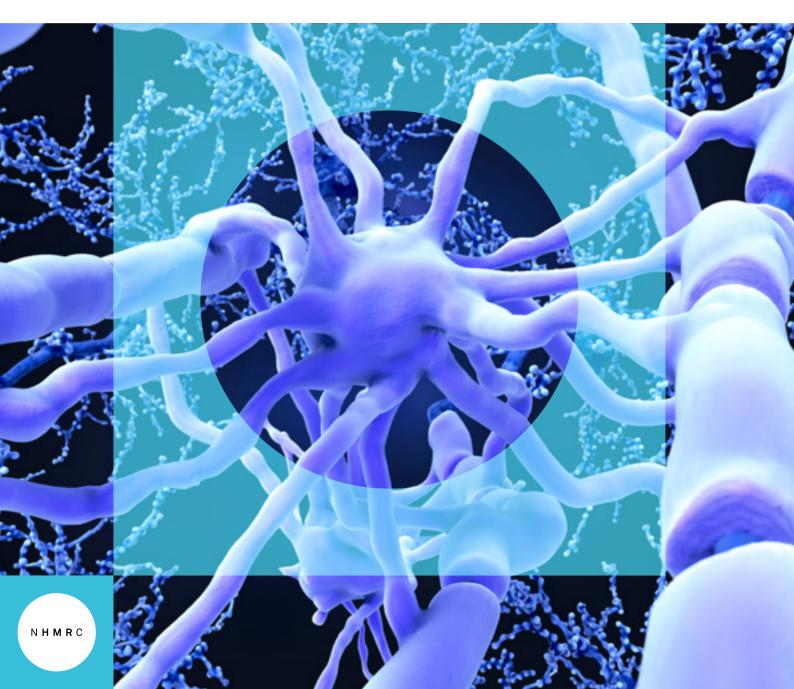
Australian Government National Health and Medical Research Council BUILDING A HEALTHY AUSTRALIA

# **10 BEST**

### Showcasing significant projects that support the improvement of human health

NHMRC Research Projects (Twelfth Edition)





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# **CEO FOREWORD**

This twelfth edition of NHMRC's 10 of the Best is published in 2020, to be remembered as the year of the COVID-19 pandemic.

Many people have commented on the critical role that science has played in Australia's response to COVID-19. When faced with this new global threat to our health and wellbeing, governments and communities have turned to scientists to explain, predict, advise and solve.

The trusted public health, medical and other scientists on whom we have relied this year are available to us because of Australia's support for research in our universities, medical research institutes, hospitals and companies over decades. The Australian Government has been a patient investor in research in the laboratory, the clinic and the community, supporting researchers who see a problem in their daily lives or practice and decide to work on a solution.

10 of the Best celebrates success stories from Australia's health and medical researchers whose work has been funded by the Australian Government through NHMRC.

This edition highlights research projects across a broad spectrum of topics, including cancer immunology, youth mental health, Indigenous workforce building, neurosurgical devices, tuberculosis, coronary disease, respiratory disease rehabilitation, depression and the economic evaluation of cancer treatment. The projects showcased here are representative of hundreds of successful high-quality projects funded each year by NHMRC. Selected from 1,020 completed NHMRC grants, it was challenging to choose only 10. We used blinded review to produce a short list which was then reviewed by a scientific panel for scientific merit to select the *10 of the Best*.

All NHMRC projects, including the 10 presented here, are evidence of the deliberative and collaborative scientific method which underpins Australia's reputation for research integrity and quality.

We know that research is a long game, not a race an ongoing endeavour driven by human curiosity and, at times, the urgent need to find solutions.

I encourage you to read "the next steps" accompanying each project and to follow these researchers and their exemplary work in the years ahead.

The response to COVID-19 has shown us the importance of our long-term national investment in health and medical research and underlined the direct link between good health, the quality of our lives and our national prosperity.

On behalf of NHMRC, I hope you enjoy discovering how some of our best researchers are leading the way.

- Kelo

Professor Anne Kelso AO CEO



### ADDRESSING THE NEGLECTED GLOBAL BURDEN OF CHILD AND DRUG-RESISTANT TUBERCULOSIS



# PRACTITIONER

**OF SYDNEY** 

**FELLOWSHIP** \$278,407 2013-2016

#### **TEAM MEMBERS**

Associate Professor Greg Fox Professor Vitali Sintchenko Professor Jan-Willem Alffenaar Professor Warwick Britton

**Professor Ben Marais** 

Ever since completing his PhD whilst working as a young paediatrician in South Africa, Professor Ben Marais has been on a mission to raise awareness of childhood tuberculosis (TB) and the transmissibility of drug-resistant TB — having seen first-hand the deadly impacts when this disease is left undiagnosed and untreated.

