



The Institute

basil hetzel institute for translational health research

Research Report 2014

Translational health research creating
positive outcomes for thousands of
South Australians



the hospital
research foundation
finding cures improving care

the leading cause
of death in Australia is
cardiovascular
disease

by 2050 frailty
will impact 4 million
Australians

over 11,000
Australians are on
renal dialysis

5% of Australians
have diabetes

colorectal cancer is
the second most
common cancer
in Australia





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Bench



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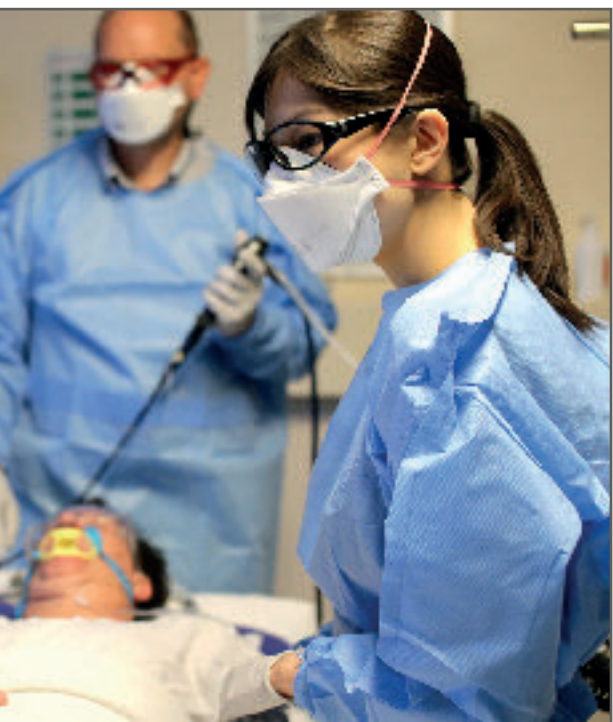
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Research Report 2014

You



Bedside



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The translational bench to bedside research undertaken at the Basil Hetzel Institute and The Queen Elizabeth Hospital has a positive effect on the lives of thousands of Australians every year.



The Institute

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TQEH Director of



Research Report



2014 has presented some challenges and significant opportunities to the research activities at the Basil Hetzel Institute.

On a positive note, the publications emanating from the groups have continued to grow and not only in their absolute numbers but also in the quality of the journals in which they are found. The various research groups within the Institute have undergone appreciable expansion and the links to other groups around South Australia have consolidated and grown.

The success of the NHMRC grant round in 2014 has been somewhat disappointing, however Professor Renuka Visvanathan has been successful in her group obtaining significant support over the next three years for her research initiative in falls prevention in the geriatric population. Associate Professor Sandy Peake was successful also in gaining a project grant in excess of \$5 million over five years in collaboration with the RAH, Monash University and the Austin Hospital to look at nutritional issues in intensive care patients.

During the year, considerable progress has been made in working with the Royal Adelaide Hospital research initiatives in better understanding what funding sources are available to them and the relationship between research at the Royal Adelaide Hospital and The Queen Elizabeth Hospital. As the two hospitals develop single service multiple site activities, the need to more closely align their research agendas seems to be a practical and pragmatic one, aimed at harnessing the research agendas at both sites. This has been facilitated by a joint committee chaired by myself and Professor Peter Bardy and slowly we are beginning to understand the resources available and the processes used at both the Royal Adelaide Hospital and The Queen Elizabeth Hospital. It may well be that the future sees both sites independently branded but co-operatively working towards the shared research agendas of the staff serving the two clinical entities but with a common research goal. This transition will take time, but hopefully when the move to the new Royal Adelaide Hospital occurs in 2016 the relationships and structures will be in place to facilitate the maximum output from the two sites.

2014 also saw the commencement of the Beat Cancer grant which has been jointly funded by The Hospital Research Foundation and the South Australian Health and Medical Research Institute. This is the first joint initiative of the two organisations and hopefully will lay a framework for future co-operative initiatives at the two sites.

In summary, the year has seen new directions, consolidated activities and success at the NHMRC, although not quite as prolific as might have been hoped for. In 2015 we will need to access further funds from a range of sources in order to consolidate the well established groups now based within the BHI facility.

Guy Maddern
Director of Research
The Basil Hetzel Institute for Translational Health Research
The Queen Elizabeth Hospital

Research leaders making an impact

Professor John Horowitz

AM, B Med Sci (Hons), MBBS, PhD, FRACP

Cardiology Unit, The Queen Elizabeth Hospital

John Horowitz became interested in the role of research in advancing medical practice during his medical training at the University of Adelaide. He spent 12 months as an honours student in the Department of Human Physiology and Pharmacology, and even now, over 40 years later, remembers how easy research seemed. He was involved in studies related to the physiology of diving in normal man, and early research about the pharmacology of the plasma kinen system. After finishing his medical degree and internship he could not wait to get back to research, undertaking PhD studies at the University of Melbourne.

In retrospect, this was quite a mistake: his PhD experiments mostly did not work properly and he found the going very hard. Even after finishing his degree he was not sure what value could be attached to the process! He returned to clinical medicine, obtaining specialist physician's qualifications in cardiology and clinical pharmacology at the Austin Hospital in Melbourne. And somewhat to his surprise he started becoming interested in research once again, and actually did some work that turned out to be useful!

The group with whom he worked demonstrated that the drug phenylpropanolamine, freely available "over the counter" to suppress appetite, was capable of dangerously raising blood pressure: this finding led to its withdrawal from the market. Conversely, he became interested in an anti-anginal agent called perhexiline, which seemed very effective, but also very poisonous. Together with colleagues in the Austin Clinical Pharmacology Department he showed that perhexiline toxicity was mainly due to the tendency of the drug to accumulate in the body in some patients, and that this risk could be averted by measuring its levels in blood and adjusting dosage. Eventually, the finding prevented perhexiline from disappearing from the market.

In 1980 he was awarded a Merck International Fellowship for postgraduate studies at Harvard University, Boston. Over the next 2 years he immersed himself in the intense academic environment of the Brigham and Women's Hospital, performing studies related to the pharmacology of digoxin, beta-blockers, calcium antagonists, perhexiline and nitroglycerine. Perhaps the most exciting finding related to the fact that responses to nitroglycerine could be increased by its combination with sulphhydryl donors, such as N-acetylcysteine. This became the basis of a long standing research interest.



In 1982, he took up a position as a research fellow at Melbourne University, and then as a NHMRC Senior Research Fellow. The main focus of his work included the process of nitrate tolerance, or progressive loss of response to agents such as nitroglycerine. He was part of two successful NHMRC Program Grant applications.

Professor Horowitz took up his current position in Adelaide at the end of 1988. Coming to The Queen Elizabeth Hospital (TQEH) was quite a challenge because there was no previous cardiology research here and the first research laboratory established was in the hospital basement ("Room 19 1/2"). However, the real advantage was the enthusiasm shown by his colleagues for widening the academic scope of the department. It quickly became "normal expectancy" for cardiology trainees to do PhD studies, and they were joined by pharmacists, science graduates and even some nurses. Over the past 25 years, Professor Horowitz has supervised/co-supervised approximately 30 postgraduate students many of whom have gone on to strong academic careers.

There have been quite a few highlights in research at TQEH over this period of time, but also plenty of disappointments: many ideas were simply wrong, or led to no real advances. However among the more pleasant experiences were:

1. The idea by a PhD student (Dr John Beltrame) that the coronary slow flow phenomenon (CSFP) was worthy of study. This turned out to be very correct: the phenomenon is a form of coronary spasm which causes severe angina and requires specific treatments.
2. The idea by a nurse doing PhD studies (Simon Stewart) that heart failure could best be treated by specialised nurses focusing individually on patients' needs, including visiting the patients' homes. This has now become a world-wide practice, and (now) Professor Stewart is an authority in this area.
3. The recruitment (in 1990) of Dr Yuliy Chirkov and Professor Ivan de la Lande, who contributed considerable insights into the actions of nitric oxide and nitric oxide donors in platelets and blood vessels, adding a new dimension to research at TQEH.
4. The finding by Professor Jenny Kennedy and Dr Steve Unger that perhexiline inhibited the enzyme CPT-1, allowing it to enable the heart to generate energy in spite of a lack of oxygen.

Over the last 10 years three main new areas of research have emerged in cardiology: the problem of aortic valve disease, new nitric oxide-like drugs such as nitrite and nitroxyl donors, and the extraordinary condition of Tako-Tsubo Cardiomyopathy ("broken heart syndrome"). Fortunately good progress has been made in all these areas.

Today, the group in the Cardiology Unit has active collaborations with researchers in Melbourne, the UK and Germany. Productivity has never been greater. Paradoxically, the availability of research funds has become a matter of increasing concern. Young researchers today often have a very difficult time establishing themselves because of a shortage of funds.

"The bottom line," Professor Horowitz says "is that if you don't do any research it is easy also not to think, and then progress is difficult".

He hopes the Australian Government is listening!



Research leaders making an impact

Professor Renuka Visvanathan

PhD GradCertEd (Higher Ed.) FRACP FANZSGM MBBS ATCL

Aged and Extended Care Services

Renuka Visvanathan has been the Clinical Director of the Aged & Extended Care Services at the The Queen Elizabeth Hospital (TQEH) since 2005. Supported by an AUSAID Merit Scholarship and then an International Postgraduate Research Scholarship from the Australian Department of Education, Training and Youth Affairs, she was awarded a medical degree (MBBS; 1996) and then a doctorate (PhD; 2005) from the University of Adelaide. She is now Professor of Geriatric Medicine at the University of Adelaide. Professor Visvanathan has had the privilege also to train clinically at multiple hospitals in Adelaide including TQEH, the Lyell McEwin Hospital and the Royal Adelaide Hospital, qualifying professionally as a geriatrician with a Fellowship from the Royal Australasian College of Physician (FRACP) in 2004.

Professor Visvanathan is especially interested in the design and delivery of quality health care for older people with the ultimate goal of helping older people remain independent longer. She is honoured to have had the opportunity to lead the establishment of a clinical and academic 'Centre of Excellence' in geriatric medicine at the University of Adelaide and TQEH. This centre operates with a clear vision of contributing to the health and well-being of older South Australians through excellence and innovation in geriatrics and gerontology training, research and clinical services.

Professor Visvanathan has an international research reputation in the area of nutritional frailty. She has established research collaborations with three international centres of excellence in geriatric medicine and frailty research: Professor John Morley (St Louis University, USA), Professor Matteo Cesari (Toulouse, France) and Professor Ken Rockwood (Dalhousie, Canada). Professor Visvanathan is an Expert Advisory Board Member to the European Sarcopenia and Physical Frailty In Older Persons: Multicomponent Treatment Strategies [SPRINTT] Project. She is also a member of the Editorial Board to Frailty.net, an international education resource that aims to help primary care physicians and other health professionals involved in the care of older persons implement frailty into clinical practice.

In 2005, Professor Visvanathan was awarded the prestigious Merck New Investigators Award by the American Geriatrics Society. This Award recognises individuals committed to a career in ageing research and was especially significant because she was not an American scholar.



She has also received the following awards from the Australia and New Zealand Society for Geriatric Medicine (ANZSGM): the RM Gibson Prize in 2002 which is awarded to the best oral presentation from an advanced trainee in geriatric medicine; the Bristol Myer Squibb Career Investigator Award in 2007, which is awarded to the best oral research presentation from a fellow less than 5 years post specialisation, and in 2009 the Lundbeck Fellowship, which is awarded annually to an accomplished geriatrician with a track record in dementia care.

As part of research teams, she has secured \$7.4 million in research funding. She has also been awarded education and training grants totalling approximately \$3 million since 2010. It is therefore not at all surprising that she was awarded the Fellowship of the Australia and New Zealand Society for Geriatric Medicine (FANZSGM) in 2013, in recognition of her contribution to academic and clinical geriatric medicine.

Professor Visvanathan is an Associate Investigator with the University of Adelaide's NHMRC Centre of Research Excellence Translating Nutritional Science to Good Health. This project (2012-2017) is based at the Royal Adelaide Hospital campus and the South Australian Health and Medical Research Institute (SAHMRI).

Professor Visvanathan's research has directly contributed to increased awareness nationally that under-nutrition is a major contributing factor to adverse health outcomes such as increased risk of hospitalisation and falls in older people living in our community. Her research has also contributed to the development of nutritional screening methods allowing primary care clinicians to detect at-risk older individuals earlier. Recently, together with geriatrician colleague and PhD candidate Dr Solomon Yu, a screening method to identify sarcopenia (lack of muscle mass and weakness) requiring assessment of weight, gender, height, age and gait speed has been developed. These assessments can easily be completed in general practice or outpatient clinics. This is therefore an implementable screening method. Furthermore, they have alerted clinicians in Australia to the fact that one in five Australians aged 80 years and older may have sarcopenia, a clinical syndrome that puts the older person at-risk of adverse health events such as falls, disability and hospitalisation.

In the last decade Professor Visvanathan has also contributed to two international initiatives in relation to nutritional health. One was to improve the Mini Nutritional Assessment Short-Form, a widely used nutritional screening tool internationally. The second was to develop an international consensus as to the optimal protein intake for older people. More recently, in collaboration with Professor John Morley, they have proposed a new screening tool for frailty to be used in the residential aged care, the FRAILNH.

Understanding that older people are susceptible to drug related side effects, Professor Visvanathan has also investigated non-pharmacological treatment options for health syndromes common in older people. Post-prandial hypotension (PPH) is the large fall in blood pressure following a meal, observed in some older people. PPH has been associated with falls. Dr Shailaja Nair, a geriatrician and Masters of Philosophy (MPhil) research candidate at TQEH, was awarded the ANZSGM RM Gibson prize for her research on PPH. Under the supervision of Professor Visvanathan and Dr Diana Gentilcore (University of South Australia), Dr Nair has demonstrated that intermittent walking post meal is a treatment strategy for PPH.

Professor Visvanathan has more recently strived to establish a new research program in 'gerontechnology' at The Queen Elizabeth Hospital and University of Adelaide by bringing together gerontology and technology research. With project funding from The Hospital Research Foundation and in collaboration with Dr Damith Ransinghe (Computer Engineer, University of Adelaide), Professor Keith Hill (renowned falls prevention expert, Curtin University) and TQEH clinicians, a new technology system to prevent falls in hospitals has been developed. Pilot research has established that this technology can accurately identify movement transitions associated with increased likelihood of falling, such as getting out of the bed or chair unsupervised. In 2014, this research team was awarded a

National Health and Medical Research Council (NHMRC) Project Grant to further investigate the movement sensor alarm system as a method to prevent falls in older people in hospitals. The researchers hope to commence this exciting research trial at TQEH towards the end of 2015.

Professor Visvanathan is a keen contributor to education and training programs. She has supervised two PhD students who were awarded the Dean's commendation and one honours student who received 1st class honours. She is currently supervising 4 PhD and 5 MPhil research students. Professor Visvanathan also led the development of the innovative partnership initiative between the University of Adelaide and Resthaven Inc. (a large aged care organization in Adelaide) which resulted in the establishment of an academic teaching, training and research centre on an aged care campus: 'The Adelaide Geriatrics Training and Research with Aged Care (GTRAC) Centre' [<https://health.adelaide.edu.au/medicine/g-trac/>]. Launched by the Federal Minister of Aging in February 2013, this model to support medical student teaching was a first for South Australia. Providing medical students with training experience outside of the hospital sector better prepares our future medical workforce to work with older consumers in the community.

Professor Visvanathan is a current board member of Resthaven Inc., member to the Nestle Australia malnutrition board and advisory group member to the board of the Alzheimer's Association South Australia. She has previously been a member of the Clinical Governance Advisory Group, Royal District Nursing Service (RDNS) in South Australia and Deputy Chair (until July 2014) of the Older Peoples Clinical Network, SA Health. She is a current committee member of the Australasian Association of Gerontology Executive SA Division and a member of the Policy and Planning committee of the Australia and New Zealand Society for Geriatric Medicine. Through these activities she actively contributes to policy and planning for better healthcare outcomes for older people.



Students making an impact

Kristin Carson

PhD Candidate - Respiratory Medicine Unit and Clinical Practice Unit

Kristin Carson has been working as a research scientist with the Respiratory Medicine Unit and the Clinical Practice Unit since January 2008 across a wide array of studies. All studies have had an emphasis on clinical practice improvement initiatives and advances in public health (i.e. translational health research).

In 2011 Kristin commenced a part-time PhD alongside her existing employment, supervised by the Director of Respiratory Medicine, Professor Brian Smith. Her PhD focusses on tobacco cessation and prevention amongst Indigenous populations, with particular reference to Aboriginal and Torres Strait Islander (TSI) Australians. Through several meta-analyses, focus groups, one-on-one interviews and quantitative surveys Kristin has identified the barriers and facilitators to smoking cessation, tobacco prevention programs and health service utilisation for Aboriginal and TSI Australians. This knowledge has been used to influence policy, practice and research across Australia. Closing the health gap between Indigenous and non-Indigenous Australians has been highlighted as a key national priority. When considering that current tobacco prevalence estimates for Indigenous Australians is 2.5 times greater than use amongst the non-Indigenous population, research into reducing tobacco use has the potential to significantly diminish these health inequalities. Kristin expects to complete her PhD in 2015 and she has received a joint NHMRC and Cancer Australia Translating Research Into Practice (TRIP) Fellowship to continue her work into smoking cessation and prevention amongst Aboriginal Australians for 2015-2016 through a multi-centre randomised controlled trial.

The research activities Kristin has contributed to over the past seven years have resulted in over 50 peer reviewed publications, 36 as either first or second author. In addition she has had over 80 accepted conference abstracts, over 300 media citations and contributions to policy and practice locally, nationally and internationally. She has been the recipient of several prestigious awards including the Young Australian of the Year in South Australia, the Premier's and Channel 9's Young Achiever of the Year, the Young Citizen of the Year for the City of Holdfast Bay, the Thoracic Society of Australia and New Zealand (TSANZ) Janet Elder International Travel Award, the Robert Pierce Grant-In-Aid, SA/NTTSANZ Young Investigator Award as well as recipient of the Tobacco Control Prize for best oral presentation at a TSANZ conference. Kristin is also a member of decision making bodies including SA Aboriginal Health Research Network and the Aboriginal and Torres Strait Islander Health working party.

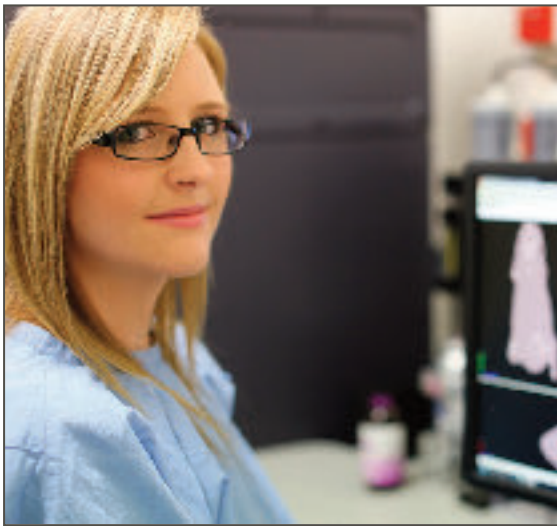


“I never realised the implications my research could have on the everyday lives of patients not only here at The Queen Elizabeth Hospital but all around the country and internationally.”

Aneta Zysk

PhD Candidate - Breast Cancer Research Unit

After completing her Honours degree in Biochemistry at the University of Adelaide, Aneta Zysk joined the Breast Cancer Research Unit within the the Discipline of Surgery at the University of Adelaide, based at the Basil Hetzel Institute, to undertake a PhD with the highly regarded Professor Andreas Evdokiou.



Bone metastases occur in many patients with advanced breast cancer leading to bone destruction, which in turn is responsible for reduced quality of life. Currently, there is no cure for cancer which has spread to the bone and treatments are only palliative. Aneta's project is investigating how to use the body's own immune system to target bone metastases using a novel immunotherapeutic approach. She has examined the role of a rare population of immune cells called gamma delta ($\gamma\delta$) T-cells, which have potent anti-cancer properties. Aneta has isolated these cells from the blood of normal human donors and increased their numbers using cell culture techniques in the laboratory. She has then used a small animal model of metastatic breast cancer to examine their efficacy. Results from her research will be published during 2015.

"Undertaking a PhD at the Basil Hetzel Institute (BHI) has given me a fantastic opportunity to work with some very gifted researchers" she said. "Not only does the BHI produce world-class research, but the atmosphere here encourages collaboration within The Institute. During my time here, I have received an enormous amount of support and encouragement from my research group, supervisors and peers. Over the past year, I have also been on the BHI Management Committee as a Postgraduate Student Representative. This has given me the opportunity to build leadership skills by organising student focused activities which in turn helps form friendships and support networks between students. Working at the BHI has been one of the most rewarding times of my life."

Since commencing her PhD, Aneta has presented the results of her research both locally and nationally. In 2014 she presented a poster at the 10th Annual Asia Pacific Musculoskeletal Tumour Society Meeting in Melbourne and at the University of Adelaide Health Science Postgraduate Research Day, where she was awarded a School of Medicine prize. She was also awarded Best Lay Description of her project at the TQEH Research Day in 2014. To date, Aneta has published as a contributing author in a manuscript prepared in collaboration with the School of Chemical Engineering. While Aneta is still unsure where her career will take her once she has completed her PhD, working at the Basil Hetzel Institute has firmly established her desire to continue working in research.

*"Working at the
Basil Hetzel Institute has
been one of the most
rewarding times of my life"*

first author

STUDENT PUBLICATIONS

2014

Our students continue to publish,
many in leading specialised and
high impact journals

AGED AND EXTENDED CARE SERVICES

Papers

Dent E, Chapman I, Piantadosi C, Visvanathan R. Performance of nutritional screening tools in predicting poor six months outcome in hospitalised older people. *Asia Pacific Journal of Clinical Nutrition* 2014; 23(3): 394-9.

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Invited Review

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CARDIOLOGY UNIT

Papers

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CLINICAL PHARMACOLGY UNIT

Papers

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Papers

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NEUROLOGY UNIT

Papers

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OTOLARYNGOLOGY, HEAD AND NECK SURGERY, Department of

Papers

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Miljkovic D, Bassiouni A, Cooksley C, Ou J, Hauben E, Wormald PJ, Vreugde S. 2014. Association between group 2 innate lymphoid cells enrichment, nasal polyps and allergy in chronic rhinosinusitis. *Allergy* 69:1154-1161.

Murphy J, Ali MJ, Psaltis AJ. Biofilm Quantification on Nasolacrimal Silastic Stents After Dacryocystorhinostomy. *Ophthalmol Plast Reconstr Surg*. 2014 Dec 3. [Epub ahead of print]

Naidoo Y, Bassiouni A, Keen M, Wormald PJ. 2014. Long-term outcomes for the endoscopic modified Lothrop/Draf III procedure: a 10-year review. *Laryngoscope* 124:43-49.

Padhye V, Valentine R, Parasivan S, Jardeleza C, Bassiouni A, Vreugde S, Wormald PJ. 2014. Early and late complications of endoscopic hemostatic techniques following different carotid artery injury characteristics. *Int Forum Allergy Rhinol* 4:651-657.

OTOLARYNGOLOGY, HEAD AND NECK SURGERY, Department of

Papers

Tan NC, Cooksley CM, Parasivan S, Vreugde S, Wormald PJ. 2014a. Safety evaluation of a sinus surfactant in an explant-based cytotoxicity assay. *Laryngoscope* 124:369-372.

Tan NC, Cooksley CM, Roscioli E, Drilling AJ, Douglas R, Wormald PJ, Vreugde S. 2014b. Small-colony variants and phenotype switching of intracellular *Staphylococcus aureus* in chronic rhinosinusitis. *Allergy* 69:1364-1371.

Tan NC, Drilling AJ, Jardeleza C, Wormald PJ. 2014c. Is nasal steroid spray bottle contamination a potential issue in chronic rhinosinusitis? *J Laryngol Otol* 128 Suppl 1:S28-33.

RESPIRATORY MEDICINE UNIT & CLINICAL PRACTICE UNIT

Papers

Carson K, Jayasinghe H, Smith B, Newchurch J, Brinn M, Veale A, Peters M, Esterman A, Singh K and members of the Thoracic Society of Australia and New Zealand Indigenous Lung Health Working Party. Smoking cessation and tobacco prevention in Indigenous populations. 2014 *Evidence Base, Issue* 3; ISSN 1838-9422; Version 1.

Carson KV, Smith BJ. Methodological challenges and options for addressing them in Aboriginal and Torres Strait Islander health research. *Australasian Epidemiology* 2014; 21(2): 47-50.

Carson KV, Usmani ZA, Smith BJ. Non-invasive ventilation in Acute Severe Asthma: Current evidence and future needs. *Curr Opin Pulm Med*. 2014 Jan;20(1):118-23.

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Book chapter

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RHEUMATOLOGY UNIT

Paper

Black RJ, Spargo L, Schultz C, Chatterton B, Cleland L, Lester S, Hill CL, Proudman SM. Decline in Hand Bone Mineral Density Indicates Increased Risk of Erosive Change in Early Rheumatoid Arthritis. *Arthritis Care Res* (Hoboken) 66, no. 4 (2014): 515-22.

SURGERY, University of Adelaide Discipline of

Papers

Gargett T, Grubor-Bauk B, Garrod TJ, Yu W, Miller D, Major L, Wesselingh S, Suhrbier A, Gowans EJ. Induction of antigen-positive cell death by the expression of Perforin, but not DTa from a DNA vaccine enhances the immune response. *Immunology Cell Biology* 2014;92(4):359-67.

Gargett T, Grubor-Bauk B, Miller D, Garrod T, Yu S, Wesselingh S, Suhrbier A, Gowans E. Increase in DNA vaccine efficacy by virosome delivery and co-expression of a cytolytic protein. *Clinical and Translational Immunology* 2014;3(6):e18.

Garrod T, Grubor-Bauk B, Yi S, Gargett T, Gowans EJ. Encoded novel forms of HSP70 or a cytolytic protein increase DNA vaccine Potency. *Human Vaccine Immunotherapy* 2014;10(9):1-5.

Garrod TJ, Gargett T, Yu W, Major L, Burrell CJ, Wesselingh S, Suhrbier A, Grubor-Bauk B, Gowans EJ. Loss of long term protection with the inclusion of HIV pol to a DNA vaccine encoding gag. *Virus Research* 2014;192:25-33.

Garrod TJ, Grubor-Bauk B, Gargett T, Li Y, Miller DS, Yu W, Major L, Burrell CJ, Wesselingh S, Suhrbier A, Gowans EJ. DNA vaccines encoding membrane-bound or secreted forms of heat shock protein 70 exhibit improved potency. *European Journal of Immunology* 2014;44:1992-2002.

Matthews TJ, Trochsler MI, Bridgewater FH, Maddern GJ. Systematic review of congenital and acquired portal-systemic shunts in otherwise normal livers. *British Journal of Surgery* 2014;101:1509-1517.

THERAPEUTICS RESEARCH CENTRE, University of South Australia

Papers

Kuswahyuning R, Roberts MS. Concentration dependency in nicotine skin penetration flux from aqueous solutions reflects vehicle induced changes in nicotine stratum corneum retention. *Pharmaceutical Research*. 2014;31:1501-1511.

Sime F, Roberts MS, Warner M, Hahn U, Robertson T, Yeend S, Phay A, Lehman S, Lipman J, Peake S, Roberts J. Altered pharmacokinetics of piperacillin in febrile neutropenic patients with haematological malignancy. *Antimicrobial Agents and Chemotherapy*. 2014;58:3564-3565.

Sime FB, Roberts MS, Roberts JA, Robertson TA. Simultaneous determination of seven beta-lactam antibiotics in human plasma for therapeutic drug monitoring and pharmacokinetic studies. *Journal of Chromatography B-Analytical Technologies in the Biomedical and Life Sciences*. 2014; 960:134-144.



SPOTLIGHT

ON PUBLICATIONS

2014

Researchers at the Basil Hetzel Institute have achieved a broad range of publication success highlighting the quality of research

Aged and Extended Care Services

Nair S, Visvanathan R, Gentilcore D. Intermittent walking: a potential treatment for older people with postprandial hypotension. *J Am Med Dir Assoc* 2014; Oct 8.pii:S1525-8610 (14) 00546-5.

Impact Factor: 4.781

The *Journal of American Medical Director's Association* is ranked second amongst the clinical journals in the Geriatrics & Gerontology category.

Older people, especially those who are frail, are at increased risk of falls and postprandial hypotension is a contributing factor. These same people are at-risk of adverse effects from pharmacological strategy. This study proposes a practical non-pharmacological strategy (i.e. intermittent walking) to treat this condition.

Yu S, Appleton S, Chapman I, Adams R, Wittert G, Visvanathan T, Visvanathan R. An anthropometric prediction equation for appendicular skeletal muscle mass in combination with a measure of muscle function to screen for sarcopenia in primary and aged care. *J Am Med Dir Assoc* 2014; Sep 16.pii:S1525-8610 (14) 00398-3.

Sarcopenia affects one in five Australians aged 80 years and older. The researchers have proposed a simple screening method that can be used in primary and aged care settings to 'rule out' sarcopenia. The researchers hope that by having provided general practitioners with a practical clinical tool, those at-risk might be identified earlier and be offered further assessment and management.

Anaesthesia

Thiruvengkatarajan V, Van Wijk RM, Rajbhoj A. Cranial Nerve Injuries with Supraglottic airway: A systematic review of published reports. *Anaesthesia*. 2014;doi:10.1111/anae.12917.

Impact factor: 3.846

Nowadays a wide variety of laryngeal mask airway derived supraglottic airway devices are used in around 50% of general anaesthetic procedures. The morbidity associated with the use of these devices is largely defined by minor pharyngolaryngeal complications such as sore throat, soft tissue abrasion, hoarseness and dysphagia. Cranial nerve injury after the use of a supraglottic airway device is an unusual but more serious complication. The true incidence is unknown. The aim of this systematic review is to analyse and summarise the features of cranial nerve injuries, with particular emphasis on contributing factors. The publication of this review in *Anaesthesia*, a high impact journal, has finally shed some light on this complex issue.

Cardiology Unit

Stewart S, Ball J, Horowitz JD, Marwick TH, Mahadavan G, Wong C, Abhayaratna WP, Chan YK, Esterman A, Thompson Dr, Scuffham PA, Carrington MJ. Standard versus atrial fibrillation-specific management strategy (SAFETY) to reduce recurrent admission and prolong survival: pragmatic. Multi-centre, randomised controlled trial. *Lancet* 2014 Nov 17. pii: S0140-6736(14)61992-9. doi: 10.1016/S0140-6736(14)61992-9. [Epub ahead of print]

Impact Factor: 39.207

This study establishes that outreach nursing-based support of patients with atrial fibrillation does not substantially affect mortality, but tends to prevent prolonged hospital admissions, and thus reduces health care costs.

Clinical Pharmacology Unit

Drury NE, Licari G, Chong C-R, Howell NJ, Frenneaux MP, Horowitz JD, Pagano D and Sallustio BC. Relationship between plasma, atrial and ventricular perhexiline concentrations in humans: insights into factors affecting myocardial uptake. *Br J Clin Pharmacol* 2014;77: 789-795.

Impact Factor: 3.69

The *British Journal of Clinical Pharmacology* is one of the finest international journals dedicated to original clinical pharmacology research, ranked in the top quartile of all pharmacology and pharmacy journals.

This publication results from a collaboration with cardiologists and cardiothoracic surgeons at the Universities of Birmingham and Aberdeen. The study investigates the anti-anginal agent perhexiline, which is increasingly being used in Europe and the USA for angina and other forms of heart disease, as a result of pioneering clinical work at The Queen Elizabeth Hospital. Its clinical use requires monitoring of patients' perhexiline concentrations in plasma to minimise the risk of side effects whilst maintaining maximum efficacy within the heart. The manuscript describes for the first time the relationship between perhexiline concentrations in plasma and in heart tissue (the site of action), confirming that there is a sound basis for monitoring plasma concentrations. Additionally the study demonstrates that uptake of perhexiline into the heart is affected by age and heart rate, suggesting that the elderly may be more sensitive to the effects of perhexiline.

Endocrinology Unit

Jesudason DR, Pedersen E, Clifton PM. Utility of Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) Equations in Obese Diabetic Individuals Before and After Weight Loss. *American Journal of Kidney Diseases* 2014. Volume 64, Issue 1:159–161.

Impact factor: 5.8

The *American Journal of Kidney Diseases* is recognized world-wide as a leading source of information devoted to clinical nephrology practice and clinical research, ranked 5th of 73 journals in the Urology & Nephrology category in 2013.

The results from this clinical trial study showed a higher precision of estimating Glomerular Filtration Rate (GFR) using equations based on cystatin C or both cystatin C and creatinine compared with the equation using creatinine alone in weight loss patients, due to the fact that weight loss has a bigger influence on serum creatinine than cystatin C. This highlighted the potential bias of using different eGFR equations in estimating weight loss patients.

Gagliardi L, Nenke MA, Thynne TRJ, von der Borch J, Rankin WA, Henley DE, Sorbello J, Inder WJ, Torpy DJ. Continuous Subcutaneous Hydrocortisone Infusion Therapy in Addison's Disease: A Randomized, Placebo-Controlled Clinical Trial. *Journal of Clinical Endocrinology & Metabolism* 2014 99(11) Pages 4149-4157.

Impact factor 6.3

The *Journal of Clinical Endocrinology & Metabolism* is the world's leading peer-reviewed journal for endocrine clinical research and clinical practice information.

This is a clinical trial to establish if continuous subcutaneous hydrocortisone infusion can improve Addison's disease patients subjective health status (SHS.) The results did not show a significant benefit from circadian cortisol delivery in trial subjects with good baseline SHS.

Gagliardi L, Schreiber AW, Hahn CN, Feng J, Cranston T, Boon H, Hotu C, Oftedal BE, Cutfield R, Adelson DL, Braund WJ, Gordon RD, Rees DA, Grossman AB, Torpy DJ, Scott HS. ARMC5 mutations are common in familial bilateral macronodular adrenal hyperplasia. *J Clin Endocrinol Metab* 2014 (9):E1784-92. doi: 10.1210/jc.2014-1265.

Impact factor 6.3

This study has detected ARMC5 mutations in 4 of 5 bilateral macronodular adrenal hyperplasia families; this finding established the genetic link between the mutation with the condition and opened the way to a possible genetic screening for the diseases.

Haematology - Oncology

Grover PK, Cummins AG, Price TJ, Roberts-Thomson IC, Hardingham JE. Circulating tumour cells: The evolving concept and the inadequacy of their enrichment by EpCAM-based methodology for basic and clinical cancer research. *Annals of Oncology* 2014;25:1506-16.

Impact Factor: 6.58

The enumeration of circulating tumour cells (CTC) in a blood sample from patients with solid tumours is becoming increasingly used in patient management as a marker of risk of metastatic disease, and in monitoring the efficacy of chemotherapy. This timely and thorough review highlights the fact that the large majority of clinical studies available to date relied on CTC isolation using positive selection, which has to assume specific criteria for isolation such as high expression of the epithelial cell adhesion marker EpCAM. Such approaches are intrinsically flawed, under-estimating the real CTC load and missing the cancer stem cell populations of likely high relevance for causing disease relapse and metastasis. The importance of this issue was recognised by the editor of *Annals of Oncology*.

Intensive Care Unit

SL Peake, A Delaney M Bailey, R Bellomo, P Cameron, DJ Cooper, A Higgins, A Holdgate, B Howe, SAR. Webb, P Williams. Goal-Directed Resuscitation for Patients with Early Septic Shock. *NEJM*, 1 October 2014.

Impact Factor: 54.42

New England Journal of Medicine has the highest impact factor of all medical journals, the publication of the ARISE study by this prestigious journal emphasizes the world-wide significance of this study in relation to the management of patients with severe sepsis.

The incidence of sepsis and its associated burden continues to drive researchers in their pursuit of improved outcomes for patients presenting to hospital with sepsis. A proof-of-concept randomized trial, published in 2001, showed that early hemodynamic resuscitation according to a specific protocol termed early goal-directed therapy (EGDT) improved outcomes in patients presenting to the emergency department with severe sepsis, as compared with usual therapy. This protocol was subsequently incorporated into the international guidelines for management of severe sepsis and septic shock. However, concerns about the considerable financial and resource implications of EGDT, the internal and external validity of the original trial and the potential risks associated with various elements of the EGDT resuscitation protocol factors, have resulted in variations in the degree to which these guidelines have been implemented globally.

SPOTLIGHT

ON PUBLICATIONS

2014

continued

Intensive Care Unit (cont.)

As a result of these concerns and the international recommendations continuing to support the implementation of EGDT, a prospective, observational study was performed in 32 ANZ hospitals between 2006 and 2007. This survey demonstrated that EGDT is not routinely practised in our countries. The Australasian Resuscitation In Sepsis Evaluation Randomised Controlled Trial (ARISE RCT) was a phase III, multi-centre, National Health and Medical Research Council (NHMRC) funded, ANZICS CTG-endorsed, randomised, controlled study designed to evaluate early goal-directed therapy (EGDT) in 1600 patients presenting to the emergency department with severe sepsis. The ARISE study was one of three collaborative, harmonized studies, along with the United States-based ProCESS trial and the Protocolized Management in Sepsis (ProMiSe) trial, conducted in the United Kingdom, designed to address the effectiveness of EGDT.

The results of the ARISE trial showed that EGDT, as compared with usual resuscitation practice, did not decrease 90-day mortality among patients presenting to the emergency department with early septic shock. The study results were presented at the European Society of Intensive Care Medicine's Annual Forum 2014 and simultaneously published on-line by the New England Journal of Medicine.

The findings of the ARISE RCT are similar to those of the ProCESS randomised controlled trial and the results of the ProMiSe trial are expected to be published in March 2015. The results of both the ARISE and ProCESS studies suggest that incorporating EGDT into the Surviving Sepsis Campaign, international guidelines for management of sepsis is questionable.

Otolaryngology, Head and Neck Surgery, Department of

Miljkovic, D., Bassiouni A, C. Cooksley, J. Ou, E. Hauben, Wormald PJ, S. Vreugde. Association between group 2 innate lymphoid cells enrichment, nasal polyps and allergy in chronic rhinosinusitis. *Allergy* 2014: 69:1154-1161.

Impact Factor: 5.995

Group 2 Innate Lymphoid cells (ILC2s) were shown to be involved in the initiation and coordination of Th2-type immune responses in allergic disease animal models. In this paper, we characterize the complex interactions between ILC2s and other Th2 response elements in the context of CRS and show that ILC2 enrichment occurs in nasal polyps and in allergic CRS patients. We also found a negative association of ILC2s with the number of previous endoscopic sinus surgeries.

Tan NC, Cooksley CM, Roscioli E, Drilling AJ, Douglas R, Wormald PJ, Vreugde S. Small-colony variants and phenotype switching of intracellular *Staphylococcus aureus* in chronic rhinosinusitis. *Allergy* 2014b: 69:1364-1371.

Impact Factor: 5.995

Chronic rhinosinusitis is characterised by chronic inflammation and bacterial infections, in particular those mediated by *Staphylococcus aureus* (*S. aureus*), that are believed to hold an important role in the recalcitrant nature of this condition. In this paper, we show that *S. aureus* infects the mucosal surface of the sinuses in some patients. Within the mucosa, we have found that the phenotype is changed and *S. aureus* exists as small colony variants that are known to be resistant to antibiotics. These intracellular variants switch off their toxin production in a reversible manner and enable the bacteria to survive within the sinonasal epithelium without inducing an immune response.

Respiratory Medicine Unit & Clinical Practice Unit

Singh K, Carson K, Usmani Z, Sawhney G, Shah R, Horowitz J. Systematic review and meta-analysis of incidence and correlates of recurrence of Takotsubo Cardiomyopathy. *Int J Cardiol.* 2014 Jul 1;174(3):696-701. doi: 10.1016/j.ijcard.2014.04.221. Epub 2014 Apr 26.
Impact Factor 6.175

This systematic review on the incidence of recurrence in Tako-Tsubo cardiomyopathy highlights an important facet of successful research, which is to conduct multi-disciplinary collaborations. Tako-Tsubo cardiomyopathy (TTC) is a well-known cardiac condition predominantly affecting women, which can be associated with chronic and acute complications. The meta-analysis revealed that TTC is associated with a 1-2% annual recurrence rate but a substantially greater frequency of ongoing symptoms. The *International Journal of Cardiology* is one of the leading journals devoted to cardiology in the broadest sense and is pitched to both practicing clinicians and basic/clinical researchers.

Rheumatology Unit

Lee EB, Fleischmann R, Hall S, Wilkinson B, Bradley JD, Gruben D, Koncz T, Krishnaswami S, Wallenstein GV, Zang C, Zwilllich SH, van Vollenhoven RF; ORAL Start Investigators. Tofacitinib versus methotrexate in rheumatoid arthritis. *N Engl J Med* 2014: Jun 19;370(25):2377-86.
Impact factor: 54.42.

The *New England Journal of Medicine* is one of the most prestigious medical journals, particularly in the area of clinical trials.

This multi-national phase III clinical trial for tofacitinib (an oral Janus kinase inhibitor) compared to methotrexate in Rheumatoid Arthritis highlights the importance of clinical trials research performed in the Rheumatology Department. The major findings of the study were that tofacitinib is superior to methotrexate in reducing signs and symptoms of rheumatoid arthritis and inhibiting the progression of structural joint damage

Surgery, University of Adelaide Discipline of

Trochsler M, Maddern G. Adhesion barriers for abdominal surgery: a sticky problem. *The Lancet* 2014;383(9911):8-10.
Impact factor: 39.207

Adhesion formation after abdominal surgery is an area of significant morbidity and mortality in surgery and has frustrated research for many years. We need to be vigilant to pick up exciting new approaches as they become available. This paper highlights an important area in surgery and the possible ways forward in order to change surgical practice with regard to adhesion prevention.

Therapeutics Research Centre, University of South Australia

Liu X, Kruger P, Maibach H, Colditz PB, Roberts MS. Using skin for drug delivery and diagnosis in the critically ill. *Adv Drug Deliv Rev.* 2014 Nov 20;77C:40-49.
Impact Factor: 12.707

This work brings together much of our interest in targeted drug delivery by the skin as it applies to intensive care medicine. This was an invited article in the highest impact specialist journal for the field.

Aged and Extended Care Services

The Aged & Extended Care Services (Geriatric Medicine) aims to provide a clinical service of excellence to older people across the healthcare continuum (acute, sub-acute and community). The academic department also has a strong focus on translational research and clinical education. The department is associated with the NHMRC Centre of Research Excellence 'Translating Nutritional Science To Good Health' where Professor Visvanathan is an associate investigator. The Aged and Extended Care Services is also linked to the Adelaide Geriatrics Training and Research with Aged Care (G-TRAC) Centre located at Resthaven's Paradise campus, where Professor Visvanathan is Director.

Frailty, Sarcopenia and Under-nutrition

Frailty In Residential Aged Care (Professor R Visvanathan):

The aim of this research is to investigate the prevalence of frailty in residential aged care and the performance of a frailty screening tool developed in collaboration with Professor John Morley at St Louis University, USA (FRAIL NH).

Frailty and Nutrition (FAN) Study (Dr C Piantadosi, Professor R Visvanathan):

This study investigated the effectiveness of 12 months combined treatment with testosterone and nutritional supplementation on health outcomes compared to placebo in under-nourished, community dwelling, older people. This NHMRC funded study recruited across 3 states (SA, NSW and Victoria) and has been completed.

Sarcopenia (Dr S Yu, Professor R Visvanathan):

Dr Yu has developed a prediction equation for appendicular skeletal muscle (ASM) mass. Cut-offs for low ASM were identified. When used in combination with grip strength, Dr Yu has developed a 'rule out' screening method for sarcopenia, which may be useful in primary and aged care settings. Dr Yu completed his PhD in 2014.

Exercise and Protein Supplementation To Treat Sarcopenia (Ms Agathe Jadczyk, Dr S Yu, Professor R Visvanathan):

The team plan to commence a pilot investigation of the effect of exercise in combination with high protein supplementation over 3 months on gait speed in older people at-risk of sarcopenia. This study is a collaboration with Dr Schultz and Professor Kitson, School of Nursing, University of Adelaide and Dr Natalie Luscombe, CSIRO.

Population Data

- > By 2050 **frailty** (or risk) could impact 4 million Australians aged 70 years and over.
- > 1 in 5 Australians aged 80 years and over are at risk of **sarcopenia**, a condition due to reduced muscle quantity and performance.
- > **Under-nutrition** (or risk) affects 43% of South Australians receiving community services.
- > **Falls** by Australians aged 65 years and over accounted for 83,800 hospitalised injury cases in 2009-2010. In hospitals, falls occurred at a rate approximating 2.5 per 1,000 separations during 2010-2011.
- > By 2050 almost 1 million Australians will be living with the diagnosis of **dementia**.

Research Focus

- Frailty, Sarcopenia and Under-nutrition
- Falls and Fracture Prevention and Management
- Technology in Health and Aged Care
- Dementia Management
- Geriatric Pharmacotherapy

Falls and Fragility Fractures

Orthogeriatrics (Dr P Shibu, Ms D Hudson, Ms Carla Smyth):

Dr Pazhvoor Shibu has identified that there is a significant care gap in terms of falls and osteoporosis management in patients presenting to our acute care hospital. He is currently undertaking a quality improvement study to determine the benefit of a liaison nurse on improving falls and osteoporosis management in our hospitals.

Post-prandial hypotension and mobility (Dr S Nair, Ms Zoe Kopsaftis, Dr D Gentilcore, Professor R Visvanathan):

Dr Nair has demonstrated that intermittent walking attenuates the fall in blood pressure normally seen following a glucose drink. This is simple lifestyle advice that can be provided to older patients to treat this condition and prevent falls. She has also demonstrated that the fall in blood pressure following a glucose drink affects gait detrimentally. Ms Kopsaftis, as part of her honours research, has demonstrated that the benefits of intermittent walking are seen only during the period of intervention.

Post-prandial hypotension and cardiovascular changes (Mr L Trahair, Dr S Rajendran, Professor K Jones, Professor R Visvanathan):

This NHMRC funded study, which includes collaboration with the Department of Cardiology at The Queen Elizabeth Hospital, is exploring the cardiovascular mechanisms contributing to post-prandial hypotension in older people.

Technology to prevent falls in hospital (Dr R Teh, Mr R Shinmoto Torres, Mr WMASB Wickramasinghe, Mr S Hoskins, Dr P Shibu, Dr D Ranasinghe, Dr Neha Mahajan, Professor R Visvanathan):

The team are developing a customizable technology system to recognize postural transitions associated with increased falls risk in real time. This might allow for timely caregiver intervention to prevent falls. The team has secured NHMRC project funding to investigate the effectiveness and acceptability of this system.

Dementia Management

The Dementia Care In Hospitals Program national rollout and evaluation (Dr Faizal Ibrahim, CALHN Dementia Care and Challenging Behaviour Group):

This national roll-out of a communication strategy and program includes four health care organisations nationally. The aim is to introduce DHCP across CALHN, evaluate the impact of the program and consider translation across South Australian health sites.

Technology to prevent malnutrition in consumers living alone with dementia (Ms Asangi Jayatilaka, Dr Damith Ranasinghe, Professor Renuka Visvanathan):

This research aims to develop an artificial intelligence system to support the nutritional intake of older people living alone with dementia.

Older peoples experience of dementia diagnosis (Professor J Ratcliffe, Professor R Visvanathan):

This pilot collaborative research with Flinders University aims to provide insights into the journey to a dementia diagnosis for a sample of older people recently diagnosed with mild dementia.

Identifying neurophysiological markers of early cognitive decline (Dr Goldsworthy, Associate Professor Ridding, Dr Yu):

This research is funded by an Alzheimer's Australia Dementia Research Foundation grant to Dr Goldsworthy. The purpose of this project is to develop a combined transcranial magnetic stimulation- electroencephalography (TMS-EEG) tool to identify early synaptic dysfunction in Alzheimer's Disease.

Geriatric Pharmacotherapy

Analgesic load, pain and daytime sedation (Dr Tan E, Associate Professor Hilmer S, Associate Professor S Bell, Professor Visvanathan R):

Funded by an Alzheimer's Australia-Resthaven Grant and in collaboration with researchers at Universities, the aim of this research project is to investigate the association between use of pain relieving medicine, pain and drowsiness in residential aged care residents.

