

Anaesthesia and
Pain Medicine Foundation

Review and Research Highlights 2015



Supporting medical research
and education that saves lives,
helps people to reclaim their
health and works to make life
as pain-free as possible



Contents

About the foundation	
Mission	1
How we pursue our mission	1
Why are we needed? Urgent health issues and the search for solutions	2
Why anaesthetists and pain medicine specialists can help save more patients	4
Finding more effective treatments for chronic pain	5
ANZCA Clinical Trials Network	6
The increased cost of healthcare	9
Research highlights	10
Exploratory projects	10
Clinical trials and large studies	16
Foundation governance	22
Financial highlights	23
Seed funding for government grants	23
How you can help	24
Donor-provided awards	26
Donors and sponsors	27



Mission

To support medical research and education that works to save lives, help people to reclaim their health, and make life as pain-free as possible.



About the foundation

The Australian and New Zealand College of Anaesthetists (ANZCA) established the Anaesthesia and Pain Medicine Foundation in 2007 to help more patients survive and recover from surgery without complications or disabilities, including chronic pain.

To pursue this humanitarian goal of delivering enjoyable, productive and healthy lives that are as pain-free as possible, the foundation works to increase funding for vital exploratory research and education projects across perioperative and pain medicine. These projects are conducted by highly qualified anaesthetists and pain medicine researchers.

ANZCA Fellows are aware of the great need for such outcomes in developing countries and indigenous communities. Therefore the foundation also seeks to raise funds to support innovative education programs being delivered by Fellows in these areas.



How we pursue our mission

The foundation's purpose is to raise funds to:

- Increase the safety and comfort of patients undergoing anaesthesia and sedation.
- Improve outcomes for critically ill patients following surgery or trauma.
- Improve the treatment of acute pain, cancer pain and persistent non-cancer pain

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Why are we needed? Urgent health issues and the search for solutions

The high standards of healthcare available to most Australians and New Zealanders are well known. Yet the high rate of chronic pain and post-surgical complications and deaths that still occur among high-risk patients remains a major, and under-recognised, public health challenge.

Across our healthcare systems, there are serious needs we need to address if we are to improve the proportion of patients who recover well from surgery and serious illness.



The following urgent health needs are examples of those being targeted by foundation-funded investigators and their teams. Foundation funding grants allow them to pursue unanswered questions and potential health solutions through exploratory medical research projects. These projects are in progress.

Healthier ageing		
Problem	Opportunity	Project
One in five people aged 70 years and over suffer serious complications within 30 days of surgery and anaesthesia. One in 20 die. ¹	A simple fitness test could help identify risks, target treatments and help more people recover fully after surgery.	The six-minute walk test (Alfred Hospital, Vic).
Women's health		
Problem	Opportunity	Project
Breast cancer is one of the most common causes of death for women in Australia and New Zealand.	Using opioid anaesthetic agents during surgery could significantly reduce the spread of cancer cells in women with breast cancer.	Can surgical pain relief influence cancer growth and spread? (Mater Adult Hospital, Brisbane, and School of Pharmacy, University of Queensland, Qld).
Preeclampsia, a life-threatening condition, affects 20,000 pregnant Australian women every year. It causes serious organ damage, disease and deaths.	Understanding how preeclampsia affects heart and blood vessels could stop it killing pregnant women and prevent many brain, kidney, heart and lung injuries.	Heart function and structure in women with preeclampsia (The Royal Women's Hospital, Vic).
Osteoarthritis affects at least 50 per cent of people over 65 years of age. Most suffer severe, often intractable, pain.	Understanding the role of cytokines could lead to more effective pain relief strategies for osteoarthritis sufferers with fewer side effects.	Osteoarthritis pain; mechanisms and mediators – the roles of NGF and IL-1 (University of Western Australia, WA).
Surgery for fractured hip has one of the highest rates of post-operative complications of all types of surgery.	Echocardiography checks to identify heart disease before hip fracture surgery could reduce its high rate of post-operative death and disability.	Does cardiac ultrasound improve patient recovery after hip fracture surgery? (University of Melbourne, Vic, Sir Charles Gairdner Hospital, WA, University of Tasmania, Tas, Royal Melbourne Hospital, Vic).

Relief from chronic pain		
Problem	Opportunity	Project
Chronic pain has an enormous impact on the quality of life of its sufferers. It's estimated total cost to the Australian economy in 2007 was \$34.3 billion. ² One in five Australians, including children, lives with chronic pain. One in three over 65 years of age suffer chronic pain. ³	Understanding the epigenetics of chronic pain could release potential to relieve suffering.	Proteolytic mechanisms of chronic pain: research translation (Alfred Hospital, Monash University, Vic)
Chronic pain for months or years is a well-recognised complication after major surgery.	Choice of anaesthetic agent could significantly reduce the incidence of chronic pain developing after surgery.	Preventing long-term pain after surgery (Austin Health, Vic).
Diabetes		
Problem	Opportunity	Project
Severe diabetes can lead to ulcers, which, in the worst cases, can ultimately lead to amputation of limbs.	Hyperbaric oxygen therapy for diabetes ulcers could help to reduce limb amputations resulting from diabetes.	Hyperbaric oxygen therapy for foot ulcers in diabetes (Royal Brisbane and Women's Hospital, Qld).
Overseas and Indigenous medical education		
Problem	Opportunity	Project
Many people in less developed countries and communities face extremely limited access to safe anaesthesia and pain medicine.	Provide capacity to deliver pain management healthcare in developing country communities, by training local health workers to teach a course in improving pain-management skills, knowledge and abilities.	Essential Pain Management (EPM) (ANZCA Overseas Aid Committee)
Many indigenous communities have limited access to essential healthcare services and the related health outcomes often are markedly below acceptable national standards.	Support and prepare clinicians to work in remote indigenous communities, provide education on indigenous cultural and health issues, mentor indigenous high school students and medical students, and organise a future scholarship to support research into anaesthesia and indigenous patients.	ANZCA Indigenous Health Program (ANZCA Indigenous Health Committee).