Professor Marais points out that TB remains the number-one infectious diseases killer on the planet and a top 10 cause of death in children under the age of five.

"Wealthy countries with good socioeconomic conditions and health care systems like Australia are at low risk of major TB outbreaks — but Australia can make a big contribution through research and advocacy."

Research into the transmission of drug-resistant TB was traditionally neglected, because it was believed to occur when patients do not take their medicine and therefore all that is required to address the problem is better treatment supervision to 'turn off the tap'.

"For many years the spread of drug-resistant TB was overlooked by the TB community, in much the same way as childhood TB was before, because of the perception that it does not pose a transmission risk.

"In the case of children, the fact that they rarely transmit TB does not imply that they are unaffected. In fact, TB is a leading cause of death in young children living in TB endemic areas, while easily preventable if appropriate care is provided. In addition, since drug-resistant TB is readily transmitted, children in close contact with an adult who has drug-resistant TB are also at risk.

"Our program of research focuses on a number of aspects. We document the burden and spectrum of disease suffered by children in different developing country settings and aim to identify better ways of preventing and treating their disease.

"We also map the spread and evolution of drug-resistant strains of TB. Regionally, the use of genome sequencing allowed us to assess drug resistance patterns and track transmission pathways within communities, in order to guide appropriate public health interventions."

In Australia, New South Wales became the first jurisdiction in the world to introduce routine sequencing of all TB strains in 2016. This facilitates personally tailored treatment that optimises patient recovery and keeps the community safe.

TB provides a constant reminder that infectious diseases do not respect borders. In 2020, COVID-19 provided another powerful example, with efforts to contain COVID-19 employing TB control concepts, such as strict infection control and quarantine, meticulous contact tracing and the use of genomics for transmission tracking. In 2018, the last year for which there are global data, TB killed approximately 1.5 million people.<sup>1</sup>

World Health Organisation. "Tuberculosis Fact Sheet" World Health Organisation. 24 May 2020. Accessed 25 August 2020. www.who.int/news-room/factsheets/ detail/tuberculosis



oto supplied by The University of Sydney

"We all need to work together to contain the emergence and spread of deadly diseases like drug-resistant TB and COVID-19."

> THE NEXT STEPS

Professor Marais is currently looking into strategies for population-level TB elimination in the Pacific (PEARL project in Kiribati) and the prevention of drug-resistant TB in Vietnam (V-Quin project), as well as continuing his research into how children are affected by the global tuberculosis epidemic and the spread of drug-resistant TB.

## BUILDING INDIGENOUS RESEARCH CAPACITY IN AUSTRALIA

"With this grant now complete, the next steps are in the hands of researchers. Participants now have a solid foundation to progress their career in their chosen field, some of which are cardiovascular, mental and maternal health; infectious diseases; alcohol, tobacco and other drugs; housing; and youth, women and human rights."



JAMES COOK UNIVERSITY, MONASH UNIVERSITY



POPULATION HEALTH CAPACITY BUILDING GRANT \$2,438,084 2007-2016

### TEAM MEMBERS

Late Emeritus Professor Richard Speare Professor Richard Murray Professor Craig Veitch Professor Jenni Judd Dr Brian McCoy For nearly three decades, Professor Jacinta Elston has worked in higher education, furthering efforts to improve Aboriginal and Torres Strait Islander health in Australia. Professor Elston is an Aboriginal woman from North Queensland and the inaugural Pro Vice-Chancellor (Indigenous) at Monash University.

When awarded an NHMRC Capacity Building Grant, Professor Elston and the team at James Cook University had two goals: to support emerging Aboriginal and Torres Strait Islander community and academic leaders to develop their careers in research and health; and to develop partnerships with Indigenous community-controlled health services.

"NHMRC funding helped to provide the resources to create a space to share experiences, develop and discuss areas of interests and build a sense of community, as well as allowing us to foster emerging Indigenous researchers into the research community. "This project operated within a framework of Indigenous leadership, ownership and engagement. "Efforts to improve the health, wellbeing and lives of Indigenous people nationally and internationally require a skilled and supported workforce, which is increasingly being led by Aboriginal and Torres Strait Islander people in Australia.