Staff

Clinical Director & Professor

R Visvanathan PhD GradCertEd (Higher Ed.) FRACP FANZSGM MBBS ATCL

Consultant Staff

S Yu (Deputy Director) FRACP MBBS LTCL

K Parasivam FRACP MBBS

J Ng FRACP MBBS

F Ibrahim FRACP CCT UK MRCP MBBSCh LRCPSI

P Shibu FRACP MD CCT UK MRCP MBBS

S Nair MBBS MRCP Fellowship Geriatric Medicine (Malaysia)

K Tham FRAC MBBS

F Cai FRACP MBBS

Specialist Registrars in Geriatric Medicine

R Teh BPharm (hon) MBBS

H Arunasalam MBBS

K Khow MBBS

T Woo MBBS

U Mushtaq MBBS (Rotating General Medicine Advanced Trainee 1st 6 months)

J Siew MBBS (Rotating General Medicine Advanced Trainee 2nd 6 months)

TQEH Geriatrics Senior Nursing

S Hoskins (CSC- GEM Unit)

L Wakefield (CPC- GEM Liaison)

TQEH Geriatrics Allied Health and Pharmacy

M Rugari Physiotherapist, GEM Unit, Allied Health Lead

C Hewton Clinical Pharmacist, GEM Unit

E Farrant Social Worker, GEM Unit

S Dabrowski Occupational Therapist, GEM Unit

Academic Staff

C Piantadosi BAppSci (Hon) PhD Research Fellow (until Oct 2014)

J Teo MBBS FRACP GTRAC Centre Academic

N Mahajan PhD MPsych MAPsychol BA GTRAC Centre Academic

Staff

Administrative Staff

C Falcone AECS
B Cannon AECS
R Bonin G-TRAC Centre Coordinator
J Lenman G-TRAC Administrative Officer

Postgraduate Students

Higher Degrees Awarded

PhD

S Yu FRACP MBBS
'Sarcopenia in older people'
Conferred by the School of Medicine, University of Adelaide,
December 2014, with Dean's commendation.
Supervisors: Adams R, Visvanathan R

PhD Candidates

C McNally MPhil (Dent) GCHP Assoc DDH
'Oral health, general health and operative risk in hospitalised
older patients'
Supervisors: Adams R, Visvanathan R, Liberali S

A de SilvaJayatilaka BSc (Hon)
'Activity recognition for preventing malnutrition in older people'
Supervisors: Visvanathan R, Ranasinghe D, Barbar A

A Daria Jadczyk Dip Sports Science
'Exercise in older people'
Supervisors: Visvanathan R, Luscombe N

Masters Candidates

Master of Philosophy - Engineering

MWMASB Wickramasinghe BSc (Hon)
'Highly accurate human activity classifier to mitigate the risk of
falls in elderly based on wearable RFID technology'
Supervisors: Ranasinghe D, Visvanathan R

Master of Philosophy – Clinical Medicine

S Nair FRACP MRCP (UK) MBBS
'Post-prandial hypotension, gait and exercise in the elderly'
Supervisors: Visvanathan R, Gentilcore D

R Teh BPharm (Hon) MBBS
'A health information tool to prevent falls'
Supervisors: Visvanathan R, Wilson A, Mahajan N

Honours Candidate

Z Kopsaftis 'Postprandial hypotension and falls in the elderly'
Bachelor of Health Sciences Honours (First class)
Supervisors: Gentilcore D, Visvanathan R

Collaborations

Local

Associate Professor Anne Wilson, School of Medicine, Flinders
University, South Australia

Professor Ian Chapman, CRE Translating Nutritional Science To
Good Health, University of Adelaide, South Australia

Professor Jon Karnon, Health Economics, University of
Adelaide, South Australia

Professor Justin Beilby, General Practice, University of Adelaide,
South Australia

Professor Alison Kitson and Dr Tim Schultz, School of Nursing,
University of Adelaide, South Australia

Professor Graeme Hugo and Dr Helen Feist, Discipline of
Geography, University of Adelaide, South Australia

Associate Professor Mellick Chehade, Discipline of
Orthopaedics and Trauma, University of Adelaide, South
Australia

Dr Sharmalar Rajendran, Department of Cardiology, The Queen
Elizabeth Hospital, South Australia

Ms Kylie Lange, CRE Translating Nutritional Science To Good
Health, University of Adelaide, South Australia

Dr Damith Ranasinghe, Director, Adelaide Auto-ID Lab and
Faculty of Engineering and Computer Sciences, University of
Adelaide, South Australia

Associate Professor Michael Ridding, Robinson Institute,
University of Adelaide, South Australia

Professor Julie Ratcliffe, Health Economics, Flinders University,
South Australia

Dr Diana Gentilcore, Senior Lecturer in Nuclear Medicine,
University of South Australia Professor Karen Jones, CRE
Translating Nutritional Science To Good Health, University of
Adelaide, South Australia

Dr Natalie Luscombe, CRE Translating Nutritional Science To
Good Health, University of Adelaide, South Australia

Grants/Scholarships

National

Associate Professor Simon Bell, Centre of Medicine Use, Safety and Pharmaceutical Sciences, Monash University and Adjunct Professor of Geriatric Pharmacotherapy, Faculty of Health Sciences, University of Eastern Finland

Professor Keith Hill, Head of School, School of Physiotherapy, Curtin University, Western Australia

Professor Ian Cameron, Professor of Rehabilitation Medicine, Medicine, Northern Clinical School, Rehabilitation Studies Unit, University of Sydney, NSW

Associate Professor Peter Hunter, Clinical Program Director Rehabilitation and Aged Care, Alfred Health, Victoria

Associate Professor Vasi Naganathan, Centre for Education and Research on Ageing (CERA), University of Sydney and Staff Specialist in Geriatric Medicine, Concord Hospital, NSW

Associate Professor Sarah Hilmer, Northern Clinical School, University of Sydney and Staff Specialist, Clinical Pharmacology and Aged Care, Royal Northshore Hospital, NSW

International

Professor Matteo Cesari, Gerontopole, Toulouse University, France

Professor John Morley, St Louis University (SLU), Missouri, USA

Professor Kenneth Rockwood, Dalhousie University, Nova Scotia, Canada

Dr Olga Theou, Dalhousie University, Nova Scotia, Canada

Awards

R Teh

Advance Trainee Research Prize 2014 (\$400) Annual Scientific Meeting of the Australia and New Zealand Society for Geriatric Medicine SA Division

Best Vocational Trainee 2014, Alan Kerr Grant Awards, The Queen Elizabeth Hospital

S Nair

Best Oral Presentation Clinical Research Group 1 (\$1,000), TQEH Research Day, October 2014, The Queen Elizabeth Hospital

Flinders University. (DVCR (R) Near Miss Grant) Incorporating older peoples' preferences into the design and delivery of dementia diagnostic services. (\$20,000 2014) Ratcliffe J, Luszcz M, Doyle C, Visvanathan R.

NHMRC. (Project grant # 627178) The effects of testosterone and a nutritional supplement on hospital admissions in under-nourished, older people. (\$384,037 2014) 2010-2014, Chapman I, Visvanathan R, Naganathan V, Hunter P, Karnon J, Horowitz M, Lange K, Cameron I.

Novartis. (Educational grant). Impact of a pilot fracture liaison service coordinator on the care of older patients presenting to hospital with a fragility fracture. (\$20,000 2014) Shibu PK.

The Queen Elizabeth Hospital Medical Staff Society Inc. Committee of Graduate Study Scholarship (\$1,000 2014) Teh R.

University of Adelaide Beacon of Enlightenment PhD Scholarship (International Tuition Fees and Living Allowance). (\$55,000 2014) 2014-2017, Jagdczak A.

Commercialisation

Patent Application (#2012903239): A system, method and software application for determining movement. Ranasinghe D, Visvanathan R.

Editorial/Advisory Boards

Visvanathan R. Editorial Board Member, Frailty.net: An international educational resource endorsed by the International Association of Geriatrics and Gerontology and the Global Ageing Research Network.

Visvanathan R. External Advisory Board Member, SPRINTT Trial: European multi-national (13 countries) trial with two objectives: 1) to provide a scientifically sound and clinically relevant operational definition for physical frailty and sarcopenia; and 2) conduct a randomised clinical trial with two year follow-up aimed at testing the effects of multicomponent interventions over 12 months to prevent disability in community-dwelling older people with physical frailty and sarcopenia.

Anaesthesia

The Department of Anaesthesia at TQEH is part of the Division of Critical Care of the Central Adelaide Local Health Network (CALHN). We provide services to Surgery, Cardiology, Gastroenterology, Respiratory Medicine, Radiology, Psychiatry and the Pregnancy Advisory Centre. Our Acute Pain Service (APS) provides advice and post-operative pain management services throughout TQEH. The Department also provides resuscitation and airway services for TQEH. We participate in the SA & NT Rotational Anaesthesia Training Scheme (SANTRATS) for the training of Registrars in Anaesthesia. We provide lectures and bed-side teaching sessions for 3rd to 6th year medical students.

Our research has a clinical focus and involves regional anaesthesia, patient safety, new drugs and new applications of drugs.

Research activities are also focused on new techniques to provide safe and effective post-operative pain relief: a simple and safe abdominal nerve block (TAP) procedure was compared to a standard epidural technique in a randomised controlled trial. This study was published in 2013. In 2014 we have started a study comparing intermittent bolus versus continuous infusion in patients having TAP catheters for post-operative pain relief.

Patient safety is also the focus of our research. We published a case where prolonged QT interval caused severe arrhythmia during sevoflurane anaesthesia in a patient with diabetes. In 2014 we finalised a study specifically investigating the effect of sevoflurane on QTc interval in diabetic patients.

After we published a systematic review at the end of 2014 on neuropraxia in relation to laryngeal mask airway devices, an anatomical study was initiated into the causes for this.

A systematic review was done and submitted for publication on the effects of beta-blockade on analgesia, anaesthesia and post-operative nausea and vomiting. The findings may cause a paradigm shift in anaesthesia, as beta-blockade appears to significantly reduce analgesia and anaesthesia dosing, whilst reducing post-operative pain, nausea and vomiting. Further research focussing on this finding will follow.

Population Data

> Every year **more than 10% of Australians undergo a surgical procedure**. In the majority of these some form of anaesthesia is involved.

Research Focus

- The effect of sevoflurane on QTc interval in patients with type 2 diabetes
- Sugammadex and new anaesthetic strategies to facilitate surgery
- Neuropraxia and Supra-Glottic Airway Devices
- Beta-blockers as adjuvants to analgesia and anaesthesia

Staff

Head of Department

R van Wijk MD PhD FANZCA FFPMANZCA

Consultants

- R Balasingam FANZCA
- E Chye FANZCA
- A Colby FANZCA
- A Czuchwicki FANZCA
- I Elhalawani FANZCA
- S Flint FANZCA
- K France FANZCA
- T George FANZCA
- C Hildyard FRCA
- J Jeyadoss FANZCA
- M Kha FANZCA
- G Koo FANZCA
- Z Lagana FANZCA
- C Lang FANZCA
- A Laver FANZCA
- R Lea FANZCA
- PC Lim FANZCA
- R Limb FANZCA
- A Michael FANZCA
- G Miller FFARCS(I) FANZCA
- R Mitchell FANZCA
- A Moffat FFARCS
- N Nanjappa FANZCA
- D Nemeth FANZCA
- G Newcombe FANZCA
- K Osborn FANZCA
- A Rajbhoj FANZCA
- V Rao Kadam FANZCA
- R Sethi FANZCA
- R Steiner FANZCA
- VThiruvankatarajan FANZCA
- T Visvanathan FANZCA
- R Watts FRACGP
- CK Wong FANZCA
- A Zanker FANZCA

Consultant Physician

C Gibb FRACP

Visiting Medical Officers

- J Currie FFARCS
- P Naderi FANZCA
- A Sen FANZCA
- V Niculescu FANZCA
- M Wahba FANZCA

Keeping your heart beating

Ben's Story



Ben and wife Angie and their children

As a father of two small children Ben, 36, knows his life has been saved by advances in medical research teamed with expert medical care. He considers himself both lucky and thankful. Told he could no longer play sport at 16 Ben thought it was the end of the world; he loved Aussie rules with a passion. It was a dramatic and unwelcome change in his life, but it wasn't the first he'd encountered.

Ben's father died from hypertrophic cardiomyopathy (HCM) when he was just 13. The 43-year-old father of three left behind his loving wife, Ben and his two sisters aged fifteen and eight. His father's death had a deep impact on Ben, finding out he had the same medical condition was just an added strain. "It was all pretty devastating and when you were at school being told you couldn't play sport like everyone else – it was really hard. I had to give up everything," Ben said. Following the premature death of his father Ben started seeing leading cardiologist Professor John Horowitz at The Queen Elizabeth Hospital to monitor his condition.

Hypertrophic cardiomyopathy or HCM is a condition where a mutation in the chemical structure of the heart muscle reduces its efficiency and causes thickening of the muscle. It is a life-threatening condition, which can cause problems with the heart's electrical system, chest discomfort and shortness of breath; it is also associated with sudden cardiac death.

Keeping close tabs on his heart health as he grew into adulthood, Professor Horowitz advised Ben surgery would be needed to implant a defibrillator into his chest. He was 21. "It was such a big thing at that age to have surgery for a heart condition. I remember being in hospital surrounded by 70 and 80 year olds," he shared.

The procedure enabled Ben to complete school and university before deciding to venture overseas to work. "My friends always have a bit of a laugh about the fact that I have one of these machines - even my work colleagues are surprised when I tell them what I have in my chest. Once I tell them what it's for - they do a double take."

Ben's life has been saved at least twice by the constant companion he has sitting under the skin on his chest. "It's already fired off three times - once when I was playing a quiet game of cricket and again when I was in London jogging for a train," he said. He laughs as he remembers waking up on the footpath not really knowing what had happened. That's when Ben and his wife Angie who he had met during his time in London realised it was perhaps time to come back to Australia to have things checked out.

"My heart was deteriorating - I could be on my knees on the floor and when I got up I'd have head spins and have to hold the table, I was constantly short of breath," Ben said. "This was also the time that Professor Horowitz said he was going to try me on a drug called Perhexiline. He said it could do something not so good or it could be really beneficial."

Ben's heart had reached a critical point and a drastic step was needed. If his heart didn't respond to the medication they would need to look at surgical options. The Queen Elizabeth Hospital has been at the centre of extensive research into Perhexiline and it has proven to be a wonder drug for Ben.

"Perhexiline improves the electrical status of the heart and we've seen it work incredibly well for Ben who has almost no shortness of breath these days, and his heart has become less thickened," Professor Horowitz said. It's a treatment he says he is looking forward to seeing used more world-wide.

After being on the drug for five years Ben said "I can jump off things, I can pick up both the children and run around after them without any issues at all."

"As an example, we were in Melbourne where there were some spiral stairs and Ben just couldn't do them before but now he can practically run up them," Angie said. The thickness in the wall of his heart dropped significantly in the first year, there was even more improvement the second year and now it has plateaued. A significant murmur that was present before taking Perhexiline has seemingly disappeared.

"I take three different medications each day and I'm now feeling really well - I do more exercise now than I have done for a long time. We walk and take the kids walking with the pram so it's not structured exercise but I keep active." While Ben's sisters continue to be checked for HCM and appear to be clear of the condition he is concerned for his two young children.

"Last time we were in with Professor Horowitz we were starting to have that conversation about the children.... I guess we knew already that it could be passed on in some way." Ben will soon undertake genotyping for HCM.

"I've just been given the blood test to have the genotyping done again - 10 years ago nothing was proven but hopefully with all the new knowledge and technology they might find the gene responsible. With the way medicines and medical research is going already the changes we are seeing - you can't let things like this stop you. By the time they get tested when they get older - who knows what treatments might be available?" Ben said.

"Realistically, there is a chance both of our children might have HCM, there's a chance neither of them will have it and there's a chance one will be affected. So we need a way to protect them in the future."

"I'm so grateful to have been able to see the same doctor all this time - since I was 12. It has been great."

Ben and Angie consider their family is in the very best of hands.

"I'm so grateful to have been able to see the same doctor all this time - since I was 12. It has been great."

Cardiology Unit

The Cardiology Unit concerns itself with the emerging epidemic of 'new' cardiac diseases of the 21st century, as well as with the development of new treatments for 'old' diseases such as heart attacks. A central theme is the role of nitric oxide (NO) as a means of protecting blood vessels and heart muscle as well as investigating disorders of NO effect in valve disease, heart failure, stress cardiomyopathy and atrial fibrillation. We are utilising understanding of the mechanisms of these disease states to develop new treatments, with consequent reductions in disability.



Research Focus

- Roles of nitric oxide, nitrite and nitroxyl in cardiovascular homeostasis and pathology
- Management of heart failure
- Pathogenesis and management of aortic valve disease
- Heart disease in women: focus on stress (Tako-Tsubo) cardiomyopathy
- Mechanisms of action of anti-aggregatory agents
- Pathogenesis and management of atrial fibrillation
- Management of acute and chronic myocardial ischemia
- Effects of natriuretic peptides on inflammatory activation
- Therapeutic manipulation of thioredoxin-interacting protein

Population Data

> **Cardiovascular Disease** is:

- The principal cause for acute and chronic illness
- The main cause of death, and
- The main basis for health care expenditure in Australia

> By 80 years of age about 10% of Australians will have **atrial fibrillation**. This arises due to inflammation and distension of the atria. It is the main cause of strokes.

> 30% of Australians will have degeneration of their aortic valves. This causes **aortic stenosis**, the most common reason for valve replacement.

> 50 years ago **heart disease** mainly affected men. Risk factors are changing and now nearly half of patients are women. The causes of heart disease in women are quite different to those in men. Women, in particular, are prone to develop heart-attack like symptoms in response to severe emotional stress.

Overview

Role of nitric oxide, nitrate and nitroxyl in cardiovascular homeostasis

Dr Yuliy Chirkov and co-workers have demonstrated that platelets are resistant to nitric oxide in association with many forms of cardiovascular disease. This 'nitric oxide resistance' represents a major limitation to their effectiveness. This may be ameliorated by other agents such as ACE inhibitors and perhexiline.

We have also shown that nitrite, which is generated from nitrate-containing foods, is subject to this same problem, and that this limits the effects of nitrite released in hypoxic tissues.

However, nitroxyl donors partially circumvent nitric oxide resistance, offering a new avenue for treatment of acute heart failure.

Management of heart failure

In collaboration with Professor Simon Stewart, we have investigated approaches to the non-pharmacological management of patients with heart failure, including outreach supervision of individual patients. This approach is cost effective and is now being trialled in patients living in rural, regional and remote areas.

We are also investigating the question of whether cardiac resynchronisation therapy exerts any effects on vascular autocrine function in restoring vascular homeostasis.

Pathogenesis and management of aortic valve disease

Narrowing of the aortic valve (aortic stenosis) was once believed to arise from a process resembling atherosclerosis in blood vessels. We have highlighted the role of nitric oxide in maintaining normal valve function, and of thioredoxin-interacting protein (TxNIP) in modulating inflammation within the valve matrix. We have recently demonstrated that in patients with bicuspid aortic valve an additional factor is myeloperoxidase, which engenders further oxidative stress. Additional studies are investigating the potential roles of non-LDL lipoproteins.

From a therapeutic point of view, we are interested in evaluating the effects of both ACE inhibitors and myeloperoxidase inhibitors in limiting the narrowing of aortic valves.

Stress (Tako-Tsubo) Cardiomyopathy (TTC)

From a clinical point of view, we have demonstrated that TTC is associated with extensive and prolonged myocardial inflammation, and have shown that this in turn leads to slow recovery of ventricular function and persistence of symptoms for at least 4 months. Our collaborators in Aberdeen, UK, have shown that there is associated impairment of myocardial energetics.

Our mechanistic studies have demonstrated supra-normal nitric oxide signaling in patients, without evaluation of markers of nitrosative stress in plasma. However, at post-mortem, patients dying of TTC exhibit evidence of both nitrosative and oxidative stress within myocardium. These findings are recapitulated in a rodent model, which will be used to help develop therapeutic interventions to optimise recovery.

Mechanisms of action of anti-aggregatory agents

We have just published data demonstrating that a substantial cause of platelet resistance to the effects of clopidogrel is impaired function of the prostaglandin E1/adenylate cyclase pathway. Further work will evaluate:

- (a) whether this also applies to other anti-aggregatory agents
- (b) what are the mechanism(s) of pathway malfunction
- (c) whether adenylylase activity can be normalised therapeutically

We will also determine whether the accessory properties of ticagrelor protect it from variability in effect irrespective of adenylylase activity.

Pathogenesis and management of atrial fibrillation (AF)

(a) Focus on 'new onset' AF. We have recently demonstrated that patients with recent onset AF have substantial impairment of nitric oxide signaling, which may represent a basis for increased thrombotic risk. Further studies will evaluate the mechanisms and therapeutic significance of this finding.

(b) Impact of restoration of sinus rhythm. We seek to determine whether restoration of sinus rhythm ameliorates the inflammatory activation and impaired nitric oxide signaling that underlies AF.

(c) We have also conducted an evaluation of the potential impact of the arginine derivatives ADMA and SDMA on thrombotic and haemorrhagic risk during treatment for AF.

Management of acute and chronic myocardial ischaemia

(a) Efficacy of perhexiline. We are conducting an audit to evaluate the long-term utility and safety of perhexiline in the context of myocardial ischaemia/impaired left ventricular function

(b) We are evaluating the relationship between treatment of ischaemia and suppression of TxNIP expression (see below).

Effects of natriuretic peptides on inflammatory activation

Brain natriuretic peptide (BNP) has always been regarded as essentially a vasodilator and natriuretic hormone release during left ventricular distension. We have now demonstrated that:

- (a) BNP is also released during ventricular inflammation
- (b) BNP tends to suppress inflammation by reducing superoxide release from neutrophils
- (c) This effect is largely lost in heart failure.

Further experiments will evaluate the integrity of BNP/superoxide interactions in TTC, and also examine the therapeutic implications of treatment of heart failure with neprilysin inhibitors in this context.

Therapeutic manipulation of thioredoxin-interacting protein (TxNIP)

TxNIP is a major activator in inflammation in diabetes and also in ischaemic heart disease. Its expression is increased by hyperglycaemia and by loss of laminar blood flow.

We are also interested in the potential roles of TxNIP in aortic stenosis, TTC and AF.

We have recently demonstrated that perhexiline and ramipril suppress TxNIP expression, and are investigating the implications of the suppression regarding their insulin-sensitizing effects.

Staff

Director

Professor JD Horowitz AM, MBBS BMedSc(Hons) PhD FRACP FACC FAHA

Senior Clinical Staff

- C N Ajaero MD FRACP
- O Akbar Ali MBBS FRACP FCSANZ
- MA Arstall MBBS PhD FRACP
- P Averbuj MD FRACP
- JF Beltrame BSc BMBS FRACP PhD FESC RACC FCSANZ
- WP Chan MBBS FRACP
- R Dautov MBBS FRACP
- D DiFiore MBBS FRACP
- V Goh MBChB FRACP
- ADB Hains MBBS FRACP
- JTY Hii BMBS FRACP
- SB Limaye MBBS MD MRCP FRACP
- D Lypourlis MD FRACP
- G Mahadavan BMBS FRACP
- K Mishra MBBS MD MRCP FRACP
- D Ninio MBBS(Hons), PhD FRACP
- A Philpott MBBS FRACP
- S Rajendran MBBS PhD FRACP
- PR Sage MBBS PhD FRACP
- K Singh MBBS FRACP
- AL Sverdllov MBBS FRACP FCSANZ
- S Unger MBBS PhD FRACP
- AS Warner MBBS BMedSc(Hons) PhD FRACP
- CJ Zeitz MBBS PhD FRACP OstJ

Senior Research Scientists

- YY Chirkov BSc PhD
- TH Nguyen PhD
- D Ngo BPharm BHLth Sc(Hons) PhD FCSANZ
- DP Wilson BSc(Hons) MSc PhD

Laboratory Manager

- I Stafford BSc

Research Assistants

- T Heresztyn BSc

Technical Officer

- G Murphy BA

Trial Coordinators

- C Anderson-Stanford RN
- M Black RN
- J Rose RN
- G Dymmott RN
- E Jansen
- J Stansborough

Administrative Staff

- P Pachen
- B Phillippo
- D McCracken

Postgraduate Students

Higher degrees awarded

PhD

C Neil MBBS, FRACP

'Short and long-term impact of Tako-Tsubo cardiomyopathy on myocardial structure and function'

Supervisor: Horowitz JD

A Amarasekera BPharm

'Does vitamin D deficiency effect endothelial dysfunction of diabetic obese patients?'

Supervisors: Roberts MS, Horowitz JD

R Dautov MD FRACP

'Therapeutic potential of nitrites and nitroxyl donors in ischaemic heart disease'

Supervisors: Horowitz JD, Chirkov Y, Rajendran S, Ngo, D

PhD Candidates

N Hurst MBBS FRACP

'The effect of the nitric oxide and prostacyclin pathways on platelet aggregation' (thesis submitted)

Supervisors: Horowitz JD, Chirkov Y

G Mahadavan MBBS FRACP

'The pathophysiology and potential therapeutics of diastolic heart failure' (thesis submitted)

Supervisor: Horowitz JD

S Liu MSc

'Impaired tissue responsiveness to brain natriuretic peptide (BNP) in heart failure (HD): biochemical bases'

Supervisor: Horowitz JD

V Nooney BPharm

'Determinants of clinical response to platelet ADP receptor antagonists'

Supervisors: Roberts M, Horowitz J, Chirkov Y

V Goh MBChB FRACP

'Reverse genesis: does atrial fibrillation perpetuate dyshomeopathic origins?'

Supervisor: Hii J, Horowitz JD

K Singh MBBS FRACP

'Pathogenesis of Tako-Tsubo Cardiomyopathy'

Supervisor: Horowitz JD

N Procter BSc(Hons)

'Biochemical Correlates of Stroke Risk in Atrial Fibrillation' (thesis submitted)

Supervisors: Horowitz JD, Chirkov Y, Kennedy J, Ngo, D

C Chong BPharm

'A pharmacological approach towards myocardial protection: new perspectives in acute and chronic cardiac disease'

Supervisors: Horowitz JD, Sallustio B

B Raman MBBS

'Tako-Tsubo Cardiomyopathy: The role of oxidative and nitrosative stress'

Supervisors: Horowitz JD; Nguyen TH

S Surikow BSc(Hons)

'The role of oxidative and nitrosative stress in the pathogenesis of Tako-Tsubo Cardiomyopathy'

Supervisors: Horowitz JD; Nguyen TH

R Shah MBBS

'Assessment of progression of bicuspid aortic valve dysfunction and aortopathy: correlation with inflammatory activation and vascular endothelial function'

Supervisor: Horowitz JD

C Ajaero MBBS FMCP FRACP

'Vascular "remodelling" from a physiological and biochemical point of view as a potential source of variable improvement post CRT insertion'

Supervisor: Horowitz JD

Masters Candidate

M Chapman BSc

'Pathogenesis of valvular and aortic degenerative changes in association with bicuspid aortic valve'

Supervisor: Horowitz JD

Vacation Student 2014-15

K Richards

'Pathogenesis and natural history of Tako-Tsubo Cardiomyopathy (TTC)'

Supervisor: Nguyen TH

Grants

NHMRC. (Project grant # 1049133) Which Heart failure Intervention is most Cost effective in reducing Hospital care (WHICH II) Trial: A multi-centre, randomised trial of standard versus intensified management of metropolitan and regional-dwelling patients with heart failure. (\$364,564 2014) 2013-2018, Stewart S, Horowitz JD, Carrington M, Scuffham P, Wong C, Newton P, Rischbieth A.

Tenovus Scotland. (Project grant G13/10) Stress induced Heart Disease. (£9,990 2013-2014) Dawson D, Neil CJ, Horowitz JD, Frenneaux MP.

NHMRC. (Project grant) A randomised comparison evaluating the value of high sensitivity troponin in the efficient management of chest pain across the spectrum of risk for an acute coronary syndrome. (\$248,452 2014) 2013-2014, Chew D, Beltrame J, Worthley M, Zeitz C, Aylward P, Quinn S, Astley C. NHMRC. (Partnership Grant #1062331)

The ACCESS Project – Assessment of Coronary artery disease using CT Effectively for Stable Symptoms (\$312,833 2014) 2013-2017, Beltrame JF, Zeitz CJ, Tavella R, Worthley MI.

Commercialisation

Patent: preventing and/or treating of stress induced cardiomyopathy. JD Horowitz/Y Chirkov. University of Adelaide. Patent no. 2012904658 23 October 2012

Clinical Pharmacology Unit

Clinical Pharmacology has both a routine diagnostic role and a medical research role. Our aim is, wherever possible, to combine both so as to translate new research findings into new laboratory and clinical skills that contribute to state-of-the-art clinical care of patients.

Our research focuses on the areas of heart disease and kidney transplantation (lead by Associate Professor Betty Sallustio), and cancer and anaesthesia (lead by Dr Ian Westley). We aim to individualise drug therapy through the use of therapeutic drug monitoring, particularly of immunosuppressant drugs used in kidney transplantation and the anti-anginal agent perhexiline in cardiac care. Through research in these fields we strive to provide a better understanding of drug action, metabolism and disposition in patients with varied genetic makeup in order to better use these agents and tailor them to each individual, and to develop new therapies.

Heart Disease

The Unit maintains an active research interest in the treatment of ischaemic heart disease and heart failure, which has evolved from work with perhexiline, an older and very effective drug used to treat angina. Perhexiline can cause serious liver and nerve toxicity if dosages are not individualised based on the diagnostic testing provided in our laboratory. Our current research aims to better understand its mechanisms of action within the body in order to translate this understanding into safer clinical use. We also aim to develop new therapies for the treatment of heart diseases such as angina and heart failure. In 2014, following the completion of his PhD, Dr John Licari was appointed as a postdoctoral research officer to continue investigating the development of new drugs based on our growing knowledge of how perhexiline works. This has now led to a patent application in Australia and the USA. The IP developed in collaboration with the University of Adelaide and the University of South Australia licenced to Heart Metabolics Ltd., a UK pharmaceutical company, that is supporting the development of our new drugs and funding Dr Licari's position through the University of Adelaide. This work was presented at the 2014 meetings of the World Congress of Cardiology and the International Society of Cardiovascular Pharmacology.

Population Data

> **Heart disease** is the second leading cause of death in Australia. It accounted for just over 1.2 million hospitalisations in 2011-2012.

> Approximately 11,500 Australians are on dialysis due to **kidney disease** but only 845 people (6%) received a **kidney transplant** in 2012.

> **Cancer** is a leading cause of death in Australia, with approximately 128,000 new cases being diagnosed this year.

Research Focus

- Personalised Medicine
- Translating laboratory skills in therapeutic drug monitoring to the delivery of optimal testing for clinical care
- Developing new treatments for heart disease
- Developing new monitoring strategies in organ transplantation
- Therapeutic drug monitoring opportunities for cancer drugs
- Local anaesthetic drugs in post-operative pain management

Transplantation Therapy

PhD candidate Mr Zaipul Md Dom is investigating genetic factors that may influence the efficacy of immunosuppressant drugs and, hence, the incidence of rejection or organ toxicity. His studies form part of our larger transplantation pharmacogenetics project, previously funded by the NHMRC. Initial results indicate that genetic differences in some transporter proteins (MRP2) affect the body's handling of the immunosuppressant mycophenolic acid in transplant recipients. They also show that differences in the expression of another transporter protein (P-gp) within the transplanted kidney are associated with both renal exposure to other immunosuppressant drugs (cyclosporine and tacrolimus), and kidney damage. In addition, by developing a method to measure the concentrations of mycophenolic acid directly within the immune cells that cause rejection, we have demonstrated a significant improvement in predicting patients at risk of rejection. These exciting results suggest that models that predict both the immune cells' and the kidney's exposure to immunosuppressant drugs and incorporate genetic markers may be an important additional guide to individualising patients' immunosuppressant medication. Part of this work was presented at the 2014 Scientific Meeting of the Australasian Society of Clinical and Experimental Pharmacologists and Toxicologists, for which Zaipul was awarded the Clinical Special Interest Group Prize, and was a finalist for the Neville Percy Prize. Zaipul was also the recipient of the Ivan De La Lande Travel Award at this year's TOEH Research Day.

Cancer Research

A relatively new area of research for the department is the dose individualisation of chemotherapeutic agents, in particular the drug docetaxel used for the treatment of breast and prostate cancer. Dr Ian Westley, a member of a Therapeutic Drug Monitoring – Oncology Research Group which comprises scientists and clinicians from the State's Universities and Hospitals, is investigating how the current "one dose fits all" policy of chemotherapeutic agents compares to a targeted concentration approach. The ultimate aim of reducing the adverse side effects associated with this drug, docetaxel whilst optimising its effectiveness.

Local anaesthesia – novel clinical usage

A project investigating interactions between an anaesthetic reversing agent and other drugs used during surgery to prevent post-operative nausea also continued in 2014. This was a collaboration with the Department of Anaesthesia. The project aims to determine whether the efficacy of the drugs is compromised or enhanced when combined with the reversing agent.

Staff

Principal Medical Scientist/Associate Professor

BC Sallustio BSc PhD

Senior Medical Scientist

IS Westley BMedSc PhD (resigned September 2014)

Grant Funded Scientist

J Licari BHSc(Hons), PhD

Senior Technical Officers

FA Wicks BSc

A Kalaitidis BSc

Technical Officers

Z Boaden BAppSci

D Dinow BSc

C de Nichilo BSc

Postgraduate Students

PhD Candidates

Z MD Dom BHSc(Hons)

'Pharmacogenetics of renal transplantation'

Supervisors: Sallustio BC, Somogyi AA, Collier JK

C-R Chong BPharm

'A pharmacological approach towards myocardial protection: new perspectives in acute and chronic cardiac disease'

Supervisors: Horowitz JD, Sallustio BC

Honours Candidate

Helen Dimitroff BSc

'The Effect of Perhexiline on the Efficacy & Toxicity of Doxorubicin'

Supervisors: Sallustio BC, Evdokiou A

Grants

Endeavour Post-Graduate Award. (Australian Federal Government PhD award) 2011-2014, MD Dom Z.

NHMRC Postgraduate Research Scholarship (\$43,033 2014), Chong C-R.

Adelaide Research and Innovation (\$91,626 2014), Sallustio BC.

Awards

Z MD Dom

Clinical Special Interest Group Prize, 2014 Scientific Meeting of the Australasian Society of Clinical and Experimental Pharmacologists and Toxicologists, joint ASCEPT meeting 7 – 11 December, Melbourne, VIC

Finalist for the Neville Percy Prize, 2014 Scientific Meeting of the Australasian Society of Clinical and Experimental Pharmacologists and Toxicologists, joint ASCEPT meeting 7 – 11 December, Melbourne, VIC

Ivan De La Lande Travel Award, TQEH Research Day 2014, Adelaide

Commercialisation

March 2014, Provisional patent application US Provisional Patent Appli 61/948,513 'Methods for using (-)- Perhexiline' DIP ref PPUS140301 "New Indications for (-)-Perhexiline". BC Sallustio, G Licari, P Milner, P Druzgula

Acknowledgements

We would like to acknowledge 20 years of service to The Queen Elizabeth Hospital and the Basil Hetzel Institute by Dr Ian Westley, who resigned in September 2014, to take up a senior position with CPR Pharma.

Collaborations

Local

Professor GR Russ, Associate Professor PT Coates and Dr R Carroll, Renal Unit, Central Adelaide Local Health Network

Professor AA Somogyi and Dr JK Collier, Discipline of Pharmacology, University of Adelaide

Professor RW Milne, School of Pharmacy and Medical Sciences, University of South Australia

Dr Michael Wiese, School of Pharmacy and Medical Sciences, University of South Australia

Dr Andrew Rowland and Dr Michael Sorich, School of Medicine, Flinders University

Dr Ganessan Kichenadasse, Medical Oncology, Flinders Medical Centre

Dr Richard Watts, Department of Anaesthesia, The Queen Elizabeth Hospital

International

Dr NE Drury, Cardiothoracic Surgery, Birmingham Heartlands Hospital & University of Birmingham, UK

Professor ME Frenneaux, School of Medicine, University of Aberdeen, UK

Dr Iain Greig, Kosterlitz Centre for Therapeutics, University of Aberdeen, UK

Professor T Van Gelder and Dr DA Hesselink, Department of Internal Medicine, Renal Transplant Unit, and Department of Hospital Pharmacy, Erasmus University Medical Centre, Rotterdam, the Netherlands



Endocrinology Unit

The Endocrinology Unit conducts research in areas relating to diabetes and osteoporosis. We aim to enhance knowledge in endocrinology through clinical trials, translational research and patient care quality improvement.

We are the Adelaide site of the multi-centre double-blind, randomised, placebo-controlled trial (T4DM). Patient recruitment for this trial is currently in its second year. The principal investigator of this clinical trial is Professor Gary Wittert of University of Adelaide while Dr David Jesudason is the chief investigator at The Queen Elizabeth Hospital. This study is supported by the NHMRC and also receives support from The Hospital Research Foundation. Mr Sam Jose, a research nurse, is the research coordinator for the trial. Eighty patients have been recruited after screening over 2000 volunteers. There have been no serious adverse events. Participants have been positive in their feedback regarding trial participation. The data collected on the utility of screening for pre-diabetes to fulfil the inclusion criterion with fasting capillary blood glucose levels and fasting venous blood glucose levels has been analysed for publication. We also conduct the body composition and bone density assessments for the participants of the T4DM trial.

Dr David Jesudason has continued the study on kidney function and bone density in overweight and obese patients using data collected in a clinical trial conducted in collaboration work with Professor Peter Clifton, Division of Nutrition, CSIRO. Mr Chris Seaborn has been involved in a North West Adelaide Health Study of diabetes and cardiovascular disease. Dr Jason Tan, in collaboration with Dr David Jesudason and Professor Gary Wittert, has initiated a study using data from The Men Androgen Inflammation Lifestyle Environment and Stress (MAILES) cohort to analyse the relationship between testosterone levels and the development of diabetes in the follow-up period. Dr Jim Wang has been involved in statistical analysis of the above studies.

Nurse educators in the Diabetes Centre have conducted the following patient care improvement oriented studies: Insulin adjustment clinic data analysis with the view of assessing the effectiveness of the clinic work; the Self Management and Review Type 1 Intensive Education (SMaRT1E) for the improvement of type 1 diabetes patient self-care. These studies are in progress.

Population Data

> About 5% of Australians have **diabetes**: 120,000 with type 1 diabetes and 956,000 with type 2 diabetes. Another 23,600 Australian women suffer from **gestational diabetes**.

> Over 100,000 Australians have developed **diabetes** in the past year, which equates to 280 people each day.

> At least 2 million Australians have **pre-diabetes or metabolic syndrome** which disposes them to a high risk of developing type 2 diabetes.

> Indigenous Australians are 3 times more likely to have type 2 diabetes compared with non-indigenous Australians.

Research Focus

- Randomised Clinical Trial in collaboration with the Royal Adelaide Hospital
- Diabetes patient care quality improvement
- Development of efficient strategies to diagnose and monitor diabetes and osteoporosis

Osteoporosis and its associated fractures are a major cause of preventable disability and dependence for South Australians and a major cost to our community. Our strong links with the community organisation Osteoporosis Australia, the Royal Australian College of General Practitioners and the Medical Services of the central, northern and western suburbs of Adelaide enable us to review the management of osteoporosis in our community. Our combined services now see about 5,500 patients per year and we have two databases containing records for around 35,000 individuals. These databases are an important source of clinical data for investigating many aspects of the overall bone health of the communities that we serve, the treatment options currently in use and of determining long term trends and changes.

Recently, we have implemented a system for assessing and reporting estimated total body percentage fat using soft tissue measurements from spine and femur bone density acquisitions. In the coming year we will evaluate the usefulness of these measurements for assessing the impact of weight and body composition changes on bone density measurements and changes in bone mineral density.

Grants

NHMRC. (Project grant #1030123) Testosterone intervention for the prevention of diabetes mellitus in high risk men: a randomised trial. (\$88,000 TQEH 2014) 2012-2016, Wittert, G, Yeap B, Grossman M, Conway A, Allan C, Daniel M.

Collaboration

The Endocrinology Unit, TQEH is the Adelaide site of T4DM, the NHMRC multi-centre double-blind, randomised, placebo-controlled trial listed above.

Staff

Head

D Jesudason MBBS FRACP

Endocrinologists

N Laddipeerla MBBS FRACP (Endo)

K Campbell MBBS FRACP

L Gagliardi MBBS FRACP PhD

Senior Registrars

C Marathe MBBS, FRACP (until Aug 2014)

U Mushtaq, MBBS, FRACP

Registrars

F Ameer MBBS, FRACP (until Feb 2014)

J Tan MBBS, FRACP (until Aug 2014)

Scientists

J Wang BSc PhD MPH

C Seaborn BSc

E Robinson BSc

T4DM Clinical Trial

S Jose BSc RN PGDCR

Diabetes Centre Nurses

T Willson RN BNg (Hons) Grad Cert Health (Diab Man and Ed) CDE

R Cox CN BN MN

M Hodgson RN RM BMid Grad Cert (Diab Ed)

D Barrow RN Grad Cert (Diab Ed)

C Nitschke RN RM Grad Cert (Diab Man & Ed)

M Kinasz RN B app sci (Food Science and Nutrition) Cert (Diab Man & Ed)

R Wilson RN

Dietitians

C Stanton BSc DipEd MND

C Roberts BSc MND

Administration

C Bouthémy (Dip.Hlth.Sc)

A Gazzard

V Watson

J Cocks

Gastroenterology and Hepatology

2014 has been a year of further change in the research personnel of the Unit. Professor Ian Roberts-Thomson has retired after 29 years as Clinical Director of the Unit. He has been involved in many clinical research and basic science studies spanning giardiasis, chronic abdominal pain, sphincter of Oddi dysfunction, DNA adducts, colon cancer and inflammatory bowel disease.

Professor Ian Roberts-Thomson will continue to be a supervisor for PhD candidate, Dr Sam Costello, and was a co-investigator on a successful NH&MRC grant on faecal transplantation for the treatment of ulcerative colitis. He will continue to work part-time at the Basil Hetzel Institute and the CSIRO, largely on the potential role of intestinal bacteria in gut inflammation. He has been awarded the title of Emeritus Professor by the University of Adelaide.

Associate Professor Adrian Cummins, while clinically retired, continues to have a research interest in intestinal stem cells during postnatal growth of the small intestine and in regeneration of the small bowel after small bowel resection. There has been a long collaboration on these projects with Professor Gordon Howarth, Department of Animal and Veterinary Sciences, Roseworthy, University of Adelaide. Along with Dr Kumar Grover, Dr Cummins also has an interest in a subgroup of cancer cells called cancer stem cells that may be responsible for the development of metastases in gastrointestinal cancer. Interestingly, these cells can sometimes be detected in peripheral blood in patients with cancer, particularly those with advanced disease. Research with cancer stem cells is being undertaken in collaboration with Dr Jenny Hardingham and Associate Professor Tim Price in TQEH Department of Haematology and Oncology. Dr Cummins is also supervising PhD candidate Dr James Fon in his study of changes in mucosal cytokines in patients with both ulcerative colitis and Crohn's disease.

Dr Dan Worthley has been an important addition to our research staff. He trained as a gastroenterologist but has been involved in basic science research for the past decade in both Australia and the USA. Dr Worthley currently has appointments at The Queen Elizabeth Hospital, the South Australian Medical Research Institute and the University of Adelaide. His particular interests include the role of mesenchymal cells in the wall of the small intestine and the development of new animal models for the study of bowel cancer. If satisfactory new models can be developed, this could enhance our understanding of cancer and provide easier ways to examine the potential benefit of new drugs. The research will be funded, in part, by a new project grant from the NHMRC.

Drs Cummins, Grover and Worthley are working with Professor Joanne Young in the Department of Haematology and Medical Oncology on aspects of colon cancer. Professor Ross Butler has a major link with the University of South Australia and continued to work part-time in our Unit during 2014. His main theme is the potential use of breath analysis for the diagnosis of cancers in the gastrointestinal tract. Thus far, most of the work has involved the analysis of gaseous products from cancer cell lines maintained in the laboratory. The plan is to extend these studies to human subjects in 2015.

Population Data

> In 2012, 16,000 Australians were diagnosed with **colon cancer**. 3,800 died from their disease.

> In 2013, 75,000 Australians were affected by **inflammatory bowel disease** (Crohn's disease and ulcerative colitis).

Research Focus

- Faecal transplantation for ulcerative colitis
- Intestinal cytokines in inflammatory bowel disease
- Circulating cancer stem cells in colon cancer

Dr Roger Yazbeck is leading a research team that is developing and validating new, transformational breath analysis tools that will offer new opportunities for early detection of gastrointestinal diseases, leading to improved clinical management. Breath analytics represents a powerful, cutting edge technology that can be used to non-invasively, rapidly and with high sensitivity and specificity detect abnormal changes in the gastrointestinal tract.

The incidence of oesophageal cancer has increased almost six-fold in some Western societies over the past 30 years. A key challenge for the early detection of oesophageal cancer is the absence of low cost, non-invasive (or minimally invasive) tools that can detect early pre-cancerous or cancerous changes in the oesophagus. PhD candidate, Michelle Squire, is undertaking a project to optimise candidate new breath tests for the diagnosis of oesophageal cancer.

Inflammatory Bowel Disease (IBD) is a chronic, debilitating condition that affects more than 60,000 people around Australia. PhD candidate, Simone Jaenisch, is investigating the molecular events that occur during immune response in IBD, which may lead to the identification of new breath biomarkers to better diagnose and monitor this lifelong condition.

Staff

Professors

IC Roberts-Thomson MD FRACP
RN Butler PhD

Associate Professor

AG Cummins BSc(Med) MD PhD FRACP

Senior Lecturer

DL Worthley MBBS PhD MDH FRACP

Consultants

I Lidums MBBS PhD FRACP
JT Fon MBBS FRACP
SP Costello MBBS FRACP

NHMRC Early Career Research Fellow

R Yazbeck BSc(Hons) PhD

Research Scientist

PK Grover PhD

Hospital Scientist

W Butler BSc

Postgraduate Students

PhD Candidates

JT Fon MBBS
'The cytokine profile of inflammatory bowel disease'
Supervisors: Roberts-Thomson IC, Cummins AG

SP Costello MBBS
'The role of faecal transplantation in the treatment of ulcerative colitis'
Supervisors: Andrews J, Roberts-Thomson IC, Conlon M, Hughes P

M Squire BSc LabMed (Hons)
'Development of a Dipeptidyl Peptidase-IV Breath Test for Oesophageal Cancer'
Supervisors: Yazbeck R, Brooks D, Butler R

S Jaenisch BSc LabMed (Hons)
'The role of Dipeptidyl Peptidases in innate immune responses during Inflammatory Bowel Disease'
Supervisors: Yazbeck R, Parkinson-Lawrence E

Grants

Grant funding commencing 2015

NHMRC. (Project grant) Faecal microbiota transplantation for active ulcerative colitis - a randomised controlled trial: clinical, microbial & immune outcomes. 2015-2017, Andrews J, Hughes P, Conlon M, Roberts-Thomson IC, Costello S.

NHMRC. (Project grant) Gastrointestinal mesenchyme supports intestinal stem cells, promotes intestinal regeneration and drives cancer. 2015-2017, Worthley D.

Collaborations

Professor Gordon Howarth, Department of Animal and Veterinary Sciences, Roseworthy, University of Adelaide

Associate Professor Tim Price, Department of Haematology and Medical Oncology, The Queen Elizabeth Hospital

Associate Professor Joanne Young, Department of Haematology and Medical Oncology, The Queen Elizabeth Hospital

Gynaecology

The Gynaecology Unit provides a comprehensive range of general gynaecological and sub-specialised investigation and management of female reproductive and urological system disorders. These include minimally invasive surgery, colposcopy, pelvic organ prolapse, urinary incontinence, abnormal uterine bleeding, gynaecological malignancy and severe endometriosis. There is a growing interest in the management of benign lower genital tract disease.

All consultants in our unit have an active role in clinical research and RANZCOG trainees undertake their compulsory research project under the supervision of these consultants. In 2014 we have focussed on research of treatment for abnormal uterine bleeding and pelvic organ prolapse. This follows audits undertaken in these areas the previous year and our ongoing contribution to the Urogynaecology Society of Australia peri-operative database.

Five percent of all visits to general practitioners are for menstrual disorders, as are twelve percent of new presentations to gynaecology clinics. After auditing the results of day surgery endometrial ablation as a treatment for menstrual disorders in 2013 we have begun studying the ability to visualise the endometrial cavity following use of this modality.

A woman's lifetime risk of developing pelvic organ prolapse is around thirty percent with one in three requiring surgery. With newer types of vaginal repair, the necessity to remove the uterus at the time of repair has been questioned. Drs P Knight (senior registrar), D Munday and C Barry have secured a grant from the Australian Gynaecological Endoscopy Society for their pilot study 'Management of Uterovaginal Prolapse: Anterior Approach Sacrospinous Hysteropexy compared to Vaginal Hysterectomy and Sacrospinous Fixation.'

We have continued to strengthen the educational role of our department with workshops in minimally invasive surgery and colposcopy, and we were especially pleased to receive an extremely positive report from the RANZCOG re-accreditation team, receiving the maximum four years accreditation of our educational program. Drs Barry and Watson are on the organising committee for the 2015 SA/NT/WA RANZCOG Regional Scientific Meeting.

Research Focus

- Treatment options for female pelvic organ prolapse, pelvic floor dysfunction and menstrual disorders

Staff

Director

R Watson MBBS FRANZCOG FRCOG

Staff specialist with interests in premalignancy, lower genital tract disease and abnormal uterine bleeding.

Chair SA&NT Regional Committee RANZCOG

Senior Consultants

D Munday MB BS FRANZCOG

Staff specialist with interests in minimally invasive surgery, endometriosis, Essure sterilisation and pelvic floor repair.

Member of the Australian Gynaecological Endoscopy Society Research Committee

C Barry MBBS FRCOG FRANZCOG PhD

Staff specialist with interests in urogynaecology and pelvic floor dysfunction.

Member of the Scientific Committee of the Continence Foundation of Australia

A Singla MBBS FRANZCOG

Staff specialist with interests in premalignancy and menopause.

J Miller MBBS FRANZCOG CGO

Staff specialist, certified sub-specialist in Gynaecological Oncology.

R Yoong MBBS FRANZCOG

Staff Specialist with an interest in minimally invasive surgery.

Grant

Australian Gynaecological Endoscopy Society. (Pilot project) Management of Uterovaginal Prolapse: Anterior Approach Sacrospinous Hysteropexy compared to Vaginal Hysterectomy and Sacrospinous Fixation (\$7,000 2014) Knight P, Munday D, Barry C.

Haematology and Medical Oncology

The Haematology and Medical Oncology departments undertake research in major forms of cancer including colorectal cancer and acute myeloid leukaemia.



Research Focus

- Identification of risk factors in groups of under-recognised colorectal cancer patients
- Development of a pre-clinical model of pharmacological blockade of aquaporin channels to prevent tumour growth and metastasis in colon cancer
- Use of genome-wide Single Nucleotide Polymorphism (SNP) arrays to identify a SNP marker profile to predict tumour response to therapy in metastatic colon cancer
- Identification of mutations important in the initiation and progression of Acute Myeloid Leukaemia (AML)

Population Data

> **Colorectal cancer (CRC)** is still the 2nd most commonly diagnosed cancer in Australia (after prostate cancer). 14,860 new cases were identified in 2010.

> CRC is also the 2nd leading cause of cancer death with 3,999 Australians dying from CRC in 2011.

> CRC incidence is higher in males than females (72 compared with 52 new cases per 100,000 people), with both incidence rates stabilising as of 2010.

> Until now the **National Bowel Cancer Screening Program**, which detects CRC earlier than in the general population, has had a 35% participation rate. In 2015 this program will be expanded to offer 2-yearly screening for people aged 50-74 years. This should bring about the decline in incidence rates and mortality in the longer term.