Why anaesthetists and pain medicine specialists can help save more patients



*Dr Lindy Roberts,
Chair,
Anaesthesia and
Pain Medicine Foundation*

An effective way to help more people to survive their surgery without complications, return home disability-free, and suffer less chronic pain, is to increase funding support for medical research and education projects conducted by anaesthetists and pain medicine specialists.

Although surgery is generally safe and the quality of patient outcomes is very high in Australia and New Zealand, death and disability still occur too frequently. The consequences can be devastating. Those who are especially at risk are the very young, the very old, and those with severe medical illness.

Anaesthetists and pain medicine researchers are ideally-placed to find ways to prevent patients from suffering poor outcomes and reduce pain and disability:

- they work across all stages of perioperative medicine (before, during, and after surgery), including assessment and preparation for surgery and anaesthesia, surgery, recovery, and recuperation. Patient outcomes are influenced by each of these stages.
- they are required in almost every area of surgical medicine, not only for the vitally important consideration of patient comfort, but to help deliver the best possible quality of recovery for each person.
- their work includes trauma injuries, cancers, immune system disorders, inflammatory conditions, cardiac and respiratory diseases, disorders of the central nervous system and organ transplantation.

Many improvements to clinical practice world-wide have already been achieved as a result of research by anaesthetists and pain medicine specialists from Australia and New Zealand. Yet Foundation-supported researchers have identified many areas where too many patients are still dying or suffering disability, and are finding more opportunities to protect them. There is much more work to be done!

Finding more effective treatments for chronic pain



Chronic pain is an epidemic that requires better understanding and more effective treatment and prevention.

Chronic (or persistent) pain can develop after surgery, trauma, injury or a medical illness. Research has shown that it affects one in every five Australians³ and New Zealanders causing immense suffering, crippling their quality of life, interfering with their work, play, hopes and dreams, severely affecting their loved ones, and costing the economy billions of dollars every year².

With funding, anaesthesia and pain research has enormous potential to deliver desperately-needed relief for sufferers of chronic pain, through new discoveries, and more effective treatments and preventive therapies.

I hope you will be inspired by the current projects and highlights of research achievements that are outlined in this report.

Philanthropic donations to the Foundation are vital to increasing its ability to fund this life-saving work. Please donate to support the Foundation's cause, and be a part of delivering successful outcomes and healthy lives to more patients.

A handwritten signature in black ink, appearing to read 'Lindy Roberts'.

Dr Lindy Roberts
Chair, Anaesthesia and Pain Medicine Foundation

ANZCA Clinical Trials Network

Life-giving achievements in foundation-supported healthcare research



Professor Kate Leslie
Chair, ANZCA Clinical Trials Network
Executive

To save more patients, we must improve our ability to prevent and manage major surgery complications.

ANZCA support for medical research through the Anaesthesia and Pain Medicine Foundation has made, and will continue to make, an enormous difference to the lives of surgery patients and people who suffer acute and chronic pain.

The foundation supports medical research and education projects conducted by anaesthetists and pain medicine specialist investigators, with a focus on exploratory and proof-of-hypothesis studies. In many cases, these have paved the way for successful multi-centre clinical trials. In this way, the foundation has delivered outstanding value for money for its supporters, as the sole funder or seed funder of many studies that have formed starting points for translational research and clinical trials, which have had led to significant improvements in local and global clinical practice.

Examples of ANZCA-funded research findings improving outcomes for patients include:

- Commonly used analgesics were found not to be transferred through breast milk to nursing infants in significant quantities, allowing better pain management for breast-feeding mothers after caesarean childbirth.
- Children exposed to general anaesthesia before the age of three years may have a higher relative risk of specific cognitive deficits than unexposed children – more information is urgently needed (and is being collected in the ANZCA-supported GAS study).
- Elderly patients face a significant risk of death and/or major complications after elective and emergency non-cardiac surgery – we must find effective and safe preventative measures.
- Epidural analgesia provides better pain relief than intravenous analgesia but does not affect the rates of major complications in high-risk surgical patients.
- Bispectral index “depth of anaesthesia” monitoring is associated with lower incidence of awareness during surgery, in patients at high risk of such awareness.
- Nitrous oxide is not associated with higher risk of post-operative stroke or cardiac arrest in adult patients having non-cardiac surgery.
- Pre-existing cognitive impairment is associated with worse post-operative cognitive outcomes up to 12 months or even longer after surgery, identifying the need for further investigation of the possible effect of anaesthesia.



Professor Matthew Chan, The Chinese University of Hong Kong and the Prince of Wales Hospital, China

The role of the ANZCA Clinical Trials Network

The foundation has been instrumental in establishing and supporting the ANZCA Clinical Trials Network – a unique, multi-national collaboration of anaesthesia and pain medicine researchers. Through collaboration, research projects can be much broader in scope and have a much bigger impact. Through support from the foundation, the ANZCA Clinical Trials Network has explored awareness during anaesthesia, the long-term effects of nitrous oxide (“laughing gas”), the prevention of heart attacks during heart surgery and the effects of anaesthesia on premature babies. These trials have changed the practice of anaesthesia and pain medicine around the world.

Studies the ANZCA Clinical Trials Network has co-ordinated or participated in have featured in world-leading peer-reviewed medical publications. In 2014, publication highlights included the appearance of an article and editorial in the *New England Journal of Medicine* on the POISE-2 study on perioperative aspirin and clonidine, and publication in *The Lancet* of the ENIGMA-II trial on the perioperative use of nitrous oxide.

The future of anaesthesia and pain medicine research

We are still not sure how general anaesthetics work or their long-term effects, particularly in babies and in the elderly. As millions of Australians and New Zealanders have surgical procedures requiring anaesthesia every year, we all have an interest in solving these puzzles to ensure anaesthesia is as safe as possible.

Our populations are ageing and the costs of caring for them will be an overwhelming burden for society in the future. Yet seniors in Australia and New Zealand want to enjoy a high quality life, not just a longer one. We urgently need to find better ways to prevent and effectively manage major perioperative complications, such as myocardial infarction, stroke, wound complications and cognitive impairment.