"Decolonising views about the progression of Indigenous researchers at varying career stages, the participants partnered with investigators in a shared learning journey about research methodologies and community-driven research activities. This gave them the tools to plan their career pathways and identify impact aspirations."

Over the past decade, the cohort of participants acquired tertiary qualifications that include an undergraduate degree and 17 postgraduate degrees. The project also resulted in a number of participants being appointed to professorships and associate professorships, and the leadership of numerous research centres, grants and programs. Across the life of the project, the Indigenous research participants also increased their publication rates.



Professor Elston is currently working to strengthen efforts and grow Indigenous research contributions at Monash University.

Over two-thirds of Indigenous primary health services organisations reported the recruitment, training and support of Aboriginal and Torres Strait Islander staff as a challenge in delivering quality health services.<sup>1</sup>

<sup>&</sup>lt;sup>1</sup> Australian Institute of Health and Welfare. "Aboriginal and Torres Strait Islander health organisations: Online Services Report key results 2017-18" Australian Government. 8 July 2019. Accessed 25 August 2020. www.aihw.gov.au/reports/ihw/212/atsi-healthorganisation-osr-key-results-2017-18/contents/ at-a-glance



Professor Frances Kay-Lambkin is a psychologist and leads an international team at the Priority Research Centre for Brain and Mental Health at the University of Newcastle. Her research focuses on the development and translation of evidence-based treatments for comorbid mental disorders for young Australians.

Professor Kay-Lambkin's team has led six large randomised controlled clinical trials through face-to-face, phone-based and computerised psychological treatments for mental health and alcohol/substance use problems. Findings were then translated into clinical practice. She engaged with 426 young people, aged between 16 and 25, who experienced depression and high levels of alcohol consumption.

"The clinical trial provided young people instant access to online intervention packages. The courses taught them to use cognitive behaviour therapy and motivation enhancement to self-manage thoughts, feelings and behaviours related to depression and alcohol consumption," Professor Kay-Lambkin said. "Technology and digital health care are critical tools in addressing shortfalls in mental health service availability, particularly with our younger generation."

This trial provided the first evidence of the impact of digital tools for both alcohol use disorders and depression. This was the first time young people were engaged in an online social network to talk specifically about alcohol use and depression.

"My team needed to establish clear clinical protocols for supporting safe discussions between young people online, without seeming like we were controlling the conversation."

Whilst the mobile app was moderated by psychologists, young people embraced the technology and the ability to virtually connect this way quickly and completely.

"Some of the best advice we saw in the network came from young people themselves, helping each other through really difficult and high-risk times."

By the end of the trial, participants reported they had reduced both their frequency of binge drinking by 18% and their depressive symptoms by 35%, indicating that helping young people cope with multiple concerns at once is an effective approach.



"This program has been so important during the COVID-19 pandemic, even though the study has now finished, keeping people connected and supported while we have not been able to do so in traditional ways."

THE UNIVERSITY OF NEW SOUTH WALES, THE UNIVERSITY OF NEWCASTLE

Ο



**TEAM MEMBERS** Dr Sally Hunt Ms Jenny Geddes Ms Kathryn Woodcock Ms Erin Forbes Dr Milena Heinsch Ms Dara Sampson Dr Samineh Sanatkar Dr Matthew Sunderland Professor Maree Teesson Professor Amanda Baker Professor Kathleen Brady Associate Professor Terry Lewin Dr Mark Deady Dr Louise Thornton

### USING DIGITAL INNOVATIONS TO ADDRESS DEPRESSION AND BINGE DRINKING IN YOUNG AUSTRALIANS

"It was humbling to watch and demonstrated to us how empowering this technology and approach can be."



Photo: iStocl

The model will expand to new groups who do not usually engage with mental health care. It will be used in the first trial of social networking and online psychological support for Australians aged 60 years and over, who are experiencing untreated depression and alcohol use problems.

### TARGETING DANGEROUS HEART ATTACK AND STROKE-CAUSING PLAQUES

DETECTION OF VULNERABLE ATHEROSCLEROTIC PLAQUES

Professor Karlheinz Peter

"The major outcome from our discoveries was the development of a specialised catheter to be used in patients to identify and treat vulnerable plaques before they cause a heart attack. This intracoronary catheter can detect NIRAF as a specific feature of unstable, rupture-prone plaques.



