay. A questionnaire will be designed to focus on issues of medical history, allergies, complications, medications, procedures and care that has been delivered during the present hospitalisation. The charts and questionnaires will be validated against a group of anaesthetists prior to commencement.

The data gathered from this study will identify whether changes to the current system of intraoperative record keeping are needed, with the aim of improving the system of transferring pertinent intraoperative information to the ward and other hospital areas.

Dr Matthew Doane, Dr Mark Chemali, Dr Khoi Pham, Royal North Shore Hospital, NSW.

\$A18,381

Novice investigator grants



Prehabilitation of frail patients undergoing elective colorectal surgery – a feasibility pilot study

In the context of an increasingly elderly and frail surgical population, ways to optimise and manage patients preoperatively in order to maximise meaningful recovery and prevent complications is a priority both nationally and internationally.

This study aims to assess the feasibility of a randomised controlled trial into prehabilitation; a structured, tailored exercise program with dietary advice, as a treatment to improve outcomes for frail patients undergoing colorectal surgery, including its health economic impact. The treatment proposed is a four-week exercise program, including cardio and resistance-based exercises, tailored to each patient and supervised by exercise scientists. The patients will also receive dietary advice. A comparison group of patients will receive usual care. The primary outcome measure will be six-minute walk distance at the five to six week post-operative clinic visit, as this is a well-validated and easily measurable tool to assess functional capacity.

Frail cancer patients have not before been specifically selected for an exercise intervention. Previous exercise studies in cancer patients as a whole, however, have suggested a benefit. This study will provide important feasibility data to inform further research into improving care for this high-risk patient group. It may reveal a signal towards benefit or harm from the intervention, but the aim is to establish whether this type of intervention can be successfully studied in this population. Prehabilitation is an area of growing interest, but of limited research data. If it can be shown that increasing pre-operative fitness improves outcomes it will inform advice to patients awaiting surgery, and potentially healthcare services and policy in the longer term.

Dr Claire Furyk, Townsville Hospital, Qld.
\$A20,000



Nitrous oxide treatment of adolescents with depression (NOTAD): a randomised double-blind placebo controlled pilot study

Major depression affects one in 16 young Australians. For severe depression in young people, the recommended medicinal treatment is the use of a group of medicines called selective serotonin reuptake inhibitors (SSRIs). These medicines work by increasing serotonin in the brain, which reduces depression. Although SSRIs are known to work, they can take up to four to eight weeks before depressive symptoms are reduced. During this period, young people can be at risk of negative side effects due to an increase in activity prior to an improvement in mood.

Nitrous oxide is a safe, inhalational gas, which is commonly used in children and adults in anaesthetic procedures. There is strong biological and clinical evidence that suggests nitrous oxide may have significant acute antidepressant effects in adults with treatment-resistant depression. However, so far no studies using nitrous oxide in adolescents have been conducted.

The aim of this pilot study is to understand whether nitrous oxide will have the same antidepressant effect in adolescents, and whether having a single dose of nitrous oxide together with an SSRI will produce a greater beneficial antidepressant effect, compared to the effect of taking SSRIs alone. The participants will be administered nitrous oxide or placebo for one hour on the day of treatment and will be monitored weekly throughout the entire study, up to 12 weeks after treatment start, in regards to mood and related psychiatric symptoms.

This project has the potential to significantly change the way clinicians treat depressive symptoms in adolescents. If the proposed approach leads to clinical improvements, this in turn can significantly reduce the risk of worsening depressive symptoms in adolescents with depression who are receiving standard pharmacological SSRI-treatment. As a consequence of more effective treatment, adolescents would be able to return to their prior level of functioning earlier, decreasing the overall burden of disease in the community and reducing the length of time these individuals are involved in mental healthcare.

Dr David Sommerfield, Dr Richard Stewart,
Princess Margaret Hospital for Children, Perth, WA.
\$19,493

Simulation/Education Grant



Establishing conditions for assessment for learning in the ANZCA training program: what is the role of trust?

The education of health professionals is critical for quality healthcare. Research and innovation in medical education help to ensure future graduates can provide safe, effective and compassionate care to their patients.

The aim of this study is to investigate the extent and determinants of trust between ANZCA trainees and their supervisors and the impact of this on the efficacy of the in-training assessment process.

Workplace-based assessments (WBA) require considerable investment in supervisor time and, if they are performed meaningfully, they can make a very important contribution to trainee learning and decisions on progression through the ANZCA training program.

In higher education, trust is recognised as a vital factor in teaching and learning with great relevance to assessment and feedback interactions. In the medical education context,

the effect of the decisions trainees make regarding the extent to which they are willing to trust their supervisors on the implementation of WBAs has not been explored. In identifying the factors that influence a trainee's decisions to trust their supervisor as an assessor and the assessment/feedback process, we will provide information for trainees and supervisors to maximise the value of WBAs and hence the success of the ANZCA curriculum implementation and ultimately the quality of ANZCA Fellows.

