Australian Government
National Health and Medical Research Council

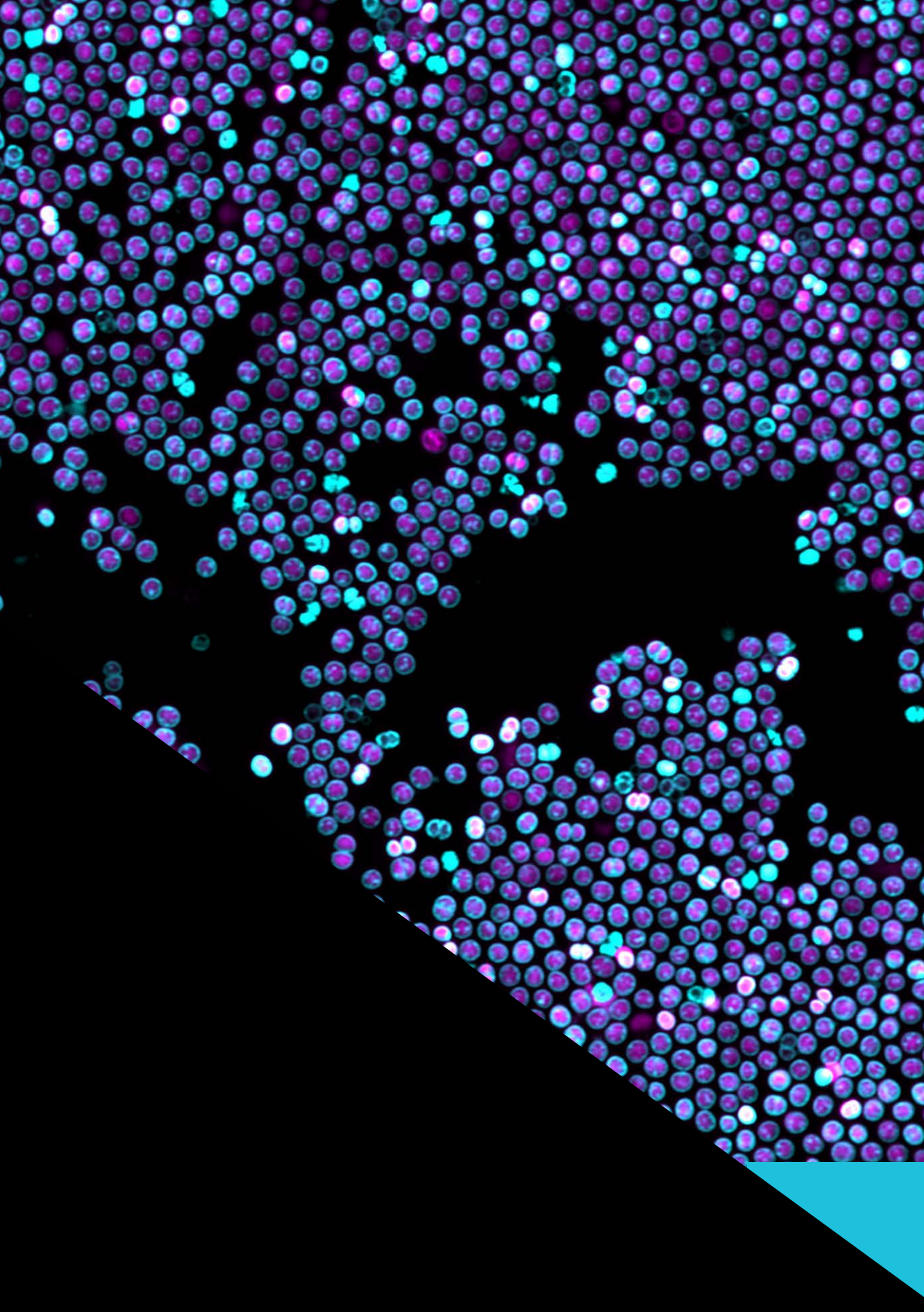
BUILDING
A HEALTHY
AUSTRALIA

1 of the BEST

NHMRC RESEARCH PROJECTS

NHMRC

SIXTEENTH EDITION



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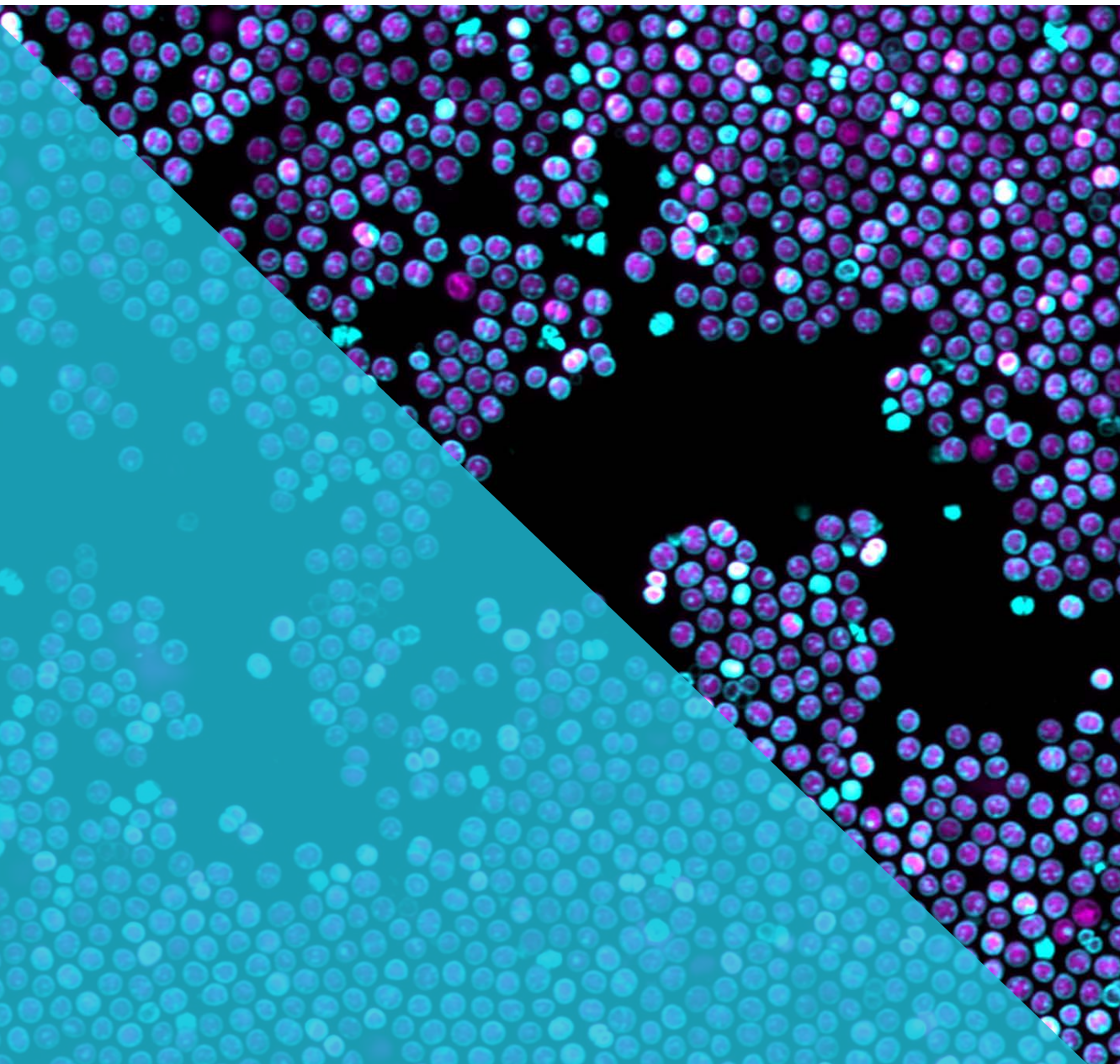
10 OF THE BEST
WELCOME

First published in 2005, *10 of the Best* showcases the success stories from Australia's health and medical researchers whose work has been funded by the Australian Government through NHMRC. The projects illustrate the diversity and quality of NHMRC-supported research and are evidence of the deliberative and collaborative scientific method which underpins our national reputation for excellence, research integrity and impact.



