## SPRE

RESEARCH AUSTRALIA SHOWCASES HEALTH & MEDICAL RESEARCH

#### COLLABORATION

**And the Bionic Eye** 

**Bioelectronics** 

The future of medicine is electric

GAUGING PUBLIC HEALTH BIT BY BIT

TOO MUCH OF A GOOD THING:

**Excess brain iron**and parkinsons

**PLUS:** 

45 and Up: Shedding light on the health of the Boomer Generation

The Fast Track: New drugs starving cancer cells

RESEARCH AUSTRALIA



#### Message from CEO

Welcome to the fourth edition of INSPIRE and the first one for 2017, providing you with latest research findings and discoveries amongst your peers. The Health and Medical Research sector hits the ground running at the start of each year with funding season well under way. Good luck to those of you who are working your way through the grant processes for your amazing ideas.

I was reminded after reading this edition of INSPIRE, the importance of collaboration and the role of the consumer or patient in our complex world of HMR. There is little doubt that we are far more effective when we work as a broad community sharing opportunity. This was highlighted in the article Gauging Public Health bit by bit (pg. 12). University of Canberra researchers delve into data driven results by consumers who joined the ACTive Community Project. So, we have an active community, voluntarily contributing their data, taking part in a collaborative research opportunity, while accessing credible information about their health and getting fitter along the way. The value of data and digital health is a powerful topic and Research Australia is focusing on how our sector and consumers can harness the transformative power of data to manage, not only our fitness, but our health too.

Data and community engagement continues in this INSPIRE edition. The 45 and Up Study (pg. 24), continues to answer key questions of healthy ageing with the help of more than 265,000 NSW residents. This study is managed by the Sax Institute in collaboration with major partners, Cancer Council NSW and The National Heart Foundation of Australia (NSW Division).

And the work coming out of the Western Australia Health Translation Network (pg. 32) again uses community engagement with researchers to guide research priorities along with policy in practice.

As the national advocacy body, the breadth of our membership is again evident, with contributors across the sector including Universities, Health and Medical Research Institutes, Health Corporates and Health Services.

There is no doubt our sector issues are abundant as are the opportunities. We look forward to a sustainably funded, innovative and healthy 2017 with you.

Nadia Levin CEO & Managing Director

#### Publisher Research Australia Ltd

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#### Who can submit articles?

Any current member of Research Australia who would like to share a relevant story that affects their organisation including, philanthropic donations and their outcomes, research findings, and any other related health and medical research topic that affects the Australian population.

#### Submission guidelines & deadlines For information regarding how to

submit and publishing deadlines visit the Research Australia

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## RESEARCH AUSTRALIA PUBLIC POLLING REPORT 2017

Every year Research Australia carries out a public opinion poll to gauge the strength of community support for health and medical research. This poll has enabled us to chart the attitudes of Australians toward the sector and the related issues surrounding this very important part of our quality of life.

#### WHAT IS ONE THING YOU'D LIKE ANSWERED?

Click here to lodge your question.\*

Benchmarking results due out in September 2017

#### **HOW WE MEASURED UP IN 2016**

87%

of Australians support the Medical Research Future Fund

91%

are willing for their data to be used for research purposes

1/3

Just over one third of Australians reported having a device for tracking their fitness.

#### RESEARCH AUSTRALIA

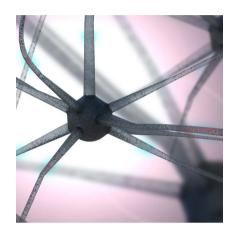
CONNECTING - ENGAGING - INFLUENCING

\* Public Polling survey 2017 questions are developed and designed at the discretion of Research Australia.

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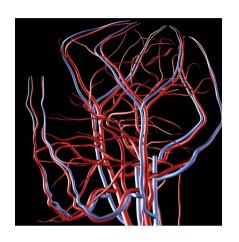
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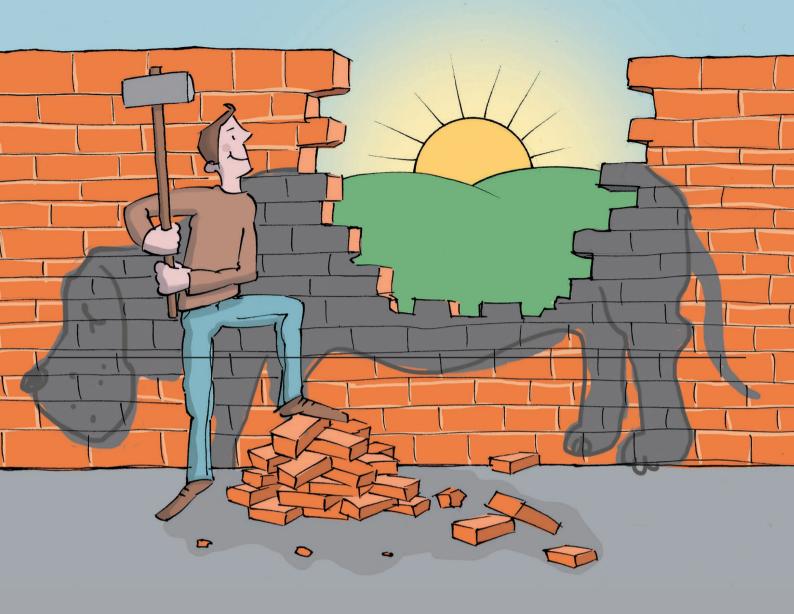
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#### **USING TECHNOLOGY TO PREVENT**



Australia has seen a 20% increase in the number of suicides in the last decade with approximately 71,600 Australians attempting suicide each year. In response to this growing health crisis, the Black Dog Institute has made suicide prevention a priority research area. Using technology and innovative approaches, the Black Dog Institute is acting now.







Using technology to prevent suicide #suicideprevention #depression #letstalk s a translational research institute, Black Dog is a world leader in putting research to practice. Black Dog's suicide prevention research team are working on a range of innovative projects to overcome the obstacles inherent to help seeking. Accessible and anonymous, technology has been found to play a key role in help seeking.

Improving aftercare and early intervention are part of Black Dog's areas of focus. RAFT (Reconnecting AFTer a Suicide Attempt) and iBobbly, the first suicide prevention app designed for Indigenous Australian youth, are two examples of the pioneering work being done at Black Dog.

Research has shown that the first few days following release from hospital, for someone who has attempted suicide or deliberate self-harm, are critical. Despite this, one-third of people discharged after such an attempt will receive no mental health follow-up. RAFT hopes to change this.