The investigators intend to use a mixed methods approach to answer these questions using a previously valid anonymous survey to gauge the extent of trust trainees have in their supervisors. We will select interviewees with diverse views from the survey respondents and conduct semi-structured interviews to explore further the conditions that afford productive trainee-supervisor assessment interactions.

The investigators expect to discover information on which to base improvements in the use of the ANZCA workplace-based assessment process for trainee learning and in-training assessment. It is anticipated that there will be broad interest in the outcome of the study within the medical education community.

Dr Damian Castanelli, Monash Medical Centre, Vic; Associate Professor Elizabeth Molloy, Associate Professor Margaret Bearman, Monash University, Vic; Associate Professor Jennifer Weller, University of Auckland, NZ.

\$A26,384

Project grants



Electroencephalographic markers of behavioural responsiveness during anaesthesia

Awareness during general anaesthesia is a rare but important complication of anaesthesia associated with significant negative psychological sequelae. During anaesthesia, relatively consistent changes occur in the electroencephalogram (EEG) as increasing doses of anaesthetic agents are administered to patients. These changes form the basis of modern depth-of-anaesthesia monitors, which usually analyse recordings taken from across the patient's forehead and output a numerical index value, reflecting the "depth" of anaesthesia.

However, these monitors do not perform well at detecting connected consciousness during anaesthesia, as revealed by simultaneous isolated forearm testing. This is possibly because only changes in the frontal cortex are measured.

Recent studies in healthy volunteers using functional magnetic resonance imaging (fMRI) and multichannel EEG have identified functional changes in other distant regions of the cortex associated with loss of behavioural responsiveness during anaesthesia. In particular, there is growing evidence that a key marker of consciousness or behavioural response is the electroencephalographic connectivity between the frontal and parietal regions of the brain.

This study is unique in that it will test responsiveness during anaesthesia and surgery, using a slow controlled anaesthetic regime, while recording multichannel EEG. The investigators will record the EEG at multiple sites across the scalp, allowing identification of key changes in activity and connectivity in a number of brain regions during transitions between responsive and unresponsive states and vice versa. These recordings will then be analysed to determine which, if any, measures can reliably distinguish between responsive and unresponsive states.

The investigators hope to gain mechanistic insights and achieve reliable measures, which may ultimately contribute to the development of improved depth of anaesthesia monitors. This might assist clinicians in optimising the dose of anaesthetic agents given to patients to minimise complications and side effects, but still ensure that the patient is unaware and unresponsive.

Dr Amy Gaskell, Professor Jamie Sleigh, Waikato Hospital, NZ.

\$A54,014 (including scholarship)

Project grants (continued)



PADDI Genomics: An investigation into the genomics of the inflammatory response to surgery and the actions of dexamethasone

The PADDI (Perioperative administration of Dexamethasone and Infection) trial is a large multi-centre randomised placebo controlled trial investigating whether the routine intraoperative use of the glucocorticosteroid drug, dexamethasone, is associated with increased or decreased risk of post-operative surgical site infection.

As a sub study of the PADDI trial, PADDI genomics aims to establish a biorepository to support genetic (DNA) and epigenetic (around DNA) investigations into the development of the inflammatory response to surgery and the impact of dexamethasone on that response. An initial analysis using state-of-the-art next generation sequencing technology and multiplex immunoassays will examine the impact of dexamethasone on inflammatory cell gene expression and protein production in patients with severe inflammatory responses. This analysis will provide fundamental preliminary data to begin more detailed explorative genetic, epigenetic, transcriptomic, proteomic and cellular (systems biology) analyses to further define the nature of perioperative inflammation and ultimately define factors that may more precisely predict harmful inflammation and the risk or benefit of intraoperative dexamethasone administration.

The biorepository will be created at 11 collaborating PADDI sites across Australia, New Zealand, Hong Kong and The Netherlands. When complete, it will support complex investigations into the molecular actions of dexamethasone and surgery on the circulating peripheral blood mononucleocytes (PBMC). The research will complement the findings of the PADDI trial by providing evidence, at a genomic level, for how a single dose of dexamethasone modifies innate and adaptive immune function in the surgical setting and how this may be associated with the risk of surgical site infection. The biorepository also will provide tissue to further investigate how dexamethasone may impact on differences in the wide range of other phenotypes monitored during the trial and, importantly, whether there are genomic markers that may predict greater risk or benefit for dexamethasone administration.

In addition, the biorepository can be used to investigate other important perioperative complications such as post-operative nausea and vomiting (PONV), persistent post-operative pain, and blood glucose variation. This project embraces the challenge of generating genomic evidence to support more precise (precision medicine) use of medication in the perioperative period.

Dr Christopher Bain, The Alfred, Melbourne, Vic; Dr Kiyomet Bozaoglu, Baker IDI Heart and Diabetes Institute, Melbourne, Vic; Dr Jan Dieleman, University Medical Centre Utrecht, The Netherlands, Professor Tomás Corcoran, Royal Perth Hospital, WA.