> CRC patients who have not participated in screening programs still present with metastatic (stage IV) disease.

> **Acute Myeloid Leukaemia (AML)** has an incidence of about 3.5 Australians in each 100,000 per year, with most cases occurring in adults (about 1000 new cases per year).

> In patients aged 50-70 years the AML survival at 12 months is less than 30% and at 5 years is less than 10%.

Overview

Blood disorders research group

The focus of the Blood disorders research group at the BHI in 2014 has been on using molecular genetic approaches to identify mutations important in the initiation and progression of Acute Myeloid Leukaemia (AML). We have recently undertaken a whole-exome screen of a large panel of 100 AML diagnostic samples derived mainly from TQEH and RAH sites in Adelaide. From this work we have identified novel mutations in the Fanconi Anaemia DNA repair pathway genes, and determined frequency and overlap with common recurrent AML mutations. Functional work is ongoing to correlate these findings with altered properties of AML cells, and with clinical outcomes.

Colorectal Cancer risk identification

Colorectal cancer (CRC) screening is most effective when targeted towards those most at-risk. Under the theme of colorectal cancer risk identification, we are seeking to investigate markers of risk in two groups of patients:

- 1) patients who develop colorectal cancer and advanced polyps aged under 50 years, and
- (2) patients with advanced serrated neoplasms.

The incidence of colorectal cancer in patients under 50 years is rising steadily in developed countries, and the reasons for this are not clear. The major concern for CRC-affected young adults is that they are being diagnosed with later stage disease. In our comprehensive study we will identify lifestyle factors which increase risk, as well as symptoms and diagnostic biomarkers which will lead to prevention and early detection.

Serrated neoplasms are the pre-cancerous lesion in 20% of all colorectal cancer. Patients with multiple serrated lesions are at increased risk for colorectal cancer. However, only 30% of these patients will develop a colorectal cancer in their lifetime. It is important to identify those individuals where the risk is high, and introduce frequent surveillance colonoscopy. We are studying factors which may predispose to cancer in serrated neoplasia, and in particular, how a common intestinal infection, carried by 1 in 20 people, may interact with the genes in some individuals to produce advanced serrated lesions.

Genetic polymorphisms in EGFR signalling pathway as predictive biomarkers of response to anti-EGFR antibody for metastatic colorectal cancer

A major focus of the Molecular Oncology Research Group is to discover biomarkers to predict resistance to targeted therapies for metastatic colorectal cancer (mCRC). The Epidermal Growth Factor Receptor (EGFR)-targeting monoclonal antibody, cetuximab is now commonly included in treatment regimens for mCRC patients with wild-type RAS and has shown significant improvement in patient survival over standard treatment. However, a significant proportion of patients still derive little or no benefit from this therapy. Ongoing research is required to identify biomarkers that will predict responsiveness to this therapy and therefore improve survival. We have a collaboration with the National Cancer Institute of Canada to analyse single nucleotide polymorphisms (SNP) in a large (> 650 patients) clinical trial cohort. The SNPs associated with resistance or sensitivity to anti-EGFR therapy will be identified from high density SNP arrays. This knowledge will significantly aid in tailoring treatment for each patient to improve efficacy and reduce the toxicity as well as cost of treatment in addition avoid treating those patients who will not benefit from this treatment.

Pharmacological blockade of aquaporin-1 water channel activity by small-molecule inhibitors restricts migration and invasion of colon cancer cells

We are excited by the possibility of a new adjuvant therapy for early stage colorectal cancer (CRC), targeting the aquaporin (AQP) 1 water channel, that would be well tolerated and without the toxic side-effects of chemotherapy. AQP1 is a dual water and cation channel and fluxes in both have been shown to be fundamental in enabling cell migration. In collaboration with Professor Andrea Yool we have shown that several synthetic derivatives of bumetanide, patented by Professor Yool and colleagues for use in cancer therapy, are effective in inhibiting migration, invasion and angiogenesis (tumour blood vessel formation) in colon cancer cell-based assays. These findings will now be tested in a pre-clinical mouse model of human colon cancer, to prevent growth and metastasis of the implanted colon cancer cells.

Staff

Chief Medical Scientist, SAHMRI Colorectal Cancer Node
JP Young PhD

Principal Medical Scientist, Group Head Molecular Oncology Research
JE Hardingham PhD

Clinical Research Staff
T Price MBBS FRACP DHlthSc Head of combined Haematology Oncology Unit/Clinical Research Program
K Pittman MBBS MD FRACP Director of Medical Oncology
A Townsend MBBS FRACP Translational Clinical Lead
P Bardy MBBS FRACP FRCPA Cancer Director CALHN
U Hahn MD FRACP Director Clinical Haematology
C Lee MBBS FRACP FRCPA
JX Gray PhD MD FRACP FRCPA
W Jaksic MBBS FRACP
W Patterson MBBS FRACP
V Broadbridge MBBS FRACP
R Roberts-Thompson MBBS FRACP
IS Tiong MBChB

Grant Funded Scientists
S Bray BSc PhD
M Bruhn BSc PhD
J Wrin BSc
H Dorward BSc (Hons)

Postgraduate Students

PhD candidates
KZY Maung BSc (Hons)
'Roles of FANC genes in Acute Myeloid Leukaemia pathogenesis'
Supervisors: Gray JX, Bray SC, Brown AL, D'Andrea RJ

S Sree Kumar BSc MSc
'Biomarkers of resistance to anti-EGFR in wild type KRAS/BRAF colorectal cancer cell lines'
Supervisors: Hardingham JE, Price TJ

Honours candidates
A Du BHSc
'Short hairpin RNA knockdown to investigate the specificity of aquaporin 1 antagonists in restricting colon cancer cell migration'.
Supervisors: Hardingham JE, Yool A, Price TJ
Awarded 1st class Honours, November 2014.

C Difelice BSc
'Targeting aurora-a to suppress cell proliferation and enhance irinotecan-induced cell death in colorectal cancer cell lines'.
Supervisors: Hardingham JE, Price TJ
Awarded 1st class Honours November 2014

Vacation Student 2014-15
R Vary
'Investigation of the expression of Aquaporin 5 in colorectal cancer'.
Supervisors: Hardingham JE

Grant

Roche Australia. Correlation of extended RAS and PIK3CA gene mutation status with outcomes from the Phase III AGITG MAX involving capecitabine alone or in combination with bevacizumab plus or minus mitomycin C in advanced colorectal cancer. (\$30,000 2014) Price TJ, Hardingham JE, Bruhn M, Townsend AR, Wrin J.

Collaborations

Local

- Associate Professor Andrew Ruszkiewicz, SA Pathology, Adelaide
- Dr Ian Lewis, Department of Haematology, SA Pathology, Adelaide.
- Professor Andrea Yool, Head Physiology, School of Medical Sciences, University of Adelaide
- Dr Oliver Frank, University of Adelaide
- Dr Dan Worthley, The Queen Elizabeth Hospital and University of Adelaide
- Mr Stephen Pederson, University of Adelaide
- Professor Luen Bik To, Clinical Haematology, Royal Adelaide Hospital
- Professor Graeme Young, Flinders University, Adelaide
- Dr Ingrid Flight, Flinders University, Adelaide
- Professor David Roder, University of South Australia
- Professor Richard D'Andrea, Centre for Cancer Biology and School of Pharmacy & Medical Sciences, University of South Australia
- Dr Anna Brown, Centre for Cancer Biology and School of Pharmacy & Medical Sciences, University of South Australia
- Associate Professor Benjamin Thierry, Ian Wark Research Institute, University of South Australia
- Associate Professor Geraint Rogers, SAHMRI, Adelaide
- Dr Stephanie Wong, Royal Adelaide Hospital, Adelaide
- Mr P Hewett, Colorectal Surgical Unit, Department of Surgery, The Royal Adelaide and The Queen Elizabeth Hospitals, Adelaide
- Dr Ilmars Lidums, The Queen Elizabeth Hospital, Adelaide
- Dr Dan Worthley, The Queen Elizabeth Hospital and University of Adelaide

National

- Dr Aung Ko Win, University of Melbourne, Victoria
- Dr Barbara-Ann Adelstein, Prince of Wales Clinical School, University of NSW
- Professor Thomas Gonda, Diamantina Institute, for Cancer, Immunology and Metabolic Medicine, University of Queensland, Brisbane
- Dr Andrew Deans, St Vincent's Institute, Melbourne, Victoria
- Associate Professor Christophe Rosty, Envoi Pathologists, Brisbane, Queensland
- Dr Paul Leo, University of Queensland, Brisbane
- Dr Brooke Gardiner, University of Queensland, Brisbane
- Dr Mhairi Marshall, University of Queensland, Brisbane
- Dr Evgeny Glazov, University of Queensland, Brisbane
- Dr Paula Marlton, Princess Alexandra Hospital, Brisbane
- Dr Devinder Gill, Alexandra Hospital, Brisbane, Queensland
- Associate Professor Niall Tebbutt, Austin Health, Melbourne, Victoria
- Dr Chee K Lee, Research Fellow, NHMRC Clinical Trials Centre, Sydney, NSW
- Dr Lavinia Gordon, Bioinformatics, AGRF, Melbourne, Victoria

International

- Associate Professor Susan Parry, NZ Familial GI Cancer Service, Auckland City Hospital, NZ
- Professor Chris O'Callaghan, Geoff Liu (statistician) NCIC Clinical Trials Group, Ontario, Canada

Acknowledgements

We would like to acknowledge patients and their families who assist in this work by their willingness to agree to enter clinical trials and importantly by allowing access to their tissues in order to help with translational research.

Intensive Care Unit



Overview

Research activities conducted within the department are a combination of:

- Investigator-initiated studies, including those by advanced trainees as part of the course requirements of the College of Intensive Care Medicine, and intensive care nurses
- Investigator-initiated studies conducted under the auspices of the Australian and New Zealand Intensive Care Society Clinical Trials Group
- Industry-sponsored clinical trials

The areas of research include:

- Sepsis studies
- Observational surveys
- Patient safety
- Nutrition studies
- Outcome studies
- Statistical method reviews
- Pharmacokinetic studies

Population Data

> There are 15,700 new cases of **septic shock** in Australia each year (0.77 per 1000 people). 69% of these patients require supportive treatment in intensive care. The estimated cost per episode is AUD\$42,300.

> The death rate for septic shock is approximately 3.5 times higher than the annual national road toll, and is also higher than the death rate for breast cancer and colorectal cancer.

Research Focus

- Improving patient safety and outcomes
- Answering pragmatic, relevant clinical questions that are of importance to the clinicians who provide patient care
- Advancements in the delivery of more efficient and effective treatments in the ICU that will not only benefit patients but also decrease costs, preserve resources and increase access to scarce critical care beds
- Statistical analysis of short and long-term outcomes relating to Intensive Care

Highlights of 2014

The completion of the Australasian Resuscitation In Sepsis Evaluation (ARISE) randomised controlled trial was the main highlight of 2014. This phase III, multi-centre, National Health and Medical Research Council funded, ANZICS Clinical Trials Group-endorsed study evaluated protocolised resuscitation, termed early goal-directed therapy (EGDT), compared to usual care in 1600 patients presenting to the emergency department with early septic shock. Study recruitment commenced in October 2008 and was completed in April 2014. Fifty one tertiary referral, metropolitan and rural hospitals in Australia, New Zealand, Finland, Ireland and Hong Kong participated in the study.

Associate Professor Sandra Peake is the Chief Investigator and Chair of the ARISE Management Committee and Patricia Williams is the Research Coordinator representative on the ARISE Management Committee. The Queen Elizabeth Hospital was the study's third highest recruiting hospital and the highest recruiting hospital per Emergency Department presentations. The results of the trial showed that EGDT, as compared with usual resuscitation practice, did not decrease 90-day mortality, the primary study outcome. The study results were presented by Associate Professor Peake in the Breaking News session at the European Society of Intensive Care Medicine's Annual Forum on the 1st October 2014 and was simultaneously published on-line by the *New England Journal of Medicine*.

Another highlight of 2014 was the success of a grant application to the NHMRC to conduct a 4,000-patient, multi-centre, double-blind, randomised, controlled, parallel-group, phase III clinical trial to determine if the enteral delivery of the full-recommended calorie (energy) requirement to critically ill patients improves 90 day survival when compared to standard practice. The funding awarded was \$3,534,236 over 5 years which was the 4th highest amount awarded in the recent project grant round.

The RAH and TQEH ICU research teams are the lead investigators for this new study. The coordinating centre for the study will be The Australian and New Zealand Intensive Care Research Centre (ANZIC RC), a bi-national intensive care clinical research methods centre, based at Monash University in Melbourne. Approximately 30 intensive care units throughout Australia and New Zealand will participate in the study.

This will be the first blinded study to evaluate the effect of optimal enteral calorie delivery in the critically ill. It will also be the largest enteral nutrition trial ever conducted in critically ill patients.

SEPSIS STUDIES

An economic evaluation of resuscitation in sepsis

An economic evaluation of the multi-centre ARISE randomised controlled trial of early goal-directed therapy in patients presenting to the Emergency Department with severe sepsis will be conducted in a cohort of patients randomised to the ARISE RCT. The study aims to evaluate 12 month survival and functional outcomes of survivors and also the cost per quality life year gained. The results of this study are expected to be published in 2015.

Australasian Resuscitation In Sepsis Evaluation (ARISE) – An Individual patient Data Meta-Analysis

A prospective, pre-planned, individual patient data meta-analysis (IPDMA) of three independent, but collaborative, multi-centre, randomised controlled trials evaluating early goal-directed therapy in patients presenting to the emergency department with early septic shock (ARISE, ProCESS [conducted in the United States] and ProMISE [conducted in the United Kingdom]) will be undertaken immediately following the completion and publication of the ProMISE trial. The ARISE and ProCESS studies have been published and the ProMISE study has completed recruitment and is in the analysis phase, with results expected to be presented in March 2015. The IPDMA represents a unique opportunity to examine the broad generalisability of the trials' findings, investigate the cause of any divergent results and conduct definitive sub-group analyses. The IPDMA is endorsed by the Australian and New Zealand Intensive Care Society Clinical Trials Group (ANZICS CTG) and the Australasian College of Emergency Medicine (ACEM) and will be undertaken in collaboration with the University of Pittsburgh Department of Critical Care Medicine (United States) and the Intensive Care and the National Audit Centre (United Kingdom). The sum of the results of all three individual trials will represent all the Phase III evidence in the world on the role of EGDT in patients presenting to the Emergency Department with severe sepsis or septic shock. Planning for this meta-analysis is underway.

Bacteraemic Load in Septic Shock (BLISS)

An NHMRC funded inception cohort study nested within the ARISE RCT aims to quantify bacterial and immune response markers in the bloodstream of patients with septic shock, the most severe form of sepsis, to determine the relationship between bacterial load, immune response and clinical outcomes. This study collected blood samples for analysis from patients enrolled in the ARISE study. These blood samples will allow us to determine whether the elevated levels of bacteria or the body inflammatory reaction to it are associated with increased risk of death. This study is being conducted under the auspices of the ANZICS-CTG. Associate Professor Sandra Peake is on the management committee for this study. Analysis is currently underway.

Tissue penetration of vancomycin in critically ill patients with sepsis

This study involves investigating the tissue penetration of vancomycin in critically ill patients with sepsis using microdialysis. We aim to use a validated technique called *in vivo* microdialysis to compare subcutaneous tissue concentrations of vancomycin with plasma concentrations and to determine the appropriateness of present dosing approaches for optimising use of this important antibiotic in critically ill patients. This study is a collaboration between The Queen Elizabeth Hospital Intensive Care Unit, the Basil Hetzel Institute Therapeutics Research Centre and the University of South Australia School of Pharmacy and The University of Queensland. Study recruitment completed in 2014. Data analysis and preparation of the manuscript is in progress.

Adjunctive corticosteroid treatment in critically ill patients with septic shock (ADRENAL)

This study is an NHMRC funded randomised blinded placebo controlled trial of hydrocortisone in 3,800 critically ill patients with septic shock. The purpose is to find out whether adult patients admitted to the Intensive Care Unit with septic shock who are given hydrocortisone compared to placebo, will have an improved rate of survival 90 days later. This study is being performed under the auspices of the ANZICS-CTG and the George Institute of Health for Global Health Recruitment. This study commenced early in 2013 and continued in 2014.

OBSERVATIONAL STUDIES

Prolonged QT interval in the ICU-incidence, risk factors and outcome, a prospective multi-centre observational study

The primary aim of this study is to determine the incidence of prolonged QTc interval and QTc dispersion in critically ill patients admitted to the ICU. Secondary aims are to identify associated risk factors, compare cardiac and non-cardiac complications, mortality, length of ICU and hospital stay in patients with prolonged QTc interval and QTc dispersion. The study was conducted in collaboration with the Royal Adelaide Hospital Intensive Care Department. Data analysis is complete and preparation is underway to submit the results of this study for publication.

Point Prevalence Program

The Point Prevalence Program, performed under the auspices of the ANZICS CTG, aims to provide the structure for individual researchers to conduct basic observational Point Prevalence Studies to inform future research, while minimising the workload on participating ICUs by combining studies using a common and standardised Case Report Form, on predictable dates. The Point Prevalence Program has been supported by two general grants from the Intensive Care Foundation, a further specific grant from the Intensive Care Foundation, a grant from the ANZICS Clinical Trials Group, and specific grants from individual hospital research foundations. The program has been financially underwritten and has received significant 'in kind' support from the George Institute for Global Health. The 2014 audit day included; 1) a point prevalence study of Treatment Intensity in Intensive Care: What interventions do they receive during ICU stay and how many patients have an advanced care directive in-place. The second component of Treatment Intensity is an independent voluntary survey of bedside clinicians and nurses; 2) Maintenance Fluids: How much and what do we give; 3) Electrolyte replacement triggers and the volume of fluid administered; 4) Stress Ulcer Prophylaxis (SUP): the incidence and practice of SUP.

A Comparison of Point of Care Capillary and Arterial Lactate Measurements in the critically ill patient

The aim of this study is to compare the measurement of lactate in paired capillary and arterial blood samples and to ascertain whether there is significant agreement between the samples, using arterial blood sampling as the 'gold standard'. The secondary aim of this study will be to compare the time and cost-effectiveness of measuring capillary blood lactate when compared to arterial blood lactate. Recruitment is ongoing.

Antimicrobial medications and the factors influencing time to administration in an adult Intensive Care Unit

This is an observational study on 'Factors that influence the timing of antimicrobial therapy administration relative to prescription within the ICU'. The results of this study are expected in 2015.

Stress ulcer prophylaxis (SUP) in the Intensive Care Unit.

The aim of this multicentre, 7-day inception cohort study was to describe the prevalence and severity of GI bleeding in 1,300 critically ill patients in the ICU, and to describe current practice of SUP. This study was part of an international initiative investigating SUP. This 7 day cohort study is to be hypothesis generating and is one part of a research program that is comprised of 4 studies.

The Fluid Translation of Research into Practice Study (Fluid-TRIPS): An International Cross - Sectional Survey of Fluid Resuscitation Practice

The aim of this project is to describe international trends in the prescription of intravenous fluid resuscitation and to determine factors influencing choice. This single day survey was conducted in 280 ICUs globally and aimed to recruit 2,100 patients.

Practice Pattern Variation in Discontinuing Mechanical Ventilation in Critically Ill Adults: An International Prospective Observational Study

A multi-centre, multi-national observational study of how clinicians discontinue invasive mechanical ventilation in critically ill adults requiring at least 24 hours of invasive ventilation. This study was conducted in approximately 150 ICUs (25 adult ICUs in each of 6 regions: Canada, USA, ANZ, UK, Europe and India).

NUTRITION STUDIES

The Augmented versus Routine approach to Giving Energy Trial: A randomised controlled trial (TARGET)

This is a pivotal, 4000-patient, multi-centre, double-blinded, randomised, controlled, parallel-group, phase III clinical trial to determine if the enteral delivery of the full-recommended calorie (energy) requirement to critically ill patients improves 90 day survival benefit when compared to standard practice. Approximately 30 Intensive Care Units throughout Australia and New Zealand will participate in the study. This study received funding from the NHMRC following the completion of a point prevalence study of energy prescription practices conducted in 2010 and a randomised, double-blind, feasibility study conducted in 2013 examining the use of a concentrated enteral nutrition solution to increase calorie delivery to critically ill patients. These data supported the conduct of a large, multi-centre, randomised, double-blind trial to determine whether the delivery of more calories by using a concentrated enteral nutrition solution can result in improved survival and functional outcomes for critically ill patients. Planning is underway to commence this study in 2015.

OUTCOME STUDIES

STandaRd Issue TrANsfusion versuS Fresher red blood cell Use in intenSive care (TRANSFUSE) – a randomised controlled trial

A multi-centre, randomised, double blind, controlled trial, testing the effect of the freshest available Red Blood Cells (RBC) compared to standard practice, on mortality in critically ill patients who require RBC transfusion. This study will determine the effect of transfusing the freshest blood in the inventory compared to transfusing the oldest blood in inventory (current standard of care). This study will provide critically important information that will help blood banks implement the findings. The results of this study will impact transfusion policy worldwide and ultimately could save many thousands of lives each year. This study is being performed under the auspices of the ANZICS CTG. Recruitment for this study commenced early in 2013 and continued in 2014.

Zinc levels in patients with chronic liver disease

This study aims to establish if low zinc levels are present in patients with chronic liver failure and if low levels equate to poor outcome and increased incidence of hepatic encephalopathy. Recruitment is ongoing.

Matched controls (zinc levels) for patients with chronic liver disease

This study is the second phase of the previously mentioned zinc study and aims to investigate zinc levels of patients without chronic liver disease as a comparison. Recruitment is ongoing.

STATISTICAL METHOD REVIEWS

A number of studies are ongoing defining the role of advanced statistical analysis in outcomes research and meta-analysis.

PHARMACOKINETIC STUDIES

SaMpling Antibiotics in Renal Replacement Therapy (SMARRT)

A large NHMRC funded, multi-centre trial in critically ill patients who are prescribed renal replacement therapy (RRT) and piperacillin-tazobactam, meropenem, vancomycin, imipenem, and linezolid. The aim of the SMARRT study is to develop optimised antibiotic dosing guidelines for ICU patients with life-threatening infections that account for patient characteristics and the type of RRT they are prescribed. Associate Professor Sandra Peake is a Chief Investigator. The SMARRT study is being performed under the auspices of the ANZICS CTG and recruitment is expected to commence in 2015.

Staff

Studies on the critically ill represent co-operative undertakings between all the nursing and medical staff in the Intensive Care Unit. Many thanks to our research coordinators Patricia Williams, JoAnne McIntyre and Jennie Phillips-Hughes and research project officer, Catherine Kurenda.

Director

MS O’Fathartaigh MB Bch BAO FFARCS (Ire.) FFICANZCA

Consultant Specialists

- SL Peake BM BS BSc(Hons) FJFICM PhD
- JL Moran MB BS FANZCA FRACP FJFICM MD
- S Moodie MB CHB FJFICM
- K Lee MBBS MBus FACEM FJICM
- S Jacobs MBChB FRCA FANZCA
- D Clayton BSc MBBS FRCA FANZCA FCICM

Research Coordinators

- P Williams RN BN IntC
- J McIntyre RN IntC Cert Grad Dip CritCareN

Research Project Officer

C Kurenda

Senior Registrar

J Raj MBBS MS

Nursing staff

- B Grealy RN RM IntCCert BN MN(Res)
- S Flynn RN IntCCert
- L Esca RN IntCCert
- R Fraser RN Int CCert
- R Kelly RN IntCCert Grad Dip CritCareN
- Y Pearce RN IntC Cert Grad Dip CritCareN

Postgraduate Students

Pharmacist/PhD candidates

MG Sinnollarredy BPharm
‘Dose optimisation of antimicrobial agent: pharmacokinetic and pharmacodynamic approach’
Supervisors: Roberts MS, Williams D

FB Sime BPharm
‘Therapeutic drug monitoring in high risk patients: pharmacokinetic and pharmacodynamics considerations for dose optimisation’
Supervisors: Roberts MS, Roberts J

Grants

Grant funding commencing 2015

NHMRC Project Grant Application: APP1078026. (2015) The Augmented versus Routine approach to Giving Energy Trial (TARGET). \$3,534,236 over 5 years. Chapman M, Peake SL, Bellomo R, Horowitz M, Davies A, Dean A, O’Connor S.

Intensive Care Foundation: (2014-15) Pharmacokinetic Australasian Collaborative. (\$39,156) Lipman J, Roberts J, Peake SL, Joynt GM, Udy AA, Nicholls MB.

Collaborations

Local

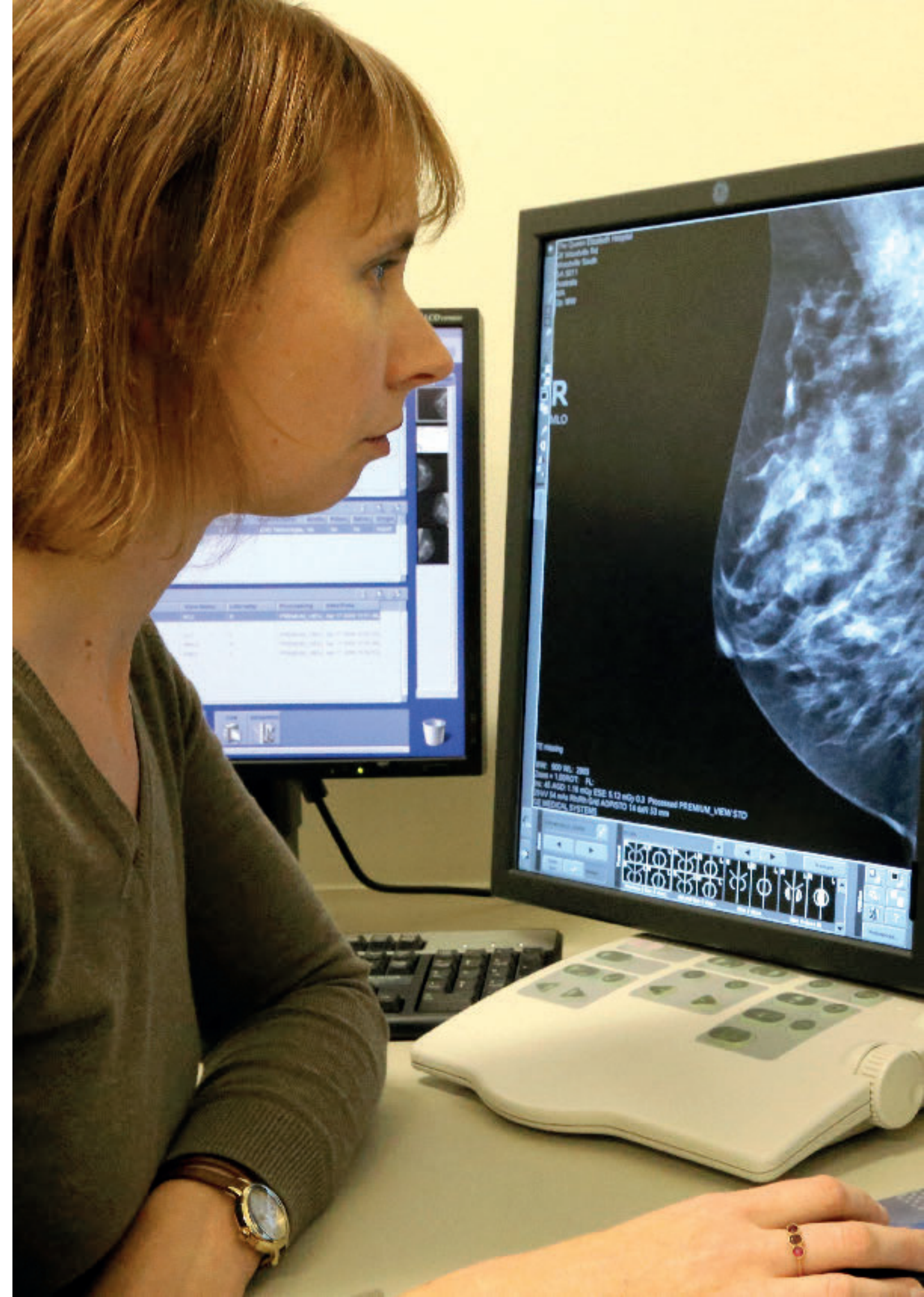
- ANZICS - Clinical Trials Group
- GlaxoSmithKline Australia Pty Ltd
- INC Research Australia
- Dr T Otto and nursing and medical staff, The Queen Elizabeth Hospital Emergency Department
- Associate Professor M Chapman, Associate Professor A Deane, S O’Connor, Intensive Care Unit, The Royal Adelaide Hospital
- Professor M Roberts, University of South Australia
- Professor M Horowitz, Dr K Lange, The University of Adelaide

National

- Professor J Roberts, Professor J Lipman, The University of Queensland
- Ms B Howe, Mrs L Little, E Ridley, Dr A Davies, Professor R Bellomo, Associate Professor J Presneill, Department of Epidemiology and Preventive Medicine, Monash University
- The George Institute for Global Health, Sydney

International

Dr P Young, Department of Critical Care, Wellington Regional Hospital, New Zealand



A Medical Mystery

Judy's Story



Judy Myers considered herself a very fit person. Through previously owning her own gym, coaching athletes at the Australian Institute of Sport in Canberra and leading an active lifestyle she is someone who understands what fitness is and the benefits it brings. So when the 54-year-old from Henley Beach started suffering from regular chest pain episodes, she was shocked. "Four years ago I was walking up the hill from the car park to my office one morning when I suddenly felt severe chest pain," recalled Judy. "From that day on whenever I exerted myself I would get the chest pains – in my jaw, down my arm, they were excruciating." Judy underwent a myriad of tests including echocardiograms and angiograms, which didn't find any blockages that could be causing her chest pain. The condition Judy was experiencing is known as Cardiac Syndrome X. For people like Judy, surgical intervention is just not an option, because the problem cannot be visualised. Treatment options are limited.

"I was so frustrated, I couldn't even walk up a flight of stairs or run around the backyard with my dog – nothing without really major chest pains. Going from being very active to being extremely debilitated in everything I did was really hard," said Judy.

In 2011, Judy was referred to see Professor John Beltrame, Professor of Medicine at The Queen Elizabeth Hospital and a leading cardiologist. At Professor Beltrame's suggestion, Judy began taking a drug which works by slowing down the heart rate. For Judy, it helped. "I could do exercise to a certain level without getting the chest pain. It was much better, I was getting my life back, to a certain extent."

But in mid-2014, this medicine had to be ceased due to unexpected side effects reported in an overseas study. "I had fallen down a flight of stairs in January and broken quite a few bones, so I wasn't very active at the time anyway." After recuperating for about three months Judy soon decided she wanted to get back to the gym. "I noticed no matter what I did I wasn't getting any chest pain. I started getting my heart rate up to 172bpm without any pain. I couldn't believe it."

Judy's experience has been an inspiration for Professor John Beltrame and Dr Kanchani Rajopadhyaya, who commenced a trial at The Queen Elizabeth Hospital in early 2014 which is investigating exercise as a therapy for people suffering with Non-obstructive Coronary Artery Disease (NCAD). Cardiac Syndrome X falls under this category of conditions. "We are undertaking this trial to find out if regular exercise actually reduces the number of chest pain episodes a person experiences and ultimately, improve quality of life for these people," explained Professor Beltrame.

Since recommencing regular exercise, Judy's fitness and attitude has made a marked improvement. "Because I have been extremely fit in the past, I know how it feels. I get a lot of energy from exercise so I feel happier. Life looks a lot brighter."

"But I am fearful of it coming back so I don't push myself too hard. I'll start to do a run on the beach with my dog and I'll be wondering... will today be the day it comes back?"

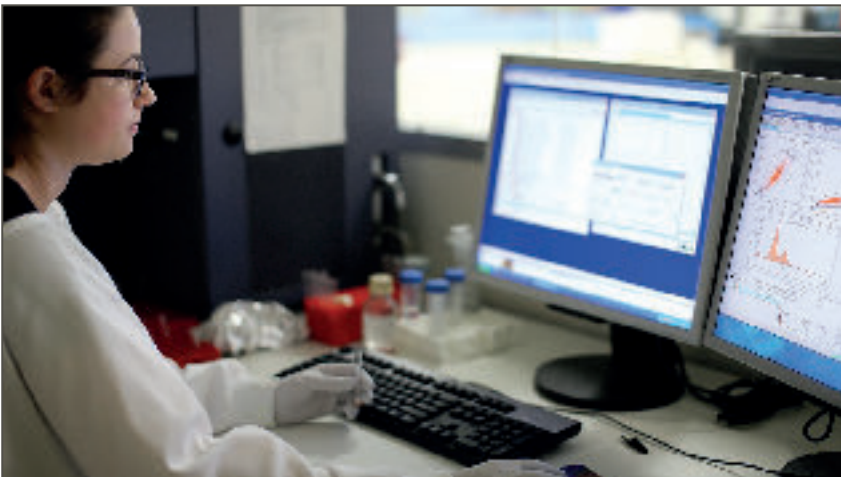
"For that reason I think medical research is really important. There's nothing worse than suffering from something that can't be explained, it's frustrating. Research is really important to get an understanding of these sorts of diseases."

"Right now there are a lot of questions but not a lot of answers! It would just be really nice to know why, and I'll help the researchers in any way I can so hopefully we can find an answer for me and others like me."

"Four years ago I was walking up the hill from the car park to my office.... when I suddenly felt severe chest pain"

Medicine

The research undertaken by the University of Adelaide Discipline of Medicine, TQEH integrates speciality medicine fields with the aim to provide more comprehensive medical care to patients. This is important in an aging population with multiple chronic problems that require a multi-disciplinary approach. The scope of the Discipline's research ensures that all aspects of health care are comprehensively considered. This extends from the discovery of new treatments in the basic research laboratory, to determining the best nutrition for our patients, and utilising our expertise in teaching to ensure that patients are appropriately educated about their illnesses as well as developing the optimal teaching methods for our future clinicians and researchers.



Overview

The Discipline of Medicine has major research and teaching responsibilities led by an experienced team of clinical academic physicians supported by an enthusiastic team of research scientists, teaching and administrative staff. The research conducted within the Discipline spans the full spectrum of research fields including basic, clinical, population and health service delivery. Areas of particular expertise include cardiology (see Cardiology Report), geriatrics (see Aged Care and Extended Care Services Report), neurology (see Neurology Report), and health literacy. The Discipline's research activities involves collaboration with other researchers within TQEH, other South Australian hospitals, as well as research institutions within Australia and internationally. The diversity in research activities is widespread but close collaboration has forged a strong department with significant outputs.

Population Data

- > **Cardiovascular disease** (includes heart attacks, stroke and peripheral artery disease) is the leading cause of death in Australia, accounting for 35% of all deaths. Women account for 55% of patients affected by cardiovascular disease
- > Apart from non-melanoma skin cancers, **breast and prostate cancer** are the most common cancer types diagnosed in women and men respectively.
- > **Obstructive Sleep Apnoea (OSA)** remains largely undiagnosed but has been increasing in line with the increase in obesity.

Research Focus

Multi-Disciplinary Research

- Epidemiology
- Vascular disease
- Stem cells in the treatment of stroke
- Zinc in the pathophysiology of disease
- Quality health care improvements
- Sleep
- Cancer biology
- Nutritional problems in the elderly
- Health literacy population research
- Undergraduate and postgraduate assessment

In addition to conducting research, the Discipline has a major teaching responsibility, both in core medical education and research training. The Discipline is responsible for clinical teaching of senior medical students within the medical school program at TQEH, as well as being involved in the pre-clinical program. Undergraduate research training undertaken by Discipline staff includes the supervision of science/medical student elective research projects and vacation electives. Postgraduate research training includes the supervision of Honours, Masters and PhD students at TQEH with projects ranging from basic laboratory science to clinical and epidemiologic studies. The Discipline is also involved in the clinical training of interns, basic and advanced physician trainees.

Professor John Beltrame is the Head of the Discipline of Medicine at The Queen Elizabeth Hospital. He is an academic cardiologist with active research, clinical and teaching roles. His international reputation and expertise focuses on coronary vascular disorders although in recent years this has broadened to include peripheral artery disease, molecular mechanisms in vascular disorders gender disparities in cardiovascular disorders, depression and cardiovascular imaging and health service delivery, with projects such as the CADOSA (Coronary Angiogram Database of South Australia) registry.

Professor Bob Adams is a respiratory physician and epidemiologist, who is Director of the Health Observatory. He is a chief investigator in the North West Adelaide Health Cohort Study (NWAHS) from which he has published on many chronic disease issues including respiratory diseases, obesity, the metabolic syndrome and nutrition. Professor Adams was also involved in initiating the Mental Health Observatory (MHO), which involves the Health Observatory, Country Health SA, Flinders University and the University of South Australia.

Professor John Horowitz is an academic cardiologist with a distinguished research career, being recognised both nationally and internationally. He is the Director of the Cardiology Unit and the Clinical Pharmacology Unit. He has an extensive publication record with important studies in the pathophysiology and therapeutics of cardiovascular disorders including coronary artery disease, heart failure, and aortic stenosis.

Professor Simon Koblar is a neurologist and the Director of the Stroke Research Program and leads an innovative research team investigating the use of dental pulp stem cells as a potential therapy for stroke patients. Professor Koblar undertook a three month sabbatical in 2014 at leading world research institutes in order to advance his collaborations in stroke stem cell therapies.

Professor Renuka Visvanathan is an academic geriatrician, Director of Aged and Extended Care Services at TQEH, and a chief investigator in the Health Observatory. She is also the academic lead for the Geriatrics Teaching and Research with Aged care Centre (G-TRAC) located at the Resthaven Paradise Campus. She is also the Deputy Chair of the Older People's Network.

Associate Professor Chris Zeitz is an academic interventional cardiologist who is the Clinical Director of Medicine in the Central Adelaide Local Health Network. He is also the founding Director of the Cardiology Assistance to Remote Districts in Australia – South Australia division (CARDIA-SA) clinical group and a member of the University of Adelaide Spencer Gulf Rural Health School. CARDIA-SA is a University of Adelaide initiative that provides consultative cardiology services to rural regions of South Australia.

Dr Sharmalar Rajendran is an interventional cardiologist and Senior Lecturer in Medicine. Her research interests focus on the cardiovascular consequences of polycystic ovary disease as well as invasive coronary studies. She is also actively involved in undergraduate teaching and supervising postgraduate research students.

Dr Peter Zalewski is a senior lecturer and the postgraduate coordinator for the Discipline of Medicine. He has an international reputation in zinc biology research, reflected by his appointment as a zinc team member on the International Collaborative Micronutrients Genome Project. The current focus of his research is on the roles of zinc and zinc transporter proteins in pancreatic islet function (with Professor Toby Coates), alveolar macrophage function (with Associate Professors Sandy Hodge and Hubertus Jersmann), and in vascular function and disease (with Professor John Beltrame). He also has collaborations with both the Rheumatology and ENT Units at TQEH.

Dr Sarah Appleton was a foundation research fellow in the Health Observatory. Her research interests focus on chronic disease issues such as diabetes, the metabolic syndrome, undiagnosed disease, health literacy and obstructive sleep apnoea.

Dr Grant Buchanan is head of the Cancer Biology Group and continues his research on the tumour microenvironment in early prostate cancer. The Cancer Biology Group's focus is on the role of the sex hormones oestrogen, testosterone and progesterone in the early stages of breast and prostate cancer. The group is keenly interested in defining the molecular mechanisms of action of these important hormones, and in translating these findings to inform the way that breast and prostate cancer patients are diagnosed and treated. In particular, in the prostate they are interested in the role of androgens in the area surrounding prostate cancer, where it plays a converse role to the action of androgens in the prostate cancer cells. In breast cancer, current interest is focused on the combinatorial role of oestrogen and progesterone, a physiological state that occurs in women during each menstrual cycle.

Dr Tiffany Gill is a physiotherapist and accomplished epidemiologist who holds an NHMRC Early Career Fellowship. Her research interests in the epidemiology of musculoskeletal disorders, chronic disease risk factors and other aspects of public health have made a major contribution to the Health Observatory.

Dr Cynthia Piantadosi, research fellow, worked with Professors Ian Chapman and Renuka Visvanathan on a national multi-centre study examining the effect of testosterone and a nutritional supplement in under-nourished older people.

Dr Rosanna Tavella is a Senior Lecturer in Medicine and the Cardiovascular Data Project Manager for the Central Adelaide Local Health Network (CALHN). She has a key role in quality assurance and health service delivery activities in both CALHN and the Data and Information Working Group of the Statewide Cardiology Clinical Network. In addition, she is the data custodian for the Coronary Angiogram Database of South Australia (CADOSA) registry. Her knowledge, experience and expertise in clinical datasets has rapidly brought her to the attention of clinical epidemiology groups around the country and internationally.

Staff

Michell Professor of Medicine

J Beltrame BSc BMBS PhD FRACP FESC, FACC, FAHA, FCSANZ

Professor in Cardiology

J Horowitz MBBS BMedSc(Hons) PhD FRACP

Professors in Medicine

RJ Adams MBBS MD FRACP

S Koblar MBBS PhD FRACP

R Visvanathan MBBS PhD FRACP

Emeritus Professor

RE Ruffin BSc (Hons) MBBS (Hons) MD FRACP

Associate Professors

CJ Zeitz MBBS PhD FRACP

Senior Lecturers

G Buchanan BSc (Hons) PhD

S Rajendran MBBS FRACP PhD

PD Zalewski BSc (Hons) PhD

Research Fellows

SL Appleton BSc (Hons) PhD

T Gill BAppSc(Physio), MAppSc(Physio), CertHlthEc, PGradDip(Hlth Sc), MBA, PGradDip(Biostats), PhD

C Piantadosi BAppSc (Hon) PhD

E Need BSc (Hons) PhD

D Leach PhD

A Trotta BHSc (Hons) BSc PhD

Peter Doherty Research Fellow

CJ Lang BSc (Hons) PhD

Clinical Data Project Manager

R Tavella B Health Sc (Hons), PhD

Hospital Scientists

AG Milton BSc (Hons)

R Jakobczak BSc

G Yong BSc BHSc (Hons)

Research Officers

K Rajopadhyaya BSc (Hons)

R Battersby

E Rees BSc

J Chan BSc

B Hoang BSc

S Tan BSc PhD

L Simeone BSc

Research Administrators

L Gallina

G Jones

Discipline Secretaries

A Brown

L Gallina

CardiaSA Secretary

K Zahra

Clinical Education

R Limb MBBS

M Denys

Postgraduate Students

Higher degrees awarded

L Giorgio, PhD conferred

E Swinstead, PhD conferred

E Roscioli, PhD conferred

S Yu, PhD conferred. Deans Commendation

Masters

Ho Yin Lau (Aden) Master of Biotech School of Med Sciences Qualified 2014

PhD candidates

M Bosco

‘Investigations into the role of zinc and zinc transporters in the pathogenesis of type 2 diabetes in db/db mice’

Supervisors: Coates T, Zalewski P, Drogemuller C

PhD candidates (cont.)

D DiFiore

'Health Outcomes in Patients with Vasospastic Angina'

Supervisors: Beltrame J, Zeitz C

A Jaghoori

'Heterogeneity in Vasomotor Responses'

Supervisor: Beltrame J

V Lamin

'Mechanical Studies in Macro and Micro-Vascular Dysfunction'

Supervisors: Beltrame J, Wilson D

C McNally

'Oral health and outcomes of patients with fractured neck of femur'

Supervisors: Adams R, Visvanathan R, Liberali S

S Pasupathy

'Myocardial Infarction with Non-obstructive Coronary Arteries'

Supervisors: Beltrame J, Worthley S

S Sidharta

'Relationship of Human Coronary Endothelial Function and Plaque Progression/Regression.'

Supervisors: Worthley S, Beltrame J, Nicholl S, Worthley M

A Sheikh

'Pathophysiological Studies in Coronary Microvascular Disorder'

Supervisor: Beltrame J

G Tucker

'Statistical and methodological aspects of assessment of health-related quality of life'

Supervisors: Adams R, Wilson D, Wittert G

R Dhillon

'The longitudinal impact of psychiatric morbidity on physical health and service use'

Supervisors: Baune B, Adams R, Bidargaddi N

Honours candidates

J Pollock

'Diet, sleep and depression interactions'

Supervisors: Adams R, Appleton S

Vacation Students 2014-15

A Burdakova

Summer Scholarship Student: Comparing patient profile, care and outcomes across four major hospitals in South Australia

J Kuppa

Summer Scholarship Student: Is Chest Pain Radiating to the Jaw Predictive of Coronary Artery Disease?

A Gupta

Summer Scholarship Student: Complication Rate from Coronary Angiography in South Australia

Grants

Cancer Australia and Prostate Cancer Foundation of Australia. (Project grant #1032970) Androgen Receptor in the Prostate Cancer Microenvironment (\$188,333 2014) 2013-2015, Buchanan G, Taylor R, Need E.

Medicare Local. Mental Health Observatory. (\$100,000 2014-2015) Adams, R.

NHMRC. (NHMRC) Early Career Fellowship - Australian Public Health (\$72,508 2014) 2011-2014, Gill T.

NHRMC. (Partnership grant #1062331) The ACCESS Project – Assessment of Coronary artery disease using Ct Effectively for Stable Symptoms. (\$312,833 2014) 2013-17, Beltrame JF, Zeitz CJ, Tavella R, Worthley MI.

SA Heart Foundation. Chronic refractory angina – defining its characteristics and exploring endothelin blockade as a new potential therapy. (\$331,913 2014) 2011 – 2014, Beltrame J, Worthley S, Chew D, Ganz P, Zeitz C, Arstall M.

SA Heart Foundation.(Tom Simpson Trust award) (\$12,500 2014) Tavella R.

The Hospital Research Foundation. (Cancer Innovation Award) Unlocking the prognostic potential of the prostate cancer microenvironment. (\$47,000 2013-2014) Buchanan G, Need E, Trotta A.

The Hospital Research Foundation. (Project grant) Exercise Therapy for the Management of the Coronary Slow Flow Phenomenon. (\$150,000 2014) 2014-2015, Beltrame JF, Elliott A, Rajopadhyaya K, Fitridge R.

The Hospital Research Foundation. (Early Career Research Fellowship) Molecular dynamics of steroid receptor crosstalk (\$57,400 2014) 2012-2016, Need E.

Grant funding commencing 2015

Arthritis Australia. Developing a patient reported outcome measure in polymyalgia rheumatic. (\$10,684 2015) Hoon E, Hill C, Gill T.

SA Heart Foundation. CADOSA Registry Continuation (\$933,502 2015-2016) Beltrame J.

New Hope for Stroke Patients

Robert's Story



Robert Lampre's colleagues thought he was joking around when he suddenly lost speech during a normal day at work as a butcher in Croydon in October 2014. "I suddenly didn't feel right, so I went outside for a smoke. I tried to roll my cigarette and I couldn't do it, it just rolled straight out of my mouth," recalled Robert from Ingle Farm.

"I went back inside and realised I couldn't speak at all. I grabbed a piece of paper and wrote 'stroke' on it and handed it to one of the girls I was working with." Although Robert is a typical joker, his workmates soon realised he was serious and dialled '000' immediately. Arriving in minutes, the ambulance drove Robert straight to The Queen Elizabeth Hospital's dedicated Acute Stroke Unit.

Stroke is essentially a 'brain attack' – similar to a 'heart attack', but located in the brain. Until only a few years ago, people who suffered a stroke were not prioritised for urgent treatment if they were brought to a hospital emergency service because medicine had essentially no special treatment for stroke.

Today, however, because of research work done by Associate Professor Jim Jannes, Professor Simon Koblar and their teams at The Queen Elizabeth Hospital, an emergency treatment designed specifically for stroke patients has been developed.

Stroke is now a treatable illness, just like a heart attack, and 2008 was the first year that a pilot Acute Stroke Unit at The Queen Elizabeth Hospital was functional. Around 350 people who have had a stroke are admitted to TQEH each year and the majority are cared for on the Stroke Unit.

Once Robert arrived at TQEH, he suffered a second stroke. "The left hand side of my face went limp," said Robert. After a whirlwind of tests, including MRI and CT scans, Robert was deemed a good candidate for the clot busting thrombolysis drug. To be effective, this drug must be administered within four hours of a person suffering a stroke. Robert was within the window.

"It did him the world of good, it definitely stopped him from getting any worse," explained Robert's wife Denise, who had witnessed the whole treatment process, arriving just moments after the ambulance delivered Robert to the hospital.

"The doctors and nurses were so efficient as soon as we arrived. It was frightening for us, there were people everywhere, but it seemed everyone knew the job they had to do," said Denise. Robert stayed in hospital for a week after the stroke, and was due to begin speech and movement therapy two days after we met him in mid-November. "I've already improved a lot, but I get tired easily which makes me drag my leg. Sometimes when I try to pick things up they slip out of my hand because I haven't gripped properly. It's frustrating."

"I am angry with myself for working so hard; 60 hours a week is average for me. Also for putting my body under stress with my health and smoking."

"But now I've given up, cold turkey." Robert is tentative about returning to work and wants to "get himself right" before going back.

"It scares me, to a certain degree. You need a lot of strength as a butcher. I just don't know how I'm going to go."

"But I am determined to get better. The people I've met through my therapy, their courage inspires me."

"You don't realise until you go through it yourself – how important medical research is."

"I'm really grateful to everyone at TQEH for doing such a good job when I came in. Anything the doctors and nurses could possibly do for you they would. The Stroke Unit is a special thing."

"You don't realise until you go through it yourself – how important medical research is."

Neurology Unit

The Neurology Unit has two main research arms:

Stroke related research which involves genetic, proteomic and clinical investigations into risk for stroke, stem cell therapy to repair the brain following stroke, inflammatory pathways involved in stroke, and primary health stroke prevention research.

Clinical trials sponsored to investigate the benefit to our patient populations of new therapeutics in dementia, epilepsy and multiple sclerosis.

STROKE RESEARCH PROGRAMME

The Stroke Research Programme (SRP), directed by Professor Simon Koblar and Co-Director Associate Professor Anne Hamilton-Bruce, collaborates with the University of Adelaide via the Schools of Medicine, Medical Science, Molecular and Biomedical Science and the Robinson Institute. The SRP is located at the Basil Hetzel Institute of The Queen Elizabeth Hospital (TQEH), and also at the South Australian Health and Medical Research Institute (SAHMRI).