#### BAKER HEART AND DIABETES INSTITUTE

**TEAM MEMBERS** 

Dr Yung Chih Chen

Dr Xiaowei Wang

Dr Nay Min Htun Dr Guy Krippner

Professor Alex Bobik Dr James McFadyen Dr Tara Schiller

Professor

Bayden Wood

Professor

(L) T

DEVELOPMENT GRANT \$545,506 2013-2016



Heart attack and stroke are major causes of death and disability worldwide. With over 500,000 Australians suffering from some form of coronary artery disease<sup>1</sup>, Professor Karlheinz Peter's research is more important than ever. Myocardial infarction, or heart attack, is caused by the build-up of atherosclerotic plaques. Bursting or rupture of inflamed and thereby vulnerable plaques can cause blood clotting, which then leads to heart attack and stroke.

Professor Peter and his team, with funding from an NHMRC Development Grant, aimed to develop a technology in a clinical setting that would reliably identify unstable, rupture-prone plaques. They knew this preventive measure has the potential to save many lives of people otherwise impacted by coronary disease and resulting heart attack. Their major breakthrough was the identification of a unique characteristic of the unstable plaque tissue. The team found a 'Near-InfraRed AutoFluorescence', or NIRAF, a characteristic specific to these dangerous heart attack and stroke-causing plaques.

The challenge for Professor Peter's team came when developing an animal model that builds up vulnerable, rupture-prone plaques as seen in patients with heart attack or stroke. The team was successful in developing such a model, which was then used to identify the characteristics of these plaques.

"We have also used the same model to test and identify several drugs that provide plaque stabilisation, which is a major achievement and addresses a great medical need."

Professor Peter described how NHMRC's support enabled the original discovery and helped propel his team's early findings. "NHMRC provided the essential basis for this research, as well as the first steps towards commercialisation to combat this heart disease which, on average, kills one Australian every 30 minutes<sup>2</sup>." "Until now, there was no method available to clinicians that would allow the identification of those dangerous plaques that are at high risk of rupture," Professor Peter explained.



For the development and testing of an imaging device that can be placed into the coronary artery the research will require further and substantial funding. Clinical evidence must be established to show evidence that the detection of unstable plaques works reliably. For Professor Peter and his team the clinical evidence that this technology saves lives and reduces costs on our health care systems is the ultimate goal.

<sup>&</sup>lt;sup>1</sup> Australian Institute of Health and Welfare. "Cardiovascular disease" Australian Government. 15 July 2020. Accessed 25 August 2020. https://www.aihw.gov.au/reports/heart-stroke-vascular-disease/ cardiovascular-health-compendium/contents/how-many-australians-have-cardiovascular-disease 2 Australian Durace of Dealth Australian 2010" Australian Courservent

<sup>&</sup>lt;sup>2</sup> Australian Bureau of Statistics. "Causes of Death, Australia, 2018" Australian Government. 25 September 2019. Accessed 25 August 2020. https://www.abs.gov.au/ausstats/abs@.nsf/ mf/3303.0



### MEASURING THE **EFFECTIVENESS OF CANCER INTERVENTIONS**

### **HEALTH STATES AND** THEIR VALUE IN ECONOMIC **EVALUATION IN CANCER**

#### **Professor Madeleine King**

Professor

Rosalie Vinev

Julie Pallant

Dr Peter Grimison





used to decide which medical services and pharmaceuticals should be publicly funded. Professor Madeline King, Director of the University of TEAM MEMBERS Sydney's Quality of Life Office. has developed ways to measure quality of life for use in economic Associate Professor evaluation of cancer interventions in Australia and across the world. Dr Monika Janda

Economic evaluation is a tool

"Economic evaluation is crucial in this age of soaring health care costs and limited health budgets. When we compare two treatments, we need to know which provides better survival. which provides better quality of life and which is the most cost effective.

"We all aspire to a good quality of life. When health is threatened, patients, families and health care providers all hope to preserve both life and quality of life."

Professor King brought together researchers from diverse fields such as economics, oncology and psychology to understand the impact of medical services and pharmaceuticals on the quality of life of cancer patients.

Through this grant, The Multi-Attribute Utility in Cancer (MAUCa) Consortium was established, with the common goal of including quality of life data in economic evaluation of new cancer treatments. Demonstrating the importance of the consumer voice in research, patients self-reported the impacts of trial treatments on their quality of life, which has informed the study's outcomes. Professor King and her team have successfully demonstrated this model and illustrated its valuable application in Australia.