\$A89,850 (including scholarship)



Myocardial structure in preeclampsia using cardiac magnetic resonance and transthoracic echocardiography

Preeclampsia is a human pregnancy specific hypertensive (high blood pressure) cardiovascular disease, which is a leading cause of global morbidity and mortality. In Australia, preeclampsia affects approximately 20,000 pregnant women each year, is the most common reason to be admitted to an intensive care unit during pregnancy and is responsible for 20 per cent of maternal deaths. Worldwide it affects 6.5 million young women each year and is a leading global cause of maternal mortality. The hypertension and its complications, including renal impairment, acute pulmonary oedema, systolic and diastolic cardiac failure, and intracerebral haemorrhage, are directly related to the cardiovascular system and altered haemodynamics (blood flow).

The proposed unique and innovative study aims to investigate the heart in women with preeclampsia using non-invasive technologies of ultrasound, transthoracic echocardiography (TTE) and cardiovascular magnetic resonance (CMR). Using these safe methods it is anticipated that the study will improve understanding of preeclampsia, lead to better monitoring and the use of different medications to reduce complications in preeclampsia.

Cardiovascular magnetic resonance (CMR) is a relatively new imaging modality for cardiovascular assessment. It is able to provide excellent, high-quality images that can be obtained in any plane and without restriction by body size and morphology. It is non-invasive and does not use radiation, both of which are important considerations in pregnant women.

As it is able to visualise the heart so well, cardiovascular magnetic resonance is an important part of the assessment of cardiovascular structure and function. Cardiovascular magnetic resonance is currently the gold standard for left ventricular volumes and function, and is the only imaging modality currently available that is able to formally quantify right ventricular volumes and function.

By observing women with preeclampsia, this study aims to further determine the differences in cardiac structure in women with preeclampsia, before and after birth. By performing observations in the antenatal period and then at six months post-birth, information will be gathered about initial cardiac changes followed by recovery of cardiac changes.

This information will then assist with understanding of cardiac changes in women with preeclampsia. This in turn may lead to additional or alternative therapeutic or monitoring interventions, such as serial echocardiography to monitor disease progress and resolution, and CMR to assess extent of myocardial oedema or fibrosis and potential for recovery.

It may also lead to consideration of the use of diuretics to reduce tissue oedema and improve cardiac function and the use of cardiac remodelling agents, such as angiotensin converting enzyme inhibitors in women after birth, who demonstrate cardiac structural changes, all of which may reduce short and long-term morbidity from this condition.

Associate Professor Alicia Dennis, The Royal Women's Hospital, Melbourne, Vic.

\$A66,591



Can free nicotine replacement therapy (NRT) increase smoking cessation before scheduled surgery? A randomised trial

Each day, 2.5 million people in Australia and New Zealand will smoke tobacco and about 300,000 of these will have elective surgery within the next 12 months. Regardless of whether this surgery is related to a smoking-related condition, many of them will make a quit attempt while on the elective surgical wait-list, and for those who do quit for four weeks or more, the risk of anaesthetic and surgical complications, particularly wound infection, is significantly lower.

Unfortunately, most quit attempts on the wait-list will occur without any behavioural or pharmacological assistance. These are likely to ultimately fail, leaving the majority of smokers arriving for elective surgery having smoked that day. Nicotine replacement therapy (NRT) is recognised as first-line therapy in smoking cessation, at least doubling quitting success compared to unaided quits, yet few perioperative services have an organised approach to ensuring this is offered to all nicotine-dependent smokers.

The investigators propose to study the effects of a systemic offer of a mailed NRT program on the population of nicotine dependent smokers who are awaiting surgery. The uptake, use, acceptability and quit-outcomes of this five-week mailed NRT supply will be quantified in nicotine dependent smokers as they enter the surgical wait-list.

The percentage of patients who quit before surgery when given open access to NRT will be compared to those that were not offered NRT. Confirmation of non-smoker status will be done on the day of surgery by carbon monoxide breath testing. Follow-up of wait-list quitters will be done at three and six months after surgery to determine the proportion of sustained abstinence after surgery in each group.

This study recognises the important position that anaesthetists have to use the perioperative period as an opportunity to improve the health of their patients.

**Dr Ashley Webb, Frankston Hospital, Peninsula Health, Vic.
\$A70,000**



Predicting disability-free survival after surgery in the elderly

People having surgery hope for a speedy recovery, with a return to good health and quality of life.

Unfortunately, it is not uncommon for patients to have complications after surgery, with poor or delayed recovery and, sometimes, persistent disability. This is particularly true for elderly people (70 years of age or older), many of who may never return to their previous level of function after major surgery.

The investigators' previous research revealed that 12 months after surgery one in seven patients had worse health than they did before surgery. The risk of a poor long-term recovery was higher in older people and those with multiple medical problems, with one in three elderly patients having died or been left with significant disability six months after surgery.