60,000 Australians suffer a stroke every year and one third are left with severe disability. The SRP aims to improve stroke outcomes by administering adult stem cells derived from dental pulp. We have previously demonstrated in animal models that these dental pulp stem cells (DPSC) injected into the brain can improve neurological function after stroke. In 2014, we continued our work on the less-invasive, intravenous administration of DPSC into stroke-affected animal models. It is our hope that this more clinically relevant method of administration will have a positive effect on brain function.

The SRP participates in the Australian Stroke Genetics Collaboration, a multi-state, multi-centre Australian study into the genetic causes of stroke. We also have international links in stroke-related genetic research via collaborations with the International Stroke Genetics Collaborative through the Australian Stroke Genetics Collaborative and Massachusetts Institute of Technology, Boston, USA.

For its research on neuroplasticity to determine the mechanisms of action of DPSC improving stroke outcome, the SRP has links with Professor James Fawcett, at the Cambridge Centre for Brain Repair, University of Cambridge and with Professor Jean-Claude Baron, Lewin Stroke & Rehabilitation Unit, Addenbrookes Hospital, Cambridge.

Research Focus

- Investigating genetic, proteomic and clinical risks for stroke
- Investigation of the therapeutic application of adult stem cells to repair the brain following stroke
- Investigation of inflammatory pathways in stroke and other diseases
- Primary health stroke prevention research.
- Statistical parametric mapping analysis of regional cerebral blood flow (Nuclear Medicine collaboration)
- Epilepsy Research (clinical trials of new anti-epileptic medication)
- Dementia Research (clinical trials of new Alzheimer's Disease and Prodromal Alzheimer's Disease medications)
- Multiple Sclerosis (clinical trials of new Relapsing Remitting Multiple Sclerosis (RRMS) treatments)

The SRP is also part of a multi-institutional research project on neuroplasticity in stroke that was awarded NHMRC project funding worth \$735,660 over four years (2014-2017). Titled 'Characterising post-stroke cortical plasticity in humans - identifying a critical window for rehabilitation', the project is enrolling patients from the Stroke Units at both the Royal Adelaide Hospital (RAH) and The Queen Elizabeth Hospital (TQEH).

PhD candidate Mr Michael Djukic took leave to undertake a Doctorate in Physiotherapy in Melbourne, which he completed in 2014. He will now finalise his proteomic biomarker research in transient ischaemic attack (TIA) patients, that has discovered further biomarkers with potential Intellectual Property applications, for submission in early 2015. His work was presented by Mr Austin Milton as a poster at the Stroke Society of Australasia conference in August and won a poster prize.

SRP team members and Stroke Unit staff presented at conferences, including the Australasian Neuroscience Society in Adelaide, the Australian Society for Medical Research (ASMR) Scientific Meeting in Adelaide, the Conference for the Stroke Society of Australasia on Hamilton Island, Queensland and at the Mt Lofty Workshop 'Frontier Technologies for Nervous System Function and Repair' in 2014.

In January 2014, the Neurology Department celebrated the promotion of Dr Anne Hamilton-Bruce to Associate Professor.

CLINICAL TRIALS

Stroke

The INSPIRE study: INternational Stroke Perfusion Imaging REgistry is an Australia-first databank of all information and data relevant to acute brain imaging. The registry will compile different stroke scans from hospitals Australia wide, allowing for comparative analysis. 24 patients are currently on the register.

Start-Extend Trial: Stroke imAging pRevention and Treatment (START) – Extend: Extending the time for Thrombolysis in Emergency Neurological Deficits. This trial is an investigator initiated, Phase III, randomised, placebo controlled, double-blinded, clinical trial that is conducted in approximately 20 study sites throughout Australia and New Zealand. 2 patients recruited, completed with no adverse effects associated with the trial medication.

Extend-IA: Extending the time for Thrombolysis in Emergency Neurological Deficits – IntraArterial. A randomised controlled trial of intra-arterial reperfusion therapy after standard dose intravenous tPA within 4.5 hours of stroke onset utilising dual target imaging selection. The study was a multi-centre, prospective, randomised, open label, blinded endpoint (PROBE), controlled phase II trial (2 arm with 1:1 randomisation) in anterior circulation ischaemic stroke patients. No patients were recruited. The study was discontinued November 2014, due to findings of international study - MR CLEAN study, indicating intra-arterial administration of tPA advantageous, so the study was stopped for ethical reasons.

National Stroke Foundation: My Stroke Journey Information pack for carers and survivors. Australian Stroke Survivors Needs Assessment Project.

Stop-Aust: The Spot sign and Tranexamic acid On Preventing ICH growth – AUStralasia Trial. A phase II randomised placebo-controlled double-blind multi-centre investigator-led academic trial of tranexamic acid within 4.5 hours of intracerebral haemorrhage in patients with contrast extravasation on CT angiography, "the Spot sign". Ethics and governance approval received and site initiation visit completed. Investigator training to be completed and patient recruitment to commence 2015.

TASTE: Tenecteplase v Alteplase for Stroke Thrombolysis Evaluation Trial. This is a phase III multi-centre, prospective, randomised open-label blinded endpoint (PROBE) study. Randomisation of patients presenting with acute stroke - to either Tenecteplase or Alteplase, no other changes to routine care. TQEH - lead site for Lyell McEwin, Royal Adelaide Hospitals and Flinders Medical Centre. Ethics and governance approval received. Trial medication received and site activated November 2014. No recruitments to date.

Socrates: A randomised, double-blind multi-national study to prevent major vascular events with Ticagrelor compared to Aspirin in patients with acute ischaemic stroke or TIA. Ethics via the Mutual agreement - approved in Melbourne July 2014. Governance Approval received and recruitment to commence 2015.

Epilepsy

The Neurology Unit has been recruiting for two new studies. USL P09-004 investigates Slow Release Topiramate as adjunctive therapy for refractory partial onset seizures with or without secondary generalisation; SP0993 and the extension SP0994 study are monotherapy controlled trials of Lacosamide 200 to 600 mg day, versus Controlled Release Carbamazepine (400 to 1200 mg day) versus placebo. Such investigative trials will allow access to new anti-epileptic drugs that may not become available to the general public until Pharmaceutical Benefits Scheme (PBS) listing and allows development of valuable clinical experience in the utilisation of these drugs. We have also undertaken a retrospective audit of Epilepsy Clinic patients from 1/3/2010 – 1/3/2012 to assess the impact of the new Assessing Fitness to Drive guidelines. This focuses on the impact of these guidelines on our patients' quality of life and also helps to review our own practice in terms of assessing fitness to drive. This was published in the Journal of Clinical Neuroscience November 2014 Vol 21 Issue 11.

Dementia

The Memory Clinic and Clinical Cognitive Research Units continue to participate in many national and international studies. Dr Karyn Boundy is the Chairperson of the Australasian Consortium of Centres for Clinical Cognitive Research (AC4R) to facilitate clinical trials in memory conditions in Australasia and further simplify their administration with Mutual Acceptance of National ethics and Lead site approval for studies coming up in 2014. She is also the South Australian and AC4R representative for Neurosciences Trials Australia – a clinical trials platform with “nodes” in each neurological subspecialty area to facilitate both investigator driven research and to also to attract pharmaceutical company early stage phase I – III research to Australia. Dr Boundy has spoken at local General Practitioner (GP) division, national and international meetings about aspects of dementia management and diagnosis of less common dementias such as, frontal lobe and tauopathies.

The CALHN review of memory services by clinical lead Dr Cathy Short with the help of Ms Kerry Mckinna and Shauna Henderson with enable the delivery of an integrated multidisciplinary service in the near future. The CALHN Memory Service has now been approved and space for the new service is being assessed. The satellite Neurology/Memory Clinic has proven popular in Port Lincoln and Tumby Bay in conjunction with Rural Health SA.

Dr Boundy is a member of a number of government committees regarding dementia service funding.

Various international publications have arisen from participation in the Prospective Research in Memory Clinics (PRIME), a database that studies all types of dementia patients attending Australian Memory Clinics.

Applications have been successfully made to PBS/PBAC to simplify prescribing of AD medications which are now streamlined and the criteria for ongoing usage have been broadened.

Alzheimer Symptomatic Trials

There has been a renewed interest in both Alzheimer symptomatic and disease modifying trials.

Lundbeck compound Lu AE58054, a selective serotonin receptor 6 (5-HT6 receptor) antagonist for patients with moderate Alzheimer's disease completed recruitment in 2011 and further studies are planned. Phase III of this study is now in the initial stages of negotiation.

Servier's CL2-38093-005 protocol for compound S 38093 trialled in both Naïve patients and as an add on to donepezil has now been advanced to phase IIb. Recruiting is now closed for this trial. (CL2 38093-012).

Disease Modifying Trials in Alzheimer's Disease

Merck MK 8931 safety and efficacy in mild to moderate AD add on to all Alzheimer drugs is currently recruiting. (BACE inhibitor Phase III), Tau RX 12 month trial of Leuco-methylthioninium in mild to moderate AD. We have commenced the randomised, double-blind WN28745 Marguerite Dementia trial for mild Alzheimer's disease patients using Gantenerumab subcut injection. This trial is now recruiting.

Prodromal AD

Roche is studying the effects of RO4919832 on Cognition and Function in Prodromal Alzheimer's Disease for two years with open label extension to four years. This study is being conducted due to Gantenerumab having a preclinical profile consistent with AB reduction effect, additionally in the multiple ascending dose (MAD) study conducted in AD patients, Gantenerumab appeared to inhibit and reduce the accumulation of brain AB observed on positron emission tomography (PET) brain scans.

The frequent MRI Brain scans required in this study have identified new amyloid therapy related imaging abnormalities ARIA-H & Aria-E, which have further enhanced our understanding of the role of amyloid in blood vessels and the effect of its removal.

Multiple Sclerosis (MS)

The treatment of MS continues to be exciting, with a further 2 oral medications (Aubagio [Teriflunomide] and Dimethyl Fumerate [Tecfidera]) reimbursed by PBS in 2014. We are pleased to have been involved in the pivotal clinical trials with those medications. We continue our association with Fingolimod, working on a long term extension trial for patients who were in the pivotal studies (protocol CFTY720D2399).

The CAMMS323 and CAMMS324 protocols trialled Alemtuzumab in treatment-naïve and previously treated MS patients respectively. CAMMS323 showed a 55% reduction in relapse at 2 years in adults treated with Alemtuzumab 12mg compared with those receiving interferon. Similarly, the 324 study showed a 49% reduction in relapse rate in patients treated with Alemtuzumab 12 mg compared to interferon beta-1a over two years of study. Importantly, there was also a 42% reduction in the risk of sustained accumulation (worsening) of disability as measured by the Expanded Disability Status Scale (EDSS). An extension study is in place to monitor the longer term effects of Alemtuzumab (CAMMS03409). This drug was approved by the TGA as another treatment for MS in early 2014 and has just received a positive recommendation by the PBS Committee. We look forward to offer this treatment to our MS patients.

Staff

Senior Consultant Neurologist/Director of Neurology

MK Robinson MBBS FRACP

Senior Visiting Neurologist

GH Purdie MBBS FRACP

KL Boundy MBBS FRACP

Senior Consultant Neurologist/Director of Stroke Unit

J Jannes BMBS FRACP PhD

Clinical Academic Neurologist/Director of Stroke Research Program

SA Koblar BMBS FRACP PhD

Chief Clinical Neuropsychologist

AC Kneebone BA Dip App Psych MA PhD FAPS

Consultant Neurologists

C Short BSc MBBS FRACP

A Tan BMBS FRACP

J Hafner BMBS FRACP

R Ghaoui BMBS FRACP

Principal Medical Scientist / Management Co-ordinator / Co-Director of SRP

MA Hamilton-Bruce BSc MSc MBA PhD AFCHSE CBiol MSB CSci FIBMS

Medical Scientist

MB Donk BHSc

Chief EEG Technologist

J Pruszkowski Diploma in Medical Analysis

Neurology Secretary

JA Greutner Cert IV Bus Admin

Administrative Assistant

K Greet (to end August 2014)

Administrative Assistant (part-time)

R Richards

Memory Unit Secretary

K McKinna

Clinical Nurse Manager

KJ Webb RN BN

Comprehensive Epilepsy Program NP

S Horn NP MNSc

Stroke Nurse

L Dodd RN BN

Transient Ischaemic Attack (TIA) Nurse

P Toner RN BN

S Castle RN

Clinical Research Trials

PCK Cheung RN

S Casey RN BN

Senior Medical Scientist for Stroke Research Programme

AG Milton BSc(Hons) Dip Comp Sci

Post-doctoral Research Fellows

K Kremer BBtech (Hons) PhD

X Kaidonis BSc (Biomed Sci) (Hons) PhD

Postgraduate Students

Higher degree awarded

K Ellis BSc (Biomed Science) BPsych (Hons)

'Neurophysiology and electrophysiology of dental pulp stem cells'

PhD conferred by University of Adelaide 2014.

Supervisor: Koblar S

PhD candidates

FC Choy BSc(Hons)

'The regulation of Npas4, a neural-specific transcription factor'

Supervisor: Koblar S

M Djukic BHSc(Hons) GradCertBus(Acc) DPT (UniMelb)

'Proteomic and genomic investigations in transient ischaemic attack'

Supervisor: Koblar S

E Leung MBBS BSc (Med) DCHFRACGP

'Transient Ischaemic Attack: a primary care perspective of stroke prevention'

Supervisor: Koblar S

J Winderlich BSc(Health Sci)(Hons)

'Investigations into the mechanisms of action of stem cell therapy for stroke'

Supervisor: Koblar S

Masters candidates

J Sutton MPhil (Med). MN. BComm. BBus (Int). CPA

'A Clinical and Economic Evaluation of TIA Care Management Models for Preventing Stroke' (leave of absence in 2014).

Supervisor: Koblar S

W Pan BSc (Biomed Science) (Hons)

'Investigation of p75 Neurotrophin Receptor on Human Dental Pulp Stem Cells'.

Supervisor: Roger ML, Koblar S

Completed Honours

H Kaur BHealthSc

'Investigating The Effects of Single Pulse Transcranial Magnetic Stimulation on Adult Human Dental Pulp Stem Cells *in vitro* and *in vivo*'

Supervisor: Koblar S

H Bridgman BSc (Animal Science)

'Relinquishment of Companion Animals by People Entering Residential Care in South Australia'

Supervisors: Koblar S, Hazel S

Vacation Students

M Gancheva BSc (Biomed.Sci)

4 weeks in 2014

Supervisor: Koblar S

E Ducher

3rd year MBBS student, worked in 2014 on a meta-analysis of stem cell therapy and Parkinsonism in pre-clinical, animal models.

Supervisor: Koblar S

Work Experience Students

The Stroke Research Programme hosted Christian Lysandrou, Rhys Kelly and Evelyn Cacas as secondary students for work experience in mid-2014.

Grants

NHMRC. (Project grant) Characterising post-stroke cortical plasticity in humans - identifying a critical window for rehabilitation (\$147,132 2014) 2014 – 2018, Ridding MC, Rothwell JC, Koblar S, Ward N, McDonnell M.

Stroke SA. Stem Cell Therapy for Stroke (\$40,000 2014) Koblar S.

Rebecca L Cooper Medical Research Foundation. (Equipment Grant) Adult Human Dental Pulp Stem Cell Therapy for Chronic Stroke (\$15,490 2014) Koblar S, Hamilton-Bruce MA, Kaidonis X, Winderlich J, Milton AG.

The Hospital Research Foundation: New computer for Zeiss Axioscope Z1 Microscope and software system update 'Zen Blue' (\$3,850 2014) AG Milton for the Basil Hetzel Institute.

Awards

K Kremer

The Peter Couche Foundation Fellowship (2 years)
Australian Brain Foundation, Elizabeth Penfold-Simpson prize (\$22,000)

J Winderlich

University of Adelaide School of Medicine travel grant, \$2,309 to study for 12 weeks in the Brain Repair Centre at Cambridge, UK, as part of his PhD candidature.
Australian Neurology Research scholarship for \$1800 to aid study at Cambridge, UK.

A Milton

Best Poster Presentation (oral) Award, Stroke Society of Australasia Annual 25th Scientific Meeting, Hamilton Island, Queensland, 1st August 2014 (\$500)

X Kaidonis

Best Flash PhD/ECR Presentation (oral) Award, Mt Lofty 'Frontier Technologies for Nervous System Function and Repair' Workshop for Brain Repair, 29 Nov. 2014 (\$100)

Collaborations

Neuroplasticity: experiments and collaborations made redetermining the mechanism of action of DPSC improving stroke outcome. These have been undertaken at Cambridge with Professor James Fawcett and Dr Jessica Kwok, Cambridge Centre for Brain Repair, University of Cambridge, UK. In 2014 PhD candidate Mr Joshua Winderlich undertook research at this prestigious institution with these collaborators to further these investigations for a prospective publication and NHMRC-UK grant application.

Investigation of Serum Biomarkers for TIA: with Dr Tim Chataway, Head of Flinders Proteomics Facility at Flinders University. This project was responsible for analysis of data with possible intellectual potential implications that arose from PhD candidate Michael Djukic's work in previous years and has now been concluded.

Animal Assisted Therapy (AAT) and relinquishment of companion animals: Collaboration and Honours co-supervision (Hayleigh Bridgman) with Dr Susan Hazel, Lecturer in Animal Science, Roseworthy Campus, University of Adelaide.

TIA Economics: Collaboration with Professor Jon Karnon, Professor in Health Economics, University of Adelaide.

Capitalising on a TIA event to positively change health behaviour in at-risk individuals: with Associate Professor Susan Hiller, Dr Svetlana Bogomolova and Dr Michelle McDonnell from the University of South Australia, started in 2014. This project provided preliminary data for an NHMRC Project Grant application in 2014 that proved unsuccessful.

Patents

An assay for determining neuroplasticity effect of stem cells PCT/AU02/01759.

Applicant: ARI, University of Adelaide & Medvet Science Pty Ltd, SA, Australia. 2007

Inventors: Koblar SA, Gronthos S, Arthur A.

Sinus Research Gives Back Life

Patrick's Story



Since his teenage years, 27-year-old Patrick Guerin has been used to an absent sense of smell and taste. A stuffy nose, pressure headaches, tiredness and feeling under the weather were part of his daily life.

Patrick suffers chronic rhinosinusitis, a common condition which affects about 18 percent of the Australian population. As in Patrick's case, chronic rhinosinusitis has a significant impact on the lives of those who suffer with it. Symptoms such as difficulty breathing, pain and swelling around the eyes and nose, a reduced sense of smell and taste and a chronic cough are common.

Patrick endured two unsuccessful surgeries to clear his nasal passages prior to being referred to Professor Peter-John Wormald; an Ear, Nose and Throat (ENT) specialist who heads the ENT Department at The Queen Elizabeth Hospital (TQEH). Patrick also tolerated a constant stream of medications, including antibiotics and steroids to treat his sinus infections, but they were largely ineffective.

A keen sportsman, Patrick felt his chronic sinusitis was holding him back, both at rest and on the court.

"Whenever I got a cold it would stick around for months and months. It was incredibly frustrating – I was really low on energy all the time and would have trouble breathing, which affected my sleep," explained Patrick.

In March 2013 Patrick underwent a frontal Sinus Drillout operation, which was performed by Professor Wormald using an endoscopic camera.

The operation involved removing polyps, eradicating the infection and opening up Patrick's sinus cavities. This created clear passages for breathing and also meant that any topical medications that Patrick was required to take to treat his sinuses could actually reach the inner sinus lining and be effective.

Adding to the success of the surgery, Professor Wormald applied Chitodex gel to Patrick's sinuses to control postoperative bleeding. This is an effective alternative to traditional nasal packing which must be removed after 1-2 days. The removal process is described by many patients as the "worst part of the operation".

Chitodex gel is an innovative new surgical product proudly designed and developed through The Queen Elizabeth Hospital and the University of Adelaide in collaboration with Otago University in New Zealand. It is a nasal dressing that is applied just once to sinuses after an operation to control bleeding, improve healing and stop scarring, whilst maintaining patient comfort. It has also now been shown to significantly improve the outcome of sinus surgery. The gel dissolves away over the course of 10 days, eliminating the need for nasal packing removal.

"Chronic rhinosinusitis is a mild but really uncomfortable thing to have. I know it's not life-threatening but it really impacted my quality of life," said Patrick.

"I am still prone to sinus infections, but now they clear up much quicker because the medication can work properly. I have a lot more energy and food tastes great!"

"I finally feel like there is nothing out of my control that's holding me back – which I felt before with my sport and my general health and well-being."

Patrick is grateful to Professor Wormald and for the research that has gone into the surgery and treatment he received.

"I will definitely support medical research in future – it's really worthwhile"

"I finally feel like there is nothing out of my control that's holding me back – which I felt before with my sport and my general health and well-being."

Otolaryngology, Head and Neck Surgery

The Department of Otolaryngology, Head and Neck Surgery, is committed to excellence in translational research and education. Research in our department is focused mainly on understanding the pathogenesis of Chronic Rhinosinusitis (CRS), using a multidisciplinary approach, aimed at identifying new diagnostic/prognostic markers and treatment strategies to the benefit of our patients. The research team currently consists of 9 MSc and PhD students, supported by four scientists and clinical staff and is recognized internationally as one of the leading rhinological research institutions in the world. Research projects cover all aspects of rhinological research from pathophysiological aspects of CRS to the identification and validation of new treatment strategies in vitro and in vivo, bringing research from bench to bedside.



Population Data

- > In Australia, **Chronic Rhinosinusitis (CRS)** is classified as a prevalent condition within the major chronic respiratory diseases group.
- > Self-reports in the National Health Survey (2004-2005) show that 9.2% of Australians (about 1.8 million people) have CRS. Of these people, 22% also have asthma.

Research Focus

- Clinical and Translational Research of Chronic Rhinosinusitis

Overview

Pathophysiological aspects of chronic rhinosinusitis

Despite extensive research in the bacteriological and immunological aspects of CRS, the pathogenetic basis of CRS remains poorly understood. Several of our research projects are aimed at understanding molecular, cellular, microbiological and immunological aspects of CRS.

Dr Clare Cooksley, post-doctoral scientist, is the department's expert in molecular microbiology and cell biology and apart from a supporting role to different projects, her research focuses on the effect of bacterial products on the host immune system. She also studies mechanisms in which *S. aureus* invades the epithelial cells.

Dr Mahnaz Ramezanzpour, post-doctoral scientist, is the department's expert in cytotoxicity studies. She is also in charge of developing a tissue and blood bank for CRS patients and studies the role of different Toll-Like Receptors and inflammasome activation in CRS.

Dr Ahmed Bassiouni, PhD candidate, is focusing on understanding the role of eosinophilic inflammatory load, fibrosis and remodelling in patients with refractory chronic rhinosinusitis and failure of surgical and medical treatment. He is also involved in different "omics" projects including the sinonasal microbiome in health and disease and in relation to changes in the immune signature in CRS.

Dr Jae Murphy, PhD candidate, is studying mucosal barrier dysfunction in CRS investigating molecular pathways and pathogenic entities implicated.

Dr Sakiko Oue, PhD candidate, studies prevalence and pathophysiology of neo-osteogenesis in recalcitrant CRS.

The host immune response in Chronic Rhinosinusitis (CRS)

Ms Dijana Miljkovic is the department's expert in flow cytometry, used to characterise different immune cell populations in CRS patient tissue.

Dr Judy Ou, PhD candidate, studies the role of Th2 cytokines in the development of CRS and explores the role of secondary lymphoid organ development in the disease process.

The host immune response in Chronic Rhinosinusitis (CRS)

Ms Dijana Miljkovic, PhD candidate, uses flow cytometry to characterise different immune cell populations in CRS patient tissue and blood. Part of her project focuses on different B-cell subsets and is done in collaboration with Northwestern University, USA.

Dr Judy Ou, PhD candidate, studies the role of Th2 cytokines in the development of CRS and how their activation and secretion is influenced by bacterial infections.

New treatment strategies for chronic rhinosinusitis

Treatment of CRS is aimed at controlling rather than curing the disease. However, despite optimal treatment measures, a significant subset of patients do not respond well and require multiple surgical interventions and repetitive antibiotic treatments, favouring the development of *Staphylococcus* strains resistant to all known antibiotics (MRSA). There is thus a need for the identification of further and improved therapeutic targets to treat this complex disease.

Ms Amanda Drilling, PhD candidate, is our expert in pre-clinical development studies. After a successful safety and efficacy study of the use of a bacteriophage cocktail to eliminate *S. aureus* infection *in vitro* and *in vivo*, we are now on the verge of starting a human clinical trial, the first of its kind in Australia.

Mr Dong Dong, PhD candidate and visiting scholar from China, joined our team for one very productive year. He worked in collaboration with the Department of Nanotechnology at the University of South Australia to develop novel nanoparticles aimed at delivering a nitric oxide donor to sinonasal mucosal biofilms.

Dr Chun Chan, PhD candidate, is doing bacterial interference studies aimed at developing a pro-biotic cocktail able to suppress the growth of pathogenic bacterial species within the sinuses.

Ms Katharina Richter, PhD candidate, studies antibiofilm properties and mechanism of action of different compounds on *S. aureus* biofilm *in vitro*. She also studies the dynamics of multi-species biofilms at the ultrastructural level using a Correlative Super High Resolution imaging platform. Her work is done in collaboration with The Department of Nanotechnology, Mawson Lakes, University of South Australia.

Pre-clinical and clinical studies testing the use of Chitosan gel

Dr Thanh Ngoc Ha, PhD candidate, is in charge of a clinical study evaluating the effects of Chitosan gel on wound healing following Endoscopic Sinus Surgery. She also coordinates a study in collaboration with Professor Maddern, Upper Gastro-Intestinal Surgery, studying the effect of Chitosan gel on the prevention of adhesions following abdominal surgery in a large animal model.

Treatment of large vessel injuries as a complication of sinus surgery

Dr Vikram Padhye, PhD candidate, studies different treatment possibilities to arrest bleeding from large vessel injuries in a large animal model.

Staff

Professor of Otorhinolaryngology, Head & Neck Surgery and Head of Department

PJ Wormald MD FRACS, FCS(SA) FRCS(Ed)

Head of Clinical Services

A Psaltis MBBS FRACS PhD

Senior Lecturer

G Rees MBBS FRACS

Staff Specialists

S Floreani MBBS FRACS

J Ling MBBS FRACS

S Rajapaksa MBBS FRACS

H Pant MBBS FRACS

D Close MBBS FRACS

K Ha MBBS FRACS

Rhinology Fellow

D Morrissey

ENT Registrar

D Gidley

Chief Scientist, Otolaryngology Head & Neck Surgery

S Vreugde MD PhD

ENT Research Assistants

C Cooksley BSc PhD

AJ Drilling Bsc

M Ramezanpour Msc PhD

Clinical Nurse Operating Theatres

S Hughes RN

Secretary

L Martin

Postgraduate Students

Higher Degrees Awarded

PhD

J Micklen BBTech (Hons)

‘Australian Aboriginal Head and Neck Cancer Patients: Health-related Quality of Life in South Australia and the Northern Territory’

Supervisor: Wormald PJ

Y Naidoo MBBS FRACS

‘Outcomes in Frontal Sinus Surgery’

Supervisor: Wormald PJ

C Jardeleza MD

‘Role of Nitric Oxide in the Pathophysiology of *Staphylococcus aureus* Biofilm Formation in Chronic Rhinosinusitis’

Supervisors: Wormald PJ, Vreugde S

E Cleland MBBS

‘The microbiome in CRS’

Supervisors: Wormald PJ, Vreugde S

D Cantero MD

‘The host Immune Response to *Staphylococcus aureus* biofilm in Chronic Rhinosinusitis’

Supervisors: Wormald PJ, Vreugde S

PhD Candidates

A Drilling BBiotec (Hons)

‘Use of bacteriophage to treat *Staphylococcus aureus* sinusitis in a sheep model’

Supervisors: Wormald PJ, Speck P

S Rajiv MBBS

‘The efficacy of Chitosan gel on hemostasis in neurosurgical sheep model’

Supervisors: Wormald PJ, Vreugde S

T Ha MBBS

‘The effects of Chitosan gel on wound healing following Endoscopic Sinus Surgery and Modified Endoscopic Lothrop Procedure’

Supervisor: Wormald PJ

A Bassiouni MBBCh

‘Understanding the role of eosinophilic inflammatory load, fibrosis and remodelling in patients with refractory chronic rhinosinusitis (rCRS) and failure of surgical and medical treatment’

Supervisors: Wormald PJ, Vreugde S

V Padhye MBBS

‘Early and late complications of endoscopic haemostatic techniques following different carotid artery injury characteristics’

Supervisors: Wormald PJ, Vreugde S

J Ou MBBS

‘Innate lymphoid cells and cytokines in CRS’

Supervisors: Wormald PJ, Vreugde S

D Miljkovic Bsc

‘Characterisation of the immune compartment in Chronic Rhinosinusitis’

Supervisors: Wormald PJ, Vreugde S

K Richter Msc Pharmacy

‘*Staphylococcus aureus* biofilm molecular ultrastructure and its breakdown upon challenge with antibacterial compounds’

Supervisors: Wormald PJ, Vreugde S, Prestidge C.

Postgraduate Students cont.

PhD Candidates (cont.)

C Chan MBBS

'Bacterial interference as a novel treatment against *Staphylococcus aureus* in chronic rhinosinusitis'

Supervisors: Wormald PJ, Psaltis A, Vreugde S

S Oue MBBS

'Neo-osteogenesis in CRS'

Supervisors: Wormald PJ, Vreugde S

J Murphy MBBS

'The mucosal barrier in chronic rhinosinusitis'

Supervisors: Wormald PJ, Vreugde S

Grants

NHMRC. (Project grant #1050883) *In vivo* evaluation of the safety and efficacy of a novel Chitosan gel in the reduction of adhesions following abdominal surgery in both animal and human models, (\$171,658 2014) 2013-15, Wormald PJ, Maddern G, Robinson S.

NHMRC. (Project grant #1047576) A novel nitric oxide-based treatment for recalcitrant *Staphylococcus aureus*-associated chronic rhinosinusitis, (\$174,309 2014) 2013-15, Wormald PJ, Prestidge C, Thierry B, Vreugde S.

Garnett Passe and Rodney Williams Memorial Foundation. (Project grant) The clinical significance of intracellular *Staphylococcus aureus* in CRS. (\$75,000 2014) 2013-2016, Wormald PJ, Vreugde S.

Garnett Passe and Rodney Williams Memorial Foundation. (Scholarship) Unravelling the role of type 2 innate lymphoid cells and their activating cytokines IL25, IL33 and TSLP in chronic rhinosinusitis. (\$55,000 2014) 2013-2015, Ou J, Wormald PJ.

Garnett Passe and Rodney Williams Memorial Foundation. (Research Scientist Fellowship) Treatment and prevention of injuries to large arterial vessels in the ENT surgical setting, (\$75,000 2014) 2013-15, Padhye V, Wormald PJ.

Garnett Passe and Rodney Williams Memorial Foundation. (Conjoint grant) Sinonasal microbial and immune homeostasis and its breakdown in Chronic Rhinosinusitis, (\$125,000 2014) 2014-16, Wormald PJ, Vreugde S.

The Hospital Research Foundation. (Project grant) Bacteriophage: a novel treatment of chronic rhinosinusitis (\$150,000 2014) 2014-15, Wormald PJ.

Awards

K Richter

Best Oral presentation, Junior PhD students (Laboratory), TQEH Research Day 2014, Adelaide, October 2014

S Rajiv

Best Scientific Presentation, American Rhinologic Society meeting, Orlando, Florida, USA, October 2014

Collaborations

Local

Professor A Evdokiou and Dr M DeNichilo (Breast Cancer Research): Role of leucocyte-derived factors on fibrosis and neo-osteogenesis in CRS

Dr P Zalewski (Medicine): Role of zinc transporter proteins in CRS

Professor G Maddern and Dr E Hauben (Surgery): Inflammasome activation in the gut

Professor G Maddern (Surgery): NH&MRC project grant *In vivo* evaluation of the safety and efficacy of a novel Chitosan gel in the reduction of adhesions following abdominal surgery in both animal and human models

Associate Professor M Rischmueller and S Lester (Medicine, Rheumatology): The role of inflammasome activation in auto-immune diseases and recalcitrant chronic rhinosinusitis

National

University of South Australia: Group of Professor C Prestidge and Associate Professor B Thierry (Department of Nanomedicine):

(1) NHMRC project grant, A novel nitric oxide-based treatment for recalcitrant *Staphylococcus aureus*-associated chronic rhinosinusitis

(2) Development of novel nanoparticles for use in the treatment and prevention of bacterial biofilms

Flinders University: Group of Professor J Mitchell and P Speck (Department of Microbiology): The use of a bacteriophage cocktail to treat bacterial biofilms

Special Phage Services, Sydney, The use of a bacteriophage cocktail to treat bacterial biofilms

University of Adelaide (Department of microbiology): Dr S Kidd. Genetics and genomics of small colony variants in CRS.

International

Stanford University Medical school, USA: Professor P. Hwang and Dr M.Costa (Department of ENT): The use of a bacteriophage cocktail to treat bacterial biofilms

Gillies Hospital, Auckland, New Zealand: Dr R. Douglas (Department of ENT): The use of a bacteriophage cocktail to treat bacterial biofilms

Otago University, Chemistry Department, New Zealand: Dr S Moratti, Professor L Hanton, Professor B Robinson. Development of a novel Chitosan based gel to prevent adhesion formation in the nose and sinuses, in the abdomen and in spinal surgery. NHMRC project grant.

Academic Medical Centre, Amsterdam, The Netherlands. Professor W Fokkens (Department of ENT): The use of a bacteriophage cocktail to treat bacterial biofilms

Medical University of South Carolina, Professor R Schlosser, Emory University Atlanta Associate Professor S Wise, Mt Sinai New York Professor S Govindara, University of Alabama Associate Professor B Woodworth, University of Toronto Professor I Witterick. (Departments of ENT) Factors that impact perioperative co-morbidity in endoscopic skull base procedures. Northwestern University, Chicago, Professor R Kern (Department of ENT) Characterisation of B-cells in CRS

Psychiatry

Under the guidance of University of Adelaide Professor Bernhard Baune the Discipline of Psychiatry has developed an integrated program across the Queen Elizabeth, Lyell McEwin and Royal Adelaide Hospitals, covering the Central and Northern Adelaide Local Health Networks

The Discipline's aim is to enhance the understanding of the etiology and pathophysiology of psychiatric disorders, and to strengthen the emerging knowledge and clinical application on the regenerative capacity of the human mind and brain for severe psychiatric disorders. Our research program spread from basic to clinical science, investigates the structures, systems and functions of the biological, cognitive, emotional, behavioural and environmental mediators of psychiatric disorders and their potential for clinical intervention, improvement and recovery.

The Discipline combines an active and innovative neuroscience and biomarker laboratory with prognostic modelling expertise together with research clinics at the three main hospital sites. In 2014 these groups were combined to create the Adelaide Integrated Mental Health, Biobank and Disease Marker Centre.

Research Focus

- Longitudinal studies of cognitive function and general function in mood and psychotic disorders
- Biomarkers of outcome in mood and psychotic disorders
- Pharmacogenomics of lithium
- Mental illness outcome trajectories
- Epidemiology of treatment resistant psychosis and management with clozapine
- Impact of psychiatric illness on physical health

Population Data

Globally, mental illness and substance abuse disorders together are the number one cause of years lost to disability accounting for an estimated 175.3 million lost years worldwide in 2010 (Whiteford *et al.* 2013). The individual impact of severe disorders such as psychosis is more obvious but mood disorders account for nearly 58% of this figure. The Profiles of Health, Australia, 2011-13 study by the Australian Bureau of Statistics suggests that 3.0 million Australians (13.6%) report having a mental or behavioural condition. Since 2001 this figure has been increasing (11.2% in 2007-08, 9.6% in 2001). The vast majority (13.5% of the population) report problems with mood such as depression and anxiety.

Emerging evidence suggests that mood disorders have significant long-term effects on cognition and general function beyond discrete illness episodes (Baune *et al.* 2010). Our research uses world-class methodology for the identification of multimodal predictors of cognition, function and outcomes in longitudinal studies of mood and psychotic disorders to develop better individualised treatments.

The 12-month prevalence of psychotic illness managed within Australian public mental health services is estimated at 4.5/1000 people (Morgan *et al.* 2012). Up to one half of these patients have reported a suicide attempt in their lifetime, over 60% report only partial recovery or continuous chronic illness, 32% have a severe dysfunction in the quality of self care and 85% rely on a government pension as their main source of income (Morgan *et al.* 2012). Seventy five percent were overweight or obese and there are high rates of comorbid chronic medical conditions, particularly metabolic syndrome, present in over 50% (Galletly *et al.* 2012). Life expectancy in those with schizophrenia is decreased in excess of 16 years largely due to associated diseases of the circulatory system (Laursen *et al.* 2011). Our discipline also focusses on cutting edge data linkage of public hospital and mental health electronic records, to better model the association between mental and physical illness and develop better monitoring and intervention strategies. We have developed and contributed to the successful implementation of a state-wide computer-based alerting system and nurse-led clinics to identify and intervene to prevent complications from the use of the high risk antipsychotic clozapine (Clark *et al.* 2014).

Grants

In line with its aims, research at The Queen Elizabeth Hospital focuses on large longitudinal cohort studies of cognitive and general function and outcome in mood and psychotic disorders, with participants drawn both from the clinical service and the general public. These studies collect data on standardised diagnosis, psychopathology, illness course, treatment response, cognitive and general function, specific blood biological markers (DNA, RNA, protein) and outcomes. Currently the Cognitive Function and Mood Disorders Study (CoFAMS) has recruited >240 participants across Adelaide. As part of this study our group has been awarded an RAH Research Foundation Project Grant to explore the role of neuro-immune mechanisms in depression in adults that suffered childhood maltreatment.

A subgroup of the CoFAMS, the Lifetime Lithium Response Study, has assessed >70 participants treated for bipolar disorder with lithium. In collaboration with the international CONLIGEN group this sample has been included in a genome wide association study of lithium response. Our group was awarded a RAH Research Foundation Project Grant for 2015 to explore the function of significant genes identified in the CONLIGEN GWAS.

A study similar to the CoFAMS in a sample of patients with psychotic illness, the Cognitive And Functioning in Psychosis Staging Study (CoFAPSS), will commence in 2015.

A secondary area of focus is the extraction and prediction of specific disease trajectories from these samples, and from health service level data. In 2014 Dr Clark received a SA Health data linkage grant to explore mortality, morbidity and service use in consumers with chronic psychosis across metropolitan Adelaide.

Postgraduate Students

PhD candidates

JC Chadbourne BSc(Hons)

'The relationship between neurocognitive performance and general function in Major Depressive Disorder'

Supervisors: Baune B, Clark S

R Dhillon MBBS FRANZCP

'Impact of psychiatric comorbidity on outcome in physical illness'

Supervisors: Baune B, AdamsR, Bidargaddi N

Staff

Clinical Academic

SR Clark MBBS FRANZCP PhD BSc (Hons)

NHMRC. (Project grant) 'Defining the Role of Inflammation in Depression during Aging'. (\$714,000 2014-2017) Baune BT.

SA Health Data. (Linkage grant) Chronic Psychosis: Mortality and Service Use in SA (\$7,200 2014-15) Baune B, Clark SR.

Grants commencing in 2015

Royal Adelaide Hospital Research Foundation. (Project grant) 'Lithium treatment response in bipolar disorder: functional characterisation of a genome-wide association study and a systems biology analysis using next generation RNA sequence data'. (\$48,677 2015) Stacey D, Clark SR, Baune BT.

Royal Adelaide Hospital Research Foundation. (Project grant) 'Childhood maltreatment and adult depression status: a pilot study to identify neuro-immune interaction mechanisms mediating early adversity effects on adult depression'. (\$43,000 2015) Jawahar C, Baune BT.

Collaborations

Local

Professor Julio Licinio, Professor Ma-Li Wong, SAHMRI / Flinders University of South Australia

National

Professor Pat McGorry, Professor Chris Pantelis and Professor Ian Everall, University of Melbourne

Professor Anthony Hannan, Dr Gursharan Chana, Florey Institute, Melbourne

Professor Perminder Sachdev, Professor Julian Trollor, University of New South Wales

Professor Ian Hickie, Professor Maria Fiatarone Singh, University of Sydney

Professor Heinrich Koerner, Immunology Laboratory, Menzies Research Institute, Tasmania

International

Bram Prins, University of Groningen, Netherlands

Dr Chris Murgatroyd, University of Manchester, UK

Dr Udo Dannlowski, University of Marburg, Germany

Professor Katharina Domschke, University of Würzburg, Germany

Professor Klaus Berger, Professor Volker Arolt University of Münster, Germany

ConLigen - Consortium on the genetics of treatment response to Lithium in bipolar disorder

Psychiatric Genetics Consortium - Major Depressive Disorder

BrainInflame – Consortium on Brain Inflammation in Aging

Helping others breathe easier

Ernest's Story



Ernest Hicks knows what it feels like to struggle for breath. Living with emphysema, he relies on daily oxygen therapy to help him breathe. Despite his ailing lungs he is determined to help others by joining a research trial at The Queen Elizabeth Hospital (TQEH) aimed at improving the delivery system of life-saving oxygen therapy.

Ernie was diagnosed with emphysema a number of years ago. It's a disease that causes irreversible damage to the airways and lungs. The condition, commonly linked to smoking or long-term exposure to industrial pollutants and dust, has left him dependent on oxygen therapy which sits in portable tanks by his side. "I couldn't believe it when they told me that I had emphysema. At the time I hadn't had a cigarette for eight months – I'd given up," he said proudly.

But the damage had been done. Prior to giving up Ernie had smoked on average 90 cigarettes a day – a habit he developed after taking up smoking at the tender age of nine. "I was officially allowed to smoke when I was 13. And I smoked heavily for 33 years." After several bouts of pneumonia Ernie faced increasing shortness of breath. It was during one of these bouts that he decided to see how long he could go without a cigarette. It was only after his third smoke free day that he realised he might win the battle – but his lungs were at war.

"I had worked in a foundry where there was dust and black sand everywhere. I won't blame anyone though – I should have known it was a good idea to cover my mouth and nose when I was working. But you don't think of those things at the time – you didn't see anyone else doing it back then so you didn't worry," he said.

Ernie now uses oxygen on a daily basis to help not only his breathing but the saturation of oxygen in his blood cells which is often low in emphysema sufferers. The disease also puts a strain on the heart as it works harder to pump blood through damaged and inflexible airways. "I started oxygen therapy in 2013. I use it sparingly but when I am out in the garden or doing something active I need it more," he said.

It was during one of his six monthly reviews at TQEH that he was told of the research study which is looking at a more portable oxygen device and signed on to help test the new system. Research Assistant Harshani Jayasinghe from the Clinical Practice Unit (Respiratory Medicine) at TQEH has been in constant contact with Ernie during his trial.

"It's great to have people like Ernie so willing to give up their time to be part of the study and give us invaluable feedback on new devices like the portable oxygen concentrator."

"Without help like this we just couldn't make the advancements that we are making to improve people's health through medical research," Harshani said.

Ernie believes he should give back when and where he can. "I haven't had the best of health – I've already had one heart attack and a frontal lobe stroke which has slowed me down significantly – but it has made me incredibly appreciative of the care I've been given over many years," he said.

This isn't the first time Ernie has been involved in a clinical trial. "I let the researchers come and take fat from under my stomach so they could test it after my heart attack. I can't be a blood donor because of my medication but both my children are donors. They like to give back as well. It's true though, from my heart I do like to help others where I can. If it helps one person then I'm happy and I've done something positive."

As Ernie approaches the end of the trial he has already formed his opinion of the new device - and it's not for him. "I found it a bit heavy really. It would be better for younger people and definitely not for those with a bad back."

Harshani will soon check back with Ernie to gather his final questionnaire from the study. "We didn't actually know how people would respond to the portable oxygen concentrator –we are gathering data on what people prefer and what we can do to improve oxygen delivery," she said.

"It's good to get such honest feedback like Ernie's. We want to know what our patients are experiencing, what difficulties they have and ask them for their ideas on how we might improve things. It's all good feedback and it will all be used to streamline better treatments."

Ernie wants to encourage as many people as he can to get involved when they can. "If we get everyone doing their bit for medical research then we really are giving back to the people who care for us when we need it most."

"If we get everyone doing their bit for medical research then we really are giving back to the people who care for us when we need it most."

Respiratory Medicine Unit and Clinical Practice Unit

The Respiratory Medicine and Clinical Practice Units conduct evidence based medicine evaluations with the primary aim of research translation. Our emphasis is on best-practice clinical care for Chronic Obstructive Pulmonary Disease (COPD), asthma, bronchiectasis, pneumothorax, sleep apnoea, tobacco-related illnesses and indigenous respiratory health. The research being done by our units directly impact the clinical care received by patients attending public hospitals in South Australia, as well as nationally and internationally.

Research Focus

- Innovative forms of portable oxygen delivery (POC study)
- Pharmacotherapy for anxiety and depression in patients with COPD (PAC study)
- Best Practice/medication/counselling combination intervention for inpatient smoking cessation (STOP study)
- Nicotine receptor up-regulation with transdermal nicotine patches (NRT study)
- Production of electronic evidence based guidelines for COPD management (ACCORD)
- Evidence based medicine research (Cochrane meta-analyses)
- Aboriginal health research
- Clinical evaluation of new techniques to assess gas exchange in the Hypoxic Altitude Simulation Test
- Evidence based management of spontaneous pneumothorax (SP)
- Nurse-led evidence based management evaluations for the treatment of bronchiectasis and COPD
- Mandatory reporting of sleep apnoea
- New treatment options for malignant pleural effusions
- Evaluation of pseudomonas eradication options for bronchiectasis
- Evaluating lung volume measurements to optimise standard practice

Population Data

- 6.3 million Australians were diagnosed with a **chronic respiratory condition** in 2012. Of these, 2.3 million were diagnosed with **asthma**
- **Chronic obstructive pulmonary disease (COPD)** is expected to be the 3rd leading cause of death by 2020
- 15.8% of COPD patients are estimated to experience an anxiety disorder, which is higher than levels of anxiety experienced by people with heart disease or cancer
- **Smoking** was estimated to cause the death of 15,000 Australians in 2014 at a cost of \$31.5 billion in social and economic expenditure
- 13.3% of all Australians aged over 18 years used tobacco in 2013, while tobacco use amongst adult Indigenous Australians was 41% soaring to up to 90% of adults living in Central Australia
- People with **sleep apnoea** have a 7-fold higher risk of heart disease and death regardless of severity of the disease, their age, or history of heart problems
- Increased risk of heart disease and death in people with sleep apnoea is eliminated with correct treatment
- SA and NT are the only regions in Australia that enforce mandatory reporting of health conditions such as sleep apnoea by a doctor

Overview

Portable Oxygen Concentrators (POC) Study: An evaluation comparing portable oxygen concentrators and regular oxygen cylinders across five Adelaide hospitals using a randomised, controlled cross-over design is nearing completion, to determine the efficacy and effectiveness of oxygen delivery for patients with COPD. Four abstracts based on this work were submitted for presentation at the Thoracic Society of Australia and New Zealand conference in 2014 with one being awarded equal 'Best oral presentation for the COPD Special Interest Group' out of over 80 presentations, for an economic assessment.

Role of paroxetine in treatment of anxiety and or depression in COPD patients (PAC Study): This multi-centre randomised controlled trial (RCT) is underway across five Adelaide hospitals. A total of 100 subjects are required for the study and one quarter of subjects have been recruited to date, with a follow-up of 12-months. This trial aims to determine the efficacy and safety of paroxetine for: anxiety and depression, quality of life, exercise capacity, respiratory function, and hospital utilisation and cost effectiveness of the intervention. It is also being used as part of a PhD project for a student with the University of Adelaide.

STOP Study: Long-term 24-month follow-up, cost effectiveness and smoking relapse triggers are currently being evaluated for a multi-centre randomised controlled STOP smoking trial comparing the latest smoking-cessation medication (varenicline tartrate) plus best practice counselling to best practice counselling-alone.

Nicotine Receptor trial (NRT Study): In 2014 we completed a pilot evaluation of nicotine receptor up-regulation activity through metabolic induction, changes in responsiveness and surrogate evaluation methods (NRT study). Primary analysis of this work is currently underway with an oral presentation already scheduled for the 2015 TSANZ conference in April on the Gold Coast.

Aboriginal Health: A number of Registrars, Advanced Trainees, Research Officers, Medical Students and Consultants have undergone training workshops for The Cochrane Collaboration to undertake systematic reviews in specialised areas of Respiratory Medicine, Tobacco and chronic disease management. Thirty one reviews are being conducted under the supervision of Professor Brian Smith with collaborations in the United Kingdom, Ireland, Netherlands, Scotland, New Zealand, United States of America and Iran. A number of projects including qualitative focus groups and one-on-one interviews are being undertaken with the aim of improving the health of Aboriginal Australians. These studies, developed in collaboration with Aboriginal Elders, researchers, policy-makers, healthcare workers and key community-stakeholders, are

designed to provide information from the 'grass-roots' level to identify the barriers and enablers in current practice and highlight evidence gaps. Areas of particular interest include: smoking cessation pharmacotherapies, smoking cessation during pregnancy, tobacco prevention initiatives for youth, Doctor and healthcare visits, research conducted with Aboriginal participants and the role of depression on psychological and health outcomes. To date this work has resulted in wide-spread media coverage including an article in The Australian and NT News, over a dozen radio interviews broadcast across Australia and over 50 online media news articles. This work is also being used as the foundation for three PhD students with the University of Adelaide.

Hypoxic Altitude Simulation Test (HAST Study):

A comparison of Arterial Blood Sampling (ABG) and transcutaneous monitoring used to measure arterial oxygen and carbon dioxide tensions is underway to assess gas exchange during the Hypoxic Altitude Simulation Test (HAST). This study, led by principal scientist Dr Mark Jurisevic has the potential to validate a non-invasive alternative to ABG sampling for clinical HAST studies.