CEO FOREWORD

Two decades ago, NHMRC launched its now flagship publication *10 of the Best* as a way of showcasing the first results of the Australian Government's doubling of investment in medical research which commenced from the adoption of the Wills Report. This report was instrumental in raising media attention of health and medical research and subsequently increasing funding for Australian science. This investment into medical science has contributed to the health of our nation, in which we have all since shared in the dividends.

Although our health and medical research sector has significantly evolved over this period, something that has remained constant is the quality and calibre of research that is undertaken by Australian researchers each year. The level of excellence of health and medical research in Australia is extraordinary and *10 of the Best* is representative of the talent, expertise and skills that leads to this excellence and continues to address our national health priorities.

It is an honour to launch 1*0 of the Best – Sixteenth Edition*, featuring a select yet impactful, sample of NHMRC-funded research completed in 2022. These diverse projects effectively span the health and medical research spectrum from basic science, clinical medicine and science, public health, to health services.

The sixteenth edition of *10 of the Best* details the ways in which researchers have combined fundamental scientific research with national health priorities such as Aboriginal and Torres Strait Islander health, cardiovascular disease, cancer and Alzheimer's disease.

To be a researcher, you require unrelenting dedication and commitment to quality. Within this, you need to be prepared for when science doesn't go quite the way you expected with a negative result. Among the incredible narratives told throughout this publication is a project in which reported results that supported the null hypothesis – increasing the knowledge impact and potential for future application to human health.

Our national investment into health and medical research is an asset to the future health of all Australians, and of which helps us build towards a healthy Australia. As the nation's lead agency supporting this research, I am proud to share the achievements of NHMRC-funded researchers and the major contributions they have made to medical science.

I congratulate and provide my sincerest thanks to the researchers celebrated in *10 of the Best – Sixteenth Edition*. To those who are reading, I hope you enjoy delving into these stories of how health and medical research, at its best, can contribute to significant improvements across all aspects of human health.

Professor Steve Wesselingh
Chief Executive Officer

ENGINEERING AND MEDICAL RESEARCH COMBINED IN THE FIGHT AGAINST ALZHEIMER'S

Dr Prashant Bharadwaj

Institution: Edith Cowan University and Alzheimer's Research Australia
Grant: NHMRC-ARC Dementia Research Development Fellowship
Funding: $446,770
Year: 2016–2022
Team members: Ms Fraulein (Poi) Arigo, Ms Zoe Mputhia, Dr Steve Pedrini, Mr Ajish Ariyath, Professor Ralph Martins and Mr Kevin Taddei.

Dr Prashant Bharadwaj's innovative research and work is paving the way for new treatments and offering hope to families affected by dementia.

Combining his background in engineering and biotechnology with a passion for neuroscience, Dr Prashant Bharadwaj has identified a role for the PRKAG2[1] gene in Alzheimer's disease. His research is providing a deeper understanding of amyloid buildup and potential 'cleaning processes' in the brain.

Dr Bharadwaj, from Edith Cowan University and Alzheimer's Research Australia, received an NHMRC-ARC boosting dementia research grant to test 5,000 yeast mutants to search for genes that regulate autophagy. [2]

Over 180 autophagy genes were screened in the yeast model revealing 4 genes that reduce levels of beta amyloid aggregates. Dr Bharadwaj then analysed brain samples and discovered that gene expression of PRKAG2 is increased 3-fold and its protein levels positively correlated with beta amyloid accumulation in the brain.

It has long been thought that autophagy activation is a mitigating response to beta amyloid accumulation in the Alzheimer's disease brain, but Dr Bharadwaj has discovered a counterintuitive result.

"The scientific question was: 'How do you find a particular gene or protein that you can activate and clear amyloid?' We found a gene that activates amyloid removal but is dysregulated in the Alzheimer's brain," said Dr Bharadwaj.

"Because autophagy is like a washing machine, clearing up all the garbage, we thought that by activating autophagy, it would clean better. But we found there is a defect somewhere. It's like the washing machine's taking in more and more dirty clothes, but it's not washing them. So, amyloid is getting stuck in the whole system."

"Increased autophagy doesn't clear out amyloid plaque so we will do more research to show that lowering activity of certain pathways might actually be more beneficial," said Dr Bharadwaj.

While it's not the result Dr Bharadwaj had hoped to find, he is committed to pursuing answers, inspired by witnessing a close family member with dementia.

"Ten years ago, I realised that despite an aging population and so many diagnosed neurological diseases, families don't have options. It's frustrating that despite decades of research, we still can't define what causes dementia and there are no efficient drugs to stop or reverse the progression," he said.

Despite challenges like the COVID-19 pandemic impacting international collaborations, Dr Bharadwaj has continued to strengthen efforts with researchers globally. He is also turning his attention to childhood dementia.

"Engaging with families affected by childhood dementia has been incredibly rewarding. Our findings not only contribute to scientific knowledge but also provide hope and support to those facing these rare disorders."

"It turns out that a lot of cases of childhood dementia are caused by disorder of the autophagy pathway, the same as in Alzheimer's. So, basically, if there's anything wrong with your autophagy, you're going to have dementia," he said.

"Engaging with families affected by childhood dementia has been incredibly rewarding. Our findings not only contribute to scientific knowledge but also provide hope and support to those facing these rare disorders."

Next steps

Dr Bharadwaj is continuing his research in Alzheimer's disease and childhood dementia. He has initiated a national biomarker study bringing together clinicians and paediatric neurologists across Australia. Working with Perth Children's Hospital and SA pathology, he is developing prognostic blood biomarkers for childhood dementia and is also investigating gene biomarkers in childhood dementia with Adelaide University.

Advancing his work in Alzheimer's disease, Dr Bharadwaj is investigating small molecules as drug candidates and hopes to engage more with drug developers and potentially startups and private investors. Dr Bharadwaj will also continue mentoring junior academic staff, supervising students and plans to develop his own independent research team.

SURVIVING MELANOMA HAS A NEW GENETIC STORY

Dr Sarah Ward

Institution: University of Western Australia

Grant: Early Career Fellowship

Funding: $419,526

Year: 2017–2021

Australia has the highest incidence of melanoma in the world with one Aussie diagnosed every 30 minutes.[3] Delve into the research led by Dr Sarah Ward aiming to unpack the genetic epidemiology of melanoma.

The underlying genetic and environmental factors that influence risk and survival of this aggressive skin cancer are fundamental building blocks for melanoma research, diagnosis and treatment, according to Dr Sarah Ward, a leading cancer epidemiologist.

"With a better understanding of the biology and causes of melanoma this knowledge can be built upon and translated into clinical tools that doctors can use to improve patients' lives," said Dr Ward from the University of Western Australia.