ANZCA Clinical Trials Network – continued

We also need to ensure that chronic post-operative pain, and other forms of chronic pain (cancer and non-cancer-related), do not impair the ability of our patients to enjoy their lives or ultimately to die with dignity and in comfort. The only way to do this is through high-quality research.

Millions of people in our region also suffer from acute or chronic pain as a result of injury or disease, but many lack effective treatments. As pain affects all our lives, we all have an interest in supporting endeavours to find solutions.

ANZCA's Anaesthesia and Pain Medicine Foundation and its donors play a vital role in this life-giving cause, by raising funds to support research by Fellows and trainees. We are very grateful to all those who have supported the foundation so far, including many ANZCA Fellows.

Professor Kate Leslie

*Chair,
ANZCA Clinical Trials Network Executive*

The increased cost of healthcare

“Growth in health spending above GDP over the past 11 years was greater than the growth above GDP of all other spending combined...”

Most of us, and our families and friends, will at some time undergo an anaesthetic procedure. An amazing 6.2 million anaesthetics are administered in Australia and New Zealand each year. Perhaps we do not take much notice of this part of the surgical process, as it can appear to be a subsidiary factor. And we tend to assume that medical science has vastly improved from the days of ether masks!

The Foundation's task is to convey the significance and importance of anaesthesia to the broader community, and garner support for research; critical for making procedures ever safer. Since joining the Board of Governors, I have begun to appreciate the enormity and significance of anaesthesia to patients' health in surgery and beyond. I am also more aware of anaesthetists' roles in managing consequential pain, to minimise the chances of chronic pain having major future impacts on patients.

Anaesthesia may not be especially visible to the patient undergoing surgery. Yet watching an anaesthetist alongside a patient throughout, monitoring constantly, and realising the dependence of each of us in that situation on that specialist, has really brought home to me the significance of the quality of this care - and the research which supports clinical practice. Medicine, including anaesthesia, is not static, and maintaining and enhancing this quality of care as total healthcare demand and cost grows requires continuous improvement, through research and practice.

An ageing population and greater demands from all age groups are driving up healthcare costs in Australia and New Zealand. Post-surgical complications and long intensive care visits are major contributors to this cost growth.

Research funding is finite, yet fundamental, to reducing complications. It holds enormous potential to deliver benefits to us all, through saved lives, reduced disability and suffering, and reduced economic costs for each patient and the community. More research should be a major, strategic, community health priority.

Corporate sponsorship or donations to the Foundation are extremely effective social investments for organisations and individuals, enabling pilot studies which often leverage further funding, and improving healthcare cost-effectiveness and accessibility through high-quality research. We can make a meaningful difference to patient experiences and health outcomes through ANZCA sponsored research.

Ms Kate Spargo

*Chair,
Anaesthesia and Pain Medicine Foundation Board of Governors*



*Ms Kate Spargo
Chair, Anaesthesia and
Pain Medicine Foundation
Board of Governors*



Exploratory projects

The following projects represent a small selection of the diverse range of exploratory studies supported by the foundation in recent years.

They demonstrate the many areas in which new knowledge is urgently needed to reduce risk for patients. They are excellent examples of how anaesthetists' and pain medicine specialists' unique roles across perioperative medicine allow them to identify and investigate serious questions, the answers to which could lead to better health outcomes for patients facing potentially devastating health problems.



Exploratory projects

Lung function in ventilated children – assessment of normal values

Professor Britta Regli-von Ungern-Sternberg, Princess Margaret Hospital for Children, WA.

Paediatric patients undergoing elective or emergency surgery, or who have been admitted to the neonatal/ paediatric intensive care unit, often require mechanical ventilation for the management of their underlying conditions. Pulmonary complications, more specifically respiratory failure requiring ventilation, are associated with high morbidity and mortality along with increased costs and length of hospital stay. Providing optimal ventilation strategies will reduce these risks, while failure to tailor ventilatory support to each patient can result in ventilator-induced lung injury, potentially exacerbating any underlying lung condition and ultimately may lead to hypoxia, organ failure and, in some cases, death. The “New evidence-based ventilation guidelines for children” project aims at measuring lung function outcomes in healthy children aged between one and 15 years old who are undergoing surgery under general anaesthesia and require mechanical ventilation. By measuring the respiratory resistance and pulmonary compliance of children undergoing surgery before and after anaesthesia induction, we will be able to develop robust prediction equations and nomograms that define the values of physiological parameters to be programmed in mechanical ventilators for optimal lung function in anaesthetised children having surgery or being ventilated on the neonatal/ paediatric intensive care unit. These normal values for respiratory resistance and pulmonary compliance derived from a healthy paediatric population will then assist in the development of evidence-based clinical guidelines for ventilation strategies in children.

Towards prevention and therapy for chronic pelvic pain

Dr Susan Evans, Professor Paul Rolan, and Associate Professor Mark Hutchinson, Royal Adelaide Hospital, SA.

Chronic pelvic pain is commonly suffered by young women and is traditionally associated with the condition endometriosis. There is little evidence and understanding of this correlation, however animal research evidence suggests that persistent neuropathic pain may be due to sensitivity from the activation of the connective tissue surrounding the nerve cells, with estrogen amplifying the process. The ‘Does estrogen drive period pain to chronic pelvic pain?’ project will investigate whether the rise in oestrogen levels that happens around the time that periods start might activate certain pain pathways. The particular pain pathways being investigated are called “Toll-Like Receptor Pathways”.



Exploratory projects – continued

Grappling with impaired mental function after anaesthesia and surgery

Associate Professor Brendan Silbert, Associate Professor David Scott, Associate Professor Lisbeth Evered, St Vincent's Hospital, Melbourne, Vic.