"RAFT is looking at a way of providing some follow-up care through text messaging, with links to online support, in the period after discharge," says Dr Mark Larsen, Early Career Fellow from the Society for Mental Health Research. "People have done some previous work in using things like postcards and follow-up letters, but we're using text messaging as a more technology-based solution," he explains.

Brief contact with recently discharged patients, such as postcards, letters and phone calls, has been found to reduce suicide re-attempts by up to 50%. This is the first time research is being done into the effectiveness of digital technology though.

#### USING TECHNOLOGY TO BREAK THE BARRIERS AND TO HELP SEEKING

"We feel technology has the potential to be more accepted and accessible, particularly to a younger population," says Dr Larsen. Text messaging has the added benefit of providing easy access to further resources. "We've also got links in the text messages to additional online support and resources, so we're expanding the scope of what can be delivered in just postcards."

RAFT is currently being assessed at the Royal Prince Alfred Hospital in Sydney, where people coming into the emergency department following a self-harm or suicide attempt are being offered the follow-up text messaging service. There will soon also be pilot sites in Toowoomba and Brisbane.

The iBobbly team's work also holds a critical space in suicide prevention. Currently, the suicide risk of Indigenous Australian youth (aged 15 to 34) is almost four times that of their non-Indigenous counterparts.

While the trial is still ongoing, after using iBobbly for six weeks, the 61 participants from Western Australia's Kimberly region experienced a 42% reduction in depression symptoms. They also reported a 28% reduction in psychological distress and a 30% reduction in thoughts of suicide.

"The suicide ideation result was not statistically significant, but it is promising that suicide ideation was reduced," says Joe Tighe, Black Dog researcher. Tighe explains that the main goal of the initial trial was to gauge if the app would be relevant. "We didn't know if Indigenous youth would engage

#### World Health Day APRIL 7, 2017

#### **DEPRESSION: Let's Talk**

THE GLOBAL HEALTH AWARENESS
INITIATIVE, CELEBRATED ON APRIL 7,
AIMS TO REDUCE STIGMA BY LETTING
PEOPLE AROUND THE WORLD KNOW
THAT TALKING ABOUT MENTAL ILLNESS IS
VITAL TO PREVENTION AND RECOVERY.

With increasing depression, anxiety and suicide rates, it is more important than ever to share personal experiences and knowledge. #WHD

with or like it. With version 2.0, the goal is to reduce suicidal thinking. Now we need to know with this larger trial that will include hundreds of people." Detailed research findings are available at BMJ Open.

Studies have shown geographic isolation is a barrier to Indigenous help seeking. iBobbly tries to combat this and, once downloaded, does not require internet connectivity so that users can access the resources at all times.

#### IT'S SIMILAR TO A VIDEO GAME

After incorporating community feedback and requests for more in-depth information, a wider trial of iBobbly version 2.0 is being undertaken across Australia. "Some people that really engaged with it wanted it to contain more, many more activities and many more exercises," says Tighe, comparing the new version to a video game with multiple levels. "So pretty much like gaming, we provided layers and layers of content, for people to go as deep as they wanted to go."

Collaboration with Indigenous partners informed the development of the app and the available resources, including the decision to include gender-specific audio resources. "Local community partnership was crucial to us successfully running the trial," says Tighe.

With wide community support for the pilot, and a drop-out rate of only 3%, the next version of iBobbly could have an even greater reach.

- \* Dr Mark Larsen, PhD, Early Career Fellow from the Society for Mental Health Research and the Black Dog Institute.
- \* Joe Tighe, PhD research student at UNSW Australia and the Black Dog Institute.





round breaking Australian research suggests that developing brains may 'break' along predictable 'fault lines', sparking research into the role that vitamin D plays in the development of psychiatric disorders.

Vitamin D deficiency has long been linked to bone health and a number of other diseases, such as multiple sclerosis, diabetes, heart disease, and various types of cancer. However, new research has found that vitamin D is also critical for normal brain development.

Researchers at the Queensland Centre for Mental Health Research (QCMHR) and Queensland Brain Institute have discovered that the absence of vitamin D – the hormone involved in normal bone growth and maintenance – during development and early life increases the likelihood of developing serious psychiatric conditions, such as schizophrenia and autism.

#### IMPORTANCE OF RESEARCH INTO EARLY BRAIN DEVELOPMENT

Professor Darryl Eyles and the Developmental Neurobiology research team at QCMHR have developed the technology to assess vitamin D levels in stored paediatric dried blood spots of patients and generated models to assess how the absence of vitamin D during early brain development may affect later brain function.

"We have developed analytical techniques that have allowed us to show that a maternal and/or early life absence of vitamin D during brain development increases the incidence of serious psychiatric conditions," Professor Eyles said.



The absence of vitamin D during brain development increases the incidence of serious psychiatric conditions

"Our latest research indicates that this could be due to the fact that early life vitamin D deficiency may be selectively targeting developing dopamine systems.

"This finding is particularly important as abnormalities in dopamine signalling are present prior to symptom onset and represent a major therapeutic target in the treatment of schizophrenia."

According to Professor Eyles, this research also suggests that the brain may 'break' along predictable fault lines.

"Just as dopamine systems are considered vulnerable during aging in diseases such as Parkinson's disease, they may also be vulnerable to multiple adverse events during pregnancy."

#### **DEVELOPMENTAL VITAMIN D DEFICIENCY**

While work will continue on establishing vitamin D as an important developmental neurosteroid, Professor Eyles said the realisation that developmental vitamin D deficiency – together with other models of psychiatric disorders – preferentially targets developing dopamine systems has allowing researchers to tap into a much bigger story.



"Our research suggests that abnormalities in these systems represent a common pathway in the development of many different psychiatric disorders".

Having recently received more than \$1 million in funding from the National Health and Medical Research Council, Professor Eyles and his research team will be furthering their research with two new projects.

The first project will focus on the team's previous success in treating pregnant mice subjected to an immune challenge with a hormonally active form of vitamin D. The team have shown such treatment to have completely abolished schizophrenia-like phenotypes in offspring. They hope to gain an understanding of how this occurred, and to replicate the results using a form of vitamin D that would be safe to use in humans.

The second project aims to directly replicate dopamine abnormalities in schizophrenia in a new model. This model replicates increased dopamine uptake and synthesis restricted to one part of the brain: the dorsal striatum.

This study is based on findings by collaborators at the Imperial College London, which have shown that dopamine changes exist in patients prior to symptom onset. The team at QCMHR will attempt to block such changes in adolescence with a variety of pharmacological agents. Any success could lead to future clinical trials.