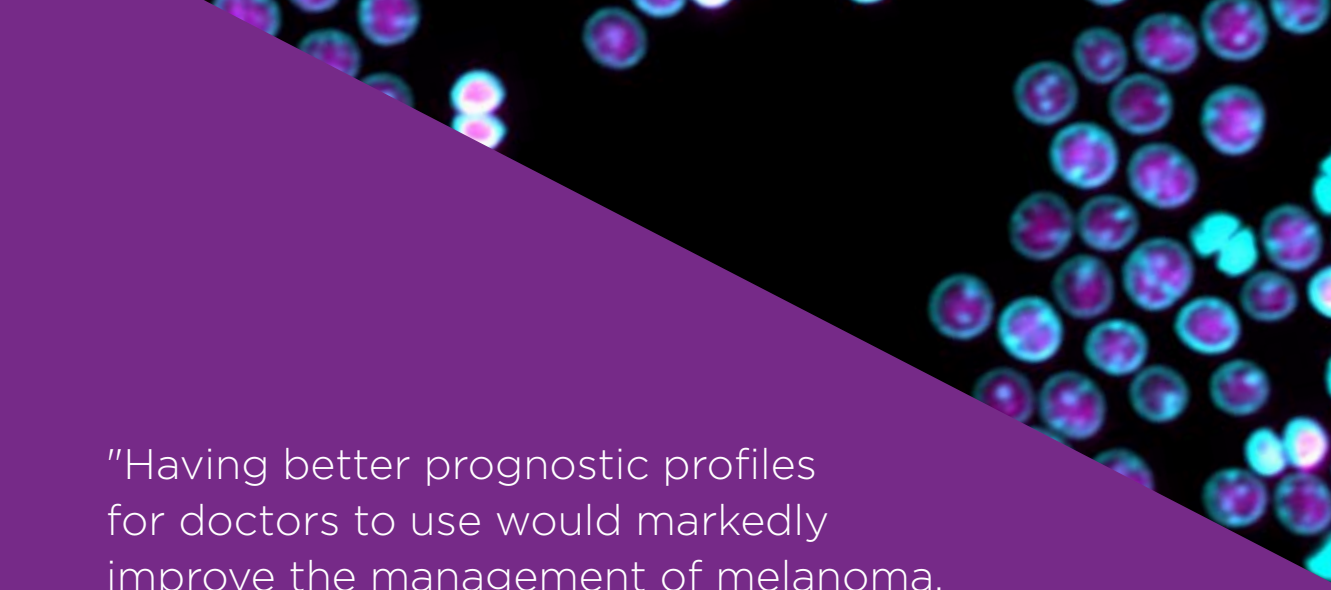
Using an NHMRC Early Career Fellowship, Dr Ward, discovered a particular melanoma risk variant in the *IRF4* gene[4] is strongly associated with melanoma at body sites with a known poor prognosis, tumour thickness and poorer survival rates. Along with her collaborators, they also found a set of variants in the vitamin D-binding protein gene are protective against death in the case of thicker tumours and a variant in the *MDM2* gene[5] reduced the risk of melanoma death in females.

To achieve these results, Dr Ward combined data from the WA Melanoma Health Study—a study analysing 1,600 cases, established during her PhD— with international datasets. Through further international collaborations, Dr Ward has also been part of a team identifying 40 new risk variants for getting melanoma.

"This body of research has substantially improved our knowledge of prognostic genetic markers and provides a platform for the development of blood tests to identify genetic markers for survival," said Dr Ward.

"Having better prognostic profiles for doctors to use would markedly improve the management of melanoma. I can also see opportunities to identify novel therapeutic targets, which is very exciting," she said.

While melanoma genetic screening tools are not yet mainstream, the potential for blood tests and other predictive measures is on the horizon. And this



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practical application to help patients and families is a key driver behind Dr Ward's more than 20 years of work in melanoma epidemiology.

"From talking with families as a student and learning more about the disease it became a passion. The more I got involved in the area I've wanted to keep going because so many people are affected by melanoma," said Dr Ward.

Dr Ward emphasises the importance of working closely with patients and collaborating with researchers to make the most of exciting advancements in genetic technology, particularly as the costs of genetic research have reduced substantially.

"People with melanoma were really enthusiastic about the work and donated their time and came in to do blood tests. Because they embraced the detailed questionnaires and were so forthcoming, we have seen incredible value from this research.

"Working with leading researchers overseas, for example at the Memorial Sloan Kettering Cancer Center in the US, has not only expanded my knowledge but also strengthened international ties in the fight against melanoma." said Dr Ward.

Next steps

Dr Ward is working towards developing polygenic (multi-gene) risk profiles to determine the combinations of genes that relate to different risks. This kind of profiling would assist doctors to know where on the body a melanoma is more likely to develop, and which melanomas are more likely to metastasise.

There are some general 'rules of thumb'—such as patients with thin melanomas (≤1 mm) having excellent prognoses—that warrant closer investigation, according to Dr Ward.

"A small proportion of patients with thin melanoma progress to metastatic disease and present a clinically challenging subset of patients to treat. Being able to identify those patients who are at high genetic risk of fatal thin melanomas means they can be monitored more closely for metastatic disease. The earlier it's diagnosed the less chance that melanoma will metastasise and spread, and that means better survival odds" said Dr Ward.

PREVENTING AND HEALING PAINFUL, CHRONIC WOUNDS THROUGH MULTIDISCIPLINARY R&D

Professor Allison Cowin

Institution: University of South Australia
Grant: Research Fellowship
Funding: $649,561
Year: 2016–2021
Team members: Dr Xanthe Strudwick, Dr Stuart Mills, Dr Chris Turner and Professor Rob Fitridge.

Discover how Professor Allison Cowin's innovative stem cell and antibody treatments are transforming chronic wound care. Her groundbreaking work offers hope and improved health outcomes for millions worldwide.

Backed by an NHMRC Research Fellowship, Professor Allison Cowin, from the University of South Australia, is on a quest to improve the health outcomes for people suffering from chronic wounds.

Describing wounds as "a spiralling epidemic affecting millions of people worldwide", Professor Cowin and her team have developed a new diagnostic blood biomarker test and 2 new treatment approaches, using stem cells and targeted antibodies. In exciting news, they have progressed a stem cell coated dressing, Cypatch, through preclinical laboratory studies and into phase I/II clinical trials with industry partners, TekCyte and Cynata Therapeutics. The results show incredible active healing and Cynata have licensed the technology for further clinical trials and product development.

"We've been able to take it from the laboratory, with incredible materials and stem cell scientists, right through to clinical trials. To show over 65% improvement in healing of diabetic foot ulcers in 12 weeks and 80% by 24 weeks is absolutely amazing," said Professor Cowin.

"For patients this means reduced pain and infection. It's usually very difficult to get a wound to heal once it's entered the chronic non-healing phase.

"Chronic wounds are an under recognised issue in Australian health care. For individuals with diabetes, the elderly, or those suffering from severe burns, there can be lifelong problems with healing," said Professor Cowin.

Wound care costs the Australian health system over $4.5 billion per year.[6] One in 4 people with diabetes will develop a diabetes-related foot ulcer and one in 5 with a moderate to severe foot ulcer will require a lower limb amputation.[7]

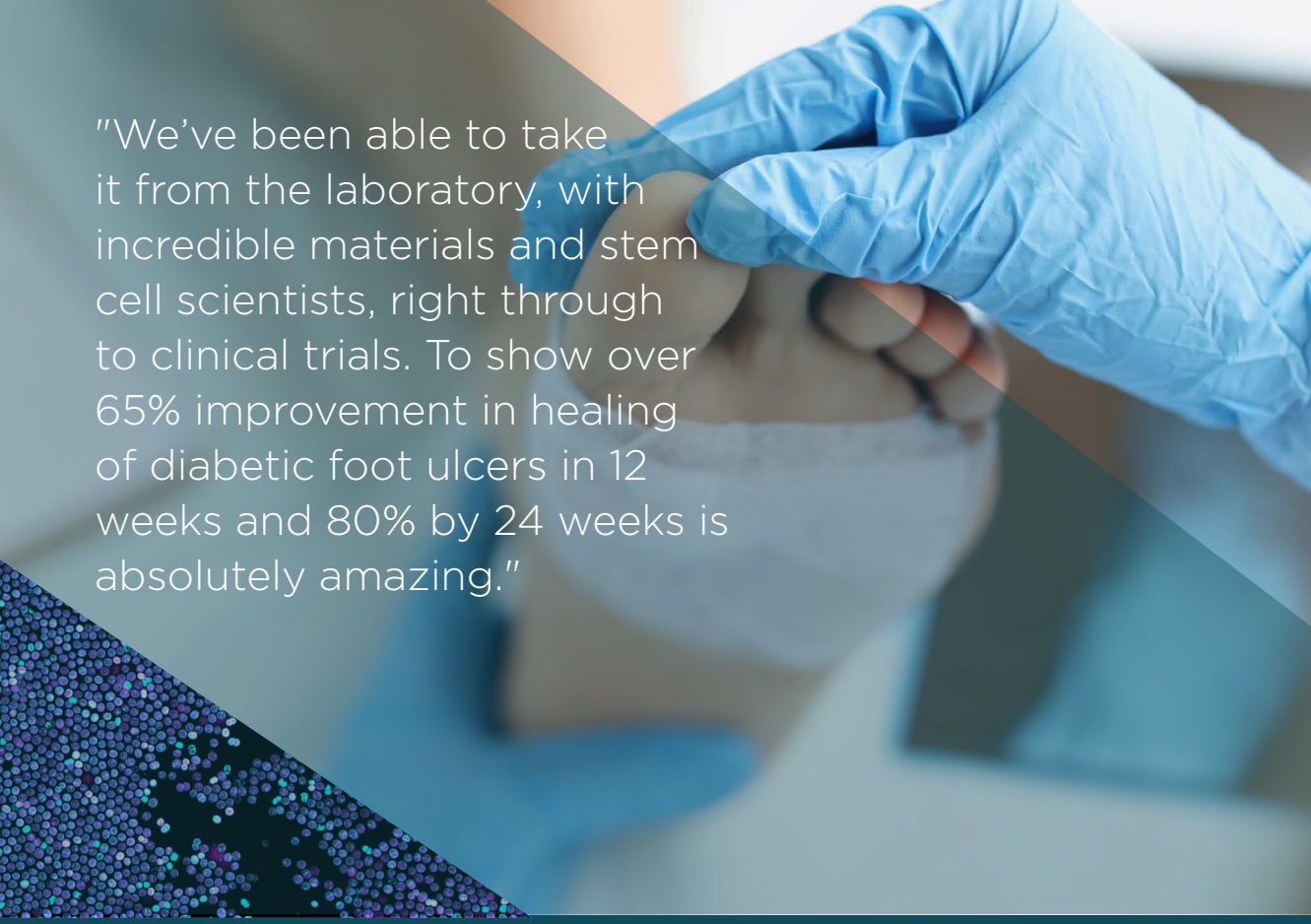
In another area close to her heart, Professor Cowin has worked for 15 years on Epidermolysis Bullosa (EB), a rare disease also known as 'fragile skin'. She has created a new antibody treatment that improves healing and addresses internal blistering, a common issue for children with EB.