Impaired mental functions after surgery, including confusion, memory loss, reduced awareness and delirium, are collectively known as post-operative cognitive dysfunction (POCD), one of the greatest challenges in anaesthesia and surgery. Mainly affecting the elderly (more than a third of Australian surgical cases), POCD is associated with distress, reduced quality of life, longer hospital stays and potential further deterioration.

Current evidence links POCD to inflammation after anaesthesia and surgery. The "Cognitive decline after anaesthesia and surgery – the role of inflammation" study will explore whether this could be a cause of POCD by establishing whether pre- and post-surgery levels of specific inflammatory proteins in the blood are related to any decline in cognitive function. Identifying such proteins is a first and vital step in developing successful POCD prevention strategies.

High-tech brain injury monitoring at point of trauma

Dr Andrew Weatherall, Dr Alan Garner, CareFlight, NSW; Professor Nigel Lovell, Dr Stephen Redmond, University of New South Wales, NSW; Professor Anna Lee, The Chinese University of Hong Kong, China; Dr Jonathan Egan, Dr Justin Skowno, The Children's Hospital at Westmead, NSW.

Traumatic brain injury (TBI) is a major cause of death and severe disability, yet outcomes have shown little improvement for 20 years. Much research has focused on optimal in-hospital TBI monitoring and management, but there is a lack of brain monitoring in the vital immediate post-trauma period, where low oxygen or blood pressure may cause further injury. Near infrared spectroscopy (NIRS) tissue oximetry using forehead probes could be applied at the accident site, to immediately monitor blood flow and oxygen utilisation. To evaluate associations between NIRS oximetry and TBI, the "Pre-hospital assessment of non-invasive tissue oximetry monitoring (PHANTOM)" project will study the use of on-site NIRS tissue oximetry, and whether there are any associations between monitoring parameters, injuries seen on cerebral imaging and patient recovery at six and 12 months after their accident. Confirming associations would be a significant first step towards the introduction of this technology on-site to improve evidence-based treatment for TBI patients.

Unravelling the interconnected reasons for chronic pain

Professor Philip Siddall, Greenwich Hospital, HammondCare, and University of Sydney, NSW.

How can we treat people's chronic pain and suffering, if we don't understand its causes? The "Assessing and treating pain: an integrated approach" project will study the complex interactions and correlations between the biological, psychological, spiritual and social factors that cause people's chronic pain. This understanding is essential to supporting the development of more effective treatments, based on identifying and assessing each of these contributors and then dealing with chronic pain cases in a holistic, tailored and informed way.

Better performance testing for trainee anaesthetists

Associate Professor Jennifer Weller, Dr Damian Castanelli and Dr Yan Chen, University of Auckland, NZ.

To produce the world's best anaesthetists, we must have a proven, tested, top quality tool to assess the performance of trainees. The "How do workplace-based assessments affect trainee supervision and learning?" project will help deliver such a tool by conducting research to establish the validity, reliability and value of the mini-CEX (mini clinical evaluation exercise), an instrument to score and provide feedback on trainee performance at work.

Helping prevent disabling pain after surgery

Professor Matthew Chan, The Chinese University of Hong Kong and the Prince of Wales Hospital, China.

Preliminary research has shown that brain-derived neurotrophic factor (BDNF) in the central nervous system is a key player in the development of chronic pain, and affects other neurological diseases. The "Brain-derived neurotrophic factor and chronic postsurgical pain: mechanisms and preventive strategy" study will evaluate the role of BDNF in chronic postsurgical pain, and construct a novel blocking peptide that will regulate the secretion of BDNF in the spinal cord. Ultimately, it is hoped the results will be translated to clinical medicine, where preoperative administration of this peptide will help to prevent disabling pain after surgery. Professor Chan was awarded ANZCA's 2015 Lennard Travers Professorship for this project.

Assessing fitness screening before surgery

Professor Paul Myles, Dr Mark Shulman and Ms Sophie Wallace, The Alfred, Vic; Associate Professor Duminda Wijeyesundera, St Michael's Hospital, Canada; Professor Brian Cuthbertson, Sunnybrook Hospital, Canada; Dr Rupert Pierce, Royal Hospital, London, UK.

The "Six-minute walk test" project will assess whether this simple and inexpensive cardiovascular fitness test can help doctors to predict how well people will recover after major surgery. This information would help specialists to better plan patient treatments and make decisions that are informed by each patient's individual prospects for fitness-based recovery, creating the potential to significantly reduce disabilities and deaths from post-operative complications.

Saving pregnant women from preeclampsia and brain, kidney, heart and lung damage

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

Preeclampsia affects 20,000 pregnant Australian women every year, often resulting in serious organ damage, long-term disease, or death. Globally, preeclampsia causes 20 per cent of all maternal deaths. The "Heart function and structure in women with preeclampsia", project aims to provide better understanding of preeclampsia and support the search for new treatments that will save the lives and future health of more pregnant women and new mothers.

Better therapies for severe osteoarthritis pain

Professor Stephan Schug and Professor David Joyce, University of Western Australia, WA.

At least half of the population over 65 year of age suffers from osteoarthritis, most with severe and often intractable pain. Studying cytokines holds the potential for better pain relief. The "Osteoarthritis pain; mechanisms and mediators – the roles of NGF and IL-1" project aims to better understand the role of cytokines in osteoarthritis pain, and discover more effective pain-relief strategies with fewer adverse side effects on patients' health.

Exploratory projects – continued

Making hip surgery safer

Dr David Canty, Prof Colin Royse, University of Melbourne; Professor John Faris, Sir Charles Gairdner Hospital, WA; Professor David Kilpatrick, University of Tasmania; and Associate Professor Andrew Bucknill, Royal Melbourne Hospital, Vic.

Hip fracture surgery is common, results in high patient mortality and disability and represents a large world health care burden. Underlying cardiac disease is common, often unrecognised during clinical assessment and poorly treated, and is believed to be a principal cause of mortality. Focused transthoracic echocardiography is the bedside application of transthoracic echocardiography, which has been shown to improve preoperative cardiac assessment by identifying major cardiac pathology and haemodynamic state guiding more appropriate perioperative management. The 'ECHONOF' study aims to determine whether preoperative focused transthoracic echocardiography improves postoperative recovery in hip fracture patients and to test feasibility of a larger trial to determine whether mortality is reduced by this powerful non-invasive diagnostic test.