The primary objective of this study is to construct and validate a risk score for the prediction of disability-free survival in older patients (aged 70 years of age or older) six months after elective or non-elective surgery in an Australian tertiary referral centre.

The investigators propose to use a large ("big data" style) prospective patient registry to create a scoring system to predict post-operative disability-free survival in older people having elective and non-elective surgery, and will investigate the patient characteristics, medical conditions (including memory impairment), types of surgery and surgical complications (including persistent pain) linked to poor recovery. The identification of these risk factors will help patients and doctors make better decisions about having surgery and plan the level of care patients need before and after surgery.

A scoring system capable of predicting disability-free survival will provide a valuable tool to facilitate patient-clinician risk-benefit discussions prior to surgery and help target high-intensity interventions to at-risk patients. Further, understanding of the epidemiology of post-operative disability will help guide future perioperative research.

**Dr Mark Shulman, Professor Paul Myles, Ms Sophie Wallace,
The Alfred, Melbourne, Vic.
\$A69,747**

Project grants (continued)



Fluid status after bowel preparation for colonoscopy: Objective assessment and relationship to hypotension under sedation

Colonoscopy is a common investigation and requires bowel preparation to empty the bowel and allow visualisation of the mucosa.

This study will investigate whether patients are significantly dehydrated after taking bowel preparation solution to undergo colonoscopy. The previous work of our research group has demonstrated that hypotension is common during sedation for endoscopy and it is not prevented by IV fluid administration prior to colonoscopy.

In this study we will combine the Clear Sight® non-invasive cardiac output monitor with a limited transthoracic echocardiography assessment to objectively record the intravascular volume status of the study cohort. Patients' intra-procedure responses to sedation along with post-operative recovery will be determined. Investigation of the fluid status of patients undergoing colonoscopy in this study will allow targeted intervention for the prevention or effective management of hypotension during colonoscopy and ultimately increasing the safety of sedation for endoscopy by anaesthetists.

Dr Megan Allen, Professor Kate Leslie, Royal Melbourne Hospital, Melbourne, Vic.

\$A54,938



The Obstructive Sleep Apnoea Study (OSATS): Making tonsillectomies safer

Obstructive sleep apnoea (OSA) is a disorder involving pauses (apnoea) or restrictions in breathing during sleep.

It is caused by the repeated collapse of the upper airways and is characterised by frequent drops in oxygen levels and repeated disruption to sleep. In children OSA has a profound effect on their daily life and development. Surgical removal of the tonsils is the first line treatment for most children suffering from OSA.

However, this airway surgery is associated with a high rate of complications with about 50 per cent of the children suffering from serious breathing problems during and/or after surgery. Disorders such as OSA and other factors, such as young age, are known to increase the risk of these breathing problems, during and after anaesthesia.

These breathing problems often result in an increased need of attention and specialised care.

The "gold standard" test for assessing presence and severity of OSA in children is polysomnography (PSG); however, PSG is a high-cost, labour-intensive test involving a complex overnight sleep study and is associated with long waiting lists. It is therefore rarely used in clinical practice in this population. The abnormally collapsible upper airway in children with OSA is evident during sleep, sedation and anaesthesia. Thus, quantifying collapsibility during anaesthesia could provide an objective tool to predict the likelihood of perioperative respiratory adverse events including post-operative obstruction and asphyxia.

While several methods have been developed for use in sleeping adults, very few studies have been performed in anaesthetised children.

The investigators have adapted one such measurement, the critical closing pressure (P_{close}), for use in children in the perioperative environment to assess upper airway collapsibility. Most importantly, the P_{close} measurement is non-invasive, quick (20 to 60 seconds per measurement), does not significantly impact theatre times and uses a measurement (pressure) that is highly familiar to anaesthetists.

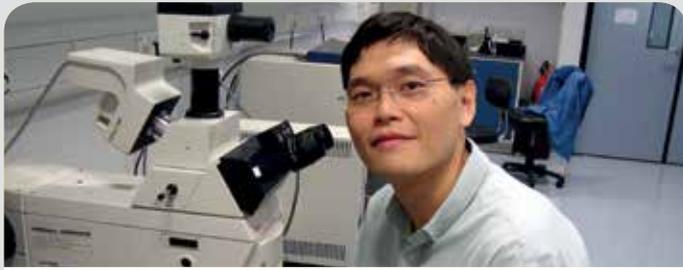
The proposed study is designed to determine the efficacy of P_{close} in assessing presence and severity of OSA compared with the gold standard technique of PSG in children undergoing elective tonsillectomy.

The results of this study have the potential to better identify children requiring higher-level care and conversely those who can have same-day discharge. Such measurements also could reduce the occurrence and severity of respiratory adverse events due to better-informed decision-making regarding perioperative management.

The study also may lead to a decrease in the number of unnecessary overnight and intensive care unit admissions.