"I first heard about EB at a conference when I saw a baby with no skin on their legs. I remember thinking if you were changing a nappy on a baby and all you did was cause pain to that poor baby, then what sort of life was that?" she recalled, her voice tinged with emotion.

"I decided there had to be something I could do as a wound healing person," she said.

Continuing to push through the major challenge of getting people to appreciate that wound healing is important, Professor Cowin is grateful to NHMRC for funding this work.

"The material scientists, physicists, stem cell biologists, nanomedicine experts, and patients… they've all been part of it. To be able to build up projects that are useful, with a group of diverse people, is fulfilling," said Professor Cowin.



"We've been able to take it from the laboratory, with incredible materials and stem cell scientists, right through to clinical trials. To show over 65% improvement in healing of diabetic foot ulcers in 12 weeks and 80% by 24 weeks is absolutely amazing."

Next steps

Professor Cowin's main drive is to take the humanised antibody therapy to phase I/II clinical trials in patients with EB.

"We are also testing the biomarker in blood samples collected from diabetic patients with different levels of wound risk to confirm predictability and reliability. And we're developing a cell-free secretome gel for the treatment of EB, which will be easy to use and provide tailored medication to promote healing responses," said Professor Cowin.

While the prospect of improving diagnostic tools and treatments is a driving force behind her work, Professor Cowin is cognisant that research requires collaboration and community. She is continuing her efforts to support the Australasian wound and tissue repair society she began to foster a vibrant research community with career opportunities.

REMOTE REHABILITATION PROGRAMS PROVE EXCELLENT OPTION FOR PEOPLE WITH CHRONIC RESPIRATORY PROBLEMS

Professor Anne Holland and Associate Professor Narelle Cox

Institution: Monash University
Grant: Project Grant
Funding: $719,745
Year: 2016–2020
Team members: Professor Christine McDonald, Professor Ajay Mahal, Professor Jennifer Alison, Dr Angela Burge, Ms Janet Bondarenko and Associate Professor Paul O'Halloran.

Learn how dedicated physiotherapists, Professor Anne Holland and Associate Professor Narelle Cox's innovative remote rehabilitation program is transforming lives for those with chronic respiratory conditions. Their groundbreaking work offers accessible, effective care from the comfort of home.

Astoundingly, 1 in 3 Australians live with a chronic respiratory condition.[8] Chronic obstructive pulmonary disease (COPD)—a group of lung conditions that includes emphysema, chronic bronchitis and chronic asthma—accounts for half of the total burden for respiratory disease. Regular exercise is a key contributor to wellbeing and staying out of hospital but access to supported exercise programs ('pulmonary rehabilitation') is a critical problem nationally and globally. Only around 5% of Australians who would benefit have ever accessed a program.

By combining digital technologies, the power of community support and access to a best-practice exercise program from home, Professor Anne Holland and Associate Professor Narelle Cox from Monash University have demonstrated a remote rehabilitation model that is both cost and clinically effective. The trial, known as REACH, is now referenced in global guidelines for treating people with COPD.

REACH ran in metropolitan and rural locations in Victoria, with some participants located more than 400km from the supervising physiotherapist. The team delivered exercise equipment, including bikes, to people's doors and participants met online with clinicians for group exercise sessions using simple technology.

"For the very disabled population—who are often very breathless, often from low socioeconomic circumstances—the burden of getting to rehabilitation programs is too much. This REACH trial is our most technologically advanced remote model," said Professor Holland.

More than 8 out of 10 people completed the program, higher than in-centre options. People completing the program had significantly lower healthcare costs in the 12 months following the program.

According to Associate Professor Cox, the flexibility and convenience from saving time and money and the social connection motivated participants.

"I learned a lot about sheep farming, as our regional trial site was in western Victoria. And so did our city patients who talked about it a lot," laughed Dr Cox.

"But seriously, a lot of the patients said being part of a group was great. They got to know others experiencing the same challenges, and they were inspired by others exercising in the same way that they were trying to." she said.

Professor Holland and Associate Professor Cox have dedicated their careers to achieving better outcomes for people with COPD, driven by the frustration of seeing unrealised potential for change.

"People with lung disease get a pretty raw deal. They not only have to deal with a debilitating condition and very distressing breathlessness, but they also have to deal with substantial stigma from society and a lack of services, said Professor Holland.

"One of the big highlights for me is that there were people in the trial that had knocked back rehabilitation many, many times over," said Associate Professor Cox.

Their innovative approach has not only proven effective but has also paved the way for a new standard of care. Almost half of the pulmonary rehabilitation programs around Australia are delivering services remotely, representing a huge shift in practice.

Next steps

The next step is to drive more widespread clinical implementation of remotely delivered models of pulmonary rehabilitation. Professor Holland and Associate Professor Cox are working with collaborators internationally to define the characteristics of patients most likely to succeed with telerehabilitation and working with clinicians and patients to develop resources to support implementation in practice.

They are also investigating less equipment-intense models of rehabilitation and new methods to accurately assess exercise capacity remotely.

"That is the missing piece of the puzzle that would enable a pulmonary rehabilitation program (assessment and intervention) to be delivered remotely, irrespective of patient location," said Professor Holland.

BETTER TREATMENT AND HEALING FROM POSTTRAUMATIC STRESS DISORDER

Professor David Forbes and Associate Professor Lisa Dell

Institution: University of Melbourne
Grant: Partnership Project
Funding: $749,156 (with co-contribution of $523,264 from partners - Departments of Veterans Affairs and Department of Defence)
Year: 2015–2021
Team members: Dr Alyssa Sbisa, Professor Meaghan O'Donnell, Professor Peter Tuerk, Professor Andrew Forbes, Professor Malcolm Battersby and Professor Richard Bryant.

Professor David Forbes has dedicated his career to helping people heal from trauma and, with Associate Professor Lisa Dell in his team from the University of Melbourne and their project collaborators, they are paving the way to improve the lives of Australians with PTSD.

"I've observed what it means to be burdened with chronic PTSD, its impact on the person's life and the lives of their loved ones. It has been an honour to be at the cutting edge of research that has the potential to be such a game changer."