It is our hope that such knowledge may allow us to understand how schizophrenia develops, leading us to treatments that either prevent or delay the onset of schizophrenia



>> Pictured above Professor Darryl Eyles

Queensland Centre for Mental Health Research Duncan McLean PhD Assistant Director, QCMHR

## COLLABORATION OF RESEARCH DISCIPLINES AND THE BIONIC EYE

ultidisciplinary research teams are essential to the development of new technologies and improving patients' quality of life, and the bionic eye is a great example.

Dianne Ashworth had been profoundly blind for many years before receiving a revolutionary medical device implant – the bionic eye. Born with normal vision, she gradually lost the ability to see in early adulthood.

Dianne suffers from *retinitis pigmentosa*, an inherited eye disorder that causes damage to and loss of photoreceptor cells in the retina, leading to degeneration of sight. She was the first patient in Bionic Vision Australia's (BVA) bionic eye study to receive a prototype implant and benefit from the groundbreaking technology.

"I recall vividly the day when Dianne's implant was 'switched on', several days after the implantation of the device. We had a lot of confidence from our pre-clinical studies that she would be able to perceive visual sensations, but it was still an enormous relief and very exciting to hear her describe visual sensations that she perceived in that first testing session," says Prof Anthony Burkitt, who leads the research team behind the bionic eye's development.



I didn't know what to expect, but all of a sudden, I could see a little flash...it was amazing. Every time there was stimulation there was a different shape that appeared in front of my eye," Ms Ashworth said.

The bionic eye is designed to restore a sense of vision to people who are blind due to a degenerative retinal condition. The device includes a retinal implant and digital camera, which is fixed to a pair of glasses worn by the patient. The camera captures and processes visual information, sending the data to the patient's implant. The implant then stimulates cells in the retina, which produces a sense of 'vision' for the patient.

The bionic eye – and Dianne's ability to perceive the world again – is a clear example of how experts from a diverse

range of research fields can unite to advance technological development and improve patients' quality of life. In this case, biomedical engineers, electrical engineers, surgeons and clinicians contributed their unique expertise to the common objective of restoring vision to patients with degenerative disease.

Prof Burkitt's team applied a broad set of criteria and involved researchers with diverse skillsets to meet the challenge of evaluating the safety and efficacy of the bionic eye prototype.

"We needed to consider the visual benefits received by the patient, long-term safety, ease of surgical implantation, stability of electrode placement and robustness of everyday use," says Prof Burkitt.

"Electrical engineers working together with neuroscientists helped determine what level of electrical stimulation is safe over long periods of time and biomedical researchers working closely with eye surgeons found a way to implant the device without damaging the surrounding tissue. A multidisciplinary approach has been absolutely essential to the success of the project," says Prof Burkitt.

#### ALIGNING MULTIDISCIPLINARY RESEARCH TEAM WITH A COLLABORATIVE CULTURE

While the benefits of a multidisciplinary research team are enormous, Prof Burkitt advises that a collaborative culture is essential to its success and must be embedded in the team from day one. It cannot be limited to formal meetings and discussion, but instead must be actively developed through side-by-side work in the lab and clinic.



It takes time to understand the language used by researchers from other disciplines and appreciate their approach to research, the techniques they use and outcomes they anticipate.

"The development of a true multidisciplinary approach is one that comes about through constant interaction with researchers from other disciplines, discussion of the research challenges, and then agreeing on how to best meet these challenges in a way that addresses all the requirements of the eventual outcome.'

A true multidisciplinary approach is one that comes about through constant interaction with researchers from other disciplines, discussion of the research challenges, and then agreeing on how to best meet these challenges.

While the current generation of vision prostheses, only provide patients with a coarse-grained view of the world and are primarily used to aid navigation around objects, Prof Burkitt believes that the technology will greatly improve in the coming years.

1

Camera captures

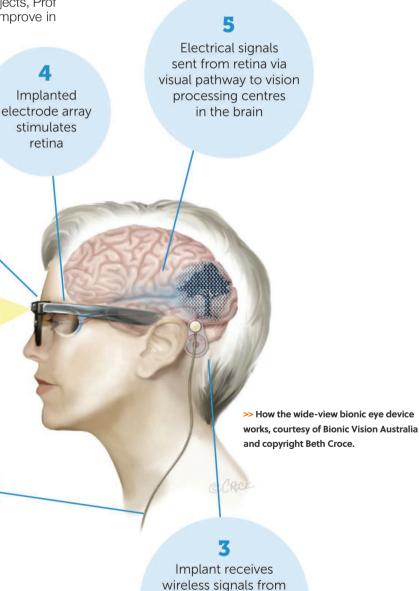
image and transmits

data to an external body word processing unit

"We can anticipate that patients may gradually be able to carry out more complex visual tasks, such as recognising faces and reading large print. This will continue to add to their quality of life, both through their ability to live more independently and to interact socially."

With the advantages of multidisciplinary research and the trend toward greater collaboration, the bionic eye may one day be as widespread and effective for blind patients as the cochlear implant has become for deaf patients.

Prof Anthony Burkitt, Director, Bionic Vision Australia, the University of Melbourne, will present, The Bionic Eye: restoring sight with vision prostheses at AusMedtech 2017 & the International Conference on Mechanics in Medicine and Biology (ICMMB) 2017.



external unit and sends them to retinal implant via implanted wire







Data processed and sent to implanted system via external wire

Collaboration of research disciplines and the Bionic Eye #medical #seeingagain #restoringsight



undreds of Canberra locals are strapping on their activity trackers and shedding new light on the health of the nation's capital, their data is providing insights into everything from health risk management to public health and urban design.

The most detailed picture of Canberra's fitness is being generated at the University of Canberra though a collaborative project harnessing the big data generated by hundreds of activity trackers.

#### THE WHAT

Launched in October 2016, the ACTive Community Project is the first ACT-wide study involving users of activity trackers, which are devices worn on the body to record movement, physical activity, heart rate and even sleep cycles.

#### **THE WHO**

This collaborative project between the University's Health Research Institute (UC-HRI) and CSIRO's Data61 is looking at the large amounts of deidentified data generated by each participant's device, including time and length of activity and location data (where possible).

#### THE DATA

The data – normally only accessible to the user, the creators of the device and operators of any linked apps – is being used by the researchers to create a detailed representation of health and wellbeing in Canberra.