Professor Britta Regli-von Ungern-Sternberg, Dr Paul Bumbak, Princess Margaret Hospital, Professor Peter Eastwood, West Australian Sleep Disorders Research Institute, Professor David Hillman, Sir Charles Gairdner Hospital, WA.

\$A52,726



The role of annexin II in opioid-induced hyperalgesia

Opioids, such as morphine, are commonly prescribed to relieve pain during and after surgery.

Paradoxically, opioid treatment also has been shown to increase sensitivity to painful stimulus and may therefore worsen post-operative pain. The investigators are working on a series of cellular and animal experiments to understand the mechanisms of this phenomenon known as “opioid-induced hyperalgesia”.

Attempts to elucidate the underlying mechanisms have suggested the possible involvement of interacting proteins that bind to the membrane μ opioid receptor (MOR). Based on a massive screen of MOR interacting proteins using high-performance liquid chromatography-tandem mass spectrometry, the investigators identified annexin II, a protein that binds to the opioid receptor, as a potential candidate that is important in the development of opioid-induced hyperalgesia.

In a series of cellular and animal experiments, the interactions between annexin II and opioid (remifentanyl/fentanyl) treatment on MOR trafficking will be measured. In addition, using an existing biobank of patient DNA samples, the investigators will also conduct a genetic association study to identify the relationship between variants on the annexin II gene and severe pain after a variety of surgical procedures.

The outcomes of this study will help to direct development of preventive and therapeutic strategies for post-operative pain, and will enhance our ability to identify patients at risk of difficult pain management in the perioperative period due to opioid-induced hyperalgesia.

**Professor Matthew Chan, Chinese University of Hong Kong, Prince of Wales Hospital, China.
\$A56,000**



Do transthoracic and transoesophageal echocardiography agree in the grading of diastolic dysfunction in cardiac surgery?

Heart failure is well established as a risk factor for adverse perioperative outcomes and has been reported present in almost 50 per cent of patients undergoing cardiac surgery.

Heart failure may reflect either systolic failure, diastolic failure or a combination of the two pathologies, with diastolic dysfunction accounting for approximately half of all new cases of heart failure. Diastolic dysfunction is typically assessed by transthoracic echocardiography (TTE) in clinical practice. The prognostic value of TTE-graded diastolic dysfunction in large numbers of patients across a range of clinical contexts supports the validity of this non-invasive method of assessment.

Intraoperative transoesophageal echocardiography (iTOE) is routinely used for diagnosis and monitoring in the majority of cardiac surgeries with expert opinion suggesting that perioperative haemodynamic strategies should be varied according to the identified grade of diastolic dysfunction. However, despite widespread use of TOE for the intraoperative evaluation of diastolic dysfunction in cardiac surgery its validity and role in this context and for this purpose remains poorly defined.

The primary objective of this study is to measure the agreement between preoperative transthoracic echocardiography (preTTE) and intraoperative transoesophageal echocardiography (iTOE), performed prior to surgical incision, for the evaluation and grading of diastolic dysfunction in adult patients undergoing cardiac surgery.

Demonstrated agreement between these two measurements for the grading of diastolic dysfunction would provide important but as yet unavailable evidence supporting the validity of iTOE for this purpose. Importantly, it would also provide the rationale and justification for larger studies to evaluate the utility of TOE for monitoring acute changes to diastolic function through the perioperative period, with potential significance for perioperative care processes including novel, targeted and dynamic approaches to goal-directed haemodynamic optimisation.

In contrast, lack of agreement would provide important justification for a large study comparing the prognostic utility of diastolic dysfunction graded by preoperative TTE and post-induction iTOE to clarify whether such disagreement reflected a meaningful change in diastolic function detected by iTOE or important misclassification by iTOE.

**Dr David McIlroy, Dr Enjarn Lin, Dr Jessica Kasza, The Alfred, Melbourne, Vic.
\$A56,000**

Project grants (continued)



Cyanotic congenital heart disease – the role of nitrogen species in adaptation to hypoxaemia

Many babies born with congenital heart disease remain cyanosed from birth until interventional therapies correct anatomical defects.

Despite this relative lack of oxygen supply for their tissues, the majority of these babies survive and remain relatively well in their early life. These babies can continue to grow and develop for variable periods of time while corrective surgeries are planned.

It is clear these babies adapt to hypoxaemia in ways that still allow the tissues to receive sufficient oxygen for survival and growth. The specific ways in which these babies have adapted are not fully understood. Some well-established mechanisms include an increased red blood cell mass (haemoglobin level) and an increase in cardiac output. Both achieve an increase in the amount of oxygen delivered to tissues but with negative impacts on myocardial work and efficiency.

Recent evidence has emerged that blue babies also have alterations in their peripheral circulation.