In a world-first partnership project, researchers have demonstrated exceptional clinical results for a shorter, more accessible gold standard treatment for posttraumatic stress disorder (PTSD). Researchers from Phoenix Australia at the Department of Psychiatry, University of Melbourne collaborated with the Departments of Defence and Veterans' Affairs to conduct a national randomised control trial in mental health treatment services. The trial showed significantly better completion rates (with non-completion down to 5% from 30%), faster recovery and outcomes equivalent to the best evidenced, lengthier PTSD treatment. These outcomes pave a way to improve the lives and wellbeing of people with PTSD across Australia.

For Professor David Forbes, helping people heal from impacts of trauma has been a career-long pursuit.

"For most of my life I've been aware of the impacts of trauma in society. Combining this with my personal family history during WWII influenced my direction into clinical psychology and PTSD," said Professor Forbes.

"I've observed what it means to be burdened with chronic PTSD, its impact on the person's life and the lives of their loved ones. It has been an honour to be at the cutting edge of research that has the potential to be such a game changer," he said.

PTSD is the second most common mental disorder in Australia with over 1.5 million Australians experiencing it in the past 12 months.[9] For military and veteran personnel, the rates are higher. PTSD is associated with significant distress, elevated risks of suicidality, long-term disability, impaired relationships, lost productivity and high healthcare costs.

For Associate Professor Lisa Dell, also with Phoenix Australia, seeing people chronically impacted for decades inspired her research.

"As researchers we have a responsibility to keep investigating innovative ways to deliver evidence-based care to support people in their recovery from PTSD. We need to keep finding options and opportunities, even for those who are chronically unwell," said Associate Professor Dell.

Both researchers are clear about their motivations: To package 'gold standard care' in a more accessible way to maximise uptake and achieve outcomes for people with PTSD, their families and society.

"It's been extremely important for us to deliver best practice treatments into real world clinical contexts, transforming service delivery and enhancing recovery. This protocol for best care for individuals with PTSD in a shorter timeframe has now been tested in a large national randomised control trial, in real life military and veteran treatment services. So, we know it works," said Professor Forbes.

The low dropout rates, very strong individual results and over 60 trained clinicians that can hit the ground running delivering the treatment, are key achievements from this research partnership.

Next steps

"We will now explore the potential to apply and evaluate this treatment for people with PTSD following exposures to other trauma types, such as physical injury, traumatic childbirth or violence. We are keen to work with other government agencies and community services to give more choice to the populations they support," said Professor Forbes.

Professor Forbes, Associate Professor Dell and Dr Alyssa Sbisa will explore biopsychosocial predictors of who benefits most from different forms of treatment. This will help guide patient clinician collaborative decision making in selecting the most suitable intervention.

They plan to continue collaborating with other partners in this research, including Flinders University, University of NSW, Monash University and the University of Virginia (USA).

ADVANCED CARDIOVASCULAR DISEASE RISK TESTS ON THE HORIZON

Professor Eric Moses and Professor Peter Meikle

Institution: University of Tasmania and the Baker Heart & Diabetes Institute
Grant: Project Grant
Funding: $2,281,268
Year: 2016–2022
Team members: Dr John Blangero, Associate Professor Phillip Melton, Dr Joseph Hung, Dr John Beilby, Dr Gemma Cadby, Professor Gerald Watts, Professor Marie-Pierre Dubé and Professor Frank Van Bockxmeer.

Some genes we inherit from our parents are linked to diseases. Explore how Professors Eric Moses and Peter Meikle are using the Busselton Health Study to uncover genetic risk factors for cardiovascular disease.

"We wanted to understand the relationship between metabolism and disease, so we combined lipidomics , genomics, statistics and clinical data and generated novel insights with incredible potential for practical applications."

To harness opportunities for better health from genetic information, scientists need access to large family datasets. In this innovative project, researchers from University of Tasmania and the Baker Heart & Diabetes Institute capitalised on the iconic and long running (50 years) Busselton Health Study (BHS) to explore risks of cardiovascular disease (CVD). The BHS includes over 4,500 people in the Shire of Busselton, Western Australia, creating one of the largest unique data resources for pivotal biochemistry and genetics studies.

The risk of developing CVD is about half due to genetic factors and half due to other external factors. But there are missing risk factors which drove the underlying research questions for Professors Eric Moses and Professor Peter Meikle.

“We wanted to understand the relationship between metabolism and disease, so we combined lipidomics[10], genomics, statistics and clinical data and generated novel insights with incredible potential for practical applications,” said Professor Eric Moses.

The lipidome provides a window into the environmental influence on metabolism and risk of CVD. The researchers analysed over 600 lipids tied to DNA sequences of over 4,500 people from the BHS. They honed lipidomic risk scores using 250 relevant lipids for predictive modelling.

“We’ve moved well beyond using basic HDL and LDL cholesterol measures and are at the stage of translating that into a new clinical test. We plan to trial it in the next few years,” said Professor Meikle.

The goal is more effective risk-based testing of specific lipidomic risk factors and preventing cardiovascular events, ultimately improving treatment strategies for individuals at risk.

The team has produced a web portal for researchers worldwide to access the datasets, achieved high-profile publications and received many requests to collaborate.

“While we’ve brought some computers to their knees with the amount of computational load and the development of new algorithms, this research has demonstrated what’s possible when you bring lipidomics and genomics together,” chuckled Professor Moses.

Importantly, the professors actively engaged with the Busselton community and believe that the sense of ownership among participants is important.

“The Busselton board, community and the Heart Foundation are thrilled with what we’ve found,” said Professor Meikle.

“This research has been an incredible enabler to drive the combination of multiple datasets and create new tests,” said Professor Moses.

“I’ve always wanted to make a difference in human health, and I thank my mother, who was a nurse, for that inspiration. We’re grateful to the families for sharing their health data with scientists like us.” he said.

Next steps

A new NHMRC grant will help Professors Moses and Meikle explore the options to develop a new tool for predicting CVD risk in women who’ve had preeclampsia. Preeclampsia, a pregnancy disorder, has been shown to be a risk factor for CVD in women.

The researchers are also using some of the same data from this project with other datasets to explore Alzheimer’s disease and autism.

GLOBAL COLLABORATIVE TRIALS LEAD TO BETTER OUTCOMES FOR YOUNG WOMEN WITH BREAST CANCER

Professor Prudence Francis

Institution: Peter MacCallum Cancer Centre/University of Melbourne
Grant: Project Grant
Funding: $753,045
Year: 2016–2022
Team members: Professor John Forbes, Professor Alan Coates, Professor Frances Boyle and Associate Professor Nicholas Wilcken.

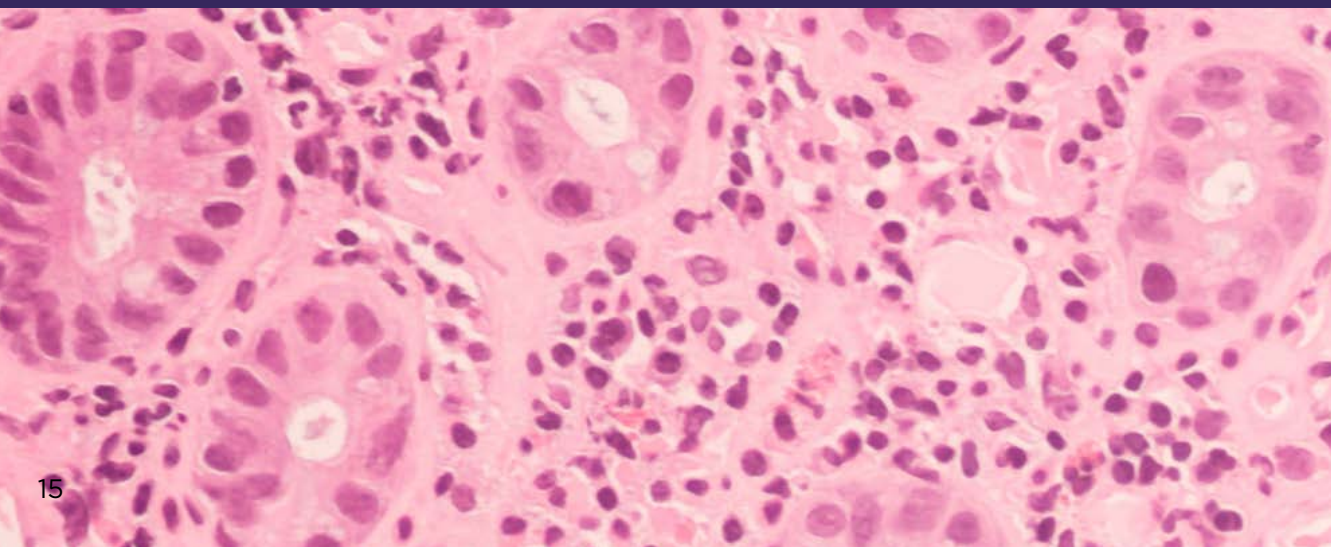
Professor Prudence Francis's dedication to young women with breast cancer is transforming treatment and saving lives. Her global trials of hormone therapy are a game changer in the fight against high-risk breast cancer.