Professor of Public Health and Director of UC-HRI Rachel Davey said that by collating and analysing the big datasets gathered in the study, they aim to uncover new details about activity levels in Canberra suburbs.

"What we are seeing is that people are more likely to engage in opportunistic exercise where their local community is well-designed for it," Professor Davey, project leader, said.



>>Pictured L-R: University of Canberra Professor Rachel Davey, Paul Samways of Data61 and UC participant Kunal Rajput



"Local parks, the proximity of shops, bike paths and walking trails, all contribute to people getting active daily.

"We hope that good examples of city planning and development, coupled with the data we're gathering, will encourage better urban design in future, something that could be adopted around the world."

More than 800 people have joined the project with over 300,000 hours of data collected so far. The project was funded by the Canberra CBR Innovation Development Fund for 12 months to establish an open data sharing commons where people could share their aggregated data.

University of Canberra Associate Professor of IT, Mathematics and Statistics Girija Chetty said preliminary analysis of the data shows that males are just slightly more active than women across all age groups, and on average they reach the widely-held goal of 10,000 steps per day, while women tend to reach between one and ten percent below that target.

Dr Chetty said the data shows varying activity levels across the 50 suburbs with registered participants, who use either FitBit™ or Garmin™ devices.

"The most active suburbs appear to be in well-established areas and we're seeing the daily average number of steps above 12,000," she said.

"The picture of Canberra's activity and health is evolving and each day we're adding more information to our datasets; as new participants sign on we're going to have more and more clarity and detail."

#### THE OUTCOMES

The researchers have designed health report cards based on the data provided by participants which are being used to offer important feedback to users.

Professor Davey explained: "We want the participants to get a better understanding of the good they are doing for themselves, so we've created a simple report card to give them a snapshot of their health.

"When they voluntarily provide information about their weight, their alcohol intake and smoking status we factor that into these report cards. It's the kind of details that people can then take to their general practitioner, to sit down and discuss their overall health and risk factors."

"The research team also hopes that the project helps to drive a competitive spirit across Canberra's suburbs, with participants able to gauge the activity level of their own suburb compared to those around them. These basic comparisons pose a challenge either individually or collectively to improve our activity levels and fitness across the city."

## BRAIN AGEING AND COGNITIVE (f) in brain aging and cognitive decline #brain #cognitive #whitematterhealth #research

hen researchers at The University of Newcastle's (UON) Functional Neuroimaging Laboratory (FNL) set out to investigate the effect of blood flow on brain functionality, they noticed some intriguing patterns in their data. Their research indicates that cardiovascular health can also impact brain health – and the cognitive decline we can experience as we get older.

It's long been assumed that decreasing cognitive capacity is merely a symptom of old age. However, new research indicates that we may be able to change our behaviour to decrease the effect of ageing on the health of our brains.

"While we know ageing produces cognitive decline, there must be a physiological mechanism by which we can explain this pattern," says group leader Associate Professor Frini Karayanidis.

"We found that those people who have cardiovascular risk factors have more evidence of brain health decline, cognitive decline and white matter decline than those without.



It isn't age – it's your brain.

#### RELATIONSHIP BETWEEN BLOOD FLOW, COGNITIVE CHANGES AND WHITE MATTER HEALTH

In a series of studies researchers were looking to explore the relationship between blood flow, cognitive changes and white matter health.

"Initially we set out to examine the link between white matter hyperintensities – a sort of neural scar tissue – and their link to cardiovascular health," explains researcher Patrick Cooper. "But the scars weren't as clearly linked to cognitive decline as we had thought. It turns out that it is the health of the white matter that the scars were embedded within that is playing more of a role, and that itself is influenced by cardiovascular risk factors."

Participants in the study, which is published in the Human Brain Mapping journal, underwent an MRI brain scan and were tested for their ability to perform in a task-switching activity. They were also assessed for a sub-set of cardiovascular risk factors - hypertension, high blood cholesterol, arterial fibrillation, diabetes and smoking and obesity status.



The data showed that mental task-switching capacity decreases with age.

Interestingly though, when the researchers controlled for cardiovascular risk factors, the effect of age on cognitive capacity disappeared.

"It is surprising - but not unexpected," explains Cooper. "It has previously been shown that cardiovascular health does influence cognition - our series of studies have demonstrated that it's these vascular changes which affect white matter and that this has an effect on cognition. So I think it's not unexpected but it is surprising that we were able to show it in such a small sample with a really elegant set of results."

Associate Professor Karayanidis and her team used diffusion MRI to look closely at the health of the white matter tracts.

"If you look at a structural MRI image you can see the white matter hyperintensities – but diffusion MRI allowed us to see not the structure of the brain, but the movement of water molecules.



>>Pictured above Researchers at the University of Newcastle's Functional Imaging Laboratory.

"Based on that, we could define the directions in which the molecules will move, and that informed us about the health of the tracts – including the integrity of the myelin."



The good news is that while declining cardiovascular health is associated with ageing, some cardiovascular risks are modifiable – so taking care of your body means taking care of your mind, too.

"It's not age per se, but how healthy your brain is," emphasises Karayanidis. "It's a positive message."

The research group is now looking to investigate a clinical population – patients who have had a *transient ischemic attack*.

"It's kind of like a mini-stroke. These people have an increased cardiovascular burden, so we want to see what happens as they recover," says Cooper. "We're trying to see if this cardiovascular idea holds true in a group that has more prolific health problems."

#### WHAT'S NEXT?

With these findings, Karayanidis is particularly excited at the prospect of her team's research becoming more translational.

"We want to start looking at whether those who are taking care of their risk factors – if they're taking their medications and so forth – still see declines in their white matter health.

"That has implications for collaborations with pharmaceutical companies, and also opportunities for the development of interventional strategies. We really want to improve people's outcomes."

These studies conducted by the FNL team were done so with support from the Australian Research Council (ARC) and the Hunter Medical Research Institute (HMRI).

- \* Associate Professor Frini Karayanidis is group leader of the FNL in the School of Psychology at UON.

  \* Dr Todd Jolly is currently studying for his Bachelor of
- \* Dr Todd Jolly is currently studying for his Bachelor of Medicine at UON.
- \* Mr Patrick Cooper is a PhD student in the School of Psychology at UON.



### SURPRISE SCURVY CASES SUGGEST

### NUTRIENT DEFICIENCIES

spate of patients suffering from wounds that refused to heal has led a clinician-researcher at a major Sydney hospital to the surprising discovery of scurvy amongst contemporary Australians.