Management of Spontaneous Pneumothorax:

Currently, treatment options for spontaneous pneumothorax (SP) vary depending on classification, presence of symptoms and severity of respiratory distress. However, despite the availability of evidence based clinical guidelines, the management of patients with SP remains largely varied across hospitals, with low compliance to published guidelines. For these reasons we are undertaking a retrospective analysis of patients presenting with SP across multiple Adelaide hospitals over a five year period to: evaluate the effectiveness of treatment options, compare existing practice across hospitals and to existing British Thoracic Society guidelines and to examine the clinical outcomes and cost-effectiveness of each intervention.

Treatment evaluation: bronchiectasis and COPD: Respiratory nurses Karen Royals and Kathy Lawton are conducting several retrospective evaluations comparing hospital records to published best-practice guidelines for the nurse-led management of bronchiectasis and COPD. A Cochrane review of Nurse Specialist care for bronchiectasis is also nearing completion as is another for Home care outreach nursing in COPD. These studies are also being used for their Master's degrees with the University of Adelaide.

Sleep Apnoea reporting: Senior sleep technician Nathan Elgar is continuing to conduct an evaluation of SA's mandatory reporting legislation which requires doctors to report patients potentially unsafe to drive. This has involved surveys of the general population, a clinical patient population and most recently of doctors and their interpretation of and compliance with the legislation.

The Respiratory Research Unit continues to evaluate a range of new medications for COPD, Asthma, IPF and Bronchiectasis led by Dr Antony Veale, Dr Zafar Usmani and Dr Jien Ni Cheng.

Staff

Director (Professor)

BJ Smith FRACP Dip Clin Epi PhD

Senior Consultants

D Grosser FRACP

S Lehmann FRACP

I Nikitins FRACP

J Polasek FRACP

A Roy FRACP

Z Usmani FRACP

A Veale PhD FRACP

Advanced Trainees

J Cheng

KV Tee

Principal Medical Scientist

M Jurisevic PhD

Senior Research Scientist (Clinical Practice Unit)

K Carson Cert III Lab Skills; Dip Lab Med

Clinical Practice Unit researchers

M Brinn BHLthSc (Life Sc) Flinders BHLthSc (Anat Hons)

H Jayasinghe BSc (BioS), BHLthSc (Hons)

Clinical Trials Unit Coordinator

K Boath Mgt Cert Adv Cert BHLthSc

Research Nurse

P Gluyas RN RM CC Cert

Pulmonary Function Laboratory

D Cotsaris BSc

K Dharmabandu BSc

X Hui Liu BSc

D Keatley BSc (Biomed) (Hons)

P Kidd BSc

Sleep Laboratory

E Besley BSc

M Bradford BSc

V Coe BSc

N Elgar BSc (Hons) BTh

T Faulkner BPsych (Hons)

D Hooper BSc

T Jones (Admin)

M Shaw BSc

M Smith BSc

A Teare BSc

Sleep Laboratory Nurses

J Byerly RN, BAN

H Dinh RN, BAN

K Musimbi RN, BAN

V Foote RN, BAN

Respiratory Nurses

L Kotal RN BAN RM CC Cert Post Grad Dip Health Counselling

K Lawton RN, BAN, Grad Dip Chronic Condition Management, Grad Cert Asthma Edu

M Peskett RN, BAN

K Royals RN, BAN, Grad Cert Chronic Condition Management

M Munro RN, BAN

Bronchoscopy Unit Supervisor

N Harrop RN, BAN

Unit Pharmacist

T Jones B Pharm Dip Ed PhD

Secretarial Supervisor

R McCawley

Secretarial

C Gilbert

M Ashley

C Deegan

Postgraduate Students

PhD candidates

K Carson Cert III Lab Skills; Dip Lab Med

‘Tobacco cessation and prevention for Indigenous populations’

Supervisors: Smith B, Clifton V, Gould G

Z Usmani MBBS, FRACP

‘Treatment of anxiety in patients with chronic obstructive pulmonary disease’

Supervisors: Smith B, Clifton V, Gould G

H Jayasinghe B.Sc (BioS), B.Hlth.Sc (Hons)

‘Advancing the understanding of tobacco use, prevention, and cessation and related illnesses caused by smoking during pregnancy in Indigenous populations’

Supervisors: Smith B, Clifton V, Gould G

Masters candidates

K Royals RN

‘Outreach respiratory nursing in the management of Chronic Obstructive Pulmonary Disease (COPD)’

Supervisors: Smith B

K Lawton BAN

‘Management of Bronchiectasis: A Tertiary Healthcare Perspective’

Supervisors: Smith B

P Kidd BSc

‘Comparing lung volume measurements: Whole-body plethysmography ‘panting’, ‘tidal breathing’ technique and single breath helium dilution washout’

Supervisor: Smith B

Grants

NHMRC (Centre for Research Excellence) Australasian Satellite of the Cochrane Airways Group (\$69,000 2014) 2013-2016, Walters J, Walters H, Holland A, Yang I, Gibson P, Smith BJ.

Australian and New Zealand School of Government.
Interventions for smoking cessation and prevention in Indigenous populations (\$10,000) 2013-2015, Carson KV, Peters M, Esterman AJ, Veale A, Smith BJ.

Grants commencing 2015

NHMRC. (Translating Research In to Practice (TRIP) Fellowship) (\$172,911), 2015-2016, Carson KV, Smith BJ.

Cancer Australia Co-funding for NHMRC TRIP Fellowship (\$100,000), 2015-2016, Carson KV, Smith BJ.

Awards

H Jayasinghe

TQEH, Research Day 2014, Best Oral Presentation in Clinical Group 2

TSANZ Travel Award to attend TSANZ 2015 conference on the Gold Coast

K Royals & K Lawton

TSANZ Best Poster Prize for the Nursing Special Interest Group at the 2014 Annual Scientific Meeting

M Jurisevic

Equal first place for 'The best COPD presentation' for the TSANZ COPD Special Interest Group at the 2014 Annual Scientific Meeting

M Brinn

TSANZ Travel Award to attend TZANZ 2015 conference on the Gold Coast

K Carson

Young Australian of the Year for South Australia

National finalist for Young Australian of the Year

Premier's and Channel 9 Young Achiever of the Year

University of Adelaide Faculty of Sciences, Science and Technology Award

Young Citizen of the Year for the City of Holdfast Bay Council

TSANZ Janet Elder International Travel Award to attend an international conference in 2014

TSANZ Travel Award to attend TZANZ 2015 conference on the Gold Coast

Clinical Trials

Dr Antony Veale, Dr Zafar Usmani and Dr Jien Ni Cheng

Boehringer Ingelheim: Roll over study for those subjects participating in the Idiopathic Pulmonary Fibrosis (IPF) study designed to evaluate efficacy of a new medication to prevent scarring of lungs and disease progression in subjects with Idiopathic Pulmonary Fibrosis; Revenue: \$594.00; Status: Study complete.

Intermune Inc: Study designed to compare the efficacy of Pirfenidone compared with placebo and effect on FVC in patients with idiopathic Pulmonary Fibrosis; Revenue: \$11,253; Status: Study complete.

Intermune Inc: Roll Over Study where patients receive open label Pirfenidone after completing the double-blind study above; Revenue: \$4,592; Status: Study complete.

Medimmune: A randomised IPF study to evaluate the efficacy of Tralokinumab in adults with Idiopathic Pulmonary Fibrosis; Revenue: \$29,400; Status: Study ongoing.

Bayer: Randomised study comparing inhaled ciprofloxacin administered 14 days on/14 days off versus 28 days on/28 days off versus placebo to evaluate time to first pulmonary exacerbation in subjects with non-cystic fibrosis bronchiectasis; Revenue: \$57,638; Status: Study ongoing.

Boehringer Ingelheim: Randomised study to assess the efficacy and safety of 12 weeks of once daily treatment of two doses of inhaled tiotropium and olodaterol fixed combination in subjects with moderate to severe COPD; Revenue: \$26,070; Status: Study complete.

Collaborations

Local

Home care outreach nursing for COPD:

The University of Adelaide, The University of South Australia, The Royal Adelaide Hospital

Anticoagulants for idiopathic pulmonary fibrosis:

The University of Adelaide, The University of South Australia, The Royal Adelaide Hospital

Mandibular advancement for Obstructive Sleep Apnoea:

Repatriation General Hospital, Flinders Medical Centre, The University of Adelaide, The University of South Australia

National

NRT study: Therapeutics Research Group TQEH, Department of Medicine, The University of Adelaide, Hanson Institute, The University of Queensland

ACAGN (Australian Cochrane Airways Group Network):

University of Tasmania, University of Newcastle, Menzies Institute, The University of Queensland, La Trobe University, Monash University

Indigenous Respiratory health: The Thoracic Society of Australia and New Zealand, Concord Hospital, The University of Sydney, The University of Western Australia, The University of Adelaide, The University of South Australia, James Cook University, Menzies School of Health Research, Aboriginal Health Council of South Australia, Murray Mallee Community Health Service, Cancer Australia, Smokers Clinic Brain Mind and Research Institute, Australian and New Zealand School of Government, NSW Health (North Coast Area Health Service), Community participants from Adelaide and Murray Bridge

Asthma self-management education: Repatriation General Hospital, University of Tasmania, The University of Adelaide, The University of South Australia, Joanna Briggs Institute, Flinders University

Lung volume reduction surgery for diffuse emphysema: John Hunter Hospital, The University of Newcastle, Repatriation General Hospital, The University of Adelaide, The University of South Australia

Consumer guidelines for chronic disease management:

The University of Adelaide, The University of South Australia, Concord Hospital, The University of Sydney, University of Tasmania

Gastro-oesophageal reflux treatment for asthma in adults and children: Flinders Medical Centre, The University of Adelaide, Alice Springs Hospital

International

Electronic best practice guidelines for the management of COPD:

Evidentia Publishing, The Netherlands, SA Health, The University of Adelaide, The University of South Australia

Indigenous tobacco cessation in adults and prevention amongst youth:

James Cook University, The University of Adelaide, The University of South Australia, Menzies School of Health Research, Robinson Institute, Aboriginal Health Council of South Australia; Community participants from Adelaide and Murray Bridge, University of Ottawa Heart Institute, Canada

Community and mass media interventions to prevent smoking in youth:

Tehran University, Iran; Menzies Institute, University of Adelaide, The University of South Australia, University of Ottawa Heart Institute Canada

Community pharmacy interventions for smoking cessation:

The University of Aberdeen, UK, The University of South Australia, The University of Adelaide, Oxford University, UK

CPAP for obstructive sleep apnoea:

St George's Hospital, UK, The Cochrane Collaboration, UK, York District Hospital, UK; Bradford Royal Infirmary, UK, The University of Adelaide, The University of South Australia

Non-invasive ventilation for COPD and asthma:

Monash University, Austin Hospital (Victoria, Australia), University of Southampton, UK, St James University Hospital, Leeds, UK, Royal Free and University College Medical School, London, UK, Katholieke Universiteit Leuven, Leuven, Belgium

Pharmacological interventions for the treatment of depression in COPD:

The University of Adelaide, The University of South Australia, Newcastle Upon Tyne NHS Foundation Trust, Newcastle Upon Tyne, UK, Newcastle University, Newcastle, UK

Nurse specialist care for bronchiectasis:

University of Sheffield, Sheffield, UK, The University of Adelaide, The University of South Australia

Prolonged antibiotics for purulent bronchiectasis:

Hemel Hempstead Hospital, Hemel Hempstead, UK, Castle Hill Hospital, Cottingham, UK, Flinders Medical Centre, The University of Adelaide, The University of South Australia

Psychological interventions for the treatment of anxiety in COPD:

Newcastle upon Tyne NHS Hospitals Foundation Trust, Newcastle upon Tyne, UK, Newcastle University, Newcastle, UK; The University of Adelaide, The University of South Australia

Psychological interventions for the treatment of depression in COPD:

The University of Adelaide, The University of South Australia, Newcastle Upon Tyne NHS Foundation Trust, Newcastle Upon Tyne, UK, Newcastle University, Newcastle, UK

Simple aspiration versus intercostal tube drainage in primary pneumothorax:

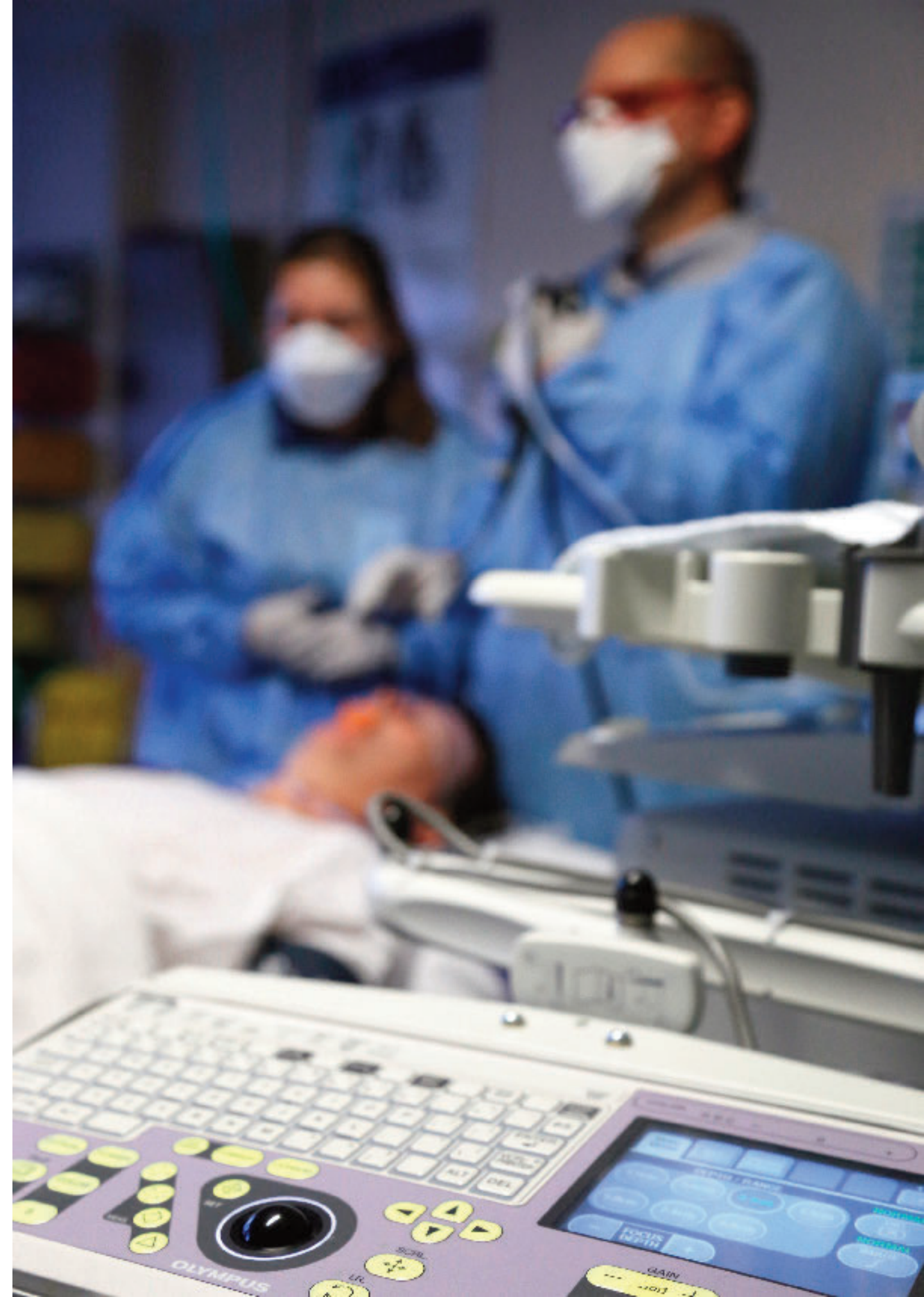
Royal College of Surgeons in Ireland, Dublin, Ireland, Our Lady's Children's Hospital Crumlin, Dublin, Ireland, Cork University Hospital, Cork, Ireland, The University of Adelaide, The University of South Australia

Training health professionals in smoking cessation:

Leiden University Medical Centre, Leiden, Netherlands, Radboud University Nijmegen Medical Centre, Nijmegen, Netherlands, The University of Adelaide, The University of South Australia

STOP study:

Royal Adelaide Hospital, Lyell McEwin Hospital, The University of Adelaide, The University of South Australia, The Cancer Council of South Australia, Flinders University, University of Sydney, University of Melbourne, Concord Repatriation General Hospital, The University of Melbourne, University of Ottawa Heart Institute Canada



Rheumatoid Arthritis no longer a handicap



Duncan's Story

When Largs North resident Duncan Low doubled over in agony while playing a shot on the golf course, he knew he couldn't push through the pain any longer. It had been a year since he'd been diagnosed with Rheumatoid Arthritis, which had been getting progressively worse as the days went by.

Rheumatoid Arthritis (RA) is a chronic disease that affects around 438,000 Australians, making it the most common autoimmune disease in Australia. It can cause joint damage, early disability and even premature mortality. For sufferers like Duncan it has a significant impact on their quality of life.

"My GP was extremely surprised when my blood tests came back showing Rheumatoid Arthritis back in 2011," recalled Duncan.

"The pain was mainly in my left wrist and it had been continually getting worse. Eventually it was at a point where I was barely doing any of the physical things I used to do; hardly any cleaning, no gardening. When my granddaughter would visit and run up to greet me, I couldn't lift her up for a big hug anymore; it was that sore and my arm was that weak."

"I was really miserable, right down I tell you." In early 2013, Duncan was referred to the Rheumatology Unit at The Queen Elizabeth Hospital (TQEH) which is directed by Associate Professor Maureen Rischmueller. Under her skilled leadership, the Rheumatology Department at TQEH has been nationally recognised as a site for best practice therapies of Rheumatic disorders and is one of the three largest Rheumatology Clinical Trial Centres in Australia.

Fortunately for Duncan, he was eligible to take part in a multi-centre international trial for a RA therapy which is currently underway at TQEH. The trial is focused on evaluating the safety and effectiveness of a combination of two drugs for people suffering early stage RA.

Within a matter of days of commencing the trial, Duncan's pain had significantly lessened, and within a week, he was back on the golf course.

"I'm really not exaggerating, that's how quick the improvement was!" said Duncan.

"It was amazing."

Associate Professor Rischmueller said one of the aims of the study is to highlight the beneficial impact of treating RA patients with this drug combination early on in their disease. Importantly, the other aim is to determine if the need for ongoing long-term therapy with the medication can be reduced through earlier treatment.

"Currently, people are only eligible for this combination therapy once their RA is significantly debilitating – they must display swelling in at least 20 joints, with raised inflammatory markers in the bloodstream. But the problem is that for many patients the damage is already done by this point, and treatment with these expensive agents is required for life" said Associate Professor Rischmueller.

By stopping the disease in its tracks early in the disease process, researchers are hopeful permanent damage to joints will be avoided and the RA will be able to be managed over the longer term by less expensive medications.

"We hope this study will illustrate that if we can prescribe this therapy to people with early symptoms of RA, the chances of full recovery are much greater. The negative impact on people's lives will be much less, as will the impact on the health system."

"Ultimately, we need the government to subsidise the treatment for early sufferers."

Duncan has been extremely grateful for the opportunity to participate in the trial. "It feels good to be a part of a trial like this – obviously because it's helped me but these trials are the only way we are going to find out these things for future people too," said Duncan.

"Everyone at TQEH has been fantastic. They make you feel relaxed and you know you can ask any questions, you don't feel silly. I can't praise them high enough."

Duncan completed the trial in January 2015, however to his delight the sponsor company granted compassionate supply of the medication for him on an ongoing basis.

"I feel so happy and really relieved that I'm back to my normal self. Well, my golf handicap is still rubbish really, but at least I'm back playing!"

"I'm really not exaggerating, that's how quick the improvement was!" said Duncan. "It was amazing."

Rheumatology Unit

Rheumatological diseases affect a large sector of the population and lead to chronic pain, disability, reduced quality of life, and in many cases, shortened life span. The monetary costs are huge with respect to lost earnings, as well as direct health care costs. The Rheumatology Unit strives to augment its clinical rheumatology services with research programs into the epidemiology, causation and complications of rheumatic diseases (“bedside to bench”), coupled with the evaluation of new generations of pharmaceutical agents for the treatment of arthritis (“bench to bedside”). These rheumatic diseases include Sjögren’s syndrome, giant cell arteritis, osteoarthritis, scleroderma, rheumatoid arthritis, ankylosing spondylitis, gout, and fibromyalgia.



Overview

Disability associated with musculoskeletal diseases is universal across both developing and developed countries. The Global Burden of Disease Study 2010, which utilised data from North West Adelaide Health Study (NWAHS) participants, concluded that “Global disease burden has continued to shift away from communicable to non-communicable diseases and from premature death to years lived with disability... The rising burden from mental and behavioural disorders, musculoskeletal disorders, and diabetes will impose new challenges on health systems...”

Population Data

- > **Musculoskeletal conditions** are the most common chronic conditions in Australia
- > 28% of Australians are estimated to have arthritis and other musculoskeletal conditions
- > The estimated health care expenditure on musculoskeletal conditions in 2008-2009 was \$5.7 billion

Research Focus

- Autoimmunity
- Epidemiology of musculoskeletal disorders
- Evidence based medicine
- Immunogenetics
- Inflammation
- Osteoarthritis
- Giant Cell Arteritis
- Fibromyalgia
- Pain
- Therapeutics

Associate Professor Maureen Rischmueller leads one of the three largest rheumatology clinical trial units in Australia, and is a principal investigator on clinical trials for patients with a wide range of rheumatological diseases, including rheumatoid arthritis (RA), psoriatic arthritis, ankylosing spondylitis, gout, scleroderma and osteoarthritis. In her current laboratory-based research projects, In collaboration with Rheumatology Medical Scientist Sue Lester she is leading a program of investigation into how people have a tendency to inherit autoimmune rheumatic diseases such as Sjögren's syndrome, lupus, scleroderma and rheumatoid arthritis, and how genes affect the pattern and severity of these diseases in patients. Other research interests include auto-antibodies: their genetic and clinical associations and inflammatory mechanisms.

Associate Professor Catherine Hill is a clinical rheumatologist and epidemiologist with research expertise in osteoarthritis, randomised clinical trials, vasculitis and population epidemiology. As Chief Investigator of the North West Adelaide Health Study (NWAHS), Associate Professor Hill was instrumental in adding the musculoskeletal data collection to this study in 2004. Work from this study has been published as part of the Global Burden of Disease study published in the Lancet (December 2012), which identified musculoskeletal diseases as one of the three most important diseases in terms of global disease burden. Associate Professor Hill previously led a multi-centre NHMRC funded project grant to study the effects of fish oil supplementation on symptoms and structural progression over two years in knee osteoarthritis in a multi-centre Randomised Controlled Trial (RCT). Subsequent collaborations have resulted in two current NHMRC-funded multi-centre Osteoarthritis trials into the role of statins and zoledronic acid in knee Osteoarthritis. Associate Professor Hill's most recent research interest is in Giant Cell Arteritis, the most common vasculitis in the elderly that can lead to blindness and stroke. She established the South Australian Giant Cell Arteritis Registry in 2009 which has resulted in further knowledge about this condition in Australia for the first time. It has also resulted in both national and international collaborations. She is involved in OMERACT (Outcome Measures in Rheumatology) which is an independent initiative of international health professionals interested in outcome measures in rheumatology. At this year's meeting, she co-chaired a SIG on remission in RA and will be involved at the next OMERACT in the areas of PMR and corticosteroid adverse events.

Dr Simon Burnet is the Medical Director, Vice President and board member of Arthritis SA. This organisation is the peak body for providing education, support and advocacy for people with rheumatic disorders in South Australia. Dr Burnet is active in the educational program of Arthritis SA which conduct multiple update and refresher courses for General Practitioners and Allied Health Professionals throughout the year. He also conducts multiple country rheumatology clinics and has spoken to the registrars and at the Annual Meeting of the Rural Doctors Workforce Agency.

Dr Samuel Whittle is undertaking research concerning fibromyalgia syndrome and chronic musculoskeletal pain, spondyloarthritis and gout. Dr Whittle is a co-founder and member of the steering committee of the Australia & New Zealand Musculoskeletal Clinical Trials Network (ANZMUSC) and is a member of the Arthritis SA Health Services, Advocacy and Research Committee. He is the convenor of the 2015 Australian Rheumatology Association Annual Scientific Meeting.

Staff

Director/Senior Lecturer

M Rischmueller MBBS FRACP

Staff Consultant Rheumatologists

C Hill MBBS MSc (Epi) FRACP

S Whittle MBBS MCLinEpi FRACP

S Burnet MBBS FRACP

F Cai MBBS

Registrar

K Ting

Rheumatology Research Administration Coordinator

S Downie-Doyle BSc(Hons) PhD

Rheumatology Clinical Research Team

S Downie-Doyle PhD – Administrator

C Schultz PhD – Clinical Trial Coordinator

L Wedding – Rheumatology Infusion Nurse

H Vanderhaak – Rheumatology Research Nurse

A Cayzer – Rheumatology Clinical Trials Nurse

S White – Rheumatology Clinical Trials Nurse

J Marrett – Clinical Trial Assistant

Chief Medical Scientist

S Lester BSc(Hons)

Research Assistants

M Bubicich BSc(Hon) – Research Assistant

M Bosco – Research/Clinical Trial Assistant

Secretary

M Devine

Postgraduate Students

PhD candidate

Dr Rachel Black MBBS, Affiliate Rheumatologist:

'Epidemiology of Glucocorticoid Use and Steroid Eye Disease in patients with rheumatoid arthritis'

Supervisor: Hill C

Masters in Biotechnology candidate

Ho Yin Lau BSc Biomedical Science

'Inflammasome priming in salivary gland epithelial cells – a disease model for primary Sjögren's syndrome'

Supervisors: Lester S, Zalewski P, Rischmueller M

Grants

NHMRC. (Project grant #1048581) Does statin use have a disease modifying effect in symptomatic knee osteoarthritis? A multi-centre randomised, double-blind, placebo-controlled trial. (\$323,670 2014) 2013-2015, Wang Y, Cicuttini F, Tonkin A, Hill C, Ding C.

NHMRC. (Project grant #1045415) A randomised trial of zoledronic acid for osteoarthritis of the knee. (\$318,199 2014) 2013-2015, Jones G, Cicuttini F, March L, Hill C, Dore D.

NHMRC. (Project grant #1068023) Dissecting the great ophthalmic masquerade: The Global Giant Cell Arteritis Genomics Consortium. (\$189,976 2014) 2014-2016, Hewitt A, Hill CL, Evans D, Merriman T, Morgan A, Smith K, McKelvie P, Martin J.

Grants commencing in 2015

Arthritis Australia. (Small grant) Developing a patient reported outcome measure in polymyalgia rheumatic. Hoon E, Hill C, Gill T. (\$10,684 for 1 year).

Acknowledgements

The Rheumatology Department acknowledges The Hospital Research Foundation for past (Centre for Inflammatory Diseases Research) and current (The Health Observatory) funding, which is continuing to bear fruit in relation to both collaborations and publications.

We also wish to acknowledge the patients who have willingly contributed their time, and samples, to our clinical research projects.

Collaborations

Associate Professor Maureen Rischmueller has an on-going collaboration with Dr Fabien Vincent and Professor Fabienne Mackay (Immunology department, B lymphocyte, BAFF and Autoimmunity Laboratory, Alfred Medical Research and Education Precinct) and Professor Eric Morand (Head of the Lupus Clinic at Southern Health/Monash Medical centre) to investigate, and compare, the role of TACI variants in Sjögren's syndrome and systemic lupus erythematosus phenotypes, B cell subsets and type I interferon expression in plasmacytoid dendritic cells.

Associate Professor Rischmueller and Sue Lester have on-going international collaborations with both SGENE and SLEGEN which are international consortia to research genetic associations with Sjögren's syndrome and systemic lupus erythematosus respectively. SGENE has already published the first genome wide association study for Sjögren's syndrome (Nature Genetics, November 2012) and patient recruitment is ongoing with the aim of studying the genetics of lymphoma risk. In 2014, SGENE and SLEGEN have combined to publish finer mapping of the associations for the IRF5-TNIP3 region, a common susceptibility region for both diseases.

Associate Professor Rischmueller, Associate Professor Hill and Sue Lester have an on-going collaboration with the Australasian Genomics Recruitment Initiative in Australasia (AGRIA), which is collecting samples from Australia and New Zealand for genetic studies of Giant Cell Arteritis, gout and ankylosing spondylitis, with Sjögren's syndrome to be added in 2015. The Giant Cell Arteritis component is funded by a current NHMRC grant. This has an international collaboration with Prof Ann Morgan (Leeds), Tony Merriman (Otago) and Javier Martin (Spain).

Associate Professor Rischmueller, Associate Professor Hill and Sue Lester are collaborators with the Australian Scleroderma Interest Group (ASIG) which currently consists of a clinical database of over 1500 patients and a biobank, which is housed at the Basil Hetzel Institute. An Immunochip genome wide association study for this cohort was published in 2014 which identified several novel associations.

Associate Professor Hill has ongoing collaboration with Associate Professor Sarah Mackie to further research into polymyalgia rheumatic and giant cell arteritis. Together, they have undertaken to chair two SIGs at OMERACT (Outcome measures in rheumatology; an international collaboration to further outcome measure development in rheumatology). These will include polymyalgia rheumatica and glucocorticoid adverse effects.

Associate Professor Hill has ongoing collaborations in investigator-led osteoarthritis studies with Professor Graeme Jones (Menzies, Tasmania), Prof Flavia Cicuttini (Monash) and Professor Lyn March (Uni Sydney). This includes 2 current NHMRC-funded randomised clinical trials.

Associate Professor Hill has ongoing collaborations with Professor Hylton Menz (La Trobe) and Professor Marian Hannan (Boston) in the epidemiology of foot pain.



Opening up the vein of life

Steve's Story



A sudden onset of cramping pain in his right leg stopped Steve Curnow in his tracks. Now, some months later he realises the seriousness of the event and how expert medical intervention helped get him back on his feet.

In November 2014, 59 year old Steve was in Whyalla pouring concrete when he experienced an excruciating pain in his right calf. In hindsight he thinks he should have stopped but he kept working through the pain. A number of hours later and still in pain he contacted his physiotherapist for treatment.

"I thought I'd just pulled a ligament or something like that. By that stage my right foot was getting cold. I was getting tingles and it was becoming numb in places," Steve said.

By the time he saw his physiotherapist in his home town of Stansbury, Steve was not alone thinking there was a serious problem with his right leg. "She was very worried about the circulation – or lack of circulation. I was then off to see my GP who referred me directly to The Queen Elizabeth Hospital and Professor Rob Fitridge," Steve said.

"It was a bit of an emergency actually with the Royal Flying Doctor Service taking me to Adelaide. My GP couldn't get a pulse in my foot so there wasn't much blood flow." Steve was diagnosed with acute occlusion of his leg artery, secondary to peripheral vascular disease, a condition where plaque build-up in the blood vessels reduces blood flow to the leg and may result in a sudden blockage of blood flow to the calf and foot. In severe cases it can lead to loss of the leg.

Steve was in hospital for three and a half days receiving treatment including a blood thinning medication. He was then started on warfarin to try to break down the clot in his right leg.

"They didn't want to operate. The decision was made to clear the blockage by conservative means rather than surgery – but it was always an option if the blood flow to my foot didn't improve," Steve said.

Looking back Steve wonders if an injury he sustained to his right leg a week or so before this incident may have contributed. "I was riding my motorbike and gave myself a good kicking in the shin – it was the same leg and it was very heavily bruised. I did notice at that time my foot was a bit cold but I still didn't think much of it – until now."

Steve was also put on a trial of a new therapy for peripheral vascular disease called Ramipril which helped with the pain in his legs. "When I first came home from hospital I would wake at night and it would be like someone had poured boiling water over my foot. It was incredibly painful, but that is happening less now," he said.

"I still have one good sized clot just below the knee – which Professor Fitridge said is like a block of concrete, but it is resolving."

Steve says he has slowed down a bit – walking too far still causes his calf muscle to go into painful spasm. "I have been incredibly lucky. I can do most things but I self-regulate – if it hurts I stop," said Steve.

"I'm so grateful for the expert medical care I have received here at the hospital. I am very fortunate that the vascular team was able to manage this conservatively rather than have to have surgery".

Steve didn't like the thought of having bypass surgery on his leg but if his condition hadn't improved it was the most likely scenario. He now reflects on what has happened to him - how quickly he received the medical assessment and emergency treatment that saved his leg.

"I hate to think what would have happened to me if I hadn't had this level of care and attention," he said.

Mr Curnow has now signed on to be part of an international clinical study for people with peripheral vascular disease to evaluate clinical features of their condition and quality of life.

The Queen Elizabeth Hospital is one of the coordinating centres of the study which also includes the Mid-American Heart Institute in Kansas City and Tilburg University in the Netherlands.

"I'm so grateful for the expert medical care I have received here at the hospital".

Surgery

The Discipline of Surgery has continued to conduct research into a number of key areas based on the clinical load and the expertise of staff currently working at The Queen Elizabeth Hospital site.

In particular, work on upper gastrointestinal malignancies such as pancreatic and gastric cancer has been conducted at a clinical level. Hepatic resection for colorectal cancer and hepatocellular cancer has also been consolidated with a number of epidemiological overviews being performed.

Within the area of colorectal cancer, trials have continued on aspects of anastomotic integrity and long-term follow up as well as the follow up of disseminated colorectal cancers within South Australia, leading to a number of important publications in collaboration with other surgical and oncological centres in South Australia.

Vascular surgery continues to make important contributions to the understanding of the aetiological factors behind the development of abdominal aortic aneurysm disease and sees the conclusion of a most successful National Health and Medical Research Council (NHMRC) research grant.

Within breast surgery, successful support from the NHMRC has led to innovative breast nurse support services being introduced within South Australia and used as a pilot for national adoption.

Within the Virology Group, based at the Basil Hetzel Institute, some important publications have emerged during the year and this group of outstanding researchers, headed by Professor Eric Gowans, continues to make important contributions into this extremely challenging but absolutely vital area of research.

Research Focus

- Early breast cancer
- Metastatic breast disease
- Functional sinus disease
- Liver function in surgical disease
- Audit of surgical mortality in Australia
- Endovascular surgery
- Outcome predictors
- Surgical simulation
- Surgical technology assessment

Population Data

> **Breast cancer** is the 2nd leading cause of cancer death in Australian women (15.5% of all cancer deaths in Australian women)

> 1 in 8 Australian women will be diagnosed with breast cancer before they reach 85 years

> In 2014 nearly 17,000 Australians are expected to be diagnosed with **bowel cancer** (9,250 men and 7,730 women)

> Nearly 20,000 Australians are expected to be diagnosed with **colorectal cancer** in 2020

> **Liver cancer** accounted for 3.3% of Australian cancer deaths in 2011 (1,423 deaths) elevating it into the top 10 causes of cancer deaths in men for the first time

> Liver cancer is rarely detected early and as a consequence has a high mortality rate

> **Abdominal aortic aneurysms (AAAs)** are more common with increasing age, male sex and the presence of chronic obstructive pulmonary disease (COPD), smoking and hypertension

> AAA is rare in people aged less than 50 years but incidence increases sharply with age (4-7% of men and 1-2% of women over 65 years are affected)

> **Prostate cancer** is the most commonly diagnosed cancer in Australia (21,808 new diagnoses in 2009) and the 4th leading cause of death in Australian males (3,294 deaths in 2011)

The Breast Cancer Research Group and Breast Biology and Cancer Group are led by scientific research leaders Professor Andreas Evdokiou and Associate Professor Wendy Ingman respectively. Over the last twelve months they have established a strong track output, both jointly and individually. They are making the most of opportunities provided by the close working relationship between clinicians and benchtop scientists.

Over the past twelve months almost 100 publications have been produced by the Discipline of Surgery in a wide range of journals from basic science through to clinical papers in premier world surgical journals.

Despite the continual squeeze on funding being constantly exerted on the healthcare sector, we have been able to secure 'Beat Cancer' grant funding from SAHMRI and The Hospital Research Foundation. This research is directed at investigating solid organ tumours. This work is being conducted by Associate Professor Joanne Young in conjunction with Dr Ehud Hauben, and looks at both the epidemiological aspects of colorectal cancer and the basic molecular science.

The challenges for maintaining all these enterprises is considerable. Despite this the Discipline of Surgery continues to have a significant research output, a large number of dedicated staff and an extremely promising future for the next five years.

Staff

RP Jepson Professor of Surgery
Head, Discipline of Surgery
Director, Division of Surgery
Director of Research, The Queen Elizabeth Hospital
GJ Maddern MBBS PhD MS MD FRACS

Professor of Vascular Surgery
R Fitridge MBBS MS FRACS

Professor of Colorectal Surgery
P Hewett MBBS FRACS

Associate Professors
N Rieger MBBS MS FRACS
M Goggin MB BCh BAO DO FRCSI (Ophth) FRCOphth FRANZCO MS

Senior Lecturers
M Bruening MBBS MS FRACS
J Miller MBBS FRACS
D Rodda MBBS FRACS
M Trochsler MD FMH MMIS FRACS
D Walsh MBBS FRACS

Staff Specialists
A Anthony MBBS FRACS
J Dawson MBBS FRACS MD ChM
S Ganesh MBBS FRACS
A Gupta MBBS FRANZCO
M Hamilton MBChB FRACS
I Harvey BMBS FRACS
M Herbert MBBS FRACS
P Hewett MBBS FRACS
H Kanhere MBBS FRACS
G Kiroff MBBS FRACS
C Lai MBBS FRACS
D Spernat MBBS FRACS
D Tonkin MBBS FRACS
D Walters MBBS FRACS

Staff

Visiting Specialists

G Benveniste MBBS FRACS
J Black MBBS FRANZCO
F Bridgewater MBBS FRCS FRACS
B Carney MBBS FRACS
D Close MBBS FRACS
P Cooper MBBS FRANZCO
S Durkin BMBS FRANZCO
D Economos MBBS FRANZCO
R Fleming MBBS FRANZCO
N Gehling BMBS FRACO
J Gilhotra MBBS FRANZCO
R Harries BMBS FRACS
A Karatassas MBBS FRACS
C Lang MBBS FRACS
M Lodge MBBS FRACS
D Lance BM FRACS
B Landers MBBS FRACS
M Lloyd MBBS FRACS
A Lord MBBS FRACS
K Moretti MBBS FRACS
R Parkyn MBBS FRACS
I Patterson MBBS FRACS
A Porter MBBS FRACS

Clinical Title Holders

S Ali Clinical Lecturer
A Anthony Clinical Lecturer
W Babidge Affiliate Associate Professor
F Bridgewater Clinical Associate Professor
J Black Clinical Lecturer
P Byrne Clinical Lecturer
B Carney Clinical Lecturer
S Chong Clinical Senior Lecturer
D Close Clinical Lecturer
P Cowled Affiliate Senior Lecturer
A Cowin Affiliate Associate Professor
P Cooper Clinical Lecturer
P Drew Visiting Research Fellow
D Economos Clinical Lecturer
R Fleming Clinical Lecturer
H Forbes Clinical Lecturer
N Gehling Clinical Lecturer
K Gibb Clinical Senior Lecturer
JS Gilhotra Clinical Associate Professor
M Hamilton Clinical Senior Lecturer
I Harvey Clinical Senior Lecturer
I Hensman Clinical Senior Lecturer
P Hewett Clinical Professor
V Humeniuk Clinical Lecturer
H Kanhere Clinical Senior Lecturer

A Karatassas Clinical Lecturer
C Lai Clinical Senior Lecturer
CM Lee Clinical Senior Lecturer
M Lloyd Clinical Lecturer
A Luck Clinical Senior Lecturer
B McCusker Clinical Lecturer
R McGovern Clinical Lecturer
K Moretti Clinical Lecturer
J Muecke Clinical Lecturer
P Nandoskar Associate Lecturer
S Neuhaus Clinical Associate Professor
S Olakkengil Clinical Senior Lecturer
R Parkyn Clinical Associate Professor
M Patkin Clinical Lecturer
C Pinnock Affiliate Senior Lecturer
R Phillips Clinical Lecturer
S Phipps Clinical Lecturer
C Pozza Clinical Lecturer
T Proudman Clinical Senior Lecturer
M Rao Clinical Associate Professor
S Raptis Clinical Senior Lecturer
T Rayner Affiliate Lecturer
D Roach Clinical Senior Lecturer
WEW Roediger Clinical Associate Professor
C Russell Clinical Associate Lecturer
C-KL Shaw Clinical Senior Lecturer
D Spernat Clinical Senior Lecturer
R Strickland Clinical Lecturer
P Stuart Clinical Lecturer
P Sutherland Clinical Senior Lecturer
LW Tan Affiliate Senior Lecturer
M Tie Clinical Lecturer
D Walters Clinical Senior Lecturer
M Wichmann Clinical Associate Professor
J Young Affiliate Associate Professor

RP Jepson Research Fellow

P Cowled PhD

University Research Fellow

P Grover PhD

Senior Research Officer

E Smith PhD

Research Officers

G Pena MD

C Kirana PhD

Technical Officers

B Hutchens

M Slawinski

M Smith

Senior Medical Scientist

E Hauben PhD

Project Coordinators

S Lauder BA(Hons)

L Leopardi BSc BEng(Biomedical)(Hons)

P Vanderzon BSc

Clinical Trials Coordinators

S Page BMedSc(Hons)

A Horner BHthSc(Hons)

Photographers (Ophthalmology)

A Drew

P Anderson

VIROLOGY GROUP

NHMRC Senior Research Fellow

Head, Virology Laboratory

Professor E Gowans PhD

Senior Research Officer

B Grubor-Bauk BSc(Hons) PhD

Research Officers

J Li BSc(Hons) PhD

W Yu BSc(Hons) PhD

D Wijesundara BSc(Hons) PhD

BREAST CANCER RESEARCH GROUP

Michelli-McGrath Breast Cancer Fellow

NHMRC Research Fellow

Head, Breast Cancer Research Unit (BCRU)

Professor A Evdokiou BSc(Hons) PhD

Senior Postdoctoral fellow

M De Nichilo PhD

Postdoctoral fellows

I Zinonos PhD

G Kaur BSc(Hons) MSc (part time)

Research Assistants

S Hay BSc

V Panagopoulos BSc (part-time)

BREAST BIOLOGY AND CANCER GROUP

THRF Associate Professor in Breast Cancer Research Fellow

NBCF Research Fellow, and Research Program Leader

Associate Professor W Ingman PhD

Senior Research Officer

D Glynn PhD

Australian Breast Cancer Research Postdoctoral Fellow

P Dasari PhD

The Hospital Research Foundation Postdoctoral Fellow

E Need PhD

Research Assistants

L Hodson BSc(Hons)

H Jayasinghe BHealthSc(Hons)

Research Nurse

K Mildren RN

NHMRC EVAR Trial

Project Manager

M Boulton BSc(Hons) GradDiplM

Project Coordinator/Database Manager

T DeLorain MA(Psych)

Postgraduate Students

Higher Degrees Awarded

PhD

L Giorgio

'Curcumin action in prostate cancer cells and fibroblasts'

Supervisor: Buchanan G, Need E

T Matthews B HthSc(Hons)

'The clinical analysis of liver function: can portosystemic shunts be measured?' PhD 2014

Supervisor: Maddern G

T Garrod BSc(Hons)

'The use of natural adjuvants to enhance prophylactic vaccines' PhD 2014

Supervisor: Gowans E, Gruber-Bauk B

Master of Surgery

G Benveniste FRACS

'The effect of alcohol on pancreatic blood flow. An experimental study' MS 2014

Supervisor: Maddern G

PhD candidates

V Panagopoulos BSc

'A novel role for peroxidases in breast cancer development progression and metastasis'

Supervisors: Evdokiou, A, DeNichilo M

A Zysk BSc(Hons)

'Targeting bone metastases using adoptive therapy of gamma delta T-cells'

Supervisors: Evdokiou A, DeNichilo M

V Liapis BAgSc

'Targeting cancer in bone with hypoxia activating pro-drugs'

Supervisors: Evdokiou A, DeNichilo M, Zinonos I

Y Wang BSc(Hons)

'Advanced material for drug delivery'

Supervisors: Losic D, Evdokiou A

J Smith PhD

'Surgery, ethics and climate change'

Supervisors: Maddern G, Hewett P

K Tomusange BSc, MSc

'Evaluation of recombinant human rhinoviruses as a vaccine strategy for HIV'

Supervisors: Gowans E, Gruber-Bauk B

J Gummow BSc(Hons)

'DNA vaccine targeting and immunomodulation'

Supervisors: Gowans E, Gruber-Bauk B

S Noordin BSc(Biotechnol) B HthSc(Hons)

'The role of C1q in mammary gland development and breast cancer susceptibility'

Supervisors: Ingman W, Robinson S

S Sun BSc(BiomedSc) B HthSc(Hons)

'TGFB-regulated macrophages in mammary gland development and tumorigenesis'

Supervisors: Ingman W, Robinson S

H Palethorpe B Med Pharm Sci (Hons), B Lab Med, Dip Biomed Sci

'The regulation of tumour cell behaviour by cancer associated fibroblasts'

Supervisors: Drew P, Smith E

Jagdale H BSc(Hons)

'Development of cytolytic replication defective recombinant adenovirus vaccines for Hepatitis C virus (HCV) and Human immunodeficiency virus (HIV)'

Supervisors: Gowans E, Gruber-Bauk B, Wijesundara D

Masavuli M BSc(Hons)

'A DNA vaccine to generate neutralising antibody to HCV'

Supervisors: Gowans E, Gruber-Bauk B

Master of Surgery candidates

M Wee MBBS

'The relation of peri-oesophageal fat to adenocarcinoma of the oesophagus'

Supervisors: Maddern G, Hewett P

K Kuan MBBS

'Ex vivo normothermic pancreas perfusion'

Supervisors: Maddern G, Trochsler M

A Cameron MBBS BMedSci

'The role of Flightless in excessive scarring and its potential as a target for a novel therapy'

Supervisor: Maddern G

Masters of Biotechnology candidate

V Atashgaran BSc(Medical Biosciences)

'Hormonal regulation of the immune micro-environment in the human breast: implications for breast cancer susceptibility'

Supervisors: Ingman W, Dasari P

Honours Students

M Iasiello BHSc

'The role of peroxidase enzymes as drivers of breast tissue fibrosis and increased breast cancer risk'

Supervisors: Evdokiou A, DeNichilo M, Ingman W

T Willsmore BSc

'Drug-eluting titania micro wires for the treatment of localised cancer'

Supervisors: Evdokiou A, DeNichilo M

A Shoubridge BSc

'The role of peroxidase enzymes during bone repair and regeneration'

Supervisors: Evdokiou A, DeNichilo M

M Archer BHSc

'The role of interleukin-10 in mammary gland development and cancer'

Supervisors: Ingman W, Glynn D, Robertson S

Postgraduate Students cont.

Postgraduate Scholarships

Australian Postgraduate Award (\$25,392 2014) M Wee

University of Adelaide Discipline of Surgery Top Up Scholarship (\$19,044 2014) M Wee

University of Adelaide Faculty of Health Sciences (\$24,653 2014)/Breast Cancer Research Unit, Surgery, Supplementary scholarship (\$16,000 2014) V Panagopoulos

Australian Postgraduate Award (\$25,392 2014) A Zysk

University of Adelaide Faculty of Health Sciences (\$12,326 2014)/Breast Cancer Research Unit, Surgery, Supplementary scholarship (\$16,000 2014) V Liapis

The Hospital Research Foundation Honours Research Scholarship (\$5,000 2014) M Iasiello

The Hospital Research Foundation Honours Research Scholarship (\$5,000 2014) A Shoubridge

The Hospital Research Foundation Honours Research Scholarship (\$5,000 2014) T Willsmore

University of Adelaide Faculty of Health Sciences Divisional Scholarship (\$24,653 2014) H Palethorpe

RACS Foundation for Surgery Scholarship in Surgical Ethics (\$45,000 2014) J Smith

Grants

Commonwealth Department of Health, Medical Services Advisor Committee, Special project funding (\$655,000 2014) Maddern G.

Commonwealth Department of Health, Medicare Benefits Schedule Reviews (\$220,000 2014) Maddern G.

Therapeutic Goods Administration, TGA Guidelines for Medical Devices (\$214,000 2014) Maddern G.

American College of Surgeons, Horizon scanning, Special project funding (\$75,000 2014) Maddern G.

ACT Department of Health (ACTASM), Special project funding (\$38,000 2014) Maddern G.

NSW Health – SESLHD, Peritonectomy Procedures Audit (\$7,000 2014) Maddern G.

Victorian Department of Health, Review of Surgical Procedures (\$85,000 2014) Maddern G.

Victorian Department of Health (VASM), Special Project funding (\$695,000 2014) Maddern G.

RACS/MMIM/CCANZ Colorectal cancer audit, Special project funding (\$10,000 2014) Maddern G.

Northern Territory Department of Health (NTASM), Special project funding (\$83,000 2014) Maddern G.

Western Australia Department of Health (WAASM), Special Project Funding (\$378,000 2014) Maddern G.

South Australian Department of Health (SAAPM), Special Project Funding (\$250,000 2014) Maddern G.

Tasmanian Department of Health (TASM), Special Project Funding (\$20,000 2014) Maddern G.

Queensland Department of Health (QASM), Special Project Funding (\$659,000 2014) Maddern G.

ARC. (Linkage Grant) On the cutting edge: promoting best practice in surgical innovation (\$63,750 2014) 2011–2014, Rogers WA, Johnson AJ, Townley C, Sheridan J, Ballantyne A, Lotz M, Meyerson D, Tomosey GF, Evers AA, Maddern GJ, Thomson CJ.

HCF Health and Medical Research Foundation. (Project grant) Use of surgical and radiology checklists in Australian hospitals: uptake, barriers and enablers (\$103,730 2014) 2013–2015, Maddern G, Runciman W, Mandel C, Schultz T, Munn Z.

National Breast Cancer Foundation (Early Career Fellowship) Immune system determinants of breast cancer susceptibility (\$120,000 2014) 2011–2015, Ingman W.

National Breast Cancer Foundation. (Novel Concept Award) A novel concept for parity-induced breast cancer protection (\$100,000 2014) 2013–2014 \$199,997, Ingman W, Hutchinson M.