Witnessing heartbreaking experiences of young women with breast cancer drove Professor Prudence Francis to lead the world's biggest trials of hormone treatment options. The global collaboration has demonstrated the value of ovarian suppression treatment, particularly in very young women with high-risk breast cancer. This treatment regime—now being applied in clinics—reduces cancer recurrence and saves lives.

"To see that you can actually impact survival in young women, that is what it's all about," said Professor Francis, a prominent oncologist with the Peter MacCallum Cancer Centre and St Vincent's Hospital Melbourne.

Breast cancer is more common in older women; however, in Australia every day approximately 3 women under 40 years old are diagnosed. Women with oestrogen-sensitive breast cancer diagnosed under 35 have a worse prognosis than older premenopausal women aged 35–50[11].

For decades it was unclear whether stopping oestrogen production from the ovaries was beneficial when added to other drug treatments



“Patients are often grateful for the chance to be on a trial, despite knowing they may randomly get the new or the standard treatment. Patients drive our learning and help us design research in a way that's meaningful for patients as well as for doctors. They’re focused on leaving a legacy for their daughters’ generation and beyond.”

for breast cancer in young women. Researchers set out to determine whether temporarily inducing a postmenopausal state in premenopausal women could also allow for the use of more effective hormone therapies, such as aromatase inhibitors, which deliver better results than traditional treatment. The completion of the SOFT and TEXT[12] premenopausal randomised adjuvant breast cancer trials represent the culmination of over 2 decades of Professor Francis’s tireless dedication to better cancer treatment for young women.

“I sent the first email to statistical colleagues in Boston in 1999 with the kernel of the idea. From there we’ve brought on numerous breast cancer groups and hundreds of institutions internationally and recruited almost 6,000 young women. At the time, global collaboration between groups was rare,” said Professor Francis.

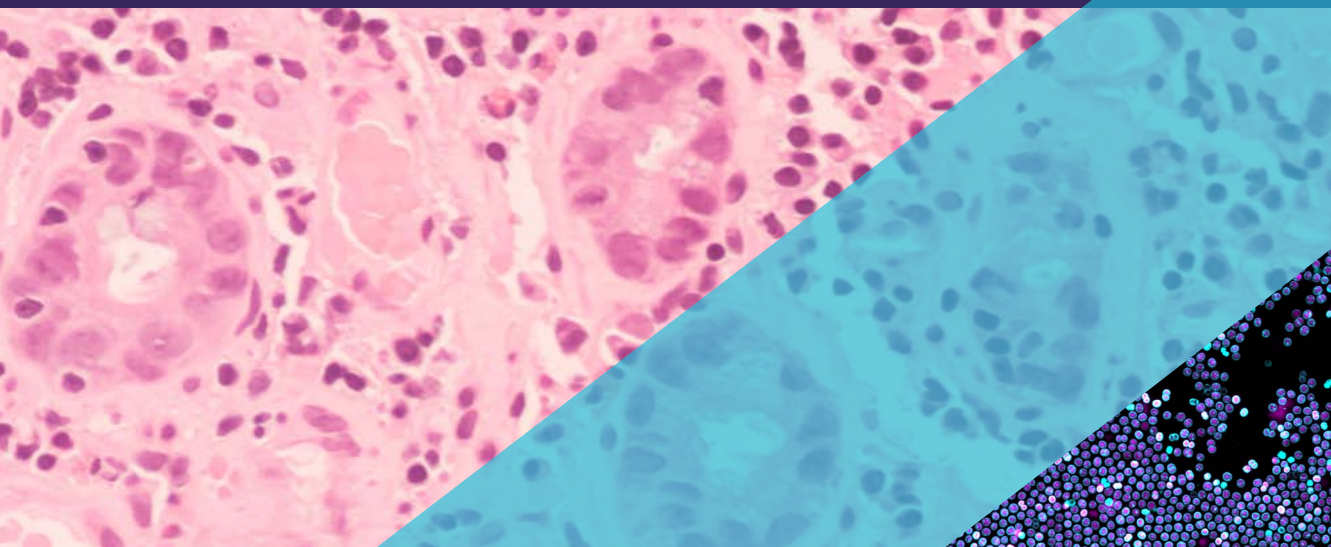
Professor Francis says that the sense of camaraderie is one reason she stayed in cancer medicine after junior doctor rotations. The other reason is the patients and consumer advocacy groups who continue to inspire her.

“Patients are often grateful for the chance to be on a trial, despite knowing they may randomly get the new or the standard treatment. Patients drive our learning and help us design research in a way that's meaningful for patients as well as for doctors. They’re focused on leaving a legacy for their daughters’ generation and beyond.”

The work has led to advancing clinical practices and transforming how clinicians advise patients, moving away from a one-size-fits-all approach to more personalised treatment strategies. The research has achieved global impact. It’s published in the New England Journal of Medicine and is inspiring changes to treatment guidelines around the world.

Next steps

Professor Francis and her colleagues are planning a further and final analysis of the long-term breast cancer outcomes and survival from the SOFT and TEXT trials in 2025. Tumour samples from patients enrolled in these clinical trials are being studied to better understand the reasons for worse outcomes in very young women. Results will provide the impetus for new trial designs with the goal of trying to optimise their future care and outcomes. Future trial sub studies will assess additional aspects such as fertility after such breast cancer treatments.



CULTURE INTRINSIC TO HEALTH FOR ABORIGINAL AND TORRES STRAIT ISLANDER PEOPLE

Professor Raymond Lovett
Institution: Australian National University
Grant: Project Grant
Funding: $2,004,365
Year: 2017–2021

Cultural factors critical to the health and wellbeing of Aboriginal and Torres Strait Islander adults have been assessed in the largest cohort study ever, conducted by Professor Raymond Lovett, yielding a new resource for health practitioners, policymakers and Indigenous communities.

The Mayi Kuwayu study, supported by an NHMRC Project Grant, drew 13,000 participants from across Australia. It explored the relationship between cultural engagement, identity formation, and health and wellbeing outcomes. The project enabled Professor Lovett and his team, from the Australian National University, to develop a suite of culturally relevant measures—a combination of existing, adapted and novel measures.

"Social determinants of health sit within a cultural context. We essentially asked Aboriginal and Torres Strait Islander people: 'What is important to your wellbeing?'" said Professor Lovett.

"Prior to this work, there were no measures for kinship systems, language and connection to country and cultural engagement. Using a salutogenic or strengths-based approach, we identified cultural and other assets that promote wellbeing. We also developed measures linked to health, like exposure to racism," said Professor Lovett.

The team analysed psychological distress levels (using the Kessler scale) of Indigenous people compared to the general Australian population. They found that rates of very high psychological distress are double for people that are exposed to any form of racism or discrimination and that racism exposure contributed to 50% of the gap in high psychological distress.

"We now know from this research that if we remove racism from the health inequity equation, half of that gap or disparity in high to very high distress will disappear. Aboriginal and Torres Strait Islander people know it's crucial to health and wellbeing. This large cohort study shines a light on the value of addressing discrimination and racism, in all its forms, to create equitable health," said Professor Lovett.