A historical disease caused by a lack of vitamin C and generally associated with old-world sailors on long voyages, it appears that scurvy is reappearing due to poor modern dietary habits.

Professor Jenny Gunton, who heads the Centre for Diabetes, Obesity and Endocrinology research at The Westmead Institute, said several of her patients at Westmead Hospital with long-running unhealed wounds were cured by a simple course of vitamin C.

"When I asked about their diet, one person was eating little or no fresh fruit and vegetables, but the rest ate fair amounts of vegetables; they were simply over-cooking them, which destroys the vitamin C," said Professor Gunton.

The irony, she says, is that it is possible for patients to be suffering scurvy, even when they are overweight or obese. "It highlights a danger that you can consume plenty of calories yet not receive enough nutrients."

A research paper by Professor Gunton, just published in the international journal Diabetic Medicine, concludes that some diabetes patients should be tested for vitamin C deficiency.

"While diabetes is not traditionally a risk factor for vitamin C deficiency, the research suggests that clinicians should have a high index of suspicion," said Professor Gunton, "particularly if their patients present with unhealed ulcers, easy bruising or gum bleeding without obvious cause."

A lack of vitamin C in the body results in defected formation of collagen and connective tissues, the results of which may include bruising, bleeding gums, petechiae (blood spots in the skin), arthralgia (joint pain) and impaired wound healing.

Common foods which are high in vitamin C include oranges, strawberries, red and green peppers including capsicums, broccoli, kiwi fruit and grapefruit. But overcooking any food is likely to destroy the vitamin C.

Her paper reported that there was no predominant social pattern to the incidence of scurvy and that patients with poor diets were observed to be from a range of socioeconomic backgrounds.

"This result suggests that despite the plethora of dietary advice readily available to consumers, there are still plenty of people – from all walks of life – who are not getting the messages."

Human bodies cannot synthesise vitamin C, so we must eat foods containing it.

Professor Jenny Gunton, who heads the Centre for Diabetes, Obesity and Endocrinology research at The Westmead Institute.







Surprise scurvy cases suggest nutrient deficiencies #medicalresearch #nutrition #diabetes



#### TOP TIPS FOR REVISING

#### JOURNAL ARTICLES

s we come up for air after another busy grant submission and fellowship applications season, we can now revisit our journal articles that have been sitting with red marks all over it. To assist you get through the feedback process, here are some practical tips for revising your journal articles.

- I. Take a deep breath. No-one likes to have their precious writing critiqued, and it can be very easy to feel defensive and annoyed. But remember a condition of academic writing is that we expose ourselves to critique. We must learn to accept this and realise how the review process can help us.
- 2. Feel gratitude for the work performed on your behalf by the reviewers and editors. Although you may not like some of their feedback, nearly all (and yes, there are some nasty exceptions) have reviewed your work in the spirit of academic generosity and have taken precious time from their own work to do this. If they have performed the review constructively, they deserve your thanks and appreciation.
- See the revision process as a way to make your work the best it can be, and a challenge to push yourself to improve it.
- If the editor has given you a decision of 'revise and resubmit', always attempt this, however extensive the work required of you. There is a very good chance that if you revise your article competently it will be accepted.
- If the editor has rejected your article, acknowledge your inevitable feelings of disappointment and frustration (or even murderous rage!) but then move on. Think about where else you can resubmit it. Consider first the comments made by the reviewers and decide whether you should address some of these before submitting elsewhere to enhance your chances of success next time around.
- Bite the bullet. Try not to leave the revisions or submission to another journal too long it can be easy to keep putting this job off, but it must be done!
- 7 If the article has been written with other authors, decide who will take leadership on the revisions. This should usually be the person who led the writing of the original manuscript. The lead author should take on as much of the revision work as they can, and then share the revised version with the other author/s for their contributions and feedback.

- 8 Block out a good chunk of time in which you will be able to begin work on the revisions. Choose a time of day if possible at which you know you will be feeling the most mentally alert. There is no denying that you have a demanding task ahead of you.
- 9. Don't rush things. Take as much time as you need to complete it properly.
- Now that you are mentally prepared ... go back and read your submitted manuscript. You will most likely have forgotten most of what you wrote and this is a good chance to read it with fresh eyes.
- Then go back to the email from the journal editors with the reviewers' comments. Copy and paste the reviewers' comments in to a new Word document. Then go through and isolate each comment which suggests or requests a revision. Then read each comment carefully.
- I2. Start to go through your original manuscript and begin addressing those points you think require revisions. It is often easiest to address the minor revisions first. In your 'response to reviewers' document, write your responses under each separate point as you go. Your response should explain the changes you have made. If you disagree with a suggested change, you are entirely within your rights to state this and explain why.
- Highlight changes in your manuscript with bold or coloured highlighting so that the editor and reviewers can easily see where you added or significantly altered material. Don't use the track changes function (unless this has been specifically requested by the editor), as track changes can leave the manuscript looking very messy and difficult to read.
- Once you think you have conducted the revisions to the best of your ability, put the revised version aside for at least a day. Come back to it and read it through again. Read your 'response to reviewers' document again. Make any further changes you deem necessary.
- ${\bf I5}$ . Take another deep breath ... and resubmit your article. Good luck!







Top tips for revising journal articles #grantwriting #funding #research

## Why we should G E

alcohol to alcoholics









Why we should give alcohol to alcoholics #managedalcoholprogram #recovery

ome homeless people who are severely alcohol dependent drink well over 30 units a day (approximately 5 bottles of wine) placing a high burden on hospitals and police as well as subjecting themselves to assault on the street. Whilst abstinence is preferred, it is unrealistic for some drinkers. A novel approach is the Managed Alcohol Program (MAP) which provide a regulated amount of alcohol, housing and other support to these drinkers to stabilise their drinking. The philosophy is harm reduction; minimising adverse health and social consequences of drinking without requiring abstinence. MAPs reduce alcohol consumption, the burden on police and hospitals and improve drinkers' health.

In the UK in 2010, people complained about the anti-social behaviour of street drinkers. The police would pour out their alcohol and move them on, but this contributed to increased reports of begging as they needed more money to replace the alcohol. Street drinkers would appear before the court, which was costly. It was estimated that 500 police staff hours were spent dealing with one individual who was drinking on the street.

In Canada, harsh weather saw a number of homeless men die from exposure and a committee was established to address this issue.