Changes in the microcirculation fundamentally affect oxygen delivery and may represent a primary compensatory mechanism in chronic hypoxaemia. However, the exact mechanism by which the microcirculatory changes occur is largely unknown. Studies in adults who have adapted to living at high altitudes suggest that an alteration in the way the body deals with nitrogen species is at the centre of peripheral microcirculatory regulation.

This study will explore the mechanism by which blue babies have adapted to low oxygen levels by measuring nitrogen species and the degree of vasodilation in babies who are awaiting corrective surgery. The study will therefore examine the relationship between nitrogen species, specifically nitrites and nitrates and nitrosyl-haemoglobin and the severity of chronic hypoxaemia. Darkfield microscopy will be used as an objective measure of microvascular flow and will allow correlations between nitrogen species and flow to be explored.

An improved understanding of the altered physiology of cyanotic heart disease will benefit all children with this condition. Careful delineation of the mechanisms by which infants and babies adapt to abnormal blood oxygen saturations creates the potential to manipulate or intervene in ways that improve long-term patient outcomes.

The proposed study will provide valuable information on the basic biology of nitrogen species in paediatric populations and on important physiological mechanisms that underpin the adaptation of neonates and infants to chronic hypoxaemia.

Dr Jonathan De Lima, Dr Marino Festa, Mr Killian O'Shaughnessy, Dr Justin Skowno, Dr Neil Street, Professor David Winlaw, Dr Harry Wark, Children's Hospital at Westmead, NSW; Professor Paul Witting, University of Sydney, NSW.

\$A41,099



Altering perceived readiness to engage in advance care planning prior to cancer surgery: a randomised control trial

Advance care planning (ACP) is a process that enables patients to plan their own healthcare for the future. It involves the patient appointing a surrogate decision-maker and then discussing their values and beliefs with that person so that if they are no longer able to communicate their wishes their right to self-determination is protected.

Despite there being widespread acknowledgement at a state, national and international level that ACP is a universal health priority, there is generally low uptake at a hospital level. Given the potential benefits to healthcare workers and patients alike, there have been several initiatives globally which attempt to increase the uptake of advance care planning. However, little research has been conducted around the most effective way to achieve this. Furthermore, there is even less research around how best to introduce the concept of ACP to patients in the perioperative period.

Most patients undergoing major surgery will attend a pre-anaesthetic clinic (PAC) where they will discuss their surgery, medical problems and anaesthetic with an anaesthetist. An important aim of this clinic is to use multidisciplinary teams to holistically prepare patients optimally for surgery. Part of this process is to ensure patients and their families have accurate understandings of the risks and benefits of their upcoming surgery. ACP has an important role in preparing patients for surgery so that in the event of complications that render a patient unable to express their wishes, their medical team will still be able to provide treatment in keeping with the patient's wishes.

This randomised control trial will examine the effect of selected interventions on patients' readiness to engage in ACP as indicated by a specific readiness to engage in ACP score. The interventions examined will include both a passive intervention, being a standardised conversation about ACP, and an active intervention, being an individualised risk discussion based on a patient's calculated American College of Surgeons National Surgical Quality Improvement Project (NSQIP) score.

The results of this study will help guide one of the first evidence-based ACP programs. Primarily it will demonstrate whether targeting patients' readiness to engage in ACP in the pre-anaesthetic clinic context is likely to be productive. Secondly, information regarding the types of patient populations who might respond better to either active or passive interventions could assist in producing easy-to-use tools that would allow the right interventions to be directed at the right individuals in order to maximise their readiness to engage in ACP. Ultimately, the aim is to improve the delivery of patient-centred cancer care by supporting a patient's right to determine their own care.

Dr Debra Leung, Associate Professor Bernhard Riedel, Dr Hilmy Ismail, Peter MacCallum Cancer Centre, Melbourne, Vic; Dr Karen Detering, Austin Hospital, Melbourne, Vic.

\$A27,495 (including scholarship)



Does cefazolin prophylaxis during elective bariatric surgery achieve therapeutic concentration in plasma and interstitial fluid?

Obesity is a risk factor for surgical site infection (SSI) and prophylactic cefazolin has been demonstrated to decrease the incidence of SSI in bariatric surgery compared to placebo and other agents. However, the evidence for optimal dosing of antibiotics in this population group is sparse and conflicting and dose adjustment for body mass index or weight is not recommended. Current Australian guidelines recommend two grams of cefazolin for all bariatric surgery patients, regardless of weight.

This study will measure the antibiotic concentrations in the blood and subcutaneous abdominal interstitial fluid in patients after a routine dose of cefazolin for bariatric surgery and a pharmacokinetic profile will be developed.

This will examine if cefazolin concentrations are sufficient to reach the minimal inhibitory concentration of common pathogens and hence prevent infections. If current doses are sub-therapeutic, the appropriate dose will be calculated. This may assist clinicians to develop guidelines for optimal dosing of prophylactic cefazolin for this increasingly common clinical scenario.