"MAUCa has developed mathematical formulae to apply the preferences of a particular country's general population so that these quality of life data can be included in economic evaluation. This helps inform decisions about which treatments will be funded by a country, and at what price.

The variety and differences in the way researchers from different disciplines think and talk about quality of life was a challenge for this multi-disciplinary research.

"Economists use the term 'utility' when talking about patient benefits, and while psychologists and oncologists also use this term, they sometimes use it differently, and they also think and talk about quality of life in other ways. While challenging, it was important to have these different areas of research working together."

"Through its success, other MAUCa members" have secured funding to fulfil its objectives in China. Japan and Singapore, as well as several countries across Europe and North America."

Cancer medicines cost the Australian Government around \$2 billion in 2016–17 around one in every six dollars of expenditure in the Pharmaceutical Benefits Scheme.<sup>1</sup>

<sup>1</sup>Department of Health. "Cancer fact sheets" Australian Government. 8 January 2018. Accessed 25 August 2020. https://www1.health.gov.au/ internet/main/publishing.nsf/Content/cancer-factsheets-1



Now that the consortium has made these tools available to the broader cancer research community, the next steps are to see if they are useful in capturing cancer-specific quality of life in economic evaluation — due not only to the effect of the disease itself, but also to side-effects associated with many common treatments. Professor King and her team's focus now is to develop user manuals and resources for the tools with the aim of expanding their use to more parts of the world.

Photo: iStocl

### MAPPING THE TRAJECTORY OF DEPRESSION IN PRIMARY CARE TO IMPROVE TREATMENT

THE DIAMOND COHORT STUDY — BETTER MANAGEMENT OF THOSE AT RISK OF PERSISTENT AND DISABLING DEPRESSION I'M FINE



#### THE UNIVERSITY OF MELBOURNE



TEAM MEMBERS

Professor Helen Herrman Dr Patty Chondros Professor Kelsey Hegarty Christopher Dowric Associate Professor Victoria Palmer Professor Michael Kyrios Associate Professor Grant Blashki Professor Gail Gilchris Professor Frances Griffiths Professor Cathrine Mihalopoulos Professor Professor Lena Sanci

"Australians take more antidepressants than almost anyone else in the world, and the number of prescriptions keeps rising, yet there is little evidence to guide for how long antidepressants should be used."

What began as a short, one-year study looking at how people who present with depressive symptoms were treated, the Diamond Study turned into a major 13-year project, following hundreds of patients through their primary care journey.

Lead Investigator, Professor Jane Gunn has had a keen interest in mental health since her days as a medical student and trainee doctor. It was very apparent to her that mental health care needs were prominent in all settings, but particularly in general practice where, in her words, "addressing these needs is a key part of helping people get better".

"During Diamond almost 800 people recruited from general practices across Victoria were followed for 10 years.

"This was the first time we had a solid understanding of how patients with depression presented to general practice and, more importantly, how they were being managed.

"After about 10 years we decided to start wrapping up the study because we kept finding the same things over and over. One big thing that really jumped out at us was the under-researched area of the connection between physical and mental health. "Our study was one of the first to comprehensively demonstrate a link between the number of physical conditions a person has, and the increased likelihood they will experience depression.

"We also found that, along with physical illness, mental illnesses often coexist when there is childhood trauma, or financial stain.

"Despite the setbacks some individuals face, we saw time and time again in Diamond that human beings have a remarkable capacity to bounce back."

Professor Gunn and her team used the findings from Diamond to develop an innovative web-based tool to help GPs identify patients at risk of depressive symptoms and match them with tailored treatment options.

"Another recurring theme we found is that too often our approach to treating mental illness is lacking a tailored, holistic approach and that much more attention needs to be paid to the way that health care is integrated in Australia."





Another issue that Professor Gunn is passionate about is the potential risk associated with long-term antidepressant use, a traditionally under-researched area, and the focus of her current research.

"I'd like to see that change, so my current research focus is looking to establish a body of research evidence, which I hope will lead to more evidenced-based, rational prescribing." "Through an effective clinical collaboration we are currently undertaking an exciting clinical trial to deliver repetitive transcranial magnetic stimulation to people with MS. This non-invasive treatment's purpose is to promote new brain cell generation and brain lesion healing."