Reducing women's pain after childbirth

Clinical Associate Professor Nolan McDonnell, King Edward Memorial Hospital for Women, WA; and Professor Michael Paech and Dr Sam Salman, University of Western Australia, WA.

Two effective and proven existing pain-relief medicines that could significantly reduce women's pain after childbirth are not being used to do so, because there is a lack of evidence that they are safe for breastfeeding babies. The "Transfer of gabapentin and pregabalin into breast milk" project aims to answer this question, and potentially safely reduce acute and chronic pain after childbirth for women across Australia.

Understanding and treating pain amplification in the central nervous system

Professor Paul Myles and Dr Nicholas Christelis, The Alfred, Vic; and Professor Nigel Bunnett, Monash University, Vic.

After traumatic injury or disease, the body's nervous system can "rewire" itself to continually amplify pain signals, producing chronic pain. In the "Proteolytic mechanisms of chronic pain: research translation" project, Professor Myles and his team will study molecular changes in the spinal fluid that can amplify pain sensitivity, to help find more effective treatments and medicines that could prevent chronic pain.

Assessing surgery performance to help prevent patient harm

Professor Alan Merry, Associate Professor Jennifer Weller and Associate Professor Simon Mitchell, University of Auckland, NZ.

Although modern anaesthesia and surgery are very safe, too many patients are still harmed in attempts to cure them. The "Checking the World Health Organization's Checklist" project will assess and validate the Behaviourally Anchored Rating Scale (BARS), a new tool developed to help assess and improve the use of the World Health Organization's Safe Surgery Checklist to improve surgical teamwork and safety culture. Once validated, the implementation of BARS has the potential to reduce patient deaths and harm across Australasia and around the world.

Using analgesia to reduce the spread of breast cancer

Dr David Sturgess, Mater Research Institute, The University of Queensland, Qld; and Associate Professor Marie-Odile Parat, Associate Professor Peter Cabot, and Professor Nick Shaw, School of Pharmacy, University of Queensland, Qld.

Anaesthetic researchers have found that using opioid drugs to control pain for women having breast cancer surgery may help stop the cancer from spreading. The "Can surgical pain relief influence cancer growth and spread?" project aims to confirm the theory so that the choice of pain control drugs could translate to standard practice and reduce the spread of breast cancer cells to other parts of patients' bodies.

Preventing long-term pain developing after surgery

Associate Professor Philip Peyton, Austin Health, Vic.

Recent results from large trials by the ANZCA Clinical Trials Network show that long-term pain is a very common complication after major surgery. Anaesthetist researchers have found that the powerful anaesthetic ketamine might help prevent the spinal cord from becoming hypersensitive to pain signals following surgery. In this project, Associate Professor Peyton's team aims to confirm that using ketamine before and after surgery can help dramatically reduce the number of patients with chronic pain six months later.

Reducing amputations among diabetes patients

Dr Susannah Sherlock, Dr Diane Smith, and Ms Kerrie Coleman, Royal Brisbane and Women's Hospital, Qld.

On current trends, three million Australians will have diabetes by 2025, increasing the number of amputations resulting from unhealed foot ulcers, and dramatically affecting more patients' quality of life. The "Hyperbaric oxygen therapy for foot ulcers in diabetes" project aims to confirm whether hyperbaric oxygen therapy can help in ulcer healing and reducing limb amputations.

Reducing the cost and environmental impact of morphine

Dr Forbes McGain, Western Health, Vic; Professor David Story, University of Melbourne, Vic; and Associate Professor Karen Haggood, Monash University, Vic.

There is growing interest in reducing the financial and environmental costs of healthcare. The carbon footprint of drug production alone contributes as much to the carbon dioxide emissions of healthcare as the direct energy consumption of all healthcare institutions combined. The "Environmental effects of morphine" project will assess the lifecycle costs of morphine to help reduce the financial and environmental costs of its production, and ultimately make anaesthetic practice more accessible and sustainable.

Improving patient safety with international database technology

Associate Professor Michael Barrington, St Vincent's Hospital, Vic.

With over 17,000 anaesthetics given daily in Australia and New Zealand, database technology is needed to collect and study unusual adverse events during and after surgery. The "International Registry of Regional Anaesthesia" project will increase anaesthetists' ability to protect surgery patients from unusual complications, and save more lives.

Predicting and preventing chronic pain after knee replacement surgery

Dr Michal Kluger, North Shore Hospital, Auckland, NZ; Professor Peter McNair and Dr Gwyn Lewis, Health and Rehabilitation Research Institute, University of Auckland, NZ; and Professor Andrew Somogyi, University of Adelaide, SA.

Up to one in three people experience chronic pain after knee-replacement surgery. The "Predictors of persistent post-surgical pain following total knee joint arthroplasty" project will help doctors find the warning signs that a patient might be at risk, so that special treatments can be provided to help prevent the body from developing entrenched, persistent pain that is ultimately very difficult to treat.

Reducing kidney injury after heart surgery

Dr David McIlroy, Associate Professor Silvana Marasco, The Alfred, Vic.

Up to a quarter of heart surgery patients suffer acute kidney injury after surgery. Our researchers believe less intravenous chloride during surgery could reduce the incidence of these kidney injuries. The "Does the composition of IV fluid alter the risk of kidney injury after cardiac surgery?" project will seek the answer, and could help more cardiac patients recover with good health, intact kidney function and the potential to enjoy good quality of life.

Reducing death and injury from acute lung injury

Dr Shay McGuinness, Dr Shailesh Bihari and Professor Andrew Bersten, Flinders Medical Centre, SA; Dr Carol Hodgson and Professor Alistair Nichol, The Alfred, Vic.