Dr Rochelle Ryan, Dr Rebecca Christensen, Dr Dwane Jackson, Professor Jason Roberts, Royal Brisbane and Women's Hospital, Queensland

\$A30,963



Does cefazolin prophylaxis during elective bariatric caesarean section achieve therapeutic concentration in plasma and interstitial fluid?

In caesarean section, prophylactic antibiotics are routinely given to women before surgery. These have been shown to significantly reduce the incidence of wound infections, endometritis and serious infectious complications.

However, the dose of antibiotics recommended for adults is the same regardless of their weight. In overweight women this dose may be too small and may result in a reduced concentration of antibiotics in the tissue where infections occur. Overweight women have an increased risk of infection in their surgical wounds and this may be in part due to reduced antibiotic concentrations.

Evidence for dosing of antibiotics in this population is sparse and conflicting. An absence of data to guide antibiotic dosing may result in antibiotic doses for surgical prophylaxis being ineffective, thus putting the mother, foetus and neonate at risk of morbidity and mortality in the event of surgical site infection. It follows that urgent pharmacokinetic data is required to guide clinicians in this increasingly common clinical scenario.

The purpose of this study is to determine optimal dosing of cefazolin prophylaxis in the obese obstetric patient (with a body mass index greater than 35) undergoing caesarean section. The investigators will measure antibiotic concentrations in the blood and in abdominal tissue after a routine dose of antibiotics. If the antibiotic concentration is insufficient, pharmacokinetic modelling will be used to calculate the dose that may be adequate.

Data generated from this study will be used to develop a pharmacokinetic model for cefazolin, which can be used to develop dosing recommendations to optimise therapeutic activity to reduce the rate of infections in the surgical wound of women having caesarean section in this patient population.

Dr Rebecca Christensen, Dr Victoria Eley, Dr Rochelle Ryan, Dr Dwane Jackson, Professor Jason Roberts, Professor Jeffrey Lipman, Royal Brisbane and Women's Hospital, Qld.

\$A30,963

These projects will describe the pharmacokinetics of prophylactic cefazolin levels in the pregnant and non-pregnant bariatric surgical patient.

Project grants (continued)



Understanding the impact of anaesthetic technique and neural-inflammatory signalling on cancer recurrence and metastasis

Cancer continues to be one of the top five disease burdens among Australians and, with a rapidly changing landscape, the impact of cancer diagnosis is expected to continue to rise exponentially. In fact, one in two patients are expected to have a cancer diagnosis by the age of 85 years.

Surgery remains the most common treatment used in the treatment of cancer, ahead of chemotherapy, radiotherapy and immunotherapy. With surgical removal of cancer indicated in over 60 per cent of patients presenting with solid tumours and up to 85 per cent of cancer patients exposed to anaesthesia as part of their treatment, it is critical to understand the impact of the perioperative period and anaesthetic agents on long-term surgical outcomes.

The aim of this research project is twofold. Firstly, we will investigate the impact of anaesthetic agents in cancer recurrence and spread in an experimental model of human breast cancer. Secondly, the investigators will explore the mechanisms driving these effects. The research will help to define optimal strategies for perioperative intervention to help guide clinical research and establish standards for anaesthetic care of the cancer patient.

This research will be performed in collaboration with the Monash Institute of Pharmaceutical Science and the Department of Anaesthesia at the Peter MacCallum Cancer Centre, bringing together clinicians and researchers at the forefront of cancer research in Australia and ensuring rapid translation of scientific research into meaningful application in the clinical setting.

The potential impact of this research is to identify anaesthetic and perioperative strategies that provide the best possible long-term cancer outcomes for patients. Novel use of existing anaesthetic agents means that findings from our research will be rapidly and easily translated into impactful changes in clinical practice. As surgery, and as such anaesthesia, continues to be a major part of cancer treatment, research into this field is vital.

Dr Julia Dubowitz, Dr Erica Sloan, Monash Institute of Pharmaceutical Sciences, Melbourne, Vic; Professor Bernhard Riedel, Peter MacCallum Cancer Centre, Melbourne, Vic.
\$A50,654 (including scholarship)



Validation of a simplified method for assessing perioperative and OSA risk

Obstructive sleep apnoea (OSA) is a common condition characterised by repetitive episodes of complete or partial airway collapse during sleep and associated with an increased risk of adverse health outcomes. Among these, individuals with OSA are at increased risk of cardiopulmonary complications in the recovery period following surgery resulting in increased admissions to high-care environments and longer hospital stays.

While these risks exist, OSA is often poorly characterised prior to surgery or not recognised at all. Further, given limited resources, high acuity care is not available for every patient in whom the possibility of having OSA has been raised.

To address these problems we propose to measure airway-closing pressure (P_{close}) on patients prior to emergence from anaesthesia as a simple means of objectively identifying and quantifying vulnerability to upper airway obstruction when unconscious. The degree of collapsibility determined by this measure will be a guide to airway behaviour during subsequent sleep and sedation. As such, it may be useful in stratifying risk, identifying those most vulnerable to obstruction.