## ADDING NEW CELLS TO THE MATURE CENTRAL NERVOUS SYSTEM

### THE UNIVERSITY OF TASMANIA



### **TEAM MEMBERS**

Professor Dr Carlie Cullen Dr Kimberley Pitman Dr Kalina Makowiecki Dr Shannon Beasley Mr Mackenzie Clutterbuck Ms Renee Pepper Mr Raphael Ricci Mr Benjamin Summers Ms Tram Nguyen Mr Loic Auderset Professor Jennifer Rodger Prof Lisa Foa Dr Jac Charlesworth Prof Bruce Taylor Dr Robert Gasperini Professor Renaud Jolivet Dr Ben Emery Dr Alexander Tang

### Associate Professor Kaylene Young

For people with Multiple Sclerosis (MS), the myelin that covers nerve fibres in the central nervous system (brain, optic nerves and spinal cord) is damaged, leading to impairment of cognitive, motor and sometimes sensory functions.

**INVESTIGATING THEIR** 

NORMAL FUNCTION AND

POTENTIAL FOR REPAIR

While undertaking a postdoctoral fellowship at University College London in 2008, Associate Professor Kaylene Young reported that an immature cell population found in the developing brain also existed in adulthood. These immature cells, called oligodendrocyte progenitor cells or 'OPCs', were not only found throughout the mature central nervous system, but continued to generate a significant number of new brain cells.



"These crucial discoveries underpinned the research that I started with funding from an NHMRC Career Development Fellowship and also resulted in additional discoveries about mature cell structure, which have significant implications for diseases ranging from MS to Alzheimer's disease and epilepsy," Associate Professor Young explained.

Over the last decade, Associate Professor Young's basic scientific discoveries have not only paved the way for further research but also led to collaborative projects to learn more about these newborn brain cells. In 2011 when Associate Professor Young started her research group at the University of Tasmania, her research efforts were directed towards understanding the function of newborn cells in the mature brain and identifying treatments that could direct these new cells towards nervous system repair. Associate Professor Young's team discovered that OPCs give rise to new cells that make myelin, the nerve cell insulation that is lost in MS. They found that the addition of new myelin and the remodelling of surviving myelin could influence the speed of information transfer in the nervous system.

"Having shown that new myelin could improve nerve cell function, we turned our attention to identifying the signals responsible. We found that OPCs responded to the electrical activity of nerve cells, and that we could use transcranial magnetic stimulation to increase the amount of new myelin," says Associate Professor Young.

Associate Professor Young's research has also contributed to MS education through the provision of content in "Understanding MS", an open online course that was launched by the MS Research Flagship at the Menzies Institute for Medical Research in 2019.

In 2017, there were over 25,000 people in Australia affected by MS, making the disease the most prevalent neurological condition affecting young adults.<sup>1</sup>

<sup>1</sup> H Ahmed, A Palmer, J Campbell, I van der Mei & B Taylor, "Health Economic Impact of Multiple Sclerosis in Australia in 2017" Multiple Sclerosis Research Australia. August 2018. Accessed 25 August 2021. https://msra.org.au/wp-content/uploads/2018/08/health-economicimpact-of-ms-in-australia-in-2017\_ms-research-australia\_web.pdf



Associate Professor Young and her team at the Menzies Institute for Medical Research at the University of Tasmania are currently working to identify the cause of MS and develop new nervous system repair treatments to improve the lives of people with this disease.

"A significant obstacle to MS research is still our lack of knowledge about what causes MS. Ultimately that means that we lack a preclinical model that recapitulates all aspects of the disease," Associate Professor Young explained.

"We are now testing potential treatments in new preclinical models, including human stem cell lines generated from people with MS, so that more aspects of MS pathophysiology can be understood".

### BREATHING EASY – IMPROVING ACCESS TO RESPIRATORY DISEASE REHABILITATION

BENEFITS AND COSTS OF HOME-BASED PULMONARY REHABILITATION IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Professor Anne Holland

In 2018, chronic obstructive pulmonary disease was the fifth leading cause of death in Australia.<sup>2</sup>

<sup>1</sup> Australian Institute of Health and Welfare. "Chronic Obstructive Pulmonary Disease (COPD)" Australian Government. 25 August 2020. Accessed 25 August 2020 https://www.aihw.gov.au/reports/acm/35/copd/data LA TROBE UNIVERSITY, MONASH UNIVERSITY



PROJECT GRANT \$364,361 2013-2016

### **TEAM MEMBERS**

Professor Christine McDonald Professor Ajay Mahal Dr Catherine Hill Dr Annemarie Lee Ms Angela Burge Dr Narelle Cox Dr Rosemary Moore Ms Caroline Nicolson Dr Paul O'Halloran Dr Aroub Lahham The average adult takes up to 20 breaths every minute<sup>2</sup>, something most people give little thought. However, breathing can be a daily struggle for people with Chronic Obstructive Pulmonary Disease (COPD), an umbrella term for a group of lung conditions that includes emphysema, chronic bronchitis and chronic asthma.