Both countries trialled the idea of a Managed Alcohol Program. A MAP is usually a residential service, where workers dispense a regulated amount of alcohol - one unit - to clients every hour from 7.30am to 9.30pm, an average of 15 drinks a day. Staff members include mental health workers, social workers, in-house support workers, nurses and doctors. The aim is to stabilise residents' drinking who are then in a position to deal with other issues. Eligibility criteria include homelessness - or at risk of it - and struggling with long-term alcohol dependence. Most consumed 30 units of alcohol a day and were not interested or able to attain abstinence. They have a high frequency of visits to hospital and regular contact with the police.

#### THE RESPONSE

Manchester's the Heavy Drinkers' project has one core house with 15 outlying houses. The core house has 14 bedsits or one-bedroom flats with support workers who also dispense alcohol. Residents can graduate to outlying houses where they are expected to live independently, including monitoring their alcohol intake, with some support.

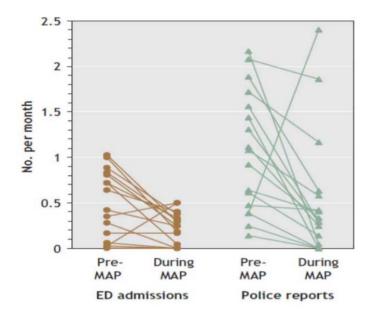
In Ottawa, the OAKS has 55 beds for alcohol dependents. Residents receive 12 units a day and can have beer, wine or Vodka which is recorded. Services include assisting clients to obtain Identification, free food, laundry facilities, toiletries, snacks, coffee, phone calls and computer access. They also monitor residents' liver function. At a MAP it can be the first visit to the doctor and dentist for many clients for some time. Several MAPs brew their own alcohol with residents assisting. The Oaks brew 810 gallons every 5 weeks for 55 people.

The overwhelming message from residents was that they had been given a chance to rejoin society, to be valued and were happy that someone still cared for them. Most had spent many years in a downward spiral where they had endured some pretty tough times. All had been subjected to violence while on the street, most had been rejected by their families and many felt a sense of failure from being heavily dependent on alcohol.

#### THE EVIDENCE

Experience suggests that it takes three to five years to see any improvement in a resident's brain function. One person had 15 visits to a hospital over a one-month period and many interactions with the police. After joining the MAP, the person has had no hospital visits and very few interactions with the police. In Ottawa, it was estimated that one MAP has saved \$2m in averted hospital costs. A study of 17 residents in a MAP found decreases after 16 months in the mean monthly visits to emergency departments (13.5 to 8, p=0.004) and in police encounters (18.1 to 8.8, p=0.018) (See graph below).

#### GRAPH NUMBER OF A & E AND POLICE CONTACTS PRE AND DURING THE MAP



#### NUMBER OF ED AND POLICE CONTACTS PRE AND DURING ATTENDING THE MAP

Some homeless people with a chronic alcohol dependency are trapped and unable to move out of their predicament. They need a comprehensive intervention to address mental health issues, alcohol and drug dependency issues, primary health care and their homelessness. Managed Alcohol Programs are a novel service for homeless with severe and intractable alcohol dependence and should be trialled in Sydney.

**About the author - Professor Kate Dolan** 2014 Churchill Fellow National Drug and Alcohol Research Centre, UNSW



he tooth fairy might have more to offer today's kids than just a gold-coin under the pillow. Dr Dominic Hare, from the Florey Institute of Neuroscience and Mental Health, hopes a bold research plan could see teeth being used to predict the future risk of developing Parkinson's disease, inform future dietary supplement policies, and lead to a therapy to stop Parkinson's disease in its tracks.

Around 1300 Australians are diagnosed with Parkinson's every year, and almost 15% of those are aged under 50. Parkinson's disease kills the cells in the brain that produce dopamine, primarily in a region of the midbrain called the *substantia nigra*. A major problem with current approaches to treating the disease is that within a year of someone being diagnosed with Parkinson's disease, more than half of the dopamine producing cells in the *substantia nigra* have died. By that point, any treatment is going to have its work cut out.

#### PREVENTION IS BETTER THAN CURE

Keeping the adage 'prevention is better than cure' in mind, biometal chemist Dr Hare recently embarked on a Master's in Medicine, specialising in public health. During his studies, he produced a chart showing that rates of Parkinson's have been steadily increasing in wealthy western nations such as Australia, the US, UK and Sweden. This was in marked contrast to Japan, where Parkinson's diagnoses per head of population have remained stable since the 1940s. Dr Hare says, "To be honest I never expected to see such a huge difference – it shocked me."

What could account for the dramatic difference? Diet was an obvious candidate, but it wasn't the food consumed by each of the different populations, rather, what had been added to it that Dr Hare suspected might be the culprit.

To prevent iron deficiency anaemia from poor diets, Western nations began fortifying staple foods like cereals and flour with iron in the 1930s, and fortified infant formula followed in the 1960s. Iron fortification was, and still is, a huge public health success story, but with sufficient dietary iron now available, iron fortification may be too much of a good thing.

Dr Hare says, "The brain especially isn't very good at getting rid of excess iron. If it gets a head start with too much iron and its 'warehouse' of iron 'spills over' as it gets older, there is a risk that the excess iron will damage brain cells."

"The idea that two chemicals that are essential for normal function could be harming the brain is a complex one. A healthy neuron does its best to keep these two reactive chemicals separated. In Parkinson's disease, it seems that this becomes too much for the cell to handle, and the mechanisms that keep them apart break down." If this is the case, it represents the fundamental chemical reaction that starts the process of a neuron dying.

#### IS EXCESS BRAIN IRON A MAJOR FACTOR?

To tease out whether excess brain iron is infact leading to higher rates of Parkinson's, Dr Hare recently published an ambitious four-point research plan in the *Nature partner journal*, on Parkinson's Disease.



The first step in the approximately \$10M plan involves examining whether 'growth lines' of iron deposits in baby teeth (much like a tree's growth rings) correlate with dietary iron. Dr Hare says "We can measure elemental distribution within baby teeth, mapping infant nutrition during childhood, from the transition between low iron breast feeding, to supplemental feeding with high iron formula, then on to solid foods with intermediate iron.'

Secondly, the team needs to confirm whether this is possible in adult teeth. Adult teeth begin to calcify at birth, and have completed the process by about age 10. This means they should also contain a record of childhood dietary iron exposure, which many people will carry right into their mid- and old age. These teeth will act as our personal 'iron passports', allowing researchers to establish the iron environment that the person has been exposed to throughout their life.