While the public health landscape is very focused on health behaviours, such as tobacco and alcohol use, according to Professor Lovett, not recognising and addressing the root causes of stress response activation (such as discrimination and racism) is unhelpful and in itself, discriminatory.

"Smoking and alcohol, for example, are major contributors to cardiovascular disease and cancer, the 2 biggest contributors to Aboriginal and Torres Strait Islander mortality.[13] If we work on things that reduce or eliminate stress response and activation, or support those salutogenic health promoting behaviours, then long term, there will be life improvements," said Professor Lovett.

Professor Lovett is a sought-after expert internationally, having worked with researchers from New Zealand, USA, Canada and Mexico in recent years. He is grateful for the enthusiasm and support from others and is committed to supporting the next generations.

"I've been so lucky to be mentored by very senior Indigenous researchers from other institutions and countries. And it's been a privilege to be able to 'pay it forward' by bringing on additional students, thanks to this project and the funding from NHMRC," he said.

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Next steps

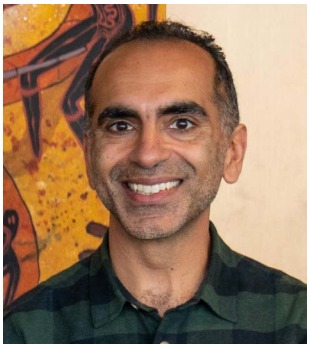
Results from the Mayi Kuwayu study are being used to train local Indigenous communities to collect and process their own data. This grassroots approach fosters ownership and relevance in health research. Professor Lovett plans to turn this project into a sustainable cohort study that spans 50 years or longer, allowing for comprehensive tracking of health outcomes and the impact of interventions over time.

Professor Lovett's team will soon be recruiting for new participants and following up past participants who have been involved since 2018. He will also be exploring digital infrastructure options to better support data collection and participant engagement.

"Having an ethical, community-focused and Indigenous-controlled resource that will contribute to a holistic and robust understanding of Aboriginal and Torres Strait Islander culture, health and wellbeing is critical. A long-term commitment is needed to drive meaningful change in life expectancy and overall health," said Professor Lovett.

TEASING OUT FACT FROM FICTION IN GLOBAL GUIDELINES FOR IRON SUPPLEMENTS IN CHILDREN

Professor Sant-Rayn Pasricha and Professor Beverley-Ann Biggs



Institution: University of Melbourne and WEHI

Grant: Project Grant
Funding: $2,893,139
Year: 2016–2022

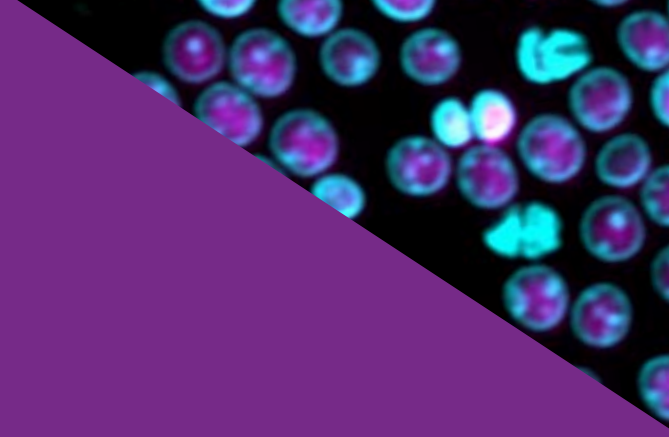
Team: Dr Jena Hamadani, Md Imrul Hasan, Associate Professor Sabine Braat and Dr Leila Larson.

Discover how Professors Sant-Rayn Pasricha and Beverley-Ann Biggs's extensive research on iron supplementation is reshaping global health recommendations. Their work offers new insights into child development and anaemia treatment.

Nearly half of the world's young children are anaemic, having low haemoglobin levels in their blood. This is often caused by a lack of iron in their diets. Anaemia may influence the burden of disease in children, particularly as it correlates with impaired cognitive development. But there have been questions about whether addressing anaemia through iron supplements improves child developmental outcomes.

Researchers from the University of Melbourne and WEHI have now determined that while iron supplements produce sustained improvements in blood levels of iron and iron stores, they do not improve developmental, behavioural or child growth outcomes in the immediate or medium term. This brings into the spotlight global recommendations for iron supplements and related aid programs to improve anaemia.

The team, led by Professor Sant-Rayn Pasricha and Professor Beverley-Ann Biggs, delivered the largest randomised controlled trial ever conducted into the effects of iron supplementation on child growth and development. Working with the International Center for Diarrheal Disease Research, Bangladesh, they studied 3,300 Bangladeshi children, visiting each child more than 20 times over the course of the research. This equated to more than 60,000 visits in villages across rural Bangladesh.



"Australian children also experience iron deficiency and anaemia, and these results help Australian agencies make better decisions about investing in aid programs that have tangible health outcomes, leading to a happier, more secure Asia-Pacific region."

"This study was so complex! And that's why I think it hasn't been done before. But it has given us a very high resolution understanding of the effects of iron interventions on child growth, child development and wellbeing," explained Professor Pasricha.

"We are so grateful to the 60 staff who helped with the study, including the trained psychologists who undertook almost 10,000 painstaking, hour long developmental tests," he said.

Completing the large study in Bangladesh, the most densely populated country in the world, provided cost benefits for Australian research and aid decisions, collaboration opportunities, and provided results that are globally relevant, explained Professor Pasricha.

"Australian children also experience iron deficiency and anaemia, and these results help Australian agencies make better decisions about investing in aid programs that have tangible health outcomes, leading to a happier, more secure Asia-Pacific region," he said.

This pivotal work is the result of an almost 20-year collaboration between Professor Pasricha, a haematologist, and Professor Biggs, an infectious disease doctor.

"As a junior doctor I was interested in haematology and global health. I approached Beverley and she took me under her wing and trained me in how to start thinking about anaemia, nutrition and hookworm," said Professor Pasricha.

"While we knew that iron supplementation reduces anaemia, this research funded by NHMRC has filled critical knowledge gaps in global health. It's been a career highlight to do this work," he said.

Next steps

Using DNA samples from the children, the researchers aim to explore the interactions between genetics, nutrition, and environmental factors. The researchers will also follow up with the children from the study until they are 6 years old to assess any long-term impacts from the original trial.

"We are also exploring if the long-standing association between anaemia and child development is causal or whether it's been observed because of confounding from other factors."

CONTACT WITH YOUTH JUSTICE SYSTEM STANDOUT MARKER FOR RISK OF PREMATURE DEATH AND POOR HEALTH

Professor Stuart Kinner

Institution: Curtin University and Murdoch Children's Research Institute
Grant: Project Grant
Funding: $620,704
Year: 2016–2020
Team members: Professor Rohan Borschmann, Professor Alan Clough, Professor Susan Sawyer, Professor Matthew Spittal, Professor Adrian Miller, Professor Yvonne Cadet-James, Dr Jesse Young and Dr Lucas Calais-Ferreira.

Discover how Professor Stuart Kinner's world-first study on the health of justice-involved young people is uncovering critical insights into the risks and causes of premature death among vulnerable young Australians.

A world-first study has documented the rates, causes, and risk factors for death among young Australians after contact with the youth justice system. The project linked youth justice, corrections, and death records for over 48,000 young people who had contact with the youth justice system in Queensland from 1994 to 2017.

"Adults released from prison die at an unacceptably high rate, but until now we've known remarkably little about what happens to young people after contact with the youth justice system," said Professor Stuart Kinner, who leads the Justice Health Group at Curtin University and Murdoch Children's Research Institute.

The study looked at 3 groups of young people who had been: in detention; under supervision in the community; or charged by the police with a crime but never convicted. Professor Kinner and colleagues observed a 'dose-response' relationship between the extent and duration of criminal justice system contact, and mortality rate. The rate of death was greatest for young people who had experienced detention.

"We found that the rate of death after youth detention was more than 6 times higher than among their age and sex matched community peers, with most deaths due to suicide— over one third—injury, overdose, or violence," said Professor Kinner, who has worked for decades with governments in Australia and with UN agencies to explore health issues in the criminal justice system.