National Breast Cancer Foundation, (Novel Concept award 2012) New and effective immunotherapeutic strategies targeting bone metastasis in breast cancer patients (\$100,000 2014) 2013–2014, Evdokiou A.

NHMRC. (Project grant #1050883) *In vivo* evaluation of the safety and efficacy of a novel chitosan gel in the reduction of adhesions following abdominal surgery in both animal and human models (\$171,650 2014) 2013–2015, Maddern G, Wormald PJ, Moratti S, Robinson B, Robinson S.

NHMRC. (Project grant #1049906) Advanced imaging to define hepatic and intestinal drug disposition in aging and liver diseases (\$245,275 2014) 2013–2015, Maddern G, Roberts M, Crawford D.

NHMRC. NBCC Shared Care Demonstration Project Phase 2. (\$120,000 2014) Walters D, Walsh D, Redman K, Lai C, Parkyn R.

NHMRC. (Project grant #1050694) Novel vitamin-E-Bisphosphonates: A new therapeutic approach targeting bone loss associated with osteoporosis and bone related malignancies (\$152,000 2014) 2013–2015, Evdokiou A, Atkins GJ.

NHMRC. (Centres of Research Excellence) National Centre of Research Excellence to improve management of peripheral arterial disease (\$499,850 2014) \$2,499,250 2010–2015, Golledge J, Kingwell B, Norman P, Tonkin A, Fitridge R, Reid C, Walker P, Hankey G, Fletcher J, Nelson M.

Grants cont.

NHMRC. (Project grant) Evaluating a decision-making model for EVAR (\$215,119 2014) \$1,075,595 2009-2014, Fitridge R, Boulton M, Maddern G, Thompson M, Barnes M.

NHMRC. (Project grant) Telmisartan in the management of abdominal aortic aneurysm (TEDY) (\$221,178 2014) 2012-2016, Golledge J, Norman P, Walker P, Ahimastos A, Dalman R, Fitridge R.

NHMRC. (Project grant) Economic evaluation and optimisation of services for the preoperative assessment and management of high risk surgical patients (\$128,718 2014) 2012-2014 Karnon J, Gibb C, Fitridge R, Marshall V, Field J.

NHMRC. (Uncoupled Research Fellowship) (\$135,000 2014) 2009-2014, Gowans EJ.

NHMRC. (Project grant) Mucosal immunity to human immunodeficiency virus (\$180,000 2014) 2012-2014, Gowans EJ, Suhrbier A, Wesselingh S.

Robinson Research Institute. Invest for Success, a new paradigm for mastitis and related breastfeeding complications (\$15,000 2014) 2014-2015, \$30,000 Ingman W, Hutchinson M.

The Hospital Research Foundation. (NHMRC Near Miss Grant) Optimisation of HCV vaccine design (\$100,000 2014) Gowans EJ.

The Hospital Research Foundation. (Project grant) DNA vaccine therapy for hepatitis C (\$150,000 2014) 2014-2015, Gowans EJ, Roberts-Thomson I.

The Hospital Research Foundation, Paracrine and juxtacrine signalling between prostate cancer cells and fibroblasts (\$34,500 2014) 2013-2014, Smith E, Drew PA.

The Hospital Research Foundation. Establishing islet isolation in South Australia (\$100,000 2014) Coates PT, Chen J, Russell C, Carroll R, Jesudason S, Voelker N, Torpy D, Radford T, Drogemuller C, Rojas-Canales, D, Penko D, Grey S, Walters S, Loudovaris T, Dennison A, Chung W, Wang L-J, Jessup C, Keating D.

University of Adelaide. (Interdisciplinary Research Fund) Nanoengineered drug nano-carriers for targeted chemotherapy (\$25,000 2014) Losic D, Evdokiou A.

University of Adelaide. (Faculty of Health Sciences Incentive Award) New and innovative strategies to enhance adoptive gamma delta T-cell based immunotherapy targeting cancer in bone. (\$10,000 2014) Evdokiou A.

University of Adelaide, Adelaide Research and Innovation. (Commercial Accelerator Scheme 2014). Using peroxidase enzymes to accelerate fracture repair in healthy or osteoporotic bone (\$30,000 2014) 2014- 2015, Evdokiou A.

Collaborations

Professor Andreas Evdokiou

Dr Vladimir Ponomarev, Memorial Sloan Kettering Cancer Centre NY USA

Professor Mike Davies, The Heart Institute, Sydney, Australia

Professor Dusan Losic, Department of Engineering, University of Adelaide

Associate Professor Wendy Ingman, Breast Biology and Cancer, BHI

Dr Jenny Hardingham, Colorectal Unit, BHI

Dr Betty Sallustio, Department of Pharmacology, BHI

Dr Paul Drew, Department of Surgery, BHI

Professor Robert Fitridge

Dr Catherine Gibb, The Queen Elizabeth Hospital

Professor John Beltrame, The Queen Elizabeth Hospital

Professor Jonathan Karnon, The University of Adelaide

Professor Allison Cowin, University of South Australia

Professor Nico Voelcker, University of South Australia

Professor Jonathan Golledge, James Cook University, Townsville QLD

Professor Matthew Thompson, St George's Vascular Institute, St George's Hospital, London, UK

Professor Eric Gowans

Dr Joseph Torresi, The University of Melbourne

Professor Ian Roberts-Thomson, The University of Adelaide.

Professor Steven Wesselingh, SAHMRI

Dr Mirielle Lahoud, Burnet Institute

Professor Andreas Suhrbier, QIMR Berghofer Medical Research Institute.

Professor Joseph Altin, The Australian National University

Professor Saumitra Das, Indian Institute of Science, Bangalore, India

Dr Paul Radspinner, FluGen Inc, Madison, Wis, USA.

Professor Suresh Tikoo, Vaccine and Infectious Disease Organisation, Saskatoon, Canada

Professor Peter Hewett

Australasian Gastro-Intestinal Trials Group (AGITG) A La Cart trial

Dr Andrew Stevenson, Royal Brisbane and Women's Hospital, Herston, Australia

Mr James Moore, Head Of Unit, Colorectal Surgery, Royal Adelaide Hospital, Australia

Mr Andrew Luck, Head Of Unit, Colorectal Surgery, Lyell McEwin Hospital, Adelaide, Australia

Dr Sid Selva-Nayagam, Consultant Medical Oncologist, Royal Adelaide Hospital, Australia

Associate Professor Tim Price, Consultant Medical Oncologist, The Queen Elizabeth Hospital, Adelaide, Australia

Dr Scott Carruthers, Radiation Oncologist, Royal Adelaide Hospital Cancer Centre, Australia

Commercialisations

Associate Professor Wendy Ingman

Professor Rik Thompson and Dr Kara Britt, University of Melbourne and Peter MacCallum Institute

Professor Fiona Pixley, University of Western Australia

Dr Marina Kotchetkova, University of Adelaide

Professor Mark Hutchinson and Prof Andrew Abell, University of Adelaide

Professor Sarah Robertson and Dr Louise Hull, University of Adelaide

Professor Andreas Evdokiou, University of Adelaide

Ingman W. Australian provisional patent "Treatment and Prevention of Mastitis" filed 05/07/2013, PCT filed 06/07/2014

Gowans EJ. Cellular vaccine and method of inducing an immune response in a subject. PCT/AU2013/000509. Held by Adelaide Research and Innovation. Entry to National Phase, November, 2014.

Professor Guy Maddern

Professor Robert Padbury, Flinders Medical Centre, Adelaide, Australia

Professor Bill Runciman, University of Adelaide, Australia

ASERNIP-S, Royal Australasian College of Surgeons, Adelaide, Australia

Royal Australasian College of Surgeons, Melbourne, Australia

Dr John Cockburn, Canberra Hospital, Australia

Dr Ashley Dennison, Leicester General Hospital, UK

Dr Wen Chung, Department of HPB Surgery, University of Leicester, UK

Dr Ajit Sachdeva, American College of Surgeons, Chicago, USA

Mr Markus Trochsler

Professor PJ Wormald, Department of Otorhinolaryngology, The Queen Elizabeth Hospital, Adelaide, Australia

Dr Ashley Dennison, Department of HPB Surgery, University of Leicester, UK

Thomas Ledowski, Anaesthesiology Unit, School of Medicine and Pharmacology, University of Western Australia

Dr Michael Goggin

Carl Zeiss Meditec AG, Germany and sponsored by Carl Zeiss Pty Ltd, in Australia "Prospective randomised clinical trial comparing efficacy and a new design of intraocular lens vs a regular intraocular lens"

Dr Eric Smith

Associate Professor Andrew Ruszkiewicz, Head of Gastroenterology Research Laboratory, SA Pathology, Adelaide, SA, Australia

Mr Tim Underwood, MRC Clinical Scientist, University of Southampton, Southampton, Hampshire, UK

Mr Jamie J Kelly, Consultant General Surgeon, Southampton University Hospitals NHS Trust, Southampton, Hampshire, UK

Dr Nicolas Clemons, Post-doctoral Scientist, Cancer Research, Peter MacCallum Cancer Centre, East Melbourne, Vic, Australia

Professor Jun Feng Liu, Fourth Military Medical University, Department of Thoracic Surgery, China

Orthopaedics and Trauma

The Queen Elizabeth Hospital Department of Orthopaedics and Trauma continues with the research focus on trialling new prostheses and technologies that have the potential to improve patient comfort and longevity of joint replacements while creating new efficiencies for surgical time and reduced costs. Trials continue looking at Ceramic versus Polyethylene liners for Total Hip Replacements, a Total Knee Replacement which will potentially reduce the occurrence of anterior knee pain post-surgery. The Research Unit continues its monitoring of metal wear particles from a variety of different size and model metal on metal hip bearings. These results will add to the accumulated data in this area allowing for more informed decisions to be made regarding joint wear and the effects on joint recipients. Funding for research in this department has been obtained entirely from industry contributions to the Orthopaedic and Trauma Research Fund. In 2014 contributions have come from Corin (\$23,056) and Johnson & Johnson (\$35,172). Acknowledgement is given to these companies for their ongoing support for research within the Department.

Staff

Director

J van Essen MBBS FRACS (Ortho)

Deputy Director

N Cullen MD FRCS(C) FRACS FAOrthA

Visiting Specialists

P Lewis MBBS FRACS FAOrthA

D Campbell BMBS PhD FRACS FAOrthA

L Ferris MBBS BSc (Med) FRACS

W Duncan MBBS FRACS (Orth)

G Nimon MBBS FRACS (Orth)

C Begg MBBS FRACS (Orth)

T Stevenson MBChB FRCS FRACS FAOrthA

N Pourgeizis MBBS FRACS (Orth)

C Gooi MBBS FRACS (Orth)

A Bajhau MBBS FRACS (Orth)

Medical Cover

Geriatric Team

Arthroplasty Fellow

S Ramawat (Trauma & Orth)

Arthroplasty Outcomes Officer/Surgical List and Patient Care Coordinator

G West

Executive Secretary

B Stoddard

Secretaries

E Smythe

J Whatling

E Parker

J. Rosser

Nursing Staff

L Thomas CPC – Joint Replacement

N Yates/D Dewick CSC – Joint Replacement

Therapeutics Research Centre

The Centre's research interests cover a spectrum of therapeutics from the chemistry of drugs, the effects drugs have on the body and the effects the body has on drugs, through to how drugs can be best used to treat disease. Current special interests include defining drug disposition and effects both in vitro and in vivo by chemical analysis using chromatography and mass spectrometry as well as bio-imaging using confocal and multiphoton reflectance, fluorescence, Raman spectroscopy and atomic force microscopy.

The Director of the Centre, Professor Michael Roberts, is an Australian National Health & Medical Research Council Senior Principal Research Fellow based at both The Institute (Basil Hetzel Institute; affiliated with the University of South Australia School of Pharmacy) and the University of Queensland School of Medicine at Princess Alexandra Hospital in Brisbane. The Therapeutics Research Centre (TRC) was established by Professor Roberts at the University of Queensland in 1989, to support his major interests of topical drug delivery, pharmacokinetics and quality use of medicines. In 2009, a new initiative led to expansion of the TRC, with the establishment of a second University of South Australia branch at the Basil Hetzel Institute. Research staff and students in the TRC now have a unique opportunity to access facilities and expertise at both universities. There are also strong clinical ties with the Princess Alexandra Hospital in Brisbane and The Queen Elizabeth Hospital in Adelaide.

Research Activities

Skin cancer, skin ageing & other conditions

Many products are applied to the skin to prevent skin cancer or to treat skin diseases. Our work seeks to better understand how we can make such products more effective, safer and appropriate for conditions such as psoriasis. One major component is concerned with the evaluation of nanotechnology products applied to the skin. We are defining rules governing the delivery of actives to the different layers of the epidermis using different formulations and certain delivery devices. This work will also define the distribution patterns of these actives in terms of both their penetration and the delivery systems used.

Population Data

- > **Melanoma** is the 6th most common cause of cancer death in Australian men and the 10th most common in Australian women
- > Melanoma of the skin accounted for 3.6% of all cancer deaths in Australia during 2011 (1,071 men and 473 women)
- > Over 14,000 Australians (8,540 men and 5,700 women) are expected to be diagnosed with melanoma of the skin in 2014

Research Focus

The focus of the Therapeutics Research Centre is to improve patient outcomes by improved diagnosis and treatment with medicines. Our work, in collaboration with a number of medical specialties, includes:

- **Skin cancer & other skin conditions:** better diagnosis and treatment using advanced non-invasive imaging technologies and topical products.
- **Intensive care:** improved use of antibiotics, antifungals and other medications in the severely ill.
- **Liver disease:** understanding how liver diseases affect medicines and how to treat patients.
- **Nanomedicines:** exploring the therapeutic potential and safety for nanomedicines.
- **Medicine efficiency & safety:** exploring how well medicines work and if other products are safe.
- **Clinical & Regulatory Toxicology:** assessing safety of medicines, consumer products, pesticides and herbicides and managing poisonings associated with exposure to them.

Intensive care

Inappropriate doses of antibiotics are likely to contribute to poor outcomes for ICU patients. Emerging data describes how clinician-led dosing frequently results in inappropriate serum antibiotic concentrations. Such inappropriate concentrations can lead to antibiotic failure, antibiotic toxicity and/or the development of antibiotic resistance. The question confronting clinicians is – what is the appropriate antibiotic dose to use in the individual patient to achieve the best outcome for this patient. Our project aims to develop dosing guidelines to achieve serum concentrations that optimise antibiotic exposure in these patients. This work also involves the Lyell McEwin Hospital and the Royal Brisbane and Women's Hospital.

Medicine efficiency

Multimodal microscopy and spectroscopy offer the exciting prospect of non-invasive imaging of human skin *in vivo* in high resolution, in three dimensions and in time. Our ability to image the skin to a depth of 200µm (papillary dermis) with this technology will enable us to use it as a potential window to study and treat cardiovascular problems such as those arising from diabetes complications, cardiovascular disease, arthritis and smoking.

Liver disease

The liver is the main organ in the body for drug metabolism and detoxification. Our work in this area seeks to address the poorly understood question: what is the *in vivo* disposition and response of the liver to drugs used for the treatment of liver diseases? The results of this work will help us better design new drugs and choose the most effective drugs for liver disease. The research may also help us find a better strategy for liver transplantation and thus improve success rates.

Nanomedicines

Nanomaterials are defined as having at least one dimension within the range 1-100 nm. Commercial applications that use nanomaterials include sunscreen (zinc oxide) and clinical imaging agents. We are investigating what happens to commercially available and therapeutic nanoparticles if they pass through the skin and enter the blood.

Safety of occupational and environmental chemicals

Assessment of skin absorption is a major regulatory requirement in registering any product that presents potentially harmful or therapeutic skin exposure. While the rigorous assessment used in regulating therapeutic drugs is well established, the main tool used for dermal regulatory human health risk assessments on potentially harmful chemicals needs further validation and refinement to provide a more reliable assessment of *in vivo* bioavailability, effects and decontamination.

Staff

University of South Australia Research Chair: Therapeutics & Pharmaceutical Science

MS Roberts BPharm PhD DSc MBA FACP

University of South Australia Research Fellows

L Mackenzie BSc PhD

Q Zhang BPharm PhD

A Holmes BForSc PhD

Postgraduate Students

PhD Candidates

A Amarasekera BPharm

'Does vitamin D deficiency contribute to endothelial dysfunction in diabetes patients with obesity?'

Supervisors: Roberts MS, Horowitz J

R To-a-nan BPharm MClPharm

'Does bioequivalence reflect therapeutic equivalence in the real population?'

Supervisor: Roberts MS

R Kuswahyuning BPharm

'Role of Formulation in Skin Delivery'

Supervisor: Roberts MS

MG Sinnollarredy BPharm

'Dose optimisation of antimicrobial agent: pharmacokinetic and pharmacodynamic approach'

Supervisor: Roberts MS

FB Sime BPharm

'Therapeutic drug monitoring in high risk patients: pharmacokinetic and pharmacodynamics considerations for dose optimisation'

Supervisor: Roberts MS

A Macedo BPharmSc MPharmSc

'The development and characterization of nanosystems for the skin delivery of actives'

Supervisor: Roberts MS, Mackenzie L, Zhang Q, Holmes A

V Nooney BPharm

'Determinants of clinical response to platelet ADP receptor antagonists'

Supervisors: Roberts M, Horowitz J, Chirkov Y

Grants

NHMRC. (Program grant # 1055176) An integrated research program in human toxicology to ensure rapid translation of results into practice and regulation (\$136,936 2014) 2014-2018, Buckley N, Isbister G, Dawson A, Roberts MS.

NHMRC. (Project grant # 1049906) Specific targeting of nanosystems by cutaneous delivery. (\$323,567 2014) 2013-2015, Roberts MS, Kendall M.

NHMRC. (Project grant # 1049979) Advanced imaging to define hepatic and intestinal drug disposition in aging and liver diseases. (\$245,273 2014) 2013-2015, Roberts MS, Crawford D, Maddern G.

NHMRC. (Project grant # 1044941) Robust antibiotic dosing for critically ill patients receiving renal replacement therapy. (\$379,929 2014) 2013-2015, Roberts J, Lipman J, Roberts MS, Paul S, Peake S, Turnidge J.

Collaborations

Local

Professor Nico Voelcker, University of South Australia; Professor Thomas Nann, University of South Australia

Dr Des Williams, University of South Australia

Dr Michael Wiese, University of South Australia

Professor Guy Maddern, University of Adelaide/TQEH

Professor John Horowitz, University of Adelaide/TQEH

Professor John Beltrame, University of Adelaide/TQEH

Professor Sepher Shaikab, University of Adelaide

Associate Professor Sandra Peake, TQEH

Dr Warren Weightman, TQEH

Professor Joe Shapter, Flinders University

National

Professor Andrew Dawson, University of Sydney

Professor Mark Kendall, University of Queensland

Professor Darrell Crawford, University of Queensland

Professor Ian Frazer, University of Queensland

Associate Professor Jeff Grice, University of Queensland

Professor Nick Buckley, University of New South Wales

Professor Zoltan Endre, University of New South Wales

Professor John Horowitz, University of Adelaide

Professor John Beltrame, University of Adelaide

Professor Sepher Shaikab, University of Adelaide

Associate Professor Sandra Peake, TQEH

International

Professor Gordon Flynn University of Michigan, USA

Professor Robert Hoffman, University of California, San Diego, USA

Professor Howard Maibach, University of California, San Diego, USA

Professor Peter So, MIT, USA

Professor Majelle Lane, University College, London UK

Professor Steven Abbott, University of Leeds, UK

Dr Klaus Suhling, Kings College, UK

Research

PUBLICATIONS

2014

Researchers at the Basil Hetzel Institute have achieved a broad range of publication success highlighting the quality of research

AGED AND EXTENDED CARE SERVICES

Papers

Dent E, Chapman I, Piantadosi C, Visvanathan R. Performance of nutritional screening tools in predicting poor six months outcome in hospitalised older people. *Asia Pacific Journal of Clinical Nutrition* 2014; 23(3): 394-9.

Dent E, Chapman I, Piantadosi C, Visvanathan R. Frailty and Functional Decline Indices Predicts Poor Outcomes of Hospitalised Older Persons. *Age & Ageing* 2014; 43(4):477-484.

Kaehr E, Visvanathan R, Malmstrom TK, Morley JE. Frailty in Nursing Homes: The FRAIL-NH Scale. *J Am Med Dir Assoc*. 2014 Dec 31. pii: S1525-8610(14)00797-X. doi: 10.1016/j.jamda.2014.12.002. [Epub ahead of print]

Gopal GK, Hewton C, Pazhvoor SK. Myoclonus associated with concomitant ciprofloxacin and oxycodone in an older patient. *Br J Clin Pharmacol* 2014 May; 77(5):906-7.

Gopal GK, Tam KL, Krishnan SP, Maddern IL. Bisphosphonate associated atypical subtrochanteric femur fractures in the older patient. *NZ Med J* 2014 Feb 14; 127(1389): 81-5.

Luscombe N, Chapman I, Visvanathan R. Hospital admission in poorly nourished, compared with well-nourished, elderly South Australians receiving 'Meals on Wheels'- findings from a pilot study. *Aus J Ageing* 2014 Sep; 33(3): 164-9.

Nair S, Visvanathan R, Gentilcore D. Intermittent walking: a potential treatment for older people with postprandial hypotension. *J Am Dir Assoc* 2014; Oct 8. pii: S1525-8610 (14) 00546-5.

Ranasinghe D, Shinmoto TR, Hill K, Visvanathan R. Detecting movements into and out of bed: preliminary development and evaluation of a movement sensor system.

Gait and Posture 2014 Jan;39(1):118-23.

Tam KL, Nair S, Yu S, Visvanathan R. A Dedicated Geriatric Medicine Teaching Block To Senior Undergraduate Medical Students Improves Attitude and Competency Scores. *Aus J Ageing* 2014; 33(4):E6-E11.

Tan ECK, Visvanathan R, Hilmer SN, Vitry AI, Quirke T, Emery T, Robson L, Sheldrick S, Reeve E, Gnjdic D, Bell JS. Analgesic load, pain and daytime sedation in people with and without dementia in aged care facilities: a prospective cohort study. *BMJ Open* 2014; 19(4):e005757.

Wimmer BC, Dent E, Bell JS, Wiese M, Johnell K, Chapman I, Visvanathan R. Medication regimen complexity and unplanned hospital admissions in older people: a prospective cohort study. *Annals of Pharmacotherapy* 2014; 48(9): 1120-1128.

Wimmer BC, Dent E, Visvanathan R, Wiese M, Johnell K, Chapman I, Bell JS. Polypharmacy and medication regimen complexity as predictors of hospital discharge directly to home: a cohort study. *Drugs and Ageing* 2014; 31(8):623-630.

Yu S, Appleton S, Chapman I, Adams R, Wittert G, Visvanathan T, Visvanathan R. An anthropometric prediction equation for appendicular skeletal muscle mass in combination with a measure of muscle function to screen for sarcopenia in primary and aged care. *J Am Dir Assoc* 2014; Sep 16. pii: S1525-8610 (14) 00398-3.

Yu S, Appleton S, Adams R, Wittert G, Chapman I, Visvanathan T, Visvanathan R. The impact of Low Muscle Mass definition on the Prevalence of Sarcopenia in older Australians. *Biomed Research International* 2014; 36170.

Invited Review

Yu S, Umapathysivam K, Visvanathan R. Sarcopenia In Older People. *Int J Evid Based Healthc* 2014; 12(4):227-243.

Abstracts

Shibu PK, Hudson D, Visvanathan R. Osteoporosis screening and management in older fallers presenting to hospital: pilot experience with a dedicated Gerontology Nurse. *Osteoporosis International* 2014; Vol25, S2, P132.

Yu S, Appleton S, Adams R, Chapman I, Wittert G, Visvanathan T, Visvanathan R. (2014). The impact of low muscle mass definition on the prevalence of sarcopenia in older Australians. *Australasian Journal on Ageing* 33 (Suppl 1):69.

Books

Visvanathan R & Rachna K. Malnutrition in Older People in the Textbook on Geriatric Medicine. 2014 (1st Edition), Editor-in-Chief P.Sanchette. Paras Medical Publishers (Hydrebadd).

Visvanathan R. Malnutrition In Older People in Geriatric Medicine-An Introduction. 2014, Editor G.Caplan. IP Communications (Australia).

ANAESTHESIA, Department of

Papers

Jeyadoss J, Kuruppu P, Nanjappa N, Van Wijk RM. Sugammadex hypersensitivity – a case of anaphylaxis. *Anaesth Intensive Care*. 2014; 42:89-92.

Jeyadoss J, Nanjappa N, Van Wijk RM, Kuruppu P, In response to Baldo. *Anaesth Intensive Care*. 2014 Jul;42(4):527.

Kumar S, Rao V, Morris RG, Watts R, Westley IS. Ropivacaine (total and unbound) and AGP concentrations following transversus abdominis plane block for analgesia following abdominal surgery- a pilot study. *Ther Drug Monit*. 2014;36(6):759-64

Macintyre P, Huxtable C, Flint S, Dobbin M. Costs and consequences: a review of discharge opioid prescribing for ongoing management of acute pain. *Anaesth Intensive Care*. 2014;42:558-574

Papers - (cont.)

Rao Kadam V. Quadratus lumborum (QL) block catheter infusion as a postoperative analgesic technique for abdominal surgery. Accepted as letter to the Editor in *JOACP*

Rao Kadam V, Howell S, Kadam V. Comparison of ultra sound guided bilateral transversus abdominis plane block and local anaesthetic infiltration technique as analgesia in day case laparoscopic cholecystectomy-retrospective study. *Anaesth Intensive Care*. 2014;42:410-11

Thiruvankatarajan V, Van Wijk R. Risk of perioperative torsade de pointes in patients with poorly controlled diabetes mellitus. *Anesthesia & Analgesia*. 2014;119(2):497.

Thiruvankatarajan V, Van Wijk RM, Rajbhoj A. Cranial Nerve Injuries with Supraglottic airway: A systematic review of published reports. *Anaesthesia*. 2014;doi:10.1111/anae.12917.

Thiruvankatarajan V, Van Wijk RMAW, Elhalawani I, Barnes AM. Lingual nerve neuropraxia following use of the Laryngeal Mask Airway Supreme. *Journal of Clinical Anaesthesia*. 2014;26:65-68.

Thiruvankatarajan V, Pruett A, Das Adhikary S. Coagulation testing in the perioperative period. *Indian Journal of Anaesthesia*. 2014;58(5):565-572.

Yu S, Appleton S, Chapman I, Adams R, Wittert G, Visvanathan T, Visvanathan R. An Anthropometric Prediction Equation for Appendicular Skeletal Muscle Mass in Combination With a Measure of Muscle Function to Screen for Sarcopenia in Primary and Aged Care. *J Am Med Dir Assoc*. 2014;doi:10.1016/j.jamda.2014.06.018.

Yu S, Appleton S, Adams R, Chapman I, Wittert G, Visvanathan T, Visvanathan R. The impact of low muscle mass definition on the prevalence of sarcopenia in older Australians. *BioMed Research International*. 2014;doi:10.1155/2014/361790.

CARDIOLOGY

Papers

Ali OA, Chapman M, Nguyen TH, Chirkov YY, Heresztyn T, Mundisugih, Horowitz JD. Interactions between inflammatory activation and endothelial dysfunction selectively modulate valve disease progression in patients with bicuspid aortic valve. *Heart* 2014;100(10):800-5.

Bailey J, Feelisch M, Horowitz JD, Frenneaux MP, Madhani M. Pharmacology and therapeutic role of inorganic nitrate and nitrite in vasodilatation. *Pharmacol Ther* 2014 Dec;144(3):303-320. Review.

Ball J, Carrington MJ, Thompson DR, Horowitz JD, Stewart S on behalf of the Standard versus Atrial Fibrillation specific management study (SAFETY) investigators. Post-discharge electrocardiogram Holter monitoring in recently hospitalised individuals with chronic atrial fibrillation to enhance therapeutic monitoring and identify potentially predictive phenotypes. *Eur J Cardiovasc Nurs* 2014 Aug 14. pii: 1474515114547650. [Epub ahead of print]

Chapman M, Henthorn R, Surikow S, Zontjens J, Stocker B, Mclean T, Zeitz CJ. Rheumatic Mitral valve disease diagnostic Tissue Quantification (backscatter). *European Journal Echocardiography Abstracts Supplement*, 2014 December, P1117.

Chong CR, Chan WPA, Nguyen TH, Liu S, Procter NEK, Ngo DT, Sverdlow AL, Chirkov YY, Horowitz JD. Thioredoxin-interacting protein: Pathophysiology and emerging pharmacotherapeutics in cardiovascular diseases and diabetes. *Cardiovasc Drugs Ther* 2014;28(4):347-60.

Chong CR, Liu S, Licari G, Heresztyn T, Chirkov YY, Ngo Dr, Horowitz JD. Reversal of hyperglycaemia: effects on nitric oxide signaling. *Am J Med* 2014 Nov 25. pii: S0002-9343(14)01080-8.

Christersson C, Wallentin L, Andersson U, Alexander JH, Ansell J, De Caterina R, Gersh BJ, Granger CB, Hanna M, Horowitz JD, Huber K, Husted S, Hylek EM, Lopes RD, Siegbahn A. D-dimer and risk of thromboembolic and bleeding events in patients with atrial fibrillation – observations from the ARISTOTLE trial. *J Thromb Haemost* 2014;12(9):1401-12, 2014.

Dautov RF, Stafford I, Liu S, Cullen H, Chirkov Y, Horowitz JD. Hypoxic potentiation of nitrite effects in human vessels and platelets. *Nitric Oxide* 2014 Aug 31;40:36-44.

Goto S, Zhu J, Lisheng L, Oh BH, Wojdyla D, Aylward P, Bahit MC, Gersh, BJ, Hanna M, Horowitz JD, Lopes RD, Wallentin L, Xavier D, Alexander JH. Efficacy and safety of apixaban compared with warfarin for stroke prevention in patients with atrial fibrillation from East Asia : A sub-analysis of the apixaban for reduction in stroke and other thromboembolic events in atrial fibrillation (ARISTOTLE) Trial. *Am Heart J* 2014;168(3):303-9.

Hijazi Z, Siegbahn A, Andersson U, Granger CB, Alexander JH, Atar D, Gersh BJ, Mohan P, Harjola VP, Horowitz JD, Husted S, Hylek EM, Lopes RD, McMurray JJV, Wallentin L on behalf of the ARISTOTLE Investigators. High Sensitivity Troponin I for risk assessment in patients with atrial fibrillation : Insights from the apixaban for Reduction in Stroke and other Thromboembolic Events in Atrial Fibrillation (ARISTOTLE) trial. *Circulation* 2014;129(6):625-34.

Horowitz JD, Nguyen TH. The role of echocardiography in Tako-Tsubo Cardiomyopathy: Beyond diagnosis? Editorial. *JACC Cardiovascular Imaging*, 2014;7(2):130-2.

Kayacelebi AA, Nguyen TH, Neil CJ, Horowitz JD, Jordan J, Tsikas D. Homoarginine and 3-nitrotyrosine in patients with takotsubo cardiomyopathy. *Int J Cardiol*, 2014;173(3):546-7.

Liu S, Ngo DT, Stewart S, Horowitz JD, Chirkov YY. B-Type natriuretic peptide suppression of neutrophil superoxide generation: mechanistic studies in normal subjects. *Clin Exp Pharmacol Physiol* 2014 Oct;41(10):739-43.

Liu S, Chirkov YY, Horowitz JD (authors to be confirmed). BNP suppression of neutrophil superoxide generation: mechanistic studies in normal subjects. *Clinical and Experimental Pharmacology and Physiology* 2014. [epub ahead of print]

Mahadavan G, Nguyen TH, Horowitz JD. Brain natriuretic Peptide (BNP): a biomarker for all cardiac disease? *Curr Opin Cardiol* 2014;29(2):160-166.

Nguyen TH, Chong Dr, Chan WP, Horowitz JD. New developments in anti-anginal therapy: role of ivabradine, allopurinol and agents modifying myocardial metabolism. *WJCD* 2014;4:368-376.

Nooney VB, Hurst NL, Chirkov YY, De Caterina R, Horowitz JD. Post receptor determinants of acute platelet response to clopidogrel in patients with symptomatic myocardial ischemia. *Vascul Pharmacol* 2014 Nov 20. pii: S1537-1891(14)00191-8.

Procter NEK, Chong CR, Sverdlow AL, Chan WPA, Chirkov YY, Horowitz JD. Aging of platelet nitric oxide signaling: pathogenesis, clinical implications and therapeutics. *Semin Thromb Hemost* 2014 Sep;40(6):660-8.

Procter NEK, Ball J, Liu S, Hurst N, Nooney VB, Goh V, Stafford I, Heresztyn T, Carrington M, Ngo DTM, Hylek EM, Isenberg JS, Chirkov YY, Stewart S, Horowitz JD, On behalf of the SAFETY investigators. Impaired platelet nitric oxide response in patients with new onset atrial fibrillation. *Int J Cardiol* Epub 2014 Oct 23.

Raman B, Singh K, Zeitz CJ, Horowitz JD. Takotsubo cardiomyopathy presenting as S-T elevation myocardial infarction: Not gone but forgotten? *Int J Cardiol*, 2014;172(1):261-2.

Sheikh AR, Westley I, Sallustio B, Horowitz JD, Beltrame JF. Interaction of Terbinafine (Anti-fungal agent) with Perhexiline: A case report. *Heart Lung Circ*, 2014;23(6):149-51.

CARDIOLOGY (cont.)

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Wunnapuk K, Gobe G, Endre Z, Peake P, Grice JE, Roberts MS, Buckley NA, Liu X. Use of a glyphosate-based herbicide-induced nephrotoxicity model to investigate a panel of kidney injury biomarkers. *Toxicology Letters*. 2014;225:192-200.

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Reeve E, Shakib S, Hendrix I, Roberts MS, Wiese MD. Review of deprescribing processes and development of an evidence-based, patient-centred deprescribing process. *British Journal of Clinical Pharmacology*. 2014;78:738-747.

Lui X, Kruger P, Maibach H, Colditz P, Roberts MS. Using the skin for drug delivery and diagnosis in the critically ill. *Advanced Drug Delivery Reviews*. 2014;77C:40-49.

Invited

Presentations

at national and international meetings

2014

Conference Title and Date	Title of Presentation/Poster	Attendee Name
AGED & EXTENDED CARE SERVICES (GERIATRIC MEDICINE)		
Inaugural Lecture, University of Adelaide, South Australia, April 2014	Achieving healthy ageing by better managing frailty managing frailty	Visvanathan R
IOF-ESCEO World Congress on Osteoporosis Osteoarthritis and Musculoskeletal Diseases, Seville, Spain, April 2014	Osteoporosis screening and management in older fallers presenting to hospital: pilot experience with a dedicated Gerontology Nurse.	Shibu PK
Acute Care For The Elderly Seminar, Monash University, Victoria, June 2014	Nutrition in the frail elderly	Visvanathan R
Centre for Medicine Use and Safety Seminar Program, Monash University, Victoria, July 2014,	Muscle mass and older people	Visvanathan R
The Role of Protein Symposium, Melbourne, Victoria, October 2014	Protein in older people	Visvanathan R
47th National Australasian Association of Gerontology Conference, Adelaide, November 2014,	Nutritional Frailty	Visvanathan R
ANAESTHESIA		
Combined ANZCA/ASA South Australian and Northern Territory Annual Scientific Meeting Adelaide, November 2014	Recent Pain Pitfalls	Flint S
OTSAN (Overseas Trained Specialist Anaesthetists Network) Meeting Adelaide, Nov 2014	Chronic Persistent Post-Surgical Pain	Van Wijk RMAW
OTSAN (Overseas Trained Specialist Anaesthetists Network) Meeting Adelaide, Nov 2014	Transfusion Update	Jeyadoss J
OTSAN (Overseas Trained Specialist Anaesthetists Network) Meeting Adelaide, Nov 2014	Reflection in Anaesthetic Practice	Rainbird A
OTSAN (Overseas Trained Specialist Anaesthetists Network) Meeting Adelaide, Nov 2014	Ethics around End of Life Issues	Balasingam R
OTSAN (Overseas Trained Specialist Anaesthetists Network) Meeting Adelaide, Nov 2014	When Bad Things happen to Good People	Nanjappa N

Conference Title and Date	Title of Presentation/Poster	Attendee Name
ANAESTHESIA (cont.)		
Medical Forum MIMS India, Aug 2014	Obstructive sleep apnoea guidelines for surgical patients.	Rao Kadam V
ANZCA Annual Scientific Meeting Singapore, May 2014	Quadratus lumborum (QL) block catheter infusion as a postoperative analgesic technique for abdominal surgery	Rao Kadam V
Australian Pain Society 34th Annual Scientific Meeting Hobart, Tasmania, April 2014	Comparison of ultra sound guided bilateral transversus abdominis plane block and local anaesthetic infiltration technique as analgesia in day case laparoscopic cholecystectomy-retrospective study	Rao Kadam V, Howell S, Kadam V
National Congress of the Indian society of Anaesthesiologists (ISACON), Madurai, Tamil Nadu, India, December 2014	Anaesthetic considerations in : Aortic aneurysm surgery	Jeyadoss J
CARDIOLOGY UNIT		
ASAN Medical Center, Korea, June, 2014	Biomarkers for thrombo-embolism in AF	Horowitz JD
Korea Heart Rhythm Society, Seoul, Korea, 1 - 14 June, 2014,	New developments re apixaban in atrial fibrillation	Horowitz JD
Laval University, Quebec, Canada, November 2014	Tako-Tsubo Cardiomyopathy: neither rare nor benign	Horowitz JD
European Society of Cardiology, Barcelona Spain, August 2014 ,	Gender-tachycardia interactions in atrial fibrillation, impact upon platelet aggregation and nitric oxide signalling	Procter N
European Society of Cardiology Congress, Barcelona Spain, September 2014	Ticagrelor potentiates the anti-aggregatory effects of adenosine via A2 receptor stimulation	Nooney VB, Chirkov Y, De Caterina R, Horowitz JD
Invited lecture, Laval University, Quebec, Canada, November 2014	Aortic stenosis: determinants of early progression	Horowitz JD
Henry Neufeld Plenary Lecture: International Society for Cardiovascular Pharmacology, Annual Scientific Meeting, Adelaide, November 2014	Energetic/inflammatory disturbances in heart disease: emerging therapeutic perspectives	Horowitz JD
American Heart Association, Chicago, United States 15th-19th November 2014	Heterogeneity of disease progression rates in patients with bicuspid aortic valve: is there a suitable bio-marker?	Nguyen TH, Shah R, Chapman M, Ali OA, Horowitz JD
International Society of Cardiovascular Pharmacology, Adelaide, November 2014	Shock in patients with Takotsubo cardiomyopathy: a role for calcium infusion?	Chong CR, Stansborough J, Raman B, Nguyen TH, Horowitz JD
International Society of Cardiovascular Pharmacology, Adelaide, November 2014	Homo-arginine increases tissue ROS production but does not affect platelet aggregation	Liu S, Nooney VB, Chong C, Nguyen TH, Chirkov YY, Horowitz JD
International Society of Cardiovascular Pharmacology, Adelaide, November 2014	SDMA: not so inert!	Liu S, Nooney VB, Chong C, Nguyen TH, Tsikas D, Chirkov YY, Horowitz JD
American Heart Association scientific session, Chicago, November 2014	Dronedarone is a potent hepatic and cardiac carnitine palmitoyl transferase-1 inhibitor	Chong CR, Licari G, Westley IS, Horowitz JD, Sallustio BC
American Heart Association conference, Chicago, November 2014	Heterogeneity of disease progression rates in patients with bicuspid aortic valve: is there a suitable bio-marker?	Nguyen TH, Shah R, Chapman M, Ali OA, Horowitz JD
World Congress of Cardiology, Melbourne, November 2014	Determinants of acute uptake of the myocardial metabolic modulator perhexiline into human myocardium	Chong C-R, Drury NE, Licari G, Frenneaux M, Horowitz JD, Pagano D, Sallustio B

Conference Title and Date	Title of Presentation/Poster	Attendee Name
CARDIOLOGY UNIT (cont.)		
World Congress of Cardiology, Melbourne, May 2014	Hyperglycemia, rather than diabetes per se, engenders impaired platelet nitric oxide signalling:	Chong C-R, Hurst N, Nooney VB,, Licari G, Chirkov YY, Ngo DT, , Horowitz JD
World Congress of Cardiology, Melbourne, May 2014	Safety profile of long-term myocardial metabolic agent perhexiline	Phuong H, Choi B, Raman B, Chong C-R, Horowitz JD
World Congress of Cardiology, Melbourne, May 2014	Mechanism of BNP interactions with neutrophil superoxide release: attenuation in acute and chronic heart failure	Liu S, Ngo DT, Chong C-R, Chirkov Y, Stewart S, Horowitz JD
World Congress of Cardiology Scientific Sessions, Melbourne, Australia, May 2014	Is there a biochemical basis for differential thromboembolic risk in atrial fibrillation? Studies with platelet nitric oxide signalling	Procter N
World Congress of Cardiology. Melbourne, May 2014	"High On-treatment" Platelet Reactivity, But Not Pre-treatment Hyperaggregability, Predicts Clopidogrel Response	Nooney VB, Chirkov Y, Horowitz J
World Congress of Cardiology, Melbourne, May 2014	Thrombospondin-1 exerts bidirectional effects on prostacyclin signalling in human platelets: implications regarding clopidogrel resistance	Nooney VB, Nicola H, Isenberg J, Chirkov Y, Horowitz J
World Congress of Cardiology, Melbourne, May 2014	Systemic inflammatory activation and endothelial dysfunction predict development of aortic valve stenosis in bicuspid aortic valve	Nguyen TH, Ali OA, Chapman M, Chirkov YY, Heresztyn T, Mundisugih J, Horowitz JD
2nd International Summit on Clinical Pharmacy, San Francisco, USA, December 2014	<i>In vitro</i> and <i>in vivo</i> performance of two warfarin brands and predicted patient outcomes	To-A-Nan R
CLINICAL PHARMACOLOGY		
5th Asia Pacific ISSX Meeting, Tianjin, China, May 10-12, 2014	Validation of a simple high performance liquid chromatography tandem mass spectrometry method for the determination of plasma perhexiline concentrations	Westley IS
World Congress of Cardiology, Melbourne, 4-7 May 2014	The enantiomers of the myocardial metabolic agent perhexiline display divergent effects on hepatic energy metabolism and peripheral neural function in rats	Licari G
World Congress of Cardiology, Melbourne, 4-7 May 2014	Determinants of acute uptake of the myocardial metabolic modulator perhexiline into human myocardium	Chong CR
International Society of Cardiovascular Pharmacology, Adelaide, Australia, 26-28 November 2014	Effects of perhexiline enantiomers on activation of myocardial pyruvate dehydrogenase in a model of isoprenaline-induced stress	Sallustio BC
American Heart Association Scientific Sessions, Chicago, USA, 15-19 November 2014	Dronedarone is a potent hepatic and cardiac carnitine palmitoyl transferase-1 inhibitor	Chong CR
Joint ASCEPT-MPGPCR Scientific Meeting, Melbourne, Australia, 7-11 December 2014	Declining intra-lymphocyte concentrations of mycophenolic acid correlate with the incidence of graft rejection in renal transplant recipients: preliminary results of a prospective study	Z MD Dom

Conference Title and Date	Title of Presentation/Poster	Attendee Name
GYNAECOLOGY UNIT		
Urogynaecology Association of Australia, Annual Scientific Meeting, Melbourne Victoria 25 – 30 March 2014	Post-operative haemorrhage	Barry C
HAEMATOLOGY- ONCOLOGY, The combined departments of		
Asia Pacific Colorectal Conference, Singapore November 16th 2014	Invited speaker and faculty member Positive for the role of anti-EGFR therapy in combination with chemotherapy for RAS and BRAF WT colorectal cancer	Price T
MOGA Conference 2014, Sydney NSW 6-8 August 2014	Cooperative groups in Australia, opportunities for collaboration	Price T
ICU - Intensive Care Unit		
European Society of Intensive Care Medicine Annual forum. Barcelona, Spain 1 October 2014	Goal-Directed Resuscitation for Patients with Early Septic Shock	Peake SL
European Society of Intensive Care Medicine Annual forum. Barcelona, Spain 29 September 2014	Optimal Calorie Delivery In The Critically Ill	Peake SL
ANZICS/ACCCN Annual Scientific Meeting. Melbourne, 9 October 2014	Goal-Directed Resuscitation for Patients with Early Septic Shock	Peake SL
MEDICINE		
American Heart Association 2014 Scientific Sessions, Chicago, United States. 15th-19th November 2014	In-hospital Management and Outcomes in Patients with Myocardial Infarction and Non-obstructive Coronaries	Tavella R
American Heart Association 2014 Scientific Sessions, Chicago, United States . 15th-19th November 2014	Predictors of Bleeding Complications in Patients Undergoing Percutaneous Coronary Intervention in an Australian Cohort	Tavella R
American Thoracic Society Annual Scientific Meeting, San Diego, United States, June 2014 Population Cohort of Men (MAILES)	Undiagnosed Obstructive Sleep Apnea is Associated with Incident Diabetes in a	Adams R
Australian Health & Medical Research Congress, Melbourne, November, 2014	Evolving epidemiology of chronic conditions	Adams R
European Respiratory Society, Munich Sept 2014	Zinc and zinc transporters in human alveolar and THP-1 macrophages and their roles in efferocytosis in COPD	Zalewski PD
Geriatric Society of Australia & New Zealand Scientific Meeting, January 2014	Sleep Apnea in the Elderly	Adams R
Internal Medical Society of Australia and New Zealand Annual Scientific Conference, Adelaide, September 2014	Achieving the National Standards: Sustaining change after the accreditors have left	Adams R
National Health & Medical Research Council 2014 Research Translation Symposium 12th -13th November 2014	A proposed minimum set of outcome metrics for coronary artery disease management from the International Consortium for Health Outcomes Measurement (ICHOM)	Tavella R
Thoracic Society of Australia & New Zealand Annual Scientific Conference, Adelaide, April 2014	Some statistical tips for projects and beyond	Adams R

Conference Title and Date	Title of Presentation/Poster	Attendee Name
MEDICINE (cont.)		
Thoracic Society of Australia & New Zealand Annual Scientific Conference, Adelaide, April 2014	Identification of Clinical Phenotypes in Obstructive Sleep Apnea (OSA) Using Statistical methods: A Population Study	Adams R
NEUROLOGY		
Australasian Neuroscience Society Annual Scientific Meeting, Adelaide 2014	Session Chairperson: "Clinical Disorders & Injury of the Nervous System"	Kobler S
Wolfson Centre for Aged Related Disease, Guy's Hospital, London, UK May 13, 2014	Invited Speaker: "Brain Repair – Stem Cell Therapy in Stroke"	Kobler S
University of Cambridge Brain Repair Centre, Cambridge, UK May 15, 2014	BRC Seminar Series Invited Speaker: "Brain Repair - Centering on stem cell therapy and neuroplasticity in stroke"	Kobler S
The Berlin Neuro Colloquium at The Charité, University of Humboldt, Berlin Germany May 30, 2014	Invited Lecture: "Cell-based Therapy for Stroke – Time for Clinical Trials"	Kobler S
Lund University Department of Physiology Sweden, June 2, 2014	Invited Lecture: "Brain Repair in Stroke"	Kobler S
Fraunhofer Institute for Cell Therapy, Leipzig, Germany June 16, 2014	Invited Lecture: "Dental Pulp Stem Cells and Stroke"	Kobler S
Center for Cranial and Dental Molecular Biology, University of Southern California, Los Angeles, USA July 14, 2014	Invited Lecture: "Dental Pulp Stem Cells – New Perspective for Brain Repair"	Kobler S
Stroke Society of Australasia 2014 Conference, Hamilton Island, QLD July 30, 2014	Invited Lecture: "Stem Cell Therapy in Stroke – Time for a Clinical Trial"	Kobler S
Florey Stroke Division 13th Annual Scientific Meeting, Ramada Resort, Newcastle, NSW 5-7 Dec. 2014	Guest Speaker: "Update on Stem Cell Therapy in Stroke"	Kobler S

Conference Title and Date	Title of Presentation/Poster	Attendee Name
OTOLARYNGOLOGY, HEAD AND NECK SURGERY Department of		
Australian Society of Head and Neck Surgeons Brisbane March 2014	Topical Therapies in CRS	Wormald PJ
2014 USC, Los Angeles 20-25 February, 2014	Skull Base/Advances Endoscopic Sinus Surgery Course	Wormald PJ
The 7th Wessex Advanced Endoscopic Sinus Surgery Course, June 8-10 2014	Keynote Lecture: Cutting edge Rhinology	Wormald PJ
25th Congress of the European Rhinologic Society, Amsterdam, The Netherlands June 22-26, 2014		Wormald PJ
Frontiers 2014, Sydney 31 July 2014		Wormald PJ
I Curso de Cirugía Endoscópica Avanzada de Cavidades Perinasales, Chile 25-27 October, 2014		Wormald PJ
The Western States Advanced Functional Endoscopic Sinus Surgery Course, Sonoma, United States, October 2014		Wormald PJ
7th Adelaide Management of Vascular Injuries Workshop, Adelaide 26 November 2014		Wormald PJ
17th Advanced Functional Endoscopic Sinus Surgery Course, Adelaide 27-29 November 2014		Wormald PJ
PSYCHIATRY		
Society for Mental Health Research Conference, Adelaide December, 2014	Alternative paths to a successful research career	Clark SR
RESPIRATORY MEDICINE UNIT AND CLINICAL PRACTICE UNIT		
Thoracic Society of Australia and New Zealand, South Australian and Northern Territory Branch Annual Scientific Meeting, Adelaide, SA, September 2014	Smoking cessation in COPD – current evidence and future directions	Carson KV
Thoracic Society of Australia and New Zealand, South Australian and Northern Territory Branch Annual Scientific Meeting, Adelaide, SA, September 2014	Management of anxiety and depression in COPD	Carson KV, Smith BJ
Thoracic Society of Australia and New Zealand, South Australian Branch State Meeting, Adelaide, SA, September 2014	Sleep apnoea and driving	Elgar N, Smith BJ
Rotary Club of Prospect, Adelaide, SA, November 2014	Respiratory research overview and how I became a scientist	Carson KV
Lung Foundation Australia 2014 Lung Health Education Day, Adelaide, SA, November 2014	How do we know this treatment works? Information for patients (consumers) needs to be a 2-way process	Carson KV
Australian Society for Medical Research Conference, Adelaide, SA, June 2014	The importance of networking in establishing a successful career: A PhD perspective	Carson KV