Thirdly, the team will recruit Parkinson's patients and agematched controls and use magnetic resonance brain scans to measure iron levels in their brains. Using data obtained from teeth removed in dental procedures, the team will correlate lifetime iron exposure with the risk of having Parkinson's disease. "We need to identify people at risk of Parkinson's, and a test that can detect early, excessive iron exposure may be a way of doing that," says Dr Hare.

#### WHAT NEXT?

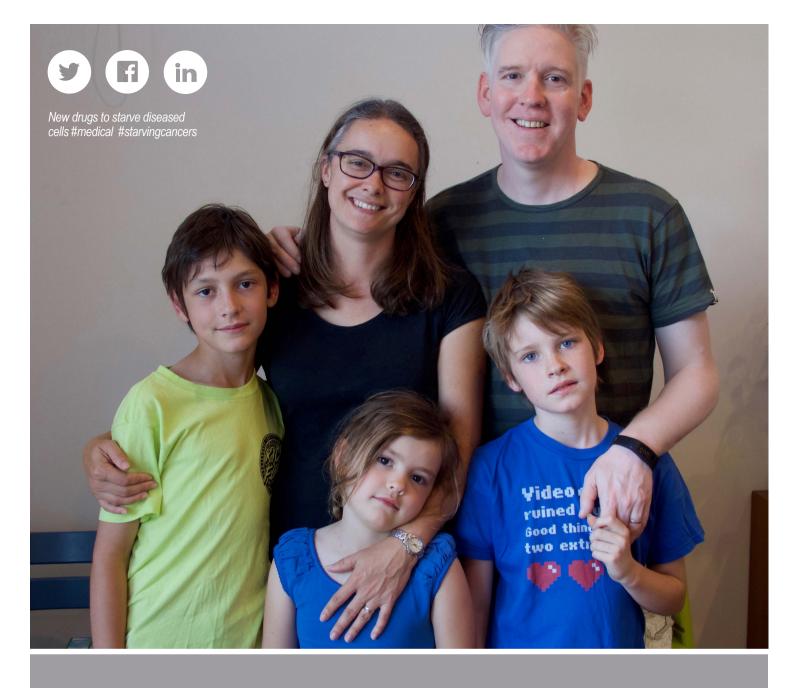
Finally, the group will recruit middle-aged people deemed to have varying risk levels for developing Parkinson's disease, then follow them for a period of years while giving them an experimental drug called deferiprone, a so-called 'iron chelator'.

Dr Hare thinks that *deferiprone* could be even more useful than just treating those diagnosed with Parkinson's disease. If someone with high brain iron can be identified early, the drug, which is thought to "mop up" excess brain iron, might even be able to stop the reaction between iron and dopamine before it can damage the cell. Although much work needs to be done, the goal of preventing Parkinson's disease might not only be better than a cure, it might just be a reality.

#### Dr Dominic Hare BSc (Hons), PhD (UTS), FRSC

Lab Head, Analytical Neurochemistry **Neurodegeneration Division of the Florey** Institute of Neuroscience and Mental Health

Dominic recieved a PhD in chemistry from the University of Technology Sydney in 2009, and has since dedicated his career to studying the biochemistry of metals in neurodegenerative diseases. Dominic joined the Florey in 2016, attracted by work being performed in the worldleading oxidation biology unit. His passion is bringing together multidisciplinary scientists to answer real world problems, recognising that discoveries are rarely made by one person alone. He has developed a wide network of collaborators to not only help paint a picture of metals in the brain throughout life, but also apply cutting-edge analytical technology to new and exciting avenues of disease research.



#### NEW DRUGS TO STARVE DISEASED CELLS

any difficult to treat cancers, including later stage melanoma, triple negative breast cancer, prostate cancer, endometrial cancer and brain cancers have relatively few therwapy options. The Centenary Institute's Origins of Cancer Program is undertaking research in how to starve these cancers, providing new hope

Rhys Thomas has a lot to live for. He is a loving husband and a father of three young children who adore him. But unlike most 38-year-olds, Rhys is facing the reality that he may not have much time left. After visiting the doctor with a seemingly minor complaint, Rhys discovered he had stage three melanoma and was given just three months to live.

"I was anxious, depressed and not sleeping. I lost 25 kilos and I couldn't keep any food down. I was ready to die, I prepared myself for that". He participated in a clinical trial which was his last hope. After a few months, the tumours began to shrink.



I thought I was still going to die but this was going to be drawn out for much longer. Then the symptoms started to improve, I was functioning, I gained weight and I realized death wasn't as imminent as I thought it was.

Three years later, Rhys is enjoying extra time with his family and is even going back to his job as an anaesthetist.

While the busy father is feeling well now, the long-term prognosis is not known – making this family's future terribly uncertain. Survival rates for many cancers have improved significantly over the past decade.

Of the 10 most commonly diagnosed cancers, the five-year survival is highest for prostate cancer, thyroid cancer and melanoma, (before it has metastasised). These encouraging improvements are largely due to the development of new therapies and diagnostic abilities. Later stage melanoma, triple negative breast cancer, prostate cancer, endometrial cancer and brain cancers are some of the most difficult-to-treat, still with relatively few therapy options currently available. The Centenary Institute's Origins of Cancer Program, led by Associate Professor Jeff Holst, continues to target these cancers with new research, which has led to some extremely exciting findings, potentially leading to game-changing drugs.

Researchers have discovered an important nutrient which is vital for helping specific cancer cells to grow and cultivate. It indicates that cells are unable to grow and change if the key nutrient pumps are blocked. "We now have three specific nutrient targets which we know are helping cancer cells to grow. If we are able to block the nutrient pumps which are feeding the cancer cells, we can essentially starve the cells and stop them from growing", states Associate Professor Jeff Holst.



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The team made these discoveries in collaboration with University of Sydney researchers Associate Professor Renae Ryan, Professor Paul Groundwater and Professor David Hibbs. These researchers have been able to identify drug compounds which inhibit these processes, using a combination of computer prediction and laboratory testing. This ground-breaking development brings us close to being able to offer a less invasive, safe option for patients such as Rhys, who are living with difficult—to-treat cancers.



>> Pictured above Associate Professor Jeff Holst (Head of the Origins of Cancer Program at the Centenary Institute) led the ground-breaking study

#### **METABLOQ PHARMACEUTICALS**

The new therapy will be developed by a newly-established privately held biotechnology company, *Metablog* Pharmaceuticals, which is focused on translating the results of Associate Prof. Holst's research into drugs for clinical trials.