Acute respiratory distress syndrome (ARDS), an inflammatory lung disease, causes high rates of patient death and disability through injury to other organs of the body. ARDS patients require intensive care and ventilator-assisted breathing. The "Do patients with lung injury have different responses to mechanical ventilation?" project is working to reveal whether varying ventilation levels for specific sub-types of the disease, a previously untested strategy, could significantly reduce death and injury rates suffered by ARDS patients.

Clinical trials and large studies



Clinical trials and large studies

The ANZCA Clinical Trials Network, the world's only specialist medical college-based clinical trials network, was established to foster multi-centre clinical trials that will answer important questions in anaesthesia, pain and perioperative medicine and improve the evidence base for clinical practice.

The Anaesthesia and Pain Medicine Foundation has provided seed funding for pilot studies and other research that has led the way for several large multi-centre trials, and has been crucial for securing grants from the National Health and Medical Research Council in Australia and the Health Research Council in New Zealand.

The use and safety of nitrous oxide (ENIGMA I and II studies)

Nitrous oxide ("laughing gas") has been used worldwide as an anaesthetic for more than 160 years, yet there had never been a definitive trial to test its overall safety and effectiveness.

Professor Paul Myles, director of anaesthesia and perioperative medicine at The Alfred hospital in Melbourne, and his colleagues established a large multi-centre randomised controlled trial, ENIGMA I, involving more than 2000 patients in 30 hospitals around the world including Australia, New Zealand, south-east Asia and Europe, to investigate its effectiveness and safety.

The trial outcomes showed that although its use appeared to reduce the development of chronic pain, nitrous oxide might also be associated with increased incidence of heart attack and stroke.

The trial raised important results and questions for the investigators. With more elderly patients, for whom heart attack and stroke are significant risks, presenting for major surgery it was important to determine once and for all whether nitrous oxide is linked to

increased risk of these complications. Therefore, ENIGMA II, a large five-year follow-up study focusing on these cardiovascular side effects, was conducted with 7000 patients in 40 hospitals around the world. This trial looked in particular at the long-term effects of nitrous oxide in patients with coronary artery disease undergoing major surgery.

The final results were released in May 2014, and demonstrated definitively for the first time that there is no significant correlation between the use of nitrous oxide and the risk of heart attack and stroke. This important finding will allow medical teams around the world to use nitrous oxide secure in the knowledge it is free of these risks.

The benefits are potentially significant. The continued availability of this low-cost anaesthetic option can be particularly useful, especially in lower-income contexts around the developing world.

Both studies have been funded by ANZCA project grants.

Research highlights:

- Despite initial indications from ENIGMA I, nitrous oxide is not linked to greater risk of cardiovascular complications.
- Medical teams can use nitrous oxide secure in the knowledge it is not linked to increased risk of heart attack or stroke.
- Millions in the developing world may now safely benefit from this low cost anaesthetic option.



Clinical trials and large studies – continued



The effectiveness and safety of aspirin and clonidine (POISE-2 study)

Although the drugs aspirin and clonidine have commonly been used around surgery in the hope of reducing the risk of heart attack, whether they actually reduce this risk had never been conclusively tested – yet studies indicated they might increase the risk of other major complications.

The POISE-2 study looked at the use of aspirin and clonidine to prevent death and heart attack in 10,000 high-risk patients having non-cardiac surgery. In March 2014 the findings were published in the *New England Journal of Medicine*, the highest-ranking general medical journal in the world, and are likely to be of significant benefit to patients.

Aspirin

The study revealed that despite aspirin's effectiveness in preventing heart attack in non-surgical cases, the perioperative use of aspirin does not affect the risk of heart attack, but it does cause more major bleeding.

The results were unaffected by whether or not patients had already been taking aspirin regularly, suggesting the problem of bleeding may overshadow any beneficial effect of aspirin.

POISE-2 investigators have now been able to make the evidence-based recommendation that surgeons

and anaesthetists advise patients to cease aspirin at least three days before non-cardiac surgery (unless the patient is at high risk of blood clots), to avoid unnecessarily increasing the occurrence and danger of major bleeding.

Clonidine

POISE-2 also found that the use of the drug clonidine in surgical cases did not reduce the incidence of death or heart attack, but did cause clinically significant hypotension (low blood pressure), and bradycardia (very slow heartbeat). This was despite its potential to protect against the stress of surgery by rebalancing oxygen supply and demand.

Importantly, the results indicated the hypotensive effect of clonidine might outweigh any benefit in the control of heart rate. Investigators have recommended that clonidine should not be used in attempts to prevent heart attacks, and should only be administered to high-risk patients for pain management with low doses and regular blood pressure monitoring.

Patients stand to benefit greatly from the prevention of the unnecessary occurrence of these complications, caused by the use of clonidine in the incorrect belief that it can significantly reduce the risk of fatal heart attack.

The Australian component of the POISE-2 study was funded by a National Health and Medical Research Council grant. It was led in Canada by chief investigator Dr PJ Devereaux of the Population Health Research Institute, and led in Australia by Professor Kate Leslie with co-ordination by the ANZCA Clinical Trials Network.

Research highlights:

- Surgeons and anaesthetists should advise patients to cease aspirin at least three days before non-cardiac surgery unless the patient is at high risk of blood clots.
- Preventing the unnecessary occurrence of clinically significant hypotension, bradycardia and non-fatal cardiac arrest due to the erroneous use of clonidine to prevent fatal myocardial infarction.

Depth of anaesthesia and long-term outcomes (the Balanced study)

To ensure patients do not experience potentially traumatic awareness during surgery, anaesthetists tend to administer relatively deep general anaesthesia.

However, five of six recent observational studies have shown that moderate or high-risk major surgery patients who receive this relatively deep anaesthesia suffer a 20 per cent higher risk of mortality. Anaesthetists face a dilemma – the possibility of a significantly increased risk of patient mortality with deeper anaesthesia, against a possible increase in the risk of awareness during surgery at lower anaesthetic doses.