For Professor Anne Holland, investigating supportive therapies for people with chronic respiratory disease has been a career focus. A Professor of Physiotherapy at Monash University and Alfred Health in Melbourne, she has been looking at in-home rehabilitation as a way to improve access for patients with COPD.

Pulmonary rehabilitation is a highly effective treatment for people with COPD, involving exercise, training and education over eight to twelve weeks.

"In Australia, COPD is responsible for more potentially preventable hospital admissions than any other chronic disease, and is a major contributor to health care costs. Only 5-10% of those with COPD ever receive rehabilitation because treatment is traditionally provided in hospitals or clinics," Professor Holland explained. "Australia's health system has delivered rehabilitation in outpatient facilities that patients usually attend twice a week. This model has not changed significantly in 30 years, raising barriers to access such as shortage of programs and patients' poor physical mobility, breathlessness and inability to travel.

"There is an opportunity to broaden the model to include home-based services. Our HomeBase trial showed that rehabilitation could be delivered entirely at home for people with COPD, with the same clinical outcomes as centre-based rehabilitation." Those who completed either type of rehabilitation program were 56% less likely to be admitted to hospital during the following year, significantly lowering health care costs.

The COVID-19 pandemic caused closure of centre-based rehabilitation programs to protect vulnerable patients from infection, highlighting the need for this type of home-based program. Queries on the HomeBase model came from around the world seeking alternatives to the centre-based model of rehabilitation.

"Overall the HomeBase model has been very well received by patients and health professionals, both in Australia and across the world, who have welcomed our work as a way to deliver this important treatment to a larger proportion of those who need it." "This study showed that about twice as many patients completed home-based rehabilitation compared to rehabilitation in centres. It requires no specialised equipment, and its delivery is within the current scope of practice of pulmonary rehabilitation professionals."

<sup>2</sup> C Chourpiliadis & A Bhardwaj. "Physiology, Respiratory Rate" StatPearls Publishing. January 28 2019. Accessed 25 August 2020. https://www.ncbi.nlm.nih.gov/books/NBK537306/



#### THE NEXT STEPS

Professor Holland's team will support programs across Australia to offer patients the choice of a home-based or centre-based program. "They will learn about patient preferences and how to support implementation of HomeBase in clinical practices, and test whether offering patients this choice can increase completion of pulmonary rehabilitation and reduce subsequent hospital admissions."

Professor Holland is currently a Chief Investigator of the NHMRC-funded Centre of Research Excellence in Pulmonary Fibrosis. Even though cancer survival rates have increased and cancer mortality rates continue to drop, cancer accounts for around three of every 10 deaths in Australia. Aboriginal and Torres Strait Islander people and people in lower socioeconomic groups have even lower cancer survival rates than other Australians.<sup>1</sup>

Associate Professor Misty Jenkins is an NHMRC fellow and Laboratory Head in the Immunology Division at The Walter and Eliza Hall Institute of Medical Research, where she researches cancer immunotherapy — a treatment which utilises the body's immune system to treat cancerous cells.

Associate Professor Jenkins has a long-standing interest in CD8<sup>+</sup> T cell — or 'killer' T cell — cytotoxicity, with her current research program focusing on killer T cell immunotherapy for brain cancer.

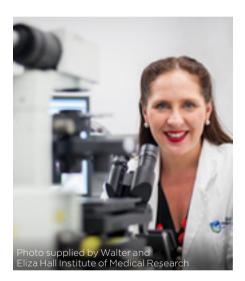
"Killer T cells are a specialised group of immune cells which destroy cancerous and infected cells. When killer T cells find a target — like a cancer or infected cell — they attach and secrete toxic molecules. They then detach from the dying target, so that they may go on to kill other cells. If they don't detach properly, they remain bound to the target cell, which can result in an improper immune response." This NHMRC Project Grant was awarded to shed light on how the killer T cell detaches, which is essential for an effective immune response.