"Importantly, our study does not suggest that contact with the youth justice system caused these deaths. Criminal justice systems tend to 'select' people from the community who have complex health needs, who are already at increased risk of premature death. Unfortunately, we don't do nearly enough to reduce this mortality risk.

"Therefore, although preventing youth detention is important, this alone will not prevent these tragic deaths. These young people need our help and support, both during and, critically, after contact with the criminal justice system," he warns.

Over his career, Professor Kinner has spent a lot of time in prisons in Australia and overseas. The portrayal of prison environments as scary or dangerous does not match with what he has witnessed, describing prisons as "often tragically banal".

"Prisons are, in important ways, like hospitals: expensive, taxpayer-funded institutions that some of the most marginalised and unwell members of our community pass through. If people discharged from our hospitals were dying at more than 6 times the rate of their community peers, we would be very concerned," said Professor Kinner.

Collaborating with government and community stakeholders has been a cornerstone of Professor

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Kinner's career and he emphasises the importance of transparency in research, even when the findings are difficult to digest.

"Despite the fact that our findings can be disturbing, organisations we've worked with have always supported publication," said Professor Kinner.

"Partnerships like this take time to develop and are based on mutual trust and respect," he said.

Next steps

"These vulnerable young people face an unacceptable risk of premature death and we need to 'open the black box' between youth justice system contact and death, to inform targeted prevention," said Professor Kinner.

Thanks to additional NHMRC funding, work is underway with the Australian Institute of Health and Welfare to develop a system for routinely monitoring the health of justice involved young people, using linked administrative data.

"Reliable data on the health of these young people is needed to drive investments in care—What gets counted gets done."

"Indigenous Australians are over-represented in prisons by a factor of 13, and in youth detention by a factor of 28. These appalling statistics must change. Our research is helping to identify the problems. We must listen to Indigenous communities to identify solutions." said Professor Kinner.

ENDNOTES

1. Protein Kinase AMP-Activated Non-Catalytic Subunit Gamma 2 (PRKAG2) control nutrient kinase regulated autophagy during stress

2. In the brain, autophagy is a cell pathway that ensures neuronal health by removing old proteins and damaged cell parts

3. Australian Institute of Health and Welfare, *Cancer data in Australia*, https://www.aihw.gov.au/reports/cancer/cancer-data-in-australia/contents/summary

4. Interferon regulatory factor 4 (IRF4) gene encodes the interferon regulatory factor 4 protein, which is a key transcription factor in the human immune system

5. Mouse double minute 2 homolog (MDM2) is a protein coding oncogene that is often overexposed in human cancers

6. Norman, R.E., Gibb, M., Dyer, A., Prentice, J., Yelland, S., Cheng, Q., Lazzarini, P.A., Carville, K., Innes-Walker, K., Finlayson, K., Edwards, H., Burn, E. and Graves, N. (2016), *Improved wound management at lower cost: a sensible goal for Australia*. Int Wound J, 13: 303-316. https://doi.org/10.1111/iwj.12538

7. Carls GS, Gibson TB, Driver VR, Wrobel JS, Garoufalis MG, Defrancis RR, et al. *The economic value of specialized lower-extremity medical care by podiatric physicians in the treatment of diabetic foot ulcers*. J Am Podiatr Med Assoc. 2011;101(2):93-115. DOI: 10.7547/1010093

8. Australian Institute of Health and Welfare, *Chronic obstructive pulmonary disease (COPD)* [website], https://www.aihw.gov.au/reports/chronic-respiratory-conditions/chronic-respiratory-conditions/contents/summary

9. Australian Bureau of Statistics (2020-2022), *National Study of Mental Health and Wellbeing*, ABS (2023)

10. Lipidomics is the study of structure and function of the complete set of lipids, the lipidome, in a given cell or organism as well as interactions with other cellular components

11. National Breast Cancer Foundation. Breast Cancer in Young Women [website], Breast Cancer In Young Women to: Breast Cancer in Young Women (Symptoms & Risks) | NBCF

12. Suppression of Ovarian Function Trial (SOFT) and Tamoxifen and Exemestane Trial (TEXT)

13. Australian Government Institute of Health and Welfare National Indigenous Australians Agency, 1.23 Leading causes of mortality [website], https://www.indigenoushpf.gov.au/measures/*1-23-leading-causes-of-mortality*

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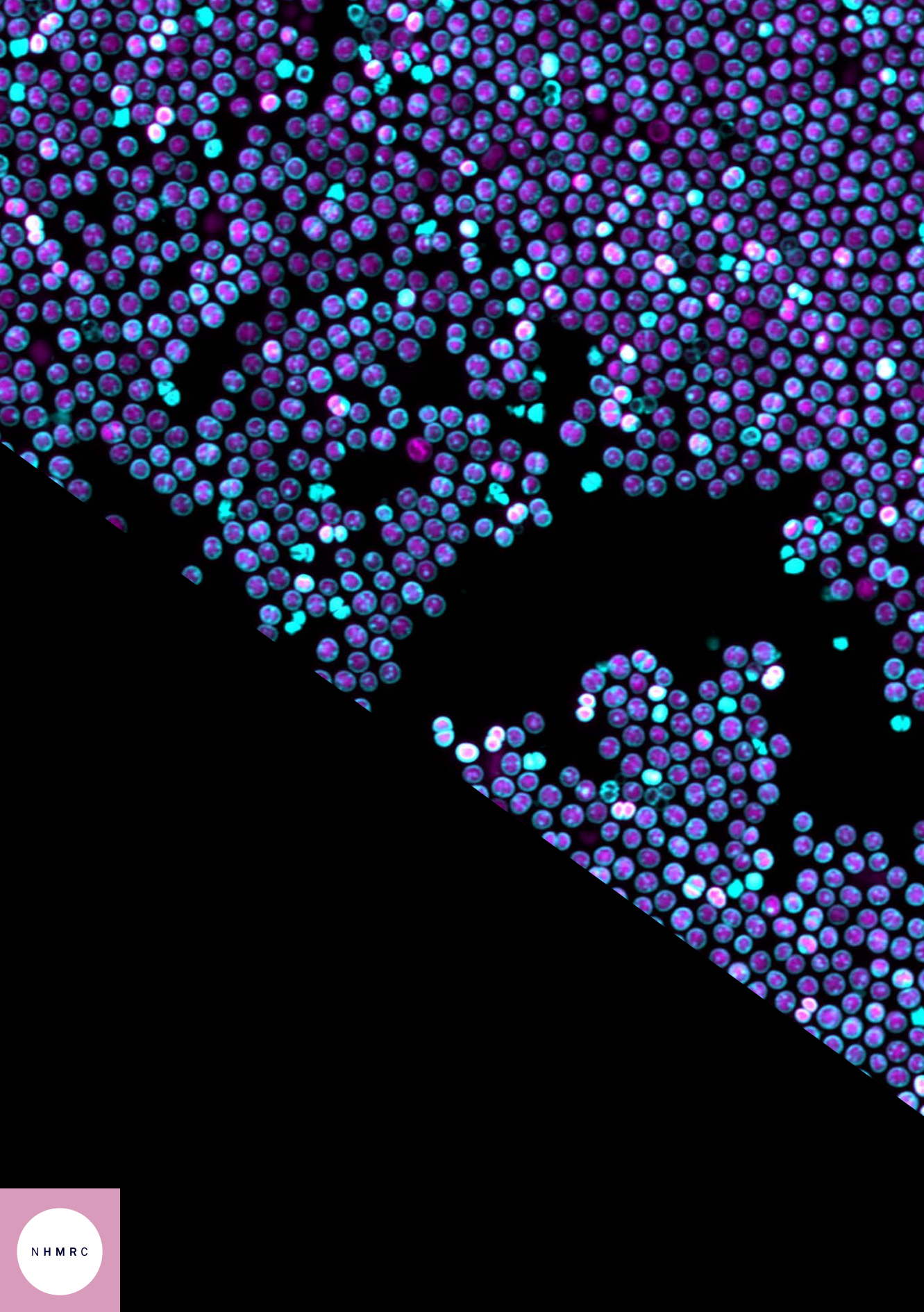

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