Although electroencephalogram (EEG) monitors used to assess anaesthetic depth in patients undergoing surgery are widely available, the dilemma remains because specialists do not know the optimal depth at which anaesthesia should be administered to minimise major complications and awareness under anaesthesia.

The Balanced study, a large scale randomised trial of “deep” versus “light” anaesthesia, aims to definitively answer the question of whether depth of anaesthesia affects total mortality one year after surgery, and whether it is linked to specific complications including wound infection, cardiovascular complications, stroke,

kidney failure, pneumonia, continuing pain and intra-operative awareness.

Balanced will be a prospective, randomised, double blind study in which patients will receive either relatively light or deep anaesthesia. Patients selected for the study will be 60 years or older, at moderate or high risk, and be having surgery lasting two or more hours with general anaesthesia.

This study holds significant promise for reducing the rate of death and disability after surgery for higher risk patients. It aims to test the ability of a widely available monitoring technology (the BIS monitor) to improve outcomes in a wide range of diseases for which major surgery is the chosen treatment.

More than 450,000 people in New Zealand, three million in Australia and around 230 million worldwide undergo surgery each year for acute and chronic conditions. About 10 per cent of these people are in higher risk categories and having extensive surgery, and are the target group for this study.

Principal Investigators for the Balanced study: Associate Professor Timothy Short, Auckland City Hospital, NZ; Professor Kate Leslie, Royal Melbourne Hospital, Vic; and Professor Matthew TV Chan, Chinese University, Hong Kong.

Research highlights:

- A positive study would have important implications for patient safety and public health costs, with an anticipated improvement in one-year survival of 20 per cent in older patients undergoing major surgery, representing a two per cent absolute risk reduction. A negative study would also have important implications for how we administer anaesthesia in sick and elderly patients.
- The findings are eminently translatable into clinical practice because most hospitals already have anaesthetic depth monitors available. The result will suggest best practice in an area where there is currently no guidance.

Clinical trials and large studies – continued



Restrictive versus Liberal Fluid Therapy in Major Abdominal Surgery (the RELIEF study)

Around 230 million people around the world, including about three million people in Australia, undergo major surgery each year. A growing proportion of these patients (40 per cent) are elderly, and they and many others have additional health problems that increase the risks of complications, long-term disability or death following surgical procedures.

There is therefore a relentlessly increasing need to find ways to reduce surgery-related complications and mortality. One of the important factors shown to influence these outcomes is the intravenous fluid regimen applied for surgery.

Anaesthetists frequently use liberal fluid administration to correct or avoid the occurrence of hypotension (low blood pressure), which reduces blood flow to vital organs including the brain, heart and kidneys. Severe uncorrected hypotension can lead to serious complications including stroke, heart attack, and foetal compromise in obstetric patients. Some small trials have suggested that fluid supplementation can also help reduce organ dysfunction, post-operative morbidity and death.

However, the administration of excess fluid also causes oedema (swelling), and this may contribute to increased

pulmonary complications, impaired coagulation, bacterial translocation and sepsis, and impaired wound healing. Some small trials of patients undergoing abdominal surgery have found that fluid restriction, rather than supplementation, can lead to reduced morbidity and hospital stay.

Clearly, there is a conflicting evidence base, which explains the diverse and varied practices around the world. The strongest and most consistent evidence supports a restrictive fluid strategy, while there is less (and more contradictory) evidence supporting the alternatives. We simply do not know whether a liberal or restrictive fluid approach improves outcomes. Secondary questions also exist, including the choice of fluid and the role of goal-directed therapy in major abdominal surgery.

A large, definitive clinical trial evaluating perioperative fluid replacement in major surgery is required. In 2011, the foundation funded a pilot study by Professor Paul Myles and his team at the Alfred Hospital in Melbourne, which demonstrated the feasibility of conducting such a clinical trial.

Following the pilot study, the proposed RELIEF trial was the National Health and Medical Research Council's most

highly ranked medical research funding application. The funding secured will allow the investigators to study the effects of a restricted versus liberal fluid regimen and the possible effect-modification of goal-directed therapy and colloid fluid replacement, to supply the evidence that is so urgently needed.

Research highlights:

- The RELIEF trial will test the hypothesis that a restrictive fluid regimen for major surgery leads to reduced complications and better disability-free survival for patients in the months after surgery, when compared with a liberal fluid regimen.
- This study will provide an evidence base that is currently lacking and assist anaesthetists in optimising perioperative fluid therapy and therefore outcomes for patients, in the context of increasing numbers of patients with high-risk profiles.

General versus spinal anaesthesia (the GAS study)

The GAS study (general anaesthesia versus spinal) is an international study designed to answer the crucial question of whether a general anaesthetic given to newborn babies undergoing surgery results in injury to the developing brain.

Determining the long-term effects of drugs on the developing brain is difficult. Yet it is vitally important that all drugs used in babies, including anaesthetics, be tested for long-term effects before being used routinely. The GAS study is determining whether spinal and general anaesthesia have the same neurodevelopment outcome in babies.

General anaesthesia renders the patient unconscious, whereas spinal anaesthesia just numbs the lower half of the patient's body. Many hospitals routinely use both forms of anaesthetic, but it is not clear whether one is superior to the other in this regard. The GAS study, one of the first large multi-site anaesthesia trials to be attempted in children, is drawing on the network of paediatric anaesthetists worldwide to answer this important question.

A total of 660 babies requiring surgery to repair a hernia have been recruited to the study from hospitals in Australia, New Zealand, the UK, the US, Italy, the Netherlands and Canada. The babies were allocated to undergo surgical procedures under either general or local anaesthetic, and then monitored for five years for differences in neurological development. Detailed neuropsychological assessments and neurological examinations are conducted at two and five years, and the data analysed to reveal any differences between the spinal and general anaesthetic groups.

The results will provide valuable information for specialists confronted with deciding on the safest choice of anaesthesia to use in babies, with far-reaching potential benefits for children and their families.