"This grant enabled further research to understand how white blood cells and natural killer cells kill their cancerous targets one after the other, sometimes referred to as 'serial killing'. Decades ago, researchers coined the term 'kiss of death' for this fatal interaction," Associate Professor Jenkins said.

The study also showed how engineered chimeric antigen receptor T cells (CAR T cells) formed an immune synapse with their targets - the vital connection that controls how the cells function. This research unveiled how these synthetic receptors on CAR T cells, which are currently being used to treat a variety of cancers, can override the killing capacity of T cells and in fact may result in faster signalling of the T cell. This information can be used to design even more effective killing receptors to target a variety of cancer types.

**Associate Professor Misty Jenkins** 

HOW OUR IMMUNE CELLS KILL CANCER



<sup>1</sup> Australian Institute of Health and Welfare. "Cancer in Australia 2019" Australian Government. 21 March 2019. Accessed 25 August 2020. https://www.aihw.gov.au/reports/cancer/cancer-inaustralia-2019/contents/summary

With her team, she discovered that, when target cells do not die quickly, it can cause inflammation, which hampers the body's immune response.



Associate Professor Jenkins and her team have been able to make predictions about the efficiency of killer T cells, which is important for designing new immunotherapies. Together, they are excited to take these findings from the laboratory into the clinic. "In our current program, we are generating novel immunotherapies to treat brain cancer in both adult and paediatric patients."

"Outcomes for patients with high-grade brain and spinal tumours are currently poor, but if we can design efficient T cell immunotherapies that kill tumours without causing inflammation in the brain, we might be able to help people."

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Associate Professor Misty Jenkins

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HALL INSTITUTE OF MEDICAL RESEARCH

PROJECT GRANT \$606,226 2014-2016

## A SMART NEEDLE FOR SAFER BRAIN SURGERY

DEVELOPMENT OF MICROSCOPE-IN-A-NEEDLE DEVICES FOR IMPROVED CLINICAL DIAGNOSTICS

Professor Robert McLaughlin

"Early trials showed promising results, with the smart biopsy needle able to detect blood vessels with a high sensitivity and specificity in a study on 11 patients undergoing brain surgery. This provides hope we can make brain surgery safer."







### TEAM MEMBERS

Professor David Sampson Associate Professor Christopher Lind Mr Bryden Quirk Mr Rodney Kirk Dr Jiawen Li Dr Dirk Lorenser Dr Loretta Scolaro Mr Hari Ramakonar Associate Professor Peter Noble Professor George Yeoh Professor John Olynyk

Almost 2000 Australians are diagnosed with a malignant brain tumour each year<sup>1</sup> and, tragically, it is the leading cause of cancerrelated death among children. Professor Robert McLaughlin's team at the University of Adelaide, with colleagues at The University of Western Australia, set out to better diagnose the specific type of tumours, which can benefit patients' treatment options and outcomes.

With a PhD in Electronic Engineering and industry experience in medical devices research and development, Professor McLaughlin wanted to use his unique skills to see survival rates for brain cancer significantly improved.

"Neurosurgeons are wonderfully supportive of anything that will improve outcomes for their patients. Spending time in surgery with them, I realised that the technologies we work with could help them do their job more safely. In particular, we could help them do a smarter diagnosis." One way of doing this is to perform a needle biopsy by taking a tissue sample, which involves inserting a large needle in the patient's brain. Professor McLaughlin explained the danger associated with this method: "If the needle hits a blood vessel, then the patient can suffer a stroke which can cause irreversible damage or death".

Funded by an NHMRC Development Grant, Professor McLaughlin and his team have developed a tiny imaging probe, the size of a human hair, and integrated it into a needle for use in brain biopsies.

"We created a 'smart needle' that has the ability to see where it is going. By integrating imaging technology used in eye and heart surgery with existing neurosurgical techniques, the device can detect blood vessels before damage is caused."

At present, 1% of patients will die because of bleeds during a brain biopsy and 2–3% will be left permanently disabled, an unnecessary risk during surgery that Professor McLaughlin is working to change.

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"If the needle hits a blood vessel, then the patient can suffer a stroke which can cause irreversible damage or death".





For the next phase, further NHMRC funding is supporting Professor McLaughlin and his team to develop the next generation smart brain biopsy needle for wider application. "The next generation needle has the ability to not only see delicate blood vessels in the brain, but also detect the cancer, allowing neurosurgeons to perform brain biopsies more accurately and in less time."

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