If so, it may be valuable in informing perioperative management decisions including required intensity of post-operative monitoring. The ability to easily and accurately stratify patients to appropriate level care would facilitate effective and cost effective use of resources and ultimately reduce the burden on tight healthcare budgets. It is also possible that the measure of P_{close} in the perioperative period may be useful for identifying those with OSA for subsequent sleep management.

The immediate post-operative period offers an opportunity to assess airway function in unconscious subjects and thereby quantify the tendency for OSA in a large, at risk, but largely undiagnosed population. New, streamlined methods for evaluating OSA are warranted as it is a very common condition with substantial economic cost to the Australian community.

Professor David Hillman, Dr Brad Lawther, Sir Charles Gairdner Hospital, WA; Professor Peter Eastwood, Dr Jennifer Walsh, Dr Kathleen Maddison, West Australian Sleep Disorders Research Institute, WA.
\$A33,850



Post-discharge opioid use following acute surgical care: a multi-centre study

As opioid prescription has increased, so too has concern about diversion, overdose, dependence and unintentional poisoning. The contribution to the community opioid pool by opioids dispensed from hospital following surgical care in Australia is unknown.

This study involves four hospitals, each servicing distinct surgical populations. We will follow the surgical cohort across these institutions. At two weeks after hospital discharge patients will be contacted to determine their pain control, adequacy or excess of discharge opioid analgesia and storage or disposal methods for any excess.

Obtaining a snapshot of the handling of prescription opioids post-surgery in Australia will reveal whether excess supply at hospital discharge is a material problem. Defining the problem is a vital first step in designing an intervention to better target opioid prescription to offer good pain relief and reduce the potential for a pool of prescription opioids in the community.

Dr Megan Allen, Dr Charles Kim, Royal Melbourne Hospital, Melbourne, Vic; Dr Tim Hucker, Peter MacCallum Cancer Centre, Melbourne, Vic.

\$A34,459



The effect of dexmedetomidine given as a premedication or intraoperatively on post-hospitalisation behavioural change in children: a randomised controlled trial

Post-operative negative behaviour, such as sleep and eating disorders, nightmares and tantrums, is a significant problem related to childhood surgery and anaesthesia with an incidence of over 50 per cent reported in various studies. It may also persist for up to a year in a small percentage of children. It is a significant problem as it may have long-term effects on a child's compliance with future medical therapy and it has been suggested that distress surrounding medical procedures in children leads to an increase in pain and anxiety surrounding medical events as adults. A recent meta-analysis of alpha-2 agonists, including dexmedetomidine, found that they effectively reduce the incidence of emergence delirium but none of the studies looked at longer-term outcomes, such as negative behaviours after discharge from hospital.

The aim of this study is to measure the incidence of negative behaviour change in three groups of children. Two to seven year-old children requiring general anaesthesia for common day-case procedures will be randomly assigned to: a dexmedetomidine pre-medication group, an intraoperative dexmedetomidine group and a control group. Baseline anxiety levels of the parent will be recorded and the anxiety of the child during induction of anaesthesia also will be recorded using validated tools. The primary outcome will be negative behaviours after hospitalisation and these will be measured using the Post Hospitalisation Behaviour Questionnaire for ambulatory surgery (PHBQ-AS) and the Strengths and Difficulties Questionnaire (SDQ).

Improving the perioperative experience for children and their families is of vital importance. Dexmedetomidine may reduce the incidence of negative behaviour change after surgery and anaesthesia, which would improve the recovery of the child, improve overall child and parental satisfaction with the perioperative period, reduce parental absence from work and reduce additional visits to the doctor. It may also have longer-term benefits by reducing stress and anxiety surrounding future episodes of healthcare.

Dr Paul Lee-Archer, Lady Cilento Children's Hospital, South Brisbane, Qld.

\$A28,792

Grant review process

Thank you to all reviewers listed below who reviewed a grant, and in some cases two, for your invaluable contribution to the grant process. The ANZCA Research Committee is extremely grateful for your assistance. Each year ANZCA Research Committee members read and review the grants, select two additional reviewers for each grant on the basis of their expertise and relevance to the project, read the reviews, collate the information and act as overall spokesperson for each grant, and make the final recommendations.

The grant review process is rigorous and transparent. Conflicts of interest are recorded and members of the committee are excluded from consideration of any grants for which they have a conflict. The presence of Dr Angela Watt, our community representative, adds an extra safeguard in this regard.

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Professor David A Scott, Deputy Chair
Professor Matthew Chan
Dr Andrew Klein
Professor Kate Leslie, AO
Associate Professor Simon Mitchell
Professor Paul Myles
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Dr Craig Walker
Dr William Weightman
Professor Daryl Williams
Dr Niall Wilton
Associate Professor Sunny Wong
Associate Professor William Wu
Dr James Yeates

*Reviewed two grants