Research highlights:

- The GAS study will provide strong evidence on whether or not general anaesthetic drugs cause significant injury to the developing brain.
- The study is one of the first large multi-site trials in paediatric anaesthesia.
- The study is acknowledged by the Australian Government as an important public healthcare priority through the award of two National Health and Medical Research Council project grants to Associate Professor Andrew Davidson and team at the Royal Children's Hospital, Melbourne Vic.
- The GAS study is supported by substantial grants from the US, UK, Italian and Canadian governments.

Foundation governance

The Anaesthesia and Pain Medicine Foundation is overseen by the Anaesthesia and Pain Medicine Foundation Committee, a sub-committee of the ANZCA Council. The committee oversees and provides advice and guidance on strategic direction, planning, financial management and compliance.

The foundation's Board of Governors is a group of influential and experienced leaders from the commercial and philanthropic sectors committed to improving patient outcomes. The board meets regularly to actively support, advise on and oversee the foundation's fundraising program, and promote the cause of improving patient outcomes through increasing the support for research and education in anaesthesia, perioperative medicine and pain medicine.

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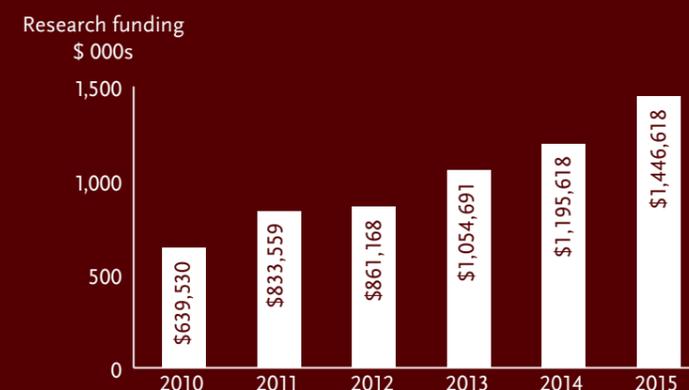
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Financial highlights

In 2015, ANZCA and its Anaesthesia and Pain Medicine Foundation provided \$1,446,618 for research grants approved by the ANZCA Research Committee. Support for research projects has grown significantly since 2010.



Seed funding for government grants

Research projects funded by the foundation have played a crucial role in the process of securing government grant funding for related major clinical trials. Since 2005, clinical trials led by Fellows who have received prior foundation research grants have been awarded more than \$A23 million in government grant funding.

Although the majority of grant funding provided through the foundation is provided by ANZCA, a strategic fundraising plan is supporting the growth of private fundraising to supplement ANZCA's contribution.

Growth in donations from the community is vital for increasing the support for research into reducing adverse health outcomes and fighting acute and chronic pain, particularly among high-risk patients.

The College covers all of the foundation's fundraising and administration expenses allowing 100 per cent of donations to be allocated directly to supporting the foundation's vital life-saving cause.

By donating to the Anaesthesia and Pain Medicine Foundation you will be helping make anaesthesia and surgery safer for more people, especially vulnerable, high-risk patients, and helping improve treatments for people in acute and chronic pain.



How you can help

Your gift will help to save lives and reduce the number of patients who suffer from disabling post-operative complications, by increasing the foundation's ability to support medical research projects led by ANZCA Fellows in leading hospitals and universities.

All donations over \$2 are fully tax-deductible in Australia, and donations over \$5 may be claimed as tax credits in New Zealand.

The foundation's online donation page allows donations to be made easily and is available on the ANZCA website at www.anzca.edu.au/fellows/foundation.

Donations can be made using Visa, MasterCard and American Express in Australia and Visa and MasterCard in New Zealand, or by cheque or money order. For electronic transfer details please contact the foundation.

Join our Patrons Program

Foundation patrons are some of the most dedicated supporters of the cause of saving lives and treating pain.

Patrons commit to annual donations of \$1000 or more, and are regularly recognised for their generous support in the College's communications.

Corporate support

The Anaesthesia and Pain Medicine Foundation welcomes and publicly recognises its corporate donors and sponsors. Sponsoring the foundation demonstrates a genuine commitment to the improvement of knowledge in anaesthesia and pain medicine, and to improving health outcomes for people in the community. Corporate support delivers significant recognition benefits and an enhanced profile among ANZCA Fellows and the community.

The foundation can tailor sponsorships to meet the needs of businesses and organisations, which seek the benefits of association with ANZCA's vital work in medical research and education.

Please contact the foundation for further information about how your business or community organisation can support this life-saving work.

Support a project

The Anaesthesia and Pain Medicine Foundation can accept donations of \$10,000 or more towards specific projects approved by the ANZCA Research Committee, until they are fully subscribed. Please contact the foundation if you would like to contribute towards a specific project.

Provide an award or a scholarship

For major gifts, the foundation can work with donors to set up one-off or recurring named research awards, scholarships, fellowships or professorships, to encourage continuing research and investigation in anaesthesia, perioperative medicine and pain medicine.

Leave a legacy

By making a bequest in your will to the Anaesthesia and Pain Medicine Foundation you will be investing in a future of continuing research into safer, life-saving anaesthesia and surgery and better pain medicine. Those who arrange a bequest to the Anaesthesia and Pain Medicine Foundation are invited to join the John Snow Society, created in honour of Dr John Snow, one of the forefathers of modern anaesthesia.

To find out more about how to make a notified bequest, please contact the foundation.

Please note bequests are not tax deductible. If you prefer to make a significant contribution to deliver future income to support research or education in the specialties, please contact the foundation for information or a confidential discussion.

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ANZCA is listed as a donee organisation by the New Zealand Inland Revenue Department, and its New Zealand National Committee is registered as a charity by the New Zealand Charities Commission under the Charities Act 2005. All New Zealand donations will fund research and education programs in New Zealand thereby meeting the requirements of New Zealand's Inland Revenue Department.

The foundation is extremely grateful to all of its donors, including the many Fellows who have included donations with their annual subscription, become patrons or included a bequest in their will.

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Thanks to the generosity and vision of several foundation donors, ANZCA and the foundation offer several recurring research awards in anaesthesia, perioperative medicine and pain medicine.

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