Conference Title and Date	Title of Presentation/Poster	Attendee Name
RESPIRATORY MEDICINE UNIT AND CLINICAL PRACTICE UNIT (cont.)		
University of Adelaide Research Highlights Meeting, Adelaide, SA, May 2014	A research overview from the Respiratory Medicine Department, TQEH: The good, the bad and the breathless	Carson KV
South Australian Branch Australasian Sleep Technology Association Meeting, Adelaide, SA, November 2014	Indigenous Sleep Health	Veale A
American Thoracic Society Conference, San Diego, California, USA, May 2014	Asthma self-management education with either regular healthcare professional review or written action plan or both in adults: A Cochrane review	Smith BJ, Carson KV, Schultz TJ, Barton C, Ali A, Brinn MP, Tan JJ, Walters EH
American Thoracic Society Conference, San Diego, California, USA, May 2014	Interventions for tobacco use cessation in Indigenous populations: A Cochrane meta-analysis	Carson KV, Brinn MP, Peters M, Veale A, Esterman AJ, Smith BJ
European Respiratory Society, Munich Germany, September 2014	Community interventions for preventing smoking in young people: A Cochrane systematic review	Smith BJ, Carson KV, Brinn MP, Sayemhiri K, Sayemhiri F, Esterman AJ
European Respiratory Society, Munich Germany, September 2014	Prolonged antibiotics for purulent bronchiectasis: A Cochrane systematic review	Hnin K, Nguyen C, Carson KV, Evans D, Greenstone M, Smith BJ
European Respiratory Society, Munich Germany, September 2014	Gastro-oesophageal reflux treatment for asthma in adults and children: A Cochrane systematic review	Yap H, Tin KS, Hnin K, Carson KV, Smith BJ
Thoracic Society of Australia and New Zealand Annual Scientific Meeting, Adelaide SA, April 2014	Barriers and enablers to the use of smoking cessation pharmacotherapy in Aboriginal and Torres Strait Islander populations: A qualitative analysis	Carson KV, Peters M, Esterman AJ, Veale A, Brinn MP, Bradley H, Newchurch J, Meagher S, Smith BJ
Thoracic Society of Australia and New Zealand Annual Scientific Meeting, Adelaide SA, April 2014	Respiratory health service delivery and utilisation by Aboriginal and Torres Strait Islander Australians: A qualitative analysis of the barriers and enablers to optimal medical management	Carson KV, Peters M, Esterman AJ, Veale A, Brinn MP, Bradley H, Newchurch J, Meagher S, Smith BJ
Thoracic Society of Australia and New Zealand Annual Scientific Meeting, Adelaide SA, April 2014	Preference for battery powered portable oxygen concentrators versus portable cylinders in patients with COPD: Evaluation of an equipment survey	Keatley D, Jurisevic M, Liu X, Kidd P, Lawton K, Kotal L, Alexander S, Liversidge C, Carson KV, Brinn MP, Esterman A, Veale A, Usmani Z, Mysore S, Smith BJ
Thoracic Society of Australia and New Zealand Annual Scientific Meeting, Adelaide SA, April 2014	Continuous positive airway pressure for obstructive sleep apnoea: A Cochrane systematic review	Usmani ZA, Carson KV, Elgar N, Smith BJ, Lasserson TJ, Mysore S, Ali A, White J, Wright J
Thoracic Society of Australia and New Zealand Annual Scientific Meeting, Adelaide SA, April 2014	Mass media interventions for preventing smoking in young people: A Cochrane systematic review	Ameer F, Carson KV, Sayemhiri K, Sayemhirir F, Brinn MP, Chang AB, Hnin K, Smith BJ
Thoracic Society of Australia and New Zealand Annual Scientific Meeting, Adelaide SA, April 2014	Physical training for asthma: A Cochrane systematic review	Carson KV, Brinn MP, Chandratilleke MG, Picot J, Esterman AJ, Smith BJ
Thoracic Society of Australia and New Zealand Annual Scientific Meeting, Adelaide SA, April 2014	Triggers resulting in relapse: Cohort analysis from the Smoking Termination Opportunity for inpatients I (STOP) trial	Hnin K, Carson KV, Brinn MP, Jannes J, Esterman AJ, Smith BJ
Thoracic Society of Australia and New Zealand Annual Scientific Meeting, Adelaide SA, April 2014	Prolonged antibiotics for purulent bronchiectasis: A Cochrane systematic review	Hnin K, Nguyen C, Carson KV, Evans D, Greenstone M, Smith BJ

Conference Title and Date	Title of Presentation/Poster	Attendee Name
RESPIRATORY MEDICINE UNIT AND CLINICAL PRACTICE UNIT (cont.)		
Thoracic Society of Australia and New Zealand Annual Scientific Meeting, Adelaide SA, April 2014	Evaluation of the hospital smoke free implementation policy: A cross-sectional cohort analysis in South Australia	Brinn MP, Carson KV, Smith BJ
Thoracic Society of Australia and New Zealand Annual Scientific Meeting, Adelaide SA, April 2014	Compliance with the British Thoracic Society guidelines in the management of pneumothoraces	Cheng J, Sarkar P, Carson KV, Brinn MP, Smith BJ
Thoracic Society of Australia and New Zealand Annual Scientific Meeting, Adelaide SA, April 2014	Smoking during pregnancy and tobacco abuse prevention in Aboriginal and Torres Strait Islander youth: A qualitative analysis	Carson KV, Peters M, Esterman AJ, Veale A, Brinn MP, Clifton V, Bradley H, Newchurch J, Meagher S, Smith BJ
Thoracic Society of Australia and New Zealand Annual Scientific Meeting, Adelaide SA, April 2014	Failure to pass the step test: Qualifying criteria in a multi-centre randomised cross-over study of portable oxygen for patients with COPD	Kidd P, Liu X, Carson KV, Lawton K, Kotal L, Liversidge C, Alexander S, Keatley D, Jurisevic M, Brinn M, Esterman A, Veale A, Usmani Z, Mysore S, Smith BJ
Thoracic Society of Australia and New Zealand Annual Scientific Meeting, Adelaide SA, April 2014	Cost effectiveness of portable oxygen concentrators compared to portable oxygen cylinders: A multi-centre RCT	Jurisevic M, Liversidge C, , Alexander S, Nguyen H, Segal L, Keatley D, Liu X, Kidd P, Kotal L, Lawton K, Carson KV, Brinn MP, Esterman A, Veale A, Smith BJ
Thoracic Society of Australia and New Zealand Annual Scientific Meeting, Adelaide SA, April 2014	Quality of life among participants of a multi-centre RCT comparing portable oxygen concentrators to portable oxygen cylinders	Lawton K, Kotal L, Nguyen H, Jurisevic M, Segal L, Liversidge C, Alexander S, Keatley D, Kidd P, Liu X, Carson KV, Brinn MP, Esterman AJ, Veale A, Smith BJ
Thoracic Society of Australia and New Zealand Annual Scientific Meeting, Adelaide SA, April 2014	Management of bronchiectasis: A retrospective hospital audit of patient care compared to British Thoracic Society guidelines	Lawton K, Royals K, Carson KV, Brinn MP, Smith BJ
World Congress of Cardiology Scientific sessions, Melbourne 2014	In-hospital mortality of Tako-tsubo cardiomyopathy: A systematic review and meta-analysis	Singh K, Carson KV, Singh B, Usmani Z, Parsaik, A, Horowitz JD
RHEUMATOLOGY		
Asia Pacific IMID Summit, Seoul, South Korea, 30 August 2014	Perspectives on Immune Mediated Inflammatory Diseases (IMID)	Rischmueller M
Asia Pacific IMID Summit, Seoul, South Korea, 30 August 2014	Understanding Rheumatism	Rischmueller M
Asia Pacific IMID Summit, Seoul, South Korea, 30 August 2014	Health Communications	Rischmueller M
Asia Pacific IMID Summit, Seoul, South Korea, 30 August 2014	Ask the Experts!	Rischmueller M
Australasian College of Dermatology Rural Dermatology Meeting. Clare SA. 25 October 2014	Spondyloarthritis	Whittle SL

Conference Title and Date	Title of Presentation/Poster	Attendee Name
RHEUMATOLOGY (cont.)		
Australian Rheumatology Association Annual Scientific Meeting, Hobart, 19 May 2014	The Cochrane Collaboration: Past, Present & Future	Whittle SL
Internal Medicine Society of Australia & New Zealand (IMSANZ) Annual Scientific Meeting, Adelaide, 18 September 2014	Fibromyalgia Syndrome	Whittle SL
Rheumatology 2014, Melbourne, 1 February 2014	Difficult Cases: Panel Discussion	Rischmueller M
SURGERY, University of Adelaide Discipline of		
Abdominal Radiology Group Australia and New Zealand Meeting, Adelaide SA, March 2014	Colorectal MDT panel discussion member	Hewett P
ACS New Zealand Annual Scientific Meeting, Queenstown New Zealand, August 2014	Simulation (interpersonal behaviour)	Maddern G
AES Postgraduate Education Workshop, Melbourne, June 2014	Mild primary hyperparathyroidism	Walsh D
ACMM23 and ICONN2014, Adelaide SA, February 2014	Bone metastasis models and therapeutic interventions	Evdokiou A
Amine Oxidase 16th International Conference and Workshop, Sydney NSW, July 2014	Peroxidase enzymes as novel modulators of collagen extracellular matrix biosynthesis	DeNichilo M
Asia Pacific HTA Policy Forum, Manila Philippines, July 2014	Variations in clinical practice between countries and the implications for transferability of HTA	Maddern G
Asia Pacific Musculoskeletal Tumour Society (APMSTS) 10th meeting, Melbourne Vic, April 2014	Targeting breast cancer bone metastases with adoptive transfer of ex vivo expanded cytotoxic gamma delta T cells	Zysk A et al
Asian Society for Vascular Surgery, Hong Kong, September 2014	Preoperative factors associated with 12 month survival after EVAR	Fitridge R
Asian Society for Vascular Surgery, Hong Kong, September 2014	Development of an automated measure of iliac artery tortuosity that successfully predicts early graft-related complications associated with endovascular aneurysm repair	Fitridge R
ASMR, SA Annual Scientific Meeting, Adelaide SA, June 2014	The effect of androgen receptor expression in fibroblasts co-cultured with prostate cancer cells	Palethorpe H, Leach D, Need E, Drew P, Smith E
Australian Society for Immunology, SAHMRI Adelaide SA, May 2014	Modern vaccine design and implementation	Gowans E
Australian Centre for HIV and Hepatitis virology, Lorne Vic, June 2014	Prime/boost vaccine strategies for HIV	Wijesundara D
Australian Medical and Health Research Congress (7th), Melbourne Vic, November 2014	Expression of androgen receptor and the androgen receptor responsive gene FKBP5 in oesophageal adenocarcinoma	Smith E, Palethorpe H, Ruszkiewicz A, Leach D, Need E, Drew P
Australian and New Zealand Society for Vascular Surgery, Canberra ACT, October 2014	Association of iliac artery tortuosity and adverse events after elective endovascular aneurysm repair (EVAR)	Fitridge R
Australian and New Zealand Society for Vascular Surgery, Canberra, ACT, October 2014	Preoperative factors associated with 12 month survival after EVAR	Fitridge R
Australian Society of Cataract and Refractive Surgeons Annual Congress, Plenary Session. Port Douglas Qld, 2014	Corneal Curvature and cataract surgery, Corneal Compendium	Goggin M

Conference Title and Date	Title of Presentation/Poster	Attendee Name
SURGERY, University of Adelaide Discipline of (cont.)		
Australasian Vaccines and Immunotherapeutics Development Meeting (5th), Melbourne Vic, May 2014	New life from dead cells-and other vaccine strategies	Gowans E
Australasian Conference on Viral Hepatitis (9th), Alice Springs NT, September 2014	Cytolytic DNA vaccines enhance immunity to hepatitis C virus	Gowans E
Breast Screen Australia Melbourne, October 2014	Mammographic density: understanding the associated biology and pathology	Ingman W
Breast Screen Australia Melbourne Vic, October 2014	Development of a new resource to support biomarker discovery	Ingman W
Bone Cancer Meeting. Concord Medical Education Centre Sydney NSW, November 2014	New therapeutic approaches targeting cancer in bone	Evdokiou A
Canadian Surgery Forum, Vancouver Canada, September 2014	Initiating a national quality agenda in hepato-pancreato-biliary surgery: How should we improve the processes of surgical care?	Maddern G
Canadian Surgery Forum, Vancouver Canada, September 2014	Surgical innovation: Do we know what we are doing	Maddern G
Canadian Surgery Forum, Vancouver Canada, September 2014	Management of liver mets for the non-liver surgeon	Maddern G
Clare valley Bone 8th Meeting, Adelaide SA, March 2014	Using mouse models to investigate novel treatments for bone cancer	Evdokiou A
Combined Medical and Surgical Grand Round, The Queen Elizabeth Hospital SA, August 2014	New surgical technology: Do we know what we are doing?	Maddern G
Centenary Institute, Sydney NSW, October 2014	Encoded natural adjuvants and cytolytic cells increase the efficacy of DNA vaccines	Gowans E
Department of Gastroenterology, Women's & Children's Hospital, Adelaide SA, November 2014	Strategies to improve the efficacy of DNA vaccines	Gowans E
Duke University/National University of Singapore, Singapore, September 2014	A unique strategy to increase the efficacy of DNA vaccines	Gowans E
Frontiers for a Healthy Start to Life, McLaren Vale SA, March 2014	Inflammatory mediators of lactation insufficiency	Ingman W
Graduates of '79 University of Adelaide, Adelaide SA, June 2014	A new RAH or an embedded institution?	Maddern G
Guangdong Provincial Symposium on Colorectal Cancer (15th), Guangzhou PR China, August, 2014	Advances in colorectal cancer	Hewett P
International Union of Microbiological Societies Congresses, Montreal Canada, July 2014	Encoded natural adjuvants increase the efficacy of DNA vaccines	Gowans E
ICONN, Adelaide SA, February 2014	Synthesis of alumina nanotubes as novel drug nano-carriers for drug delivery applications	Wang Y, Santos A, Evdokiou A, Losic D
International Conference on Nanoscience and Nanotechnology/Australian Conference on Microscopy and Microanalysis, Adelaide SA, February 2014	Live imaging of vaccine antigens after intradermal delivery to aid vaccine development	Gowans E
International Conference on Vaccines and Vaccination (4th), Valencia Spain, September 2014	DNA vaccines which encode natural adjuvants are more effective than canonical DNA vaccines	Gowans E

Conference Title and Date	Title of Presentation/Poster	Attendee Name
SURGERY, University of Adelaide Discipline of (cont.)		
Lorne Infection and Immunity Conference (4th), Lorne Vic, February 2014	Natural adjuvants encoded by DNA vaccines or released as a result of induced antigen-positive cell death enhance T cell mediated immunity	Gowans E
Mawson Institute's Materials, Minerals and Manufacturing (M3) Seminar Series, University of South Australia, Adelaide SA, May 2014	Novel role for peroxidase enzymes in regulating collagen ECM biosynthesis	DeNichilo M
MRS 2014: The 15th biennial Metastasis Research Congress Heidelberg, Germany, June 2014	Uncovering a new role for peroxidases in breast cancer development and metastasis	Panagopoulos V, Zinonos I, Leach D, Iasiello M, Hay S, Liapis V, Zysk A, Ingman W, Ponomarev V, DeNichilo M, Evdokiou A
Medical Insurance Group Australia, Adelaide SA, July 2014	Stop the Clot	Maddern G
Medical Insurance Group Australia, Sydney NSW, August 2014	Stop the Clot	Maddern G
Medical Insurance Group Australia, Melbourne Vic, September 2014	Stop the Clot	Maddern G
Medical Insurance Group Australia, Barossa Valley SA, September 2014	Stop the Clot	Maddern G
Medical Insurance Group Australia, Adelaide SA, November 2014	Stop the Clot	Maddern G
Ministry of Health Technology Advisory Committee, Singapore, May 2014	Models of implementation of HTA activities: the Australian experience	Maddern G
Ostomy Association AGM, Adelaide SA, October 2014	New developments in colorectal cancer treatment	Hewett P
OzMRS-CTx Workshop, Melbourne Vic, December 2014	Uncovering a new role for peroxidases in breast cancer development and metastasis	Panagopoulos V, Zinonos I, Leach D, Iasiello M, Hay S, Liapis V, Zysk A, Ingman W, Ponomarev V, DeNichilo M, Evdokiou A
RACS New Zealand Annual Scientific Meeting, Queenstown New Zealand, August 2014	Simulation (technical skills)	Maddern G
Royal Australasian College of Surgeons, Sydney NSW, November 2014	Summit to establish Integrated Academic Career Pathways	Maddern G
RACS Section of Academic Surgery Annual Meeting, Basil Hetzel Institute, The Queen Elizabeth Hospital, Adelaide SA, November 2014	Academics and the College	Maddern G
RACS Section of Academic Surgery Annual Meeting, Basil Hetzel Institute, The Queen Elizabeth Hospital, Adelaide SA, November 2014	Academic career pathways	Maddern G
Royal Australasian College of Surgeons Annual Scientific Congress, Singapore, May 2014	Regulation and audit in surgery – Lessons from ASERNIP-S and ANZASM	Maddern G
Royal Australasian College of Surgeons Annual Scientific Congress, Singapore, May 2014	Introduction to simulation research for surgeons	Maddern G

Conference Title and Date	Title of Presentation/Poster	Attendee Name
SURGERY, University of Adelaide Discipline of (cont.)		
Royal Australasian College of Surgeons Annual Scientific Congress, Singapore, May 2014	Optimal application of evidence-based medicine in surgery	Maddern G
Royal Australasian College of Surgeons Annual Scientific Congress, Singapore, May 2014	Trust me, I'm a surgeon	Maddern G
Society for Reproductive Biology-Endocrine Society Australasia combined meeting, Melbourne, August 2014	Hormonal regulation of the immune microenvironment in the mammary gland: implications for breast cancer risk	Ingman W
St George Hospital and Sutherland Hospital Medical Research Symposium, Sydney NSW, October 2014	Do audits of surgical mortality alter surgical outcomes?	Maddern G
St George Hospital and Sutherland Hospital Medical Research Symposium, Sydney NSW, October 2014	We can't afford new surgical technology – Debate	Maddern G
The Society of Free Radical Research Australasia, 22nd Annual Scientific Meeting, Melbourne Vic, December 2014	Peroxidase enzymes as novel modulators of collagen extracellular matrix biosynthesis	DeNichilo M
The University of Wisconsin/FluGen Inc., Madison, Wisconsin USA, August 2014	New life from dead cells-a unique strategy to increase the efficacy of DNA vaccines	Gowans E
University of Adelaide Florey International Postgraduate Research Conference, Adelaide SA, September 2014	Uncovering a new role for peroxidases in breast cancer development and metastasis	Panagopoulos V, Zinonos I, Leach D, Iasiello M, Hay S, Liapis V, Zysk A, Ingman W, Ponomarev V, DeNichilo M, Evdokiou A
Victor Chang Cardiac Research Institute, Sydney NSW, October 2014	Defining new roles for peroxidase enzymes in human health and disease	DeNichilo M
Western Health, Sunshine Hospital Melbourne Vic, November 2014	Surgical innovation: Do we know what we are doing?– Keynote address	Maddern G

THERAPEUTIC RESEARCH CENTRE, University of South Australia

6th Advanced Optical Methods Workshop AOM2014, Shenzhen China, July 2014	Imaging the tissue pharmacokinetics of drugs and nanoparticles	Roberts MS
9th Workshop on Advanced Multiphoton and Fluorescence Lifetime Imaging Techniques FLIM 2014. Saarbrücken Germany. May 2014	Multimodal imaging <i>ex vivo</i> and <i>in vivo</i>	Roberts MS
Perspectives in Percutaneous Penetration International Conference PPP2014, La Grande Motte France, April 2014.	Non-invasive imaging of the penetration of nano-materials into human skin	Roberts MS
Perspectives in Percutaneous Penetration International Conference PPP2014, La Grande Motte France, April 2014	Application of TOF-SIMS to percutaneous absorption studies	Holmes AM
North West university,Potchefstroom, South Africa, April 2014	Pamam dendromers as a topical penetration enhancer	Holmes AM
5th FIP Pharmaceutical Sciences World Congress, Melbourne Australia, April 2014	Understanding the physicochemical and biological determinants of pharmacokinetics: from humans to organs, cells and nanosystems	Roberts MS
10th International Conference and Workshop on Biological Barriers, Saarland Germany, February 2014	Extension of the Jmax concept	Roberts MS
11th Advanced Imaging Methods Workshop, San Francisco USA, January 2014.	Using <i>ex vivo</i> and <i>in vivo</i> Multiphoton Imaging and FLIM to Assess Drug Disposition and Response	Roberts MS
Australian Pesticides and Veterinary Medicines Authority Nanotechnology Regulation Symposium, Canberra ACT, October 2014	Nanoproduct safety – health implications	Roberts MS
2014 Joint Australian-New Zealand Control Release Society Student Workshop: Development of Pharmaceutical Therapeutics: From Biological Imaging to Delivery System Optimisation, Adelaide SA, October 2014	Imaging biological barriers and transport	Roberts MS
14th Hunter Meeting, Hunter Valley NSW, March 2014	<i>In vivo</i> and <i>ex vivo</i> multimodal imaging	Roberts MS

Support Structures

Supporting research at the
Basil Hetzel Institute

The Basil Hetzel Institute (BHI) Policy Committee provides strategic advice for the running of the BHI and optimises the available support for research programs across The Queen Elizabeth Hospital (TQEH).

The Institute (BHI) Policy Committee Current Members, December 2014

Professor Guy Maddern
Professor John Beltrame
Professor Alastair Burt (proxy - Professor Andrew Somogyi)
Professor Mike Roberts (proxy - Dr Lorraine Mackenzie)
Dr Prue Cowled
Dr Peter Zalewski
Dr Jenny Hardingham
Professor Andreas Evdokiou
Dr Ehud Hauben
Mr Paul Flynn
Ms Kathryn Hudson
Professor Eric Gowans
Professor Wendy Ingman
Ms Diana Brown

Executive Support

Ms Gwenda Graves

The Committee is comprised of senior representatives from:

- the two universities with whom the hospital is affiliated, the University of Adelaide and the University of South Australia;
- University of Adelaide academic heads of departments at TQEH (Medicine and Surgery);
- Allied Health
- Chair, Strategic Research Directions Working Group
- BHI Facility Manager and
- the scientific community

Professor Guy Maddern was reappointed to the position of Director of Research in April 2010 for a five-year term. This leadership position has been critical to furthering the aims of research excellence and enhancing the research reputation of TQEH.

Several sub-committees assist The Institute Policy Committee as required, notably the:

- Research Day Organising Committee, chaired by Dr Prue Cowled, University of Adelaide Discipline of Surgery, in the planning and running of the annual Research Day event.
- Scholarship Selection Committee, chaired by Professor Maddern, in awarding a range of scholarships funded by The Hospital Research Foundation.
- BHI Management Committee, chaired by Associate Professor Wendy Ingman, University of Adelaide Discipline of Surgery, in managing the Basil Hetzel Institute.

The Basil Hetzel Institute Strategic Research Directions group provides a forum for BHI Researchers to interact and discuss Institute issues and initiatives as well as focus on academic issues such as teaching and postgraduate student recruitment and completions. It reports to The Institute (BHI) Policy Committee, and in 2014 provided recommendations to The Hospital Research Foundation on the 2015 funding framework. All TQEH researchers at Associate Professor level, Postgraduate coordinators, Heads of departments, and Chief Investigators on Category 1 grants are eligible to attend each forum, as well as a postdoctoral representative. Professor Eric Gowans has chaired the group since 2012.

TQEH Research Secretariat undertakes a range of activities to assist the Director of Research in supporting, fostering and administering quality research activity across TQEH.

Research Training

The BHI Policy Committee aims to support the research capacity within basic and clinical areas through its strategy of providing a number of scholarships at Postgraduate, Honours and Vacation levels.

Research training promotion

In 2014 research training opportunities and Scholarship support were actively promoted through the Basil Hetzel Institute's Internet site with links to key university research training sites.

The Hospital Research Foundation Vacation Research Scholarships

Eight placements offered in TQEH research settings over the 2014-2015 vacation were funded by individual departments, and provided scholars with the opportunity to gain valuable research experience in a clinical/laboratory environment.

Honours Research Scholarships

Honours Scholarships continued to be offered at TQEH in 2014. Five Scholarship recipients completed projects through either the Breast Cancer Research Unit or the combined departments of Haematology and Medical Oncology; one Scholarship recipient, in the Clinical Pharmacology Unit, commenced mid year and will finish in mid 2015.

Higher Degrees

In 2014 over sixty scholars were undertaking research towards Higher Degrees at TQEH, with several domestic students supported with The Hospital Research Foundation Scholarships. In 2014 The Hospital Research Foundation Scholarships provided for stipends which matched the Australian Postgraduate Award (APA) rate. Responsibility for the selection of Honours and Postgraduate scholars lies with the BHI Scholarship Selection Committee. The Committee draws representatives from clinical academics and scientists. Both the University of Adelaide and University of South Australia are represented. Other higher degree students at TQEH have scholarship support from a range of funding bodies, including NHMRC, the University of Adelaide and University of South Australia (International scholarships, APA, and University of Adelaide Faculty 'Divisional' scholarships). The Hospital Research Foundation also supports two international scholars.

Support

Supporting research at the
Basil Hetzel Institute

Structures (cont.)

Statistical Support Service, TQEH

The Statistical Support Service, jointly funded by BHI and the Faculty of Health Sciences (FHS) at the University of Adelaide, provides 12 hours per week of statistical assistance to staff and students at the BHI and TQEH more generally.

In 2014 the Statistical Service continued to be provided by Dr Stuart Howell, of the Statistics Division of the Data Management & Analysis Centre (DMAC), School of Population Health and Clinical Practice at The University of Adelaide.

The range of services has included:

- Advice to research staff, Postgraduate and Honours students about:
 - o Design of health-related research
 - o Statistical aspects of research programs
 - o Preparing data for analysis
 - o Data analysis
 - o Manuscript preparation
- Analysis of data from research programs based at BHI, TQEH.

We are grateful to DMAC, and the University of Adelaide for their support and commitment to research at TQEH.

Research Day 2014

TQEH Research Day was held on Friday 17 October 2014 in the BHI facility. Our congratulations to all the postgraduate students and registrars who participated in Research Day 2014! Once again the scope and quality of the research presented was of a consistently high standard, which made the judges' jobs even more difficult.

The purpose of Research Day is to provide an opportunity for our post-graduate students and those in training to develop and practice writing and presentation skills under conditions that are typical of most professional society congresses. They are asked to write an Abstract and prepare either a 10-minute oral presentation or a poster with a 3-minute oral presentation. They receive guidance and encouragement from their supervisors and peers during preparation of both the Abstract and the presentations. On Research Day, they experienced giving their presentations before a large audience and then answering questions. With this experience, it is hoped that the students will feel more confident when they are presenting their studies at major national and international conferences. It is also hoped that, by holding Research Day as a significant professional development activity, high quality researchers will graduate from The Basil Hetzel Institute and The Queen Elizabeth Hospital, adding to the campus' reputation as a significant research facility.

Research Day also provides an opportunity for all researchers at the BHI/TQEH to hear about the wide range of research being undertaken on this campus. This knowledge can lead to the identification of new opportunities for inter-disciplinary collaboration. It is also important in research training that students are exposed to a wide range of disciplines, as their later careers may diverge from the topics studied during their post-graduate years. This broad exposure will produce well-rounded researchers that are equipped for their future careers in research.

Dr Prue Cowled
Chair, Research Day Organising Committee, 2014



*Back Row: S Vreugde, L Mackenzie, A Zysk, W Ingman, T Cambareri, S Appleton, I Stafford, M Smith, K Rajopadhyaya
Front Row: T Pasupathy, C Kirana, K Hudson, G Graves - Not shown: S Bray*

Basil Hetzel Institute Management Committee

Current members, December 2014

The Institute Level

Ground Level

Representative

Ms Sarah Appleton

Level 1

Dr Sarah Vreugde

Dr Chandra Kirana

Dr Sarah Bray
(Deputy Chair 2014-15)

Level 2

Dr Lorraine Mackenzie

Dr Kanchani Rajopadhyaya

Ms Irene Stafford

Surgical Suite

Mr Matthew Smith

External representative

Dr Tony Cambareri

Postgraduate Representatives

Ms Tharshy Pasupathy (Level 2)

Ms Aneta Zysk (Level 1)

Chair

Associate Professor Wendy Ingman

BHI Facility Manager

Ms Kathryn Hudson

Executive Support

Ms Gwenda Graves

Human Research

Ethics Report 2014



Associate Professor Tim Mathew - Chairman
Human Research Ethics Committee (TQEH/LMH/MH)

The current year (2014) has seen a maturing of the amended Ethics process detailed in my communication last year and several aspects have now gained clarity. Most importantly from the viewpoint of the Ethics process there has been a substantial reduction in the number of new applications requiring scientific and ethical review at the local level but no reduction in the workload involved in gaining governance approval. For the researchers there has been a reduction in workload for those projects where the local investigators are not the National 'lead' and conversely for the lead investigators more work and more responsibility.

It has been resolved that there should continue to be an accredited Ethics review process located at The Queen Elizabeth Hospital. This I believe is appropriate and should work to the advantage of TQEH located research teams through strong links and engagement with the local process and the availability of informed guidance to simplify the process of Ethics approval. Given the complexity of ethics applications this is highly desirable. However at the time of writing there has been considerable activity in the Central Local Area Network (for this purpose involving only RAH and TQEH) aimed at 'harmonising' the ethical review and approval process across the Network.

This might seem entirely rational and appropriate to the outsider and indeed there is no fundamental reason for this not to happen. However given the position from where we were four years ago prior to a system of mandated outside regulation (National accreditation, participation in the National Mutual Acceptance scheme and the mandated acquisition of a new IT platform (AuRed)) it has been a pronounced challenge to accommodate the changes whilst keeping productivity and timelines for the routine flow of applications.

One can look back to the previous era of Ethics review, where all we had to worry about was doing a thorough review of the science and ethics and leaving the governance in the hands of the hospital management and the researcher's department, as being the halcyon days! I don't believe the pharmaceutical companies who were almost solely responsible for driving change in the name of cost saving and avoidance of duplication would have anticipated the fallout that has brought probably increased cost and so far no indication of an overall reduction in timelines!

Ms Melissa Kluge and her team have guided our Ethics process through these demanding years with skill, good sense and a positive attitude towards change. Without Ms Kluge's resilience and strong commitment to the process we would have stumbled. The Human Research Ethics Committee (HREC) has also been a tower of strength and wisdom and has kept us grounded to the real world – as is their task. It has been a privilege for me to have been Chair of HREC for these past 8 years. We are particularly fortunate to have recruited Professor Richard Ruffin to take over as Chair from October 2014. Professor Ruffin brings to the task a long experience in research and indeed until recently he was a Chair of one of the Belberry Ethics Committee (a busy and highly regarded HREC active in the private hospital sphere). We could not be more fortunate in being able to hand over the Chair to someone with his qualities and background.

Associate Professor Tim Mathew
Outgoing Chairman 2014

Research day Awards 2014

Supporting research at the Basil Hetzel Institute



From Left: Helen Palethorpe, Aneta Zysk, Kati Richter, Tamsyn Willsmore, Harshani Jayasinghe, Bill Panagopoulos, Alice Du, Zaipul MD Dom with Professor Guy Maddern

Best Oral Presentation Honours Students

Tamsyn Willsmore, Gagandeep Kaur, Karan Gulati, Irene Zinosos, Ye Wang, Abel Santos, Dusan Losic, Andreas Evdokiou
'Titanium nanotube arrays for the localised treatment of cancer'

Best Oral Presentation Junior PhD Students (Laboratory)

Katharina Richter, Rowan Valentine, Sarah Vreugde, PJ Wormald
'A novel strategy to fight *Staphylococcus aureus* biofilms'

Best Oral Presentation Senior PhD Students (Laboratory)

Vasilios Panagopoulos, Irene Zinosos, Damien Leach, Matthew Iasiello, Shelley Hay, Vasilios Liapis, Aneta Zysk, Wendy Ingman, Vladimir Ponomarev, Mark DeNichilo, Andreas Evdokiou
'Uncovering a new role for mammalian peroxidases in breast cancer development and metastasis'

Best Oral Presentation Clinical Research Group 1

Shailaja Nair, R. Visvanathan, D. Gentlecore
'The postprandial blood pressure decline following a glucose drink affects gait detrimentally in older people'

Best Oral Presentation Clinical Research Group 2

Harshani Jayasinghe, KV. Carson, MP. Brinn, K. Sayemhiri, F. Sayemhiri, AJ. Esterman, BJ Smith
'Community interventions for preventing smoking in young people: A Cochrane Systematic Review'

Poster Prize (Junior)

Alice Du, Michael Deieso, Mohamad Kourgi, Timothy Price, Andrea Yool, Jennifer Hardingham
'shRNA knockdown of Aquaporin 1 (AQP1) to confirm specificity of the AQP1 antagonists AQB011, AQB013 and AQB050 in restricting migration of colon cancer cells'

Poster Prize (Senior)

Helen Palethorpe, Damien Leach, Eleanor Need, Paul Drew, Eric Smith
'Fibroblast androgen receptor expression regulates fibroblast and prostate cancer cell interactions *in vitro*'

Best Lay Description

Aneta Zysk, Vasilios Panagopoulos, Mark DeNichilo, Irene Zinosos, Vasilios Liapis, Shelley Hay, Vladimir Ponomarev, Wendy Ingman, Andreas Evdokiou
'Targeting breast cancer bone metastases with adoptive transfer of *ex vivo* expanded cytotoxic Gamma Delta T-Cells'

Ivan De La Lande Award

Zaipul MD Dom, Janet Coller, Andrew Somogyi, Graeme Russ, Bernadetta Sallustio
'Declining intra-lymphocyte concentrations of mycophenolic acid correlate with the incidence of graft rejection in renal transplant recipients: preliminary results of a prospective study'

Acknowledgements

Acknowledging our collaborators and supporters **2014**

Aberdeen University, UK
Academic Medical Centre, Amsterdam
ACAGN (Australian Cochrane Airways Group Network)
Adelaide Women's and Children's Hospital
AGRF, Melbourne
Alfred Health, Victoria
Alice Springs Hospital
Alzheimers Australia
American Chamber of Commerce
American College of Surgeons, Chicago, USA
AMGEN
Anne Marie Trimboli Trust
ANZICS
ARC
Arthritis Australia
ASERNIPS
Auckland City Hospital, NZ
Austin Health
Austin Hospital
Australian and New Zealand Intensive Care Society
Australian Breast Cancer Research
Australian Catholic University, Melbourne
Australian Genomics Recruitment Initiative
Australian Hotel Association (AHA Hotel Care)
Australian Prostate Cancer Research
Australian Red Cross Blood Service (ARCBS)
Australian Research Council
Australian Scleroderma Interest Group
Australian Society for Medical Research (ASMR)
Baker Research Institute
BankSA Staff Charitable Fund
Beat Cancer SAHMRI
BioInnovationSA AIB Labs
Biomet
Birmingham Heartlands Hospital
Boehringer Ingelheim
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Burnet Institute, Melbourne
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Cambridge UK
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Cancer Australia
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Erasmus University Medical Centre, Rotterdam, the Netherlands
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Indian Institute of Science, Bangalore, India
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Intermune Inc
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Kings College, UK
La Trobe University
Leicester General Hospital, UK
Lyll McEwin Hospital
Medical University of South Carolina, USA
Medimmune
Memorial Sloan Kettering Cancer Centre, NY, USA
Menzies Research Institute
Mid-America Heart Institute, Kansas, USA
MIT, USA
Monash Medical Centre
Monash University
Nagoya University Graduate School of Medicine, Nagoya, Japan
National Breast Cancer Foundation
National Health & Medical Research Council (NHMRC)
National Heart Foundation of Australia (NHFA)

NCIC Clinical Trials Group, Ontario, Canada
 Newcastle University, United Kingdom
 NHMRC Clinical Trials, Sydney
 Northern Territory Health
 Northwestern University, Chicago, USA
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 Resthaven
 Robinson Institute, University of Adelaide
 Royal Adelaide Hospital
 Royal Australasian College of Physicians
 Royal Australasian College of Surgeons
 Royal Australian College of General Practitioners
 Royal Brisbane and Womens' Hospital
 Royal Free and University College Medical School, London, UK
 Royal Northshore Hospital, NSW
 Royal Prince Alfred Hospital Intensive Care Unit
 SA Heart Foundation
 SA Pathology
 South Australian Health and Medical Research Institute
 Scott Salisbury Homes
 South Australian Department of Health
 Special Phage Services, Sydney
 St George's Vascular Institute, London, UK
 St James University Hospital, Leeds, UK
 St Jude's Research Institute, Memphis USA
 St Louis University, Missouri, USA
 St Vincent's Institute Melbourne, Department of Medicine
 Stanford University Medical School, USA
 Stroke SA
 Sydney University, NSW
 Tehran University, Iran
 The Australian National University, Canberra
 The Chinese University of Hong Kong, China
 The George Institute for Global Health

The Hospital Research Foundation (THRF) (formerly The
 (Queen Elizabeth Hospital Research Foundation)
 The Royal Marsden Hospital, UK
 Threshold Pharmaceuticals, Inc. California, USA
 Tilberg University, The Netherlands
 TLC Pharmacy, Hanson
 Toulouse University, France
 University College, London UK
 University Nijmegen Medical Centre, Nijmegen, Netherlands
 University of Adelaide
 University of Birmingham, UK
 University of California, San Diego, USA
 University of Cyprus
 University of Eastern Finland
 University of Groningen
 University of Hannover, Germany
 University of Leeds, UK
 University of Leicester, Leicester, UK
 University of Manchester
 University of Marburg
 University of Melbourne
 University of Michigan, USA
 University of Münster
 University of New South Wales
 University of Newcastle
 University of Nova Scotia, Canada
 University of Otago, New Zealand, Department of Chemistry
 University of Ottawa, Canada
 University of Queensland
 University of South Australia
 University of Southampton, UK
 University of Tasmania,
 University of Western Australia
 University of Würzburg
 Vaccine and Infectious Disease Organisation, Canada
 Weill Cornell Medical College, New York, USA
 Wellington Regional Hospital
 Western Australian Institute for Medical Research (WAIMR)
 Women's and Children's Hospital, South Australia
 York District Hospital, UK

Chair Report 2014



the hospital
research foundation

finding cures improving care

The Hospital Research Foundation supports medical research at The Queen Elizabeth Hospital and The Basil Hetzel Institute

If the Foundation entered 2014 at a canter it most certainly has reached full stride. It is pleasing to observe the growth and innovation that has guided the organisation towards achieving new goals and reaching new horizons in a challenging economic and political environment.

The expansion and added complexity of its operations has been shaped by the building of the Foundation's 'disease specific affiliate' brands which focus predominantly on high incidence diseases within communities across Australia.

The foresight to diversify and enter into highly competitive markets across Australia is courageous but it is what sets the Foundation apart. "You cannot lead from the back" they say and The Hospital Research Foundation is making its way on a national stage with great success.

Australian Heart Research (AHR) was launched this year as the third 'disease specific affiliate' operating under the Foundation's umbrella. It could not have been launched without the insightful guidance of our leading cardiologists and sets a new standard for the Foundation partner brands. The AHR affiliate also marks a new direction for fundraising as it seeks to achieve organic growth through clinical settings at The Queen Elizabeth Hospital and Royal Adelaide Hospital.

The affiliate program will be boosted by more brands in 2015. These include a stroke affiliate which will be launched in collaboration with Stroke Unit clinicians at The Queen Elizabeth Hospital (TQEH) and the Royal Adelaide Hospital (RAH). An affiliate in the area of Renal and Diabetes research will also launch to assist critical investigation into stem cell therapy conducted at the RAH. A further disease specific affiliate in the area of bowel cancer will follow later in 2015 which will support a Beat Cancer project in collaboration with SA Health, SAHMRI and the Cancer Council.

The affiliate program has enabled enthusiastic dialogue and interaction with clinicians and researchers at hospitals in South Australia. It has come at a pivotal time for the Foundation and blends seamlessly into the new centralisation strategy driven through the Central Adelaide Local Health Network (CALHN). It has fostered collaboration and a tacit recognition of the Foundation's ability to assist and deliver.

An Allied Health affiliate is also in planning with the lead team based at the RAH. It is an interesting area and one that will further expand the notion of organic growth from within the clinical settings of CALHN.

The rapidly approaching commissioning of the new RAH is building momentum. The Foundation is proud to be playing an active role in assisting in the development of affiliates that sit across the two hospitals. It is also delighted to be enabling an exciting new program which will focus on arts in health. The name for this new initiative is still emerging but signals a new health focused direction for the health outcomes of South Australians.



Lee Michaelis - Chair

Indeed it has been a busy but fruitful year for the Foundation. While driving new frontiers and growing its diversity it has also successfully delivered a record financial year with a Funds to Research Ratio of 79.3%. We all should be incredibly proud of this result which has been achieved despite often less than optimal conditions. It stands the Foundation in good stead as it gains recognition and support in the marketplace.

Research Grants:

Our research grants have traditionally addressed key areas of need as directed by the Strategic Research Committee at the Basil Hetzel Institute for Translational Health Research. The committee ensures that funds are allocated to translational research that has the greatest potential to provide benefits to the wider community via new treatments, therapeutics and patient care initiatives. Please refer to The Hospital Research Foundation's 'Research' section within this report for an update on the progress of research projects funded by the three major grants announced in late 2013. \$300,000 was allocated to each of these projects which are being undertaken in areas of Cardiology, Ear Nose and Throat and Virology.

We are proud to continue our long-standing commitment to key areas of research into breast cancer and prostate cancer. We have also significantly boosted funding to future growth areas reflected in our disease specific affiliates such as heart and renal research. The Foundation is delighted to have provided seed funding to the Virology Group headed up by Professor Eric Gowans who have achieved a patent on a technique which will deliver the first therapeutic vaccine for Hepatitis C and HIV. Funding to assist a collaborative project between Adelaide University and TQEH to produce a wearable patient sensor to prevent falls in hospital has led to further NHMRC funds being granted. Both the sensor and the vaccine are expected to be in clinical trials at TQEH in 2015.

Independent Research Review Committee:

To our esteemed panel of Research leaders who lend their immense skill and knowledge to our mission to support the highest quality research projects and personnel – we thank you most sincerely for your direction and candor. Our ability to achieve our strategic and translational research objectives can only be recognised with your ongoing contributions. The panel consists of Chair, Professor Colin Johnson, Senior Research Fellow at Baker IDI Heart and Diabetes Institute, Honorary Professor of Medicine at Monash University and Emeritus Professor of the University of Melbourne. He is joined on the panel by fellow members Professor Judith Whitworth from the Australian National University and Professor Richard Fox, Director of Research at St Vincent's Hospital in Melbourne.

Patient Support:

The Foundation has continued to expand patient support activities in both the local and regional communities. Through third party fundraising entities the Foundation has forged relationships and helped to grow legacy support for its many country hospital partners. Dry July revenue in 2014 was lower than expected however the value proposition in building regional awareness and support transcends the monetary value. Visits to the seven regional hospitals have reinforced the activity as beneficial to the immediate communities with plans already underway for upgrades to cancer patient areas in several of the centres. The key relationship with Mercer SuperCycle continues to grow with more than \$400,000 delivered to the Foundation from the 2014 ride. This energetic and focused group of cycling enthusiasts seems to require little downtime as they gear up for their third SuperCycle event in 2015. The target for next year's ride is conservatively estimated to be in excess of \$500,000. The funds have been directed to complete the first of the Foundation's Under Our Roof projects located at Woodville West. The project will provide vital family accommodation for country patients coming to TQEH for cancer treatment. The two 3-bedroom homes being built by Scott Salisbury Homes will be completed in 2015. Plans to expand this project to build more homes to service patients from TQEH and the new RAH are underway.

Fundraising Activities:

The Foundation's traditional fundraising model has been honed to become more donor centric, focused on creating donor validation and a defined donor journey. There has been an increase in Regular Giving for the Foundation and across the affiliate brands.

The cash lottery programs established in South Australia have now been introduced on a national scale for the Foundation and its three established disease specific affiliates.

The Foundation takes pride in its uptake of new technologies and new media and has built capabilities into its online presence and donation functionality for faster and more meaningful fulfillment for the donor. Social media channels including Facebook, Twitter and YouTube have become reliable platforms for public engagement and timely news delivery for the Foundation. Social media will continue to be a key area of growth, experimentation, testing and measurement to ensure strategic objectives including the potential for income generation are achieved.

Third party giving platforms such as Everyday Hero, Donate Planet and Just Giving have become vital fundraising partners for the Foundation and its disease specific affiliates. These sites allow engagement with people who are more inclined to show their support for health and medical research by participating in organised

events across Australia. It has given the Foundation a vital connection and interaction with new donors and additional support on a local, national and even international level

Thanks and welcome:

It is indeed a great honour to serve on The Hospital Research Foundation Board with such distinguished members. It is these key members who enable the Foundation to flourish and diversify. It is the members trust, solidarity and good governance that has given the Foundation its ability to set a record pace in 2014 and on into another remarkable year.

Into this stimulating environment come two new members of the Board and I wish them a warm welcome. Marylou Bishop and Valerie Timms are both remarkable business women with a wealth of knowledge and experience. I wish them well in their new capacity as Foundation Board members and know they will enjoy the camaraderie and professional focus of the established team.

At the operational helm of this wonderful enterprise is Paul Flynn. He is perhaps one of the most capable and knowledgeable leaders in the state. I thank him most sincerely for his direction and dedication to his role and his very talented and dexterous staff.

Summary:

It is with some sadness that I tender this Annual Report as outgoing Chairman of The Hospital Research Foundation. It has been both a proud and long association during which time the Foundation has harnessed new energy, explored and seized new directions, embraced change and strengthened its position as a market leader in the not-for-profit arena.

I am immensely proud of the achievements that have been made during my tenure and I thank my esteemed colleagues and members of the Board for their unwavering guidance, diligence and professionalism. I also thank them for helping to successfully steer the Foundation towards the close of a significant half century and onwards to the next fifty.

In our ever-changing political and economic landscape reaching a fifty year milestone is cause for celebration. The Foundation's beginnings suggest people perhaps wiser than they might have realised, provided the blueprint for a robust entity that has not only endured but thrived when others have failed; changed when others have remained static and been bold when others have not recognised opportunity.

Throughout this journey the Foundation has not lost sight of its overarching purpose – to deliver improved health and well-being to our local community informed by the very best translational medical research. This endeavour has been at the forefront of all that the Foundation is and stands for.

While my tenure may be drawing to a close my passion and interest in the Foundation's future directions and success will never diminish. I look forward with great interest as the next chapter unfolds, knowing in all likelihood that the best is yet to come.

I transfer the reins to a most accomplished and capable board member Melinda OLeary who I know will help elevate the Foundation to its next level. I wish Melinda the very best as the Foundation's new Chair.

Lee Michaelis
Chair Dec 2009 - Dec 2014

Board Members 2014



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Melinda OLeary (Chair commencing Dec 2014)

is a co-founder, and consultant with Nova Systems, an Engineering and Project Management company, which employs more than 300 staff around Australia, Singapore and The United Kingdom. Prior to joining Nova, Melinda held senior positions in several recruitment firms including State Operations Manager for Select Staff, and State Manager for both Manpower Services and Kelly Services. She joined The Hospital Research Foundation in 2010 as a Board Member and has used her extensive experience in business and HR both at a board level and as Chair of the HR committee. She joined the Board of the Lifetime Support Authority in October 2013 and is a former board member with "Time for Kids". Melinda has been a Time for Kids volunteer carer since 2006.

John MacPhail (Deputy Chair)

is a founding partner and director of NDA Law, an Adelaide-based law firm with a new and different approach, providing a full range of business law services including corporate, commercial, tax, succession planning, intellectual property and technology law. John has more than 25 years experience working in law firms in London, Sydney and Melbourne. He is a past President of the Copyright Society of Australia, and taught part-time as a postgraduate university law lecturer and professional examiner on intellectual property subjects. As a practising lawyer he advises clients working in a wide range of industries, particularly medical and healthcare, biotechnology, wine, retail, sports, marketing and sponsorship, and ITC.



Paul Flynn (Chief Executive Officer)

is an innovative and entrepreneurial Executive who has earned a stellar reputation for achievement during a multifaceted career in both the Finance and Not for Profit sectors. He has been acknowledged for his contribution by being awarded the 2005 Ernst & Young Social Entrepreneur of the Year in SA/NT and was also awarded the 2006 Equity Trustees Australian CEO Award for Innovation. Paul is passionate about the opportunity to help medical and scientific researchers in their important voyage of discovery which will benefit all Australians. Paul brings advanced skills to The Hospital Research Foundation in the areas of Leadership, Sales Management, Property Development and Management, Change Management, Financial Risk Management, Employee and Organisation Development and Employee Relations. He is delighted to be working with the team at THRF and The Institute, contributing to the health and well-being of all Australians.



Professor John Beltrame

Leading cardiologist Professor John Beltrame brings a medical perspective to the board. He has degrees in both science and medicine, and is a Fellow of the Royal Australasian College of Physicians, the European Society of Cardiology, the American College of Cardiology, the American Heart Association and the Cardiac Society of Australia and New Zealand. He is the Michell Professor of Medicine and the Cardiology Academic Lead for the Central Adelaide Local Health Network.

Professor Peter Hewett

is a Clinical Professor of Surgery with the Adelaide University Discipline of Surgery and is Head of Colorectal Surgery at The Queen Elizabeth Hospital. He has published more than 100 articles in peer reviewed journals and has held three NHMRC grants. Professor Hewett is also currently chairman of the Calvary North Adelaide Hospital Clinical Review Committee and teaches at the Adelaide University Masters Course in Minimally Invasive Surgery.



Ken Milne

is the Director of Milne Architects Pty Ltd and adds a different aspect to the board. He received a Diploma of Architecture at the University of South Australia and is a Fellow of the Royal Australian Institute of Architects. He is a Past President and former Chapter Councillor of the Royal Australian Institute of Architects, he was National Chair of RAIA Public Affairs Committee & Awards Director. He was also a Board member & Deputy Chair of the Rostrevor College for 10 years overseeing the formulation & introduction of the College Master Plan.

MaryLou Bishop

For the last 23 years MaryLou Bishop has run a surgical devices company selling highly technical operating room equipment into our largest hospitals across SA, WA and NT. MaryLou has a strong understanding of the medical world and the health industry. In 2014 MaryLou was elected a councillor to The Town of Walkerville. She joined The Hospital Research Foundation in 2014.





John Hender

is the Senior Manager for Native Title trusts and Investments for Perpetual Ltd. He has worked extensively in the financial services industry for over 30 years in sales, marketing and management roles. He has tertiary qualifications in marketing, finance and trusteeship and is currently studying towards a Post Grad Masters in Aboriginal Studies at Uni SA. John has a long history of community service and has been a board member of The Hospital Research Foundation for over 14 years.



Luciana Larkin

Luciana is the lead partner of Tregloans, an established and respected Chartered Accountancy practice. As a sharp and strategic thinker, she applies her expertise in financial, complex tax & business transactions to deliver effective outcomes. Luciana brings this professional expertise and strong focus on accountability & governance to the THRF Board together with experience as a trusted advisor to numerous other Corporate Boards and not-for-profit bodies.



Dr Stephen Rodda

is Chief Executive of ITEK Ventures, the technology commercialisation arm (TTO) of the University of South Australia. He was educated at the University of Adelaide gaining a first class honours degree, a PhD in Biochemistry and was awarded the University Medal. Subsequently he was awarded the prestigious CJ Martin and Arthritis Foundation fellowships for post-doctoral training at Harvard University. Dr Rodda has a combined 15 years of experience in the areas of scientific research, research management, technology commercialisation, investment management and corporate governance. Dr Rodda holds an MBA and is a Graduate of the Australian Institute of Company Directors.



John Woodward

is Corporate Portfolio Manager at SA Power Networks. John has more than 25 years' experience in technology related change programs, projects and consulting services across industries including the health, water, energy, and entertainment sectors. John was elected to West Torrens City Council in 2014 to represent Keswick Ward. He holds an MBA specialising in technology management, is a graduate of the Australian Institute of Company Directors and a certified Project Management Professional through the Project Management Institute. John joined the Board of The Hospital Research Foundation in 2013.



Valerie Timms

has more than 14 year's experience in Adelaide's competitive real estate industry. After only two years, Valerie was the number one sales person for a large franchise group, and went on to run her own award winning office for nine years. Three years ago she created her own independent real estate company - Timms Real Estate. Valerie is a skilled coach and mentor within the property sector and is dedicated to serving the community and helping others achieve business success.

Bringing Research News to You

THRF is delighted to share the many health and medical research advancements and achievements made by research teams at the BHI. It is these advancements that return benefit to the community through improvements in medical treatments and patient care. They are only possible through generous on-going community support.

To reach the widest possible audience with the latest research news we have forged solid relationships with local and regional television, radio and newspaper outlets. These relationships ensure the delivery of research developments that impact and improve our everyday lives. We also regularly post media stories on our website www.hospitalresearch.com.au.

Highlights and updates are also recorded in our quarterly newsletters; available in both print and electronic formats. If you would like to receive a copy of our e-Newsletter directly into your inbox, you can subscribe online via our website, or if you would like to receive a printed copy to your mailbox, please call us on (08)8244 1100.

We also enjoy a very active social media presence across a variety of platforms including Facebook, Twitter, Linked In and YouTube.

Please join the conversation and 'Like' our Facebook page, 'Follow' us on Twitter, and watch our latest media stories and more on our YouTube channel. Don't forget to subscribe to our channel while you are there and share with your friends.

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Research Achievements 2014



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Fighting a common condition with a common substance

In 2014 The Hospital Research Foundation (THRF) awarded a \$300,000 project grant to help people suffering with Chronic Rhinosinusitis (CRS), a common condition which affects 18% of Australians. Sufferers experience a very poor quality of life comparable to those who have diabetes, cardiac disease and lower back pain. As a common and extremely debilitating condition CRS is a research focus for Ear, Nose and Throat specialist Professor Peter-John Wormald and his team at The Queen Elizabeth Hospital and the Basil Hetzel Institute for Translational Health Research.

Professor Wormald explains that only one in five people treated for CRS with current methods respond to medication and recover.

"Obviously this leaves four out of five patients who don't respond to medication, so the next option for these people is surgery," he said.

"Surgery involves improving sinus ventilation and drainage, and we do have a good success rate; around 80% of patients have their CRS cured with surgery."

However, it is the remaining 20% of people who don't respond to medication or surgery who are at the centre of the research project supported by THRF. "We have limited treatment options for these people and they have a continuing poor quality of life. The THRF grant will support research to develop a new potential therapy," said Professor Wormald.

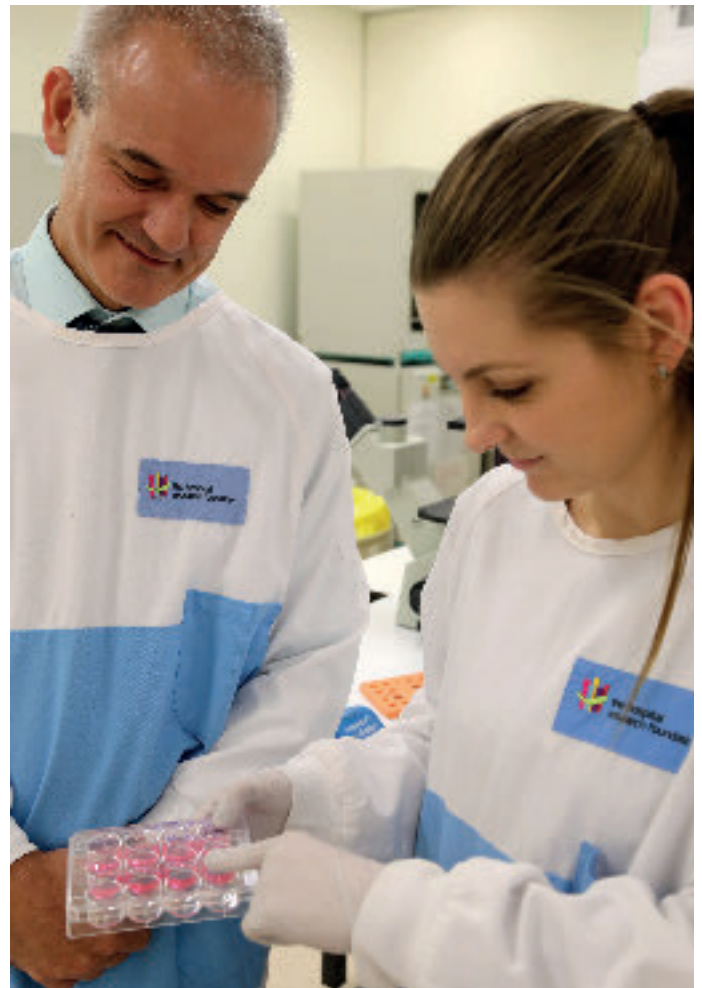
The team have been investigating a substance known as bacteriophage which has shown promising preliminary results as a potential treatment. Bacteriophage is naturally occurring in all natural substances in our environment – for example sea water contains millions of bacteriophage per millilitre. It also makes up the biology within the human nose.

"Current antibiotic treatment options for CSR are not targeted, so when applied they wipe out not just the bad inflammatory bacteria in the nose but also eliminate the good bacteria that we need for healthy sinuses. The chance of the body developing resistance to these treatments is also high because of their broad effect," said Professor Wormald. "Bacteriophage is useful as it is targeted – we think that by using it we can target two specific harmful bacteria; S.aureus and Pseudomonas, without the collateral damage caused by antibiotics and other treatments. We can maintain the balance of good and bad bacteria within the nose which may be the key to helping these patients."

The likelihood of the body developing resistance to bacteriophage is very low because it's specific and it doesn't damage the environmental surrounds. "We are the only people in the world that we know of researching bacteriophage in the sinuses," said Professor Wormald.

"We have shown it to be safe and effective *in vitro* and *in vivo*, and after a bit more in vivo work using funds from THRF we will be ready to move into human trials in early 2015."

"This is great research on a very common disease that has a direct patient benefit, and we are grateful to THRF and their donors for supporting this important work," said Professor Wormald.



ENT researchers are hopeful this \$300,000 THRF grant will lead to a successful therapy for chronic rhinosinusitis

Zooming In On Research



THRF helped fund a Zeiss LSM700 confocal microscope which will expand the possibilities of research for nearly all teams at the BHI.

Research capability at the Basil Hetzel Institute for Translational Health Research (BHI) advanced in 2014 with an exciting new arrival; a Zeiss LSM700 confocal microscope. The new microscope located at the BHI, together with its bigger brothers (the LSM710 Super High Resolution Confocal microscope and Scanning Electron Microscope), located at the University of South Australia Mawson Lakes campus, form the first facility of its kind in the Southern Hemisphere.

The imaging platform is the culmination of an Australian Research Council LIEF Grant awarded to Professor PJ Wormald (Head of the Ear Nose and Throat Department at The Queen Elizabeth Hospital) and collaborators from Uni SA and the University of Adelaide. "The system is the only one of its type in Australia and we are very fortunate to have equipment of this calibre available to us here at the BHI," said ENT Department Chief Scientist, Dr Sarah Vreugde (pictured above with colleague Mahnaz Ramezanzpour).

The purchase was also assisted by The Hospital Research Foundation (THRF) with funding given to expand the system to add extra capabilities and functions - essential to take medical research to new levels now and into the future. "The confocal microscope is a piece of equipment that is vital for many aspects of research. It can help us to visualise cells or proteins or even nanostructures relative to cells in a very detailed way. Most importantly it can be used by almost every research group located here at the BHI."

The system also features a life cell imaging incubating system which allows researchers to look at cells in real time for several days. "We can do things to the cells and see what happens to their mobility which is important in metastases formation – where the cells are mobile. We can try different treatments and see if there is a change in cell mobility as the system allows you to follow these cells for several days or several hours - whatever you need to look at."

"It's really expanding the possibilities of research. The facility will underpin the advancement of many sciences requiring structural characterisation at the nanoscale. It's not only enabling different questions and different aspects of research to be asked, it is also making our lives so much easier by not having to transport cells to the University (Adelaide) to use their microscope," said Dr Vreugde.

"We are just learning the extent that it can teach us things."

"It is unique in Australia so we will be the first to publish our work using the system. We really have to show what it can do for us; for research and for new enquiry. I expect there will be quite an impact," she said.

Towards a New Vaccine Therapy for Hepatitis C

A promising new study at The Basil Hetzel Institute and The Queen Elizabeth Hospital funded by one of The Hospital Research Foundation's 2014 Project Grants aims to develop a new therapeutic vaccine for patients with Hepatitis C (HCV). Specifically, the study will investigate a therapy for patients who have the gt3 strain of HCV, for which there are no current antiviral options. Professor Eric Gowans, who is supervising the project, says that 80% of patients who become infected with HCV are infected for life.

"Gt1 and gt3 are the most common virus strains of HCV in Australia. There are good direct acting antivirals that treat gt1 patients effectively but the same is not true for gt3 patients," said Professor Gowans.

Interestingly 20% of patients who are infected with HCV spontaneously clear it through cell mediated immunity – in other words their body fights off the virus without requiring treatment. The team at the BHI are aiming to develop a vaccine that replicates this natural immune response.

In previous studies the team have been working to develop a new, better performing DNA vaccine – with fantastic results.

"We are now hopeful with this improved drug that if we vaccinate patients we should be able to generate a cell mediated immune response which will clear the virus infected cells – effectively curing the patients," said Professor Gowans.

Professor Gowans says that people who contract the gt3 strain are generally younger than gt1 patients.

"Many of those suffering with the gt1 strain originally became infected through contaminated blood in the days before blood supply was tested," he said.

"However, the younger generation are more likely to contract HCV through intravenous drug use, and it's the gt3 strain that is most commonly contracted in this way."

"An important thing to remember about the importance of this research is that young people think they are indestructible – although many are aware of the risks, they never think contracting a disease like Hepatitis C through intravenous drug use will happen to them," said Professor Gowans.

"The sad thing is they only need to make a mistake once and they are infected for life. We need an effective therapy for these people."



The researchers at the Basil Hetzel Institute will be collaborating closely with clinicians at The Queen Elizabeth Hospital throughout the project. The Hospital Research Foundation will support the work with a project grant of \$300,000 over two years.

Professor Eric Gowans and his team are investigating a new therapeutic vaccine for patients with Hepatitis C, thanks to a \$300,000 grant from The Hospital Research Foundation.

Immune Cells Open Window to Breast Cancer Risk

Understanding the role our immune cells play in the risk of developing breast cancer has taken a big step forward.

Research into the immune cells known as macrophages, led by Associate Professor Wendy Ingman from the Breast Biology and Cancer Unit at the Basil Hetzel Institute for Translational Health Research (BHI), has shown the cells role changes in response to the hormone fluctuations that occur each month. The team's study found that the cells play a role in the normal function of the breast but at certain stages in a woman's menstrual cycle they may actually help to make the breast more susceptible to cancer.



The Breast Biology and Cancer Unit are learning more about the role our immune cells play in breast cancer risk in an effort to prevent the disease.

"These cells should be protecting our body from cancer, but at certain times of the month it appears macrophages might be allowing cancerous cells to escape detection by the immune system," Associate Professor Ingman said.

"It's a sort of Jekyll and Hyde scenario – we need the macrophages to do their job so the breast can function normally, but at the same time they're giving cancerous cells the chance to survive," she said.

Associate Professor Ingman and her team now believe there is a "window of risk" which opens when a woman has a period and the levels of the hormone progesterone drops.

"Immune defences in the breast tissue are down at this time and women could be more susceptible to the initiating factors that lead to breast cancer," she said. "We have known for some time that there is a link between the number of years of menstrual cycling a woman has and breast cancer risk. "We are now starting to understand the cell-to-cell interactions that impact this risk," she said. By increasing their knowledge of the biological factors that underpin breast cancer susceptibility, Associate Professor Ingman said they might one day be able to close these windows of risk, and reduce women's lifetime risk of breast cancer. The team are now working to unravel the mechanisms that are responsible for the increased risk and taking steps to alter them

Exercise the Answer to Coronary Slow Flow?

Patients who suffer painful recurrent chest pain due to the Coronary Slow Flow Phenomenon (CSFP) sadly don't have any effective therapies currently available. A project grant awarded by The Hospital Research Foundation in 2014 will enable Professor John Beltrame, who was instrumental in first characterising CSFP, and his team to investigate a new therapy for this condition.

Patients with CSFP have dysfunctional microscopic blood vessels causing blood to flow slower through their major heart vessels, producing recurring chest pain. The condition is extremely debilitating and has a severe impact on sufferer's quality of life.

TQEH is internationally renowned for its research studies into the CSFP. Over the past 15 years, TQEH researchers have been evaluating the effectiveness of a number of different drug therapies for CSFP. A drug called mifibradil was an outstanding therapeutic option for CSFP sufferers but unfortunately, it was withdrawn from the market because of drug interactions; thus the search for an effective therapy continues.

The \$300,000 THRF grant will enable Professor Beltrame and his research team to investigate exercise as a therapy for CSFP.

"Considering exercise as a good therapy for chest pain is not instinctive. We know chest pain can often be caused by physical activity, so to think of it as a potential therapy is counter-intuitive!" explains Professor John Beltrame, Cardiologist and Professor of Medicine at TQEH.

The concept of exercise therapy was born out of collaboration between the Cardiology and Vascular Surgery Departments at

TQEH. The Vascular Surgery team have demonstrated that patients with leg pain due to blocked blood vessels have benefited enormously from exercise therapy. "Fortuitously, a Program Grant awarded by The Hospital Research Foundation 4 years ago brought Professor Robert Fitridge, Head of Vascular Surgery, and I together as collaborators. If it wasn't for that grant we may not have had the opportunity to put our heads together and develop the exercise therapy concept for CSFP," said Professor John Beltrame. Teaming up with expert exercise physiologists at the University of Adelaide, the project team will evaluate the effectiveness of exercise therapy in a group of 56 CSFP patients, both men and women.

Many CSFP patients experience angina (chest pain) episodes several times a week, and Professor Beltrame explains that patients are desperate for some relief, as their quality of life is so poor. "We are very hopeful that the exercise therapy will be a viable treatment option, but even if the study is negative, it is likely to incite similar studies into related coronary disorders, which have largely ignored exercise therapy," said Professor Beltrame. "We are breaking new ground here at TQEH in Adelaide and it's fantastic that The Hospital Research Foundation is able to assist with getting this project started.

"Moreover, The Queen Elizabeth Hospital will continue to be at the forefront of research and therapy for CSFP"

New Treatment Hope for Heart Disease

A new drug developed by researchers at The Queen Elizabeth Hospital (TQEH) has the potential to benefit people worldwide who suffer with some types of untreatable heart disease. The team of scientists from TQEH, together with collaborators from the University of Adelaide and UniSA, have been investigating a new drug over the last six years. The new drug offers improvements over a current medicine called Perhexiline, which is used to treat angina (recurrent chest pain).

It's a research advance that gives hope to angina sufferer Catherine MacDonald, who deals with agonising angina attacks three to four times a day.

"I've tried all the medications available but without much success. The attacks I continue to have literally stop me in my tracks; when I have one it feels like something is crushing my chest, it's awful," said Ms MacDonald.

Associate Professor Betty Sallustio (Pictured below) from the Clinical Pharmacology Department at TQEH and the University of Adelaide said that Perhexiline is an older medicine and although it's been effective, its ability to help many people with heart disease is being held back because it can be potentially toxic if not closely monitored.



A new drug developed by researchers at TQEH has the potential to benefit people worldwide who suffer with some types of untreatable heart disease.

"Some of the symptoms from toxicity that can be caused by Perhexiline are nausea and dizziness; if you are an older person this may be particularly debilitating as it can increase your risk of falling and fractures. More severe toxicity can include liver damage and peripheral neuropathy (pins and needles in the fingers and toes and loss of sensation), which of course can be avoided with close monitoring; but there is a risk."

"The aim of our study was to develop a drug that has the same or more beneficial activity, but not the negative side effects," said Associate Professor Sallustio.

"And we think we have done that, fingers crossed!"

Ms MacDonald said it was exciting to hear that researchers are making headway in heart disease treatments.

"At 57 I consider myself still young, but my condition is stopping me from doing things, simple day-to-day tasks like hanging out the washing, but also enjoying life experiences, like travelling overseas with my husband. It's impacting both of our lives," said Ms MacDonald.

In addition to helping angina sufferers, Associate Professor Sallustio believes this new drug might be able to treat many more types of heart disease, including some inherited forms of heart failure, for which there is no current treatment.

"Considering we have been working on this project for six years it's extremely exciting that we have reached this point, with the drug being patented in Australian and the US," said Associate Professor Sallustio.

"We are hoping that this drug will ultimately eliminate the need for close patient monitoring and help a lot more people with different kinds of heart disease."

"At the moment Perhexiline is mainly used in Australia but if we can prove that our drug shows efficacy and lack of toxicity, this will open up markets in the US, Europe and other countries worldwide."

Funding contributors to this project have been The Hospital Research Foundation in collaboration with disease specific affiliate Australian Heart Research, and the Heart Foundation.

Old Enzymes for Growing New Bones

Researchers at The Basil Hetzel Institute for Translational Health Research (BHI), The Queen Elizabeth Hospital have patented an exciting new technology which could lead to a treatment that dramatically speeds up bone healing for people with osteoporosis and bone fractures from years to just months.

The research project is being undertaken by researchers in the Breast Cancer Research Unit (BCRU) led by Michell McGrath Breast Cancer Fellow Professor Andreas Evdokiou.

"Our focus within the BCRU is the development, progression and metastatic spread of breast cancer and we are particularly interested in learning how to treat breast cancer effectively once it has spread to the bone," said Professor Evdokiou.

"In addition to what we are learning about breast cancer I am pleased our work has led to such a valuable discovery which could be beneficial for people with osteoporosis and fractures."

The technology uses peroxidase enzymes, which are naturally occurring in products such as soy beans and cheese whey. Postdoctoral researcher Dr Mark DeNichilo, (Pictured below right) who is part of the Breast Cancer Research Group at the BHI spent eight years in a previous role working with a biotechnology company that aimed to develop new medicines from waste products generated by the dairy industry, such as cheese whey.

Dr DeNichilo and his team identified an enzyme in cheese whey called 'lactoperoxidase' which can act as a catalyst for healing damaged skin after serious burns. His initial research showed that when lactoperoxidase was applied via a dressing to a wound, the enzyme could stimulate skin cells to make new collagen and speed up the process of healing tremendously. This discovery came as a great surprise, because lactoperoxidase had only previously been known as an 'anti-bacterial' agent that helped to prevent milk from spoiling.

Having joined The Basil Hetzel Institute for Translational Health Research in 2011, Dr DeNichilo is now applying this discovery to develop new treatments for osteoporosis and bone fractures.

"I thought we could use what we had learnt about the healing properties of peroxidases in skin and apply it to bone. One similarity between bone and skin is they are mostly made of collagen."

"Naturally, our skeleton experiences wear and tear over our lifetime, so we have cells called osteoclasts which 'chew up' the old and damaged bone. We also have osteoblasts, which are responsible for repairing and making new bone," explains Dr DeNichilo.

People with osteoporosis have overactive osteoclasts and underactive osteoblasts.

"We found if we treated osteoblasts in the lab with the different peroxidase enzymes, they made collagen rapidly, just like the skin cells did. They speed up the process of taking an osteoblast from a cell that's immature to one that makes new bone."

"We now know that peroxidases prevent formation of osteoclasts and stimulate osteoblasts, with the end result being more bone produced."

Dr DeNichilo and his colleagues at the BHI have patented this exciting work.

"Our initial research suggests that to treat bone fractures in the future, surgeons could insert a sponge soaked with peroxidases in between two pieces of bone during surgery, causing the bone cells to migrate in and make new collagen."

"It could speed up the healing process to months rather than years."

In people with osteoporosis, fracture healing is a significant issue. In osteoporotic patients having hip replacements, surgeons insert a titanium rod into the bone. But because osteoporotic bones are weak, there is a limited ability to cement that piece in, so it loosens and many people need to have revision surgery, sometimes multiple times.

"We envisage that we could put the titanium material into the bone but also include a sponge or other structure that contains peroxidase to promote bone formation and also dampen the formation of osteoclasts."

"We all know the population is aging and osteoporosis is a problem as you get older. The number of people suffering with this condition is only going to grow, so there is a real need medically to help them," said Dr DeNichilo.

"Currently there is nothing really out there like this."

The research team is currently seeking further funding and a development partner to advance the project to in vivo trials.



An exciting revelation by researchers in the Breast Cancer Research Unit could lead to a treatment for osteoporosis and bone fractures.

Lighting the way to a breast cancer cure

Researchers in the Breast Cancer Research Unit at the Basil Hetzel Institute for Translational Health Research have taken an exciting step forward in understanding how the body's immune system can be used to fight breast cancer which has spread to the bone.

"There is a rare population of immune cells within our blood called gamma delta T-cells that can specifically target cancer cells," explained PhD student Aneta Zysk (Pictured below right) who has been primarily involved in the project.

"As there are not normally enough of these cells to kill the cancer, I'm working on isolating these cells in the lab and growing them to increase their numbers."

"I have fluorescently labelled these cells so that when we use them in vivo, we can actually visualise the path they are travelling – we can see if the cells are going directly to the tumour site or elsewhere.

In an exciting finding, Aneta has seen these cells travel directly to cancer in the bone.

"We know from previous research that these cells have cancer-killing properties in vitro, so this indicates they will most likely be successful at killing cancer cells *in vivo*," said Aneta.

Cancer cells have mechanisms that enable them to avoid the immune system, but the special gamma delta T-cells which Aneta is growing in the lab are able to bypass that system and can still detect the cancer cell regardless.

Aneta is using a state-of-the-art IVIS Spectrum In Vivo Imaging Machine to undertake her project, which was purchased with the help of The Hospital Research Foundation in collaboration with its disease specific affiliate Australian Breast Cancer Research in 2013. This exciting project would not have been possible without it.

"Normally when cancer research is done in vivo, researchers use instruments to measure tumour size to determine if their therapy is impacting on tumour growth," explained Aneta.

"Because I am looking at breast cancer when it has spread into the bone, we physically can't use the instruments to measure the tumour."

"So what I do is tag the cancer cells so they emit light and the amount of light we can see with the machine is proportional to the size of the tumour – if there is a decrease in the amount of light being produced then we know the tumour size is decreasing."

So far using this technique, Aneta has found that the cells can slow down cancer growth in the bone and decrease the spread to other parts of the body like the lungs.

"The next step for my work will be to increase their natural cancer killing properties by using them in combination with other therapies so they can kill cancer even more effectively."

"It's exciting work and I am very pleased to be a part of what could be a potentially life-saving treatment for people with breast cancer, and other cancers which spread to the bone."



The Breast Cancer Research Unit has identified cancer-killing cells which they hope will lead to a treatment for people with breast cancer and other cancers which spread to the bone.

Wearable Sensors to Prevent Hospital Falls

Did you know almost 26 Australians die each year as a result of a fall in hospital? In a recent study of 200,000 incident reports hospital falls also contributed to 530 hip fractures and about 1000 other fractures.

Falls in hospitals are all too common and costly, says PhD student Roberto Shinmoto Torres (Pictured below right) who is currently working on a project to develop and pilot a technology system that might help reduce hospital based falls. The project has been supported by a grant from The Hospital Research Foundation to Dr Damith Ranasinghe from the Auto-ID Lab at the University of Adelaide and has involved a multi-disciplinary team at The Queen Elizabeth Hospital and the university.

"We are working on a system that alerts nursing staff that at-risk patients require supervision. We hope that the provision of earlier intervention or supervision will help to reduce the number of falls each year," he said.

The psychological consequences of falls are also costly and include anxiety, depression, loss of confidence and fear of falling and ultimately a downward spiral of decline in health.

"A patient might decide to get out of bed and go to the toilet and slip. They might have made this choice because they did not want to trouble the nurse," said Roberto.

"This might not have happened if the nurse was alerted ahead of time – and this is where we hope our system can help."

Development of the Wearable Wireless Identification and Sensing Platform (or W2ISP) was developed at the Auto-ID Lab at the University of Adelaide where Roberto is based, and in collaboration with Intel Research in Seattle.

"The W2ISP is a device that is worn by patients – it's light and does not require a battery," Roberto said.

"It is powered by a reader located on the ceiling, which also receives transmitted data about patients' movements from the W2ISP."

The data is then relayed to a computer system, which automatically identifies the movement using algorithms that have been developed, and then makes a decision if the movement is risky.

Where a risk movement has been detected, the system will alert nursing staff. The nursing staff will then be able to immediately check on the patient.

With a background in science and engineering Roberto's research focus has been to help develop algorithms that can be used by the computer system to detect risk movement.

"To do this, I have evaluated data collected from the wearable sensor (W2ISP) with young volunteers, older volunteers and hospitalised older patients in the Geriatric Evaluation and Management Unit at The Queen Elizabeth Hospital," he said.

As part of his experiments Roberto has also investigated the perception of research participants to the W2ISP and confirmed that it is acceptable and well tolerated.

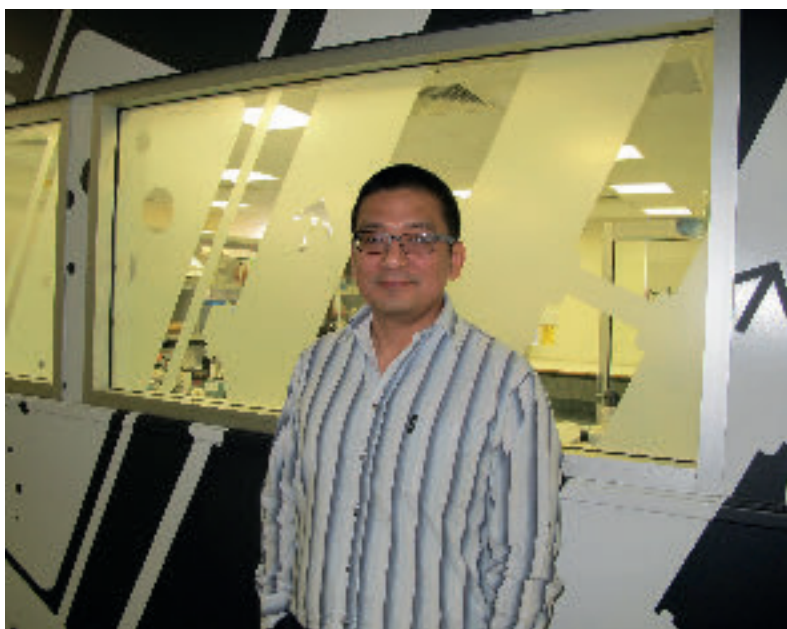
"It is incredibly exciting working on a project that will directly benefit people – that provides a lot of motivation," Roberto said.

"I particularly like the idea that my research can help people remain healthy by preventing injuries in hospitals."

Roberto and the team hope that the W2ISP system will help our hospital staff ensure the safety of patients in hospital, especially older patients and those with dementia.

Clinical trials for the next phase of testing will take place at The Queen Elizabeth Hospital in 2015.

As a direct result of this initial research, Professor Visvanathan (Director, Aged & Extended Care Services) and her team have received a larger grant from the NHMRC to further investigate if this system, when deployed in hospital wards, is able to reduce falls in hospitals. The researchers will also investigate if the system is acceptable to consumers and clinicians. This research will provide the researchers with the opportunity to improve the system in response to their research findings.



This TQEH based study aims to reduce hospital falls, thanks to a THRF grant.

SuperCycle Wonderful Success

Mercer SuperCycle raised almost \$450,000 for The Hospital Research Foundation in 2014 with 50 riders cycling and raising vital funds for THRF's Under Our Roof program. This was the second year THRF has been the proud beneficiary of the cycling event.

Fifty riders took part in the first two days, while 34 continued to complete 1000km in seven days riding throughout country South Australia, including Kangaroo Island.

"This year's Mercer SuperCycle was a fantastic success," said Mercer SuperCycle chairman Mark Day.

"With the support of so many corporate teams and volunteers we are keen to continue to grow Mercer SuperCycle and work towards more accommodation for country patients when they need treatment away from home."

The cyclists and volunteers were welcomed home by friends and family on Friday, April 11 where a \$50,000 donation from epc Pacific was announced.

One of the 2014 riders was Bendigo Bank Team's Rebecca Edmiston.

She was diagnosed with liver cancer at just four years of age. After chemotherapy and radiotherapy, doctors found cancer in her lungs. Although the lung cancer was successfully treated, her liver cancer wasn't, so she and her family moved to Sydney to wait for a transplant.

Rebecca will always remember her time in Sydney, where she and her family stayed in shared accommodation with eight other families. It was a stressful time, especially for her parents, without a private space to call their own.



Mercer SuperCyclists rode 1000kms in 7 days during April 2014 raising more than \$450,000 for The Hospital Research Foundation.

Luckily for Rebecca a liver became available and since she's lived a happy life with no complications.

"The cause is something that really hit home for me as it's something I went through with my family-it would have been impossible for us to stay in Sydney as a family if we didn't have free accommodation."

Thank you to all the riders, volunteers, sponsors and supporters who made Mercer SuperCycle such a wonderful success in 2015.

Find out more about Mercer SuperCycle by visiting www.supercycle.com.au

Community Tours & Speaking Engagements

The Hospital Research Foundation is proud of its Community Awareness Program which plays an important role in increasing awareness of medical research, health and wellbeing within the community.

In 2014, THRF held five tours of The Basil Hetzel Institute for Translational Health Research. Each tour focused on a different area of research and was hosted by a researcher undertaking work in

that area. We also coordinate a program which allows local community groups the opportunity to have a researcher attend their meeting and speak about a topic of research. Researchers attended 35 speaking engagements in 2014 for groups such as Probus Clubs, Lions Clubs, University of the Third Age and Rotary Clubs.

If you are interested in your community group having a guest speaker or attending a tour of the BHI, please visit our website for more information: www.hospitalresearch.com.au.

Dinner for 800 raises \$70,000+ for Cancer Research

More than 800 people around Australia had dinner with friends to fight cancer on Saturday the 28th of June 2014 as part of The Longest Table.

This is the second year The Hospital Research Foundation has held The Longest Table; a fun and simple event which encourages people to sign up online to host a dinner with their family and friends, and raise funds for cancer research.

Over \$72,900 was raised thanks to 110 hosts, who held parties ranging from pizza and movie nights, intimate Mexican fiestas, to elaborate French-themed banquets for more than 50 guests.

"The variety of dinners we saw on the night was phenomenal and that's one of the beauties of The Longest Table; it enables people to embrace their own inspiration and hold an event that suits them and their friends, for a wonderful cause," said THRF CEO Paul Flynn.

The Longest Table Ambassador and My Kitchen Rules 2014 Champion Bree May was the highest fundraiser, raising a wonderful \$6,000 at her BBQ Spit party on her balcony for 50 friends and family.

Bree was thrilled to be a part of The Longest Table, which combines her passions of cooking and helping others.

"I'm someone that thinks you should give back if you can. Cancer is something that has touched my family a lot," said Bree.



More than 110 people hosted a Longest Table in 2014 to raise over \$72,900 for cancer research

"After being diagnosed three years ago, my cousin Paul passed away recently of cancer. His funeral was actually while we were filming for My Kitchen Rules so I couldn't say goodbye with the rest of my family, which was heartbreaking for me."

"I was absolutely blown away by the support I received from my family and friends, and the local businesses I approached for donations – the success of my dinner wouldn't have been possible without them and I am so thankful."

Bree said her Longest Table dinner was in honour of her cousin Paul.

"We celebrated him and every other courageous person who has fought cancer and survived, or battled with intense bravery, but tragically had to leave us," she said.

"I dream of a world without this terrible disease, and by getting involved in The Longest Table I feel like I am making a difference."

Visit www.thelongesttable.com.au to find out more about the event.

American Chamber of Commerce in Australia

The Hospital Research Foundation was again the proud charity partner of the AMCHAM business lunch series in 2014. Throughout the year the lunch series provides THRF with the opportunity to engage with the South Australian corporate community and provide them with valuable insight into the vital medical research undertaken at the Basil Hetzel Institute for Translational Health Research. More than \$5,300 was raised for medical research in 2014 through the auctions and raffle.

Australia-Israel Chamber of Commerce

The Hospital Research Foundation is a member of the AICC; one of the country's most prestigious and active national business organisations. The AICC's national membership exceeds 1,000 leading Australian companies across a broad range of industry sectors, giving THRF the valuable opportunity to network and increase awareness about South Australian medical research. THRF attends numerous lunches throughout the year.

Dry July

For the sixth year The Hospital Research Foundation (THRF) was a proud beneficiary of Dry July in 2014; a nationwide fundraising program which encourages people to give up the booze for a month and raise funds to support adult cancer patients.



THRF CEO Paul Flynn visited all regional hospitals including Murray Bridge, Clare and Berri (pictured) to present funds raised through the 2014 Dry July campaign

More than 630 people in South Australia had an alcohol free July and raised \$98,000!

Dry July funds have assisted greatly with The Hospital Research Foundation's Under Our Roof project which will provide accommodation for country cancer patients and their families while they receive treatment at The Queen Elizabeth Hospital.

The Hospital Research Foundation's Dry July campaign also helped hospitals in Mount Gambier, Murray Bridge, Berri, Victor Harbor, Clare, Port Lincoln and Whyalla.

"The Hospital Research Foundation has been very impressed with the regional communities commitment to the services in their area. We are also committed to assisting the regional centres and are very proud to be able to contribute to the total amounts raised in their local communities for their local hospitals," said Mr Paul Flynn, CEO of THRF.

THRF allocated \$25,000 across the hospitals to help further increase the comfort of cancer patients.

"It is wonderful that there are so many treatment facilities in regional South Australia, but if we can brighten their waiting rooms, or provide some additional services through this fundraising initiative we hope their journey may be a little easier.

Basil Hetzel Society Thank you Luncheon

More than 125 guests attended the Basil Hetzel Society Thank you Luncheon at Kooyonga Golf Course in October 2014.

Guests were treated to a panel discussion with two of South Australia's finest clinical researchers – Professor Guy Maddern, the Director of Research at the Basil Hetzel Institute for Translational Health Research, TQEH, and Associate Professor Maureen Rischmueller, Director of Rheumatology, TQEH.

Guests Ossy Grotto and Sylvia Bridgeman thoroughly enjoyed the afternoon and said "the presentation of the venue, the quality of the food and the professionalism of the dining staff and the presentations were excellent".



BHS Luncheon guests were treated to a panel discussion with two of South Australia's finest clinical researchers – Professor Guy Maddern and Associate Professor Maureen Rischmueller, picture here with THRF CEO Paul Flynn (right).



Around 125 people attended the 2014 annual Basil Hetzel Society Thank you Luncheon.

"The luncheon was absolutely wonderful - it was the best we have been to yet," said Raymond and Betty Jackson.

THRF CEO Paul Flynn said the luncheon was an important opportunity to thank some of our most generous donors.

"This annual event acknowledges the research advances in health care that have been possible with our donor's kind support," said Mr Flynn.

"We congratulate and thank our generous supporters for making a true and lasting contribution to the health and well-being of our local South Australian community and more broadly, across Australia and world-wide through their support of medical research."

Emotional Rollercoaster for Lucky Lottery Winners

Kevin and Ann Diener from the Adelaide Hills were thrilled to be the owners of a brand new \$1.3 million Scott Salisbury home in West Beach as the winners of the amazing Grand Prize in the first 2014 Hospital Home Lottery. Kevin, a mechanic from Meadows, was about to be discharged from hospital after having two tumours removed from his bladder when he received the life-changing phone call from The Hospital Research Foundation CEO Paul Flynn. "I was sitting on the edge of the hospital bed with Ann right beside me. We didn't believe Paul when he told us we were the winners," said Kevin. "I was absolutely stunned, my legs turned to jelly and my head was spinning," said Ann. "It was a worrying time while Kevin was having surgery, but to get this fantastic news straight after is just amazing."

As they walked around their new home the following day with their children and grandchildren the Dieners were clearly blown away. "We own the oldest house in Meadows and now one of the newest in West Beach," said Kevin. "I feel like I've stepped into someone else's shoes and am living someone else's life, these things just don't happen!" THRF CEO Paul Flynn was delighted to hand the keys to such a lovely couple who were clearly overjoyed with the win.

"We thank the Dieners and every other person who bought tickets in this Hospital Home Lottery," he said.

"The funds raised through the lottery go towards vital medical



Kevin and Ann Diener were the thrilled winners of the first Hospital Home Lottery for 2014, pictured here with their family.

research and improving patient care in hospitals, and it's just wonderful that the South Australian community is generously supporting such a worthwhile cause."

The lottery was a complete sell out with 3,624 prize winners.

The Dieners had never bought tickets in the lottery before, but this time they bought eight.

"I'm so thrilled I decided that day after hearing the lottery advertised on radio to go and buy some tickets, even though I never expected to win."

"But as of now, I'm retired! It's crazy!"

Lottery Win for Young Family

Regular Hospital Home Lottery ticket buyers Trudie and Craig were the winners of our second 2014 Hospital Home Lottery, walking away with keys to the \$1.25 million Grand Prize Showhome located at picturesque Lightsvue. The win came as a complete shock for the couple and their two children.



Regular Hospital Home Lottery ticket buyers Trudie and Craig pictured with CEO Paul Flynn and Scott Salisbury were the winners of our second 2014 Hospital Home Lottery, walking away with keys to the \$1.25 million Grand Prize Showhome.

"We've been buying tickets in each lottery for a few years now and this is our first prize – and wow we are just blown away by all of this – we can't thank everyone enough," said Trudie.

The family immediately began contemplating a move from their nearby property to the beautiful Scott Salisbury Home which came fully furnished, professionally decorated and landscaped.

Trudie said winning the major prize was a dream come true.

"With two growing children we were wondering how we would all fit into our current home."

"It's such a terrific lottery – that's why we always enter. The odds of winning are great plus the money goes to a cause that helps everyone," said Trudie. "We are always delighted to meet some of the wonderful supporters of the two lotteries we have each year. Seeing people like Trudie and Craig who are so thrilled by their unexpected win and what it will mean for their family, is a great part of my role," said THRF CEO Paul Flynn.

"Thank you to all of our lottery supporters. Each year your contributions enable us to support health and medical research here in South Australia that delivers the very best medical treatment for all in our community," he said.

Under Our Roof Program

The Hospital Research Foundation's Under Our Roof program progressed significantly in 2014, with the slab poured in October and the framework on schedule to be complete by December. The Under Our Roof program is providing accommodation for country cancer patients receiving treatment at The Queen Elizabeth Hospital.

The project at 30 Nicolls Terrace Woodville West will feature two three bedroom homes for patients and their families to stay.

The Queen Elizabeth Hospital is one of South Australia's busiest cancer treatment centres. It also has the State's largest Breast Cancer Clinic. Each year more than 15,000 patients receive cancer treatments in the Day Centre alone.

There is currently no short stay accommodation in the western suburbs for families. Finding a place to stay close to the hospital during treatment periods is one of the major stressors for country patients, as identified by the Haematology/Oncology Specialists at The Queen Elizabeth Hospital. Having suitable accommodation and

family members close by we hope will help improve the level of comfort for many country cancer patients at a crucial time.

The Hospital Research Foundation (THRF) has a long standing relationship with multi-award winning builder Scott Salisbury Homes who are building the Under Our Roof homes. Each home has been specifically designed to cater for families and those who may be feeling unwell.

THRF has been able to fund the project largely thanks to fundraising partners SuperCycle Inc and Dry July. Over the last few years Mercer SuperCycle; a 1000km ride around country South Australia and Dry July; a nationwide fundraising campaign which encourages people to give up alcohol for the month, have raised an outstanding amount to make the Under Our Roof project possible.

The expected completion date for the homes is August 2015 - stay tuned throughout the year for updates.



The Under Our Roof project is due for completion in mid-2015 and will provide accommodation for country cancer patients receiving treatment at The Queen Elizabeth Hospital.

Dinner and Dancing for Breast Cancer



More than \$21,000 was raised for cancer research thanks to the hard work of long-term THRF supporters Maria & Chris Giannoudis at their annual dinner dance.

Maria and Chris Giannoudis held their annual Cancer Support Dinner Dance at the Krystal Function Centre, Adelaide in March 2014.

On the night guests enjoyed a delightful Greek feast and plenty of dancing. A fantastic \$21,260 was raised to support the work of Professor Andreas Evdokiou and his team from the Breast Cancer Research Unit at the Basil Hetzel Institute for Translational Health Research at The Queen Elizabeth Hospital. Thank you so much to Maria and Chris for your amazing efforts.

Disease Specific Affiliate Community & Corporate Supporters

The Hospital Research Foundation is honoured to have the support of many other individuals and organisations who support our disease specific affiliate brands; Australian Breast Cancer Research, Australian Prostate Cancer and Australian Heart Research. We are grateful to the following groups who have made a significant contribution in 2014;

- Intimo Lingerie
- Leaders and Lattes Networking Group, Melbourne
- The Chartered Accountants Women's Group, Adelaide
- Schmelzkopf Cosmetics, Adelaide
- Anna Giorgianni

Wendy's Walk

When Wendy Deer was told she had cancer, and only had a month to live she decided to do something not for herself but others.

She convinced her friend David Turvey to walk 100 kilometres and raise money for The Hospital Research Foundation.

"Wendy did appreciate all the research that's done at the (Queen Elizabeth) hospital, it obviously helped to extend her life, and this was a way of her giving back," David said.

Unfortunately Wendy didn't live to see David fulfil his promise. Shortly after she died, David started the walk. He had suffered cancer as well so he split the walk into 18 kilometre journeys, from his home in Wirrabara to the Laura Hospital.

Then to finish off Wendy's Walk her husband, daughter, grandchildren and friends joined David for the final 10 kilometres. In all they raised \$1440.

Colour Fun at the Color Run



THRF was pleased to be the local charity of choice for the Adelaide Color Run in 2014.

You couldn't imagine a more colourful sight than when over 14,000 people converged at Victoria Park Racecourse for The Color Run on September 14th 2014.

The Hospital Research Foundation was the local charity of choice for the Adelaide run, raising funds through the sale of trendy Swisse glass water bottles and gold coin donations. Runners completed a 5km track and as they crossed the finish line there wasn't a colourless body in sight!

Thanks to everyone who bought a water bottle or made a donation at the charity tent, \$3,554.10 was raised for hospital research in South Australia.

Big W Support

Big thanks to Big W Kilkenny who supported local medical research with their Father's Day Raffle in September.

Five prizes were donated by the store, all of which were a big hit with customers.

They raised a total of \$653.90 for The Hospital Research Foundation which

was well above their goal of \$100! Ngan Tran who organised the fundraiser said; "We were pleased to support a charity that is within our local community, and that benefits the local community through research."

Thanks again to the team at Big W Kilkenny and everyone who bought a raffle ticket for your kind support.



Big W Kilkenny donated \$653.90 to THRF raised through a raffle.

Drake Supermarkets Charity Show Bags

The Hospital Research Foundation received more than \$21,995 to support health and medical research in 2014 thanks to the South Australian community and the generosity of Drakes Supermarkets and their suppliers.

The money was raised through the sale of Drakes Supermarkets Charity Show Bags. THRF was one of four charities who received an equal share of the more than \$87,980 raised during the 2013 Show Bag campaign.

At the cheque handover Drakes Supermarkets CEO Roger Drake made special mention of their generous suppliers who donate their products each year as part of the campaign which is now in its 15th year.

"The Foundation is incredibly grateful to Roger, his wife Wendy, their suppliers and stores for their wonderful community spirit and generosity," said THRF CEO Paul Flynn.

"We also thank the people of South Australia for getting behind the campaign – by doing so they are supporting local medical research that is helping to restore and improve the lives of the people we love."

Community Donation Saves the Day



The Ladies Auxiliary (Philloptohos) of the Port Adelaide Greek Orthodox Community came to the rescue to fund a replacement piece of equipment for the BHI in December 2014.

A donation of \$14,839 from the Ladies Auxiliary (Philloptohos) of the Port Adelaide Greek Orthodox Community enabled the urgent purchase of a replacement piece of equipment at the Basil Hetzel Institute for Translational Health Research (BHI) in 2014.

Rheumatology Unit Director Professor Maureen Rischmueller said the news of the ladies' kind donation was a "god send".

"We are so grateful for their support, we never know when key pieces of equipment like this are going to let us down, but to have support from the community for a replacement so quickly is just wonderful," she said.

Father John, from the Port Adelaide Greek Orthodox Church, spoke on behalf of the ladies and said they value very much the importance of medical research and the wonderful work undertaken by the researchers at the BHI which is improving the health of our community.

The group has been supporting medical research at The Queen Elizabeth Hospital for more 25 years and in the last 10 years alone

has donated more than \$110,000 to numerous areas of medical research and equipment.

Karaoke for Research



More than \$28,000 was raised by The Vietnamese Community in Australia SA Chapter through their 2014 Karaoke dinner.

The Vietnamese Community in Australia SA Chapter are extremely passionate about medical research. The group held a Karaoke dinner in 2014 and with the help of 400 guests raised an outstanding \$28,896 for The Hospital Research Foundation.

Organiser Chau Huynh said "Many people who couldn't make it on the night still donated, they really believed in the cause."

Thank you so much to the organisers and everyone who went along to the event.

Breast Cancer High Tea



CABPSA raised a wonderful \$6,076 for the Breast Cancer Research Unit in 2014.

The Cyprus Association of Business & Professionals of SA Inc (CABPSA) held a high tea to support local breast cancer research in 2014.

Almost 200 people attended the event and funds were raised from entrance fee proceeds as well as a raffle and silent auction held on the day. The group raised a wonderful \$6,076 for the Breast Cancer Research Unit.

Luke Kouzapa from the CABPSA said the committee were fortunate to have a number of generous members of their business community who believed in the cause who donated a variety of food items for the High Tea and also items for the silent auction.

"We believe this breast cancer research led by Professor Andreas Evdokiou is very important," said Mr Kouzapa.

Christmas Dance



Chloe from THRF gratefully accepts the donation from the Vietnamese Arts and Literature Association.

The Vietnamese Arts and Literature Association generously donated \$12,100 to The Hospital Research Foundation in 2014.

They held their annual Christmas Dinner Dance in December for 435 people which was full of colour, singing, dancing and fantastic food.

We thank the Association for their kind support.

Heartfelt Support



Alexandra Vakitsidis and her dedicated group of friends have been raising funds for THRF for more than 13 years.

Supporting cancer research is something that is very close to Alex Vakitsidis' heart.

Alex and her dedicated group of friends have been raising funds for The Queen Elizabeth Hospital's Haematology-Oncology Unit for more than 13 years, continually inspired after losing a number of close friends to cancer.

Each year Alex rallies her friends together to bake and sell a delicious spread of Greek goodies in the foyer at The Queen Elizabeth Hospital. The group also host an annual Christmas Carolling tour of the suburbs. The community show their appreciation for the group's festive spirit with donations. Through their cake stall and Christmas Carolling in December 2013 the group raised a wonderful \$8,398!

Thank you so much to Alex and her tireless group of friends who continue to support medical research.

Giving Cancer the Boot

The anniversary of a loved one's death is a sad time. But for Scott Martin's family, they decided to do something different. Scott, or 'Boots' as he was better known died of stomach cancer two years ago.

His siblings Janice Silbey and Paul Martin organised a fundraiser in his honour.

They put boots on the bar collecting donations at the Grange Hotel and held a silent auction. The event raised \$3,467.55 for The Hospital Research Foundation.

Be the Cure

The Hospital Research Foundation ran two of its Be the Cure national cash lotteries in 2014. More than 5400 people supported medical research by purchasing a ticket! Congratulations to the winners and thank you for your support





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