Dr Melissa McBurnie, Chair of *Metabloq*, and an investment analyst with the Medical Research Commercialization Fund (MRCF) says, "We are very pleased to be working with the high calibre team at the Centenary Institute and the University of Sydney, to develop this entirely novel class of drugs for difficult-to-treat cancers. *Metabloq* are working aggressively to get these drugs to the point where they can be tested in patients". *Metabloq* Pharmaceuticals is funded by the MRCF and Uniseed, with additional investment from CSIRO. In kind support for the basic research was also provided through the Centenary Institute, University of Sydney and NSW Ministry of Health.

It is conceivable that the drugs produced by *Metabloq* could help patients such as Rhys, giving his small children more time with their father. Unfortunately, it is likely that he will eventually require additional treatment options; however, the production of new drugs – potentially available in the next 5 years - brings great hope for patients like Rhys, and thousands of Australians. For now, this young family is staying positive by seeing every day as a gift. "It really is the simple things, having coffee with my wife and reading to my kids."

By Jessica Bowditch, Media and Communications Manager, The Centenary Institute.





f you are overweight, can you offset the risk of diabetes by being active? How likely are the cigarettes going to kill you if you keep smoking? And can good access to GP services cut end-of-life healthcare costs?

These are some of the many complex questions being asked and answered thanks to the Sax Institute's 45 and Up Study, the largest ongoing study of healthy ageing in the Southern Hemisphere.

The Study is tracking the health of more than 265,000 NSW residents, one in ten men and women in NSW aged 45 and over, and is being used by hundreds of researchers and policy makers to help answer important health and quality-of-life questions, and help manage and prevent illness through improved knowledge of conditions such as cancer, heart disease, depression, obesity and diabetes.

Study scientific director Professor Emily Banks, said the Study data could now be linked to other datasets including 69 million Medicare records, 54 million pharmaceutical records, two million hospital separations and 24,000 death records.

"Having access to such a large-scale, longitudinal study reduces the need for researchers to reinvent the wheel and recruit new participants for every study," said Professor Banks, who also leads Epidemiology for Policy and Practice at the National Centre for Epidemiology and Population Health at Australian National University. "This enables significant time and cost savings and supports researchers in conducting high-quality work that can yield faster answers to important policy questions."

"It's an incredibly valuable research resource and the data is growing richer every year."

Over 650 researchers and policy makers have now drawn on the Study, with findings contributing to more than 200 papers published in peer-reviewed journals.

Professor Banks said findings published recently had given valuable insights into the health and health service use of older Australians, as well as busting a few myths. These included:

#### **BUSTING THE "FAT AND FIT" MYTH**

Being active is no protection against type 2 diabetes if you're also overweight, researchers from the University of Sydney's Prevention Research Collaboration revealed, after investigating levels of physical activity and sitting time in 29,572 Study participants.

Their findings, published in *Human Kinetics Journal*, showed that people who were obese but had high levels of physical activity and spent little time sitting still had five times the risk of developing type 2 diabetes compared to people who were of normal weight, and with low levels of physical activity and higher sitting levels.

#### SHEDDING LIGHT ON END-OF-LIFE HEALTHCARE COSTS

Greater use of GP services in the final years of life is not linked to lower hospital costs in the six-month end-of-life period, surprising research from the Study has shown.

The researchers, from the Centre for Big Data Research in Health at the University of New South Wales and the Centre for Health Research at Western Sydney University had hypothesised that high healthcare costs in the final six months of life might be contained by delivering better endof-life care through primary, community and palliative care services. However, they found that patients who used more GP services in the 7–18 months before death actually had higher total healthcare costs in the six month period before they died.

If GPs had a role in preventing hospitalisations at the endof-life, it was likely to be much earlier in patients' lives, they suggested in study published in *BMJ Open*.

#### POPULAR HEARTBURN DRUGS LINKED TO HOSPITALISATION

People who take the popular heartburn drugs, *proton pump inhibitors* (PPIs), have a 70 per cent increase in the risk of being admitted to hospital with infectious gastroenteritis, per research using the *45 and Up Study* that was led by researchers from Australian National University.

Lead author, Dr Yingxi Chen said the findings, published in the journal *PLOS ONE*, were based on cases of infectious gastroenteritis among 38,019 Study participants over a six-year period, and showed that the elderly and people with chronic bowel problems were at the highest risk of hospitalisation.

#### 1.8 MILLION AUSTRALIAN SMOKERS WILL DIE FROM THEIR HABIT

The Study was used to produce the first large-scale, direct evidence on smoking and mortality in Australia, that showed that up to two in three smokers – or 1.8 million of the 2.7 million smokers – would die from their habit if they continued to smoke.

Professor Banks, who led the study published in *BMC Medicine*, said the research highlighted the importance of staying the course on tobacco control. The findings had already proved influential: they were cited in new Tobacco Excise legislation and are being widely used by quit smoking organisations, she said.

The 45 and Up Study is managed by the Sax Institute in collaboration with major partner Cancer Council NSW; and partners: The National Heart Foundation of Australia (NSW Division); NSW Ministry of Health; NSW Government Family & Community Services – Ageing, Carers and the Disability Council NSW; and the Australian Red Cross Blood Service.

By Megan Howe, Publications Manger, Sax Institute.







Study answers key questions on the health of older Australians #45andupstudy #ageingpopulation #health #research



#### PROVIDING CONSUMERS AND COMMUNITY THE

#### OPPORTUNITY TO HAVE A

## VOICE

IN HEALTH RESEARCH

he value of consumer and community involvement in research is increasingly being recognised and embraced by funding bodies, research institutions and governments across the world with a wide range of initiatives being developed to support and facilitate partnerships between researchers and the community. There has been a steady increase in the uptake of meaningful consumer and community involvement across the Australian research arena over the past two decades.

The University of Western Australia's School of Population Health and the Telethon Kids Institute established a consumer and community involvement program in 1998 in response to community concerns about the development of linked data research being undertaken at that time. This program achieved national and international recognition as a good practice model for consumer and community involvement

in research. It is underpinned by the joint NHMRC and Consumers Health Forum's Statement on Consumer and Community Involvement (2016).

Three-year funding provided by WA's Lotterywest in 2016 enabled the establishment of the Western Australian Health Translation Network's, Consumer and Community Health Research Network (the Network). This exciting initiative, which is a first for Australia, will see the involvement program expand across WA universities, research institutes and tertiary health services.

The establishment of the Network has facilitated the development of a strategic framework to support consumer and community involvement across the partner organisations of the Western Australian Health Translation Network via a team of consumer advocates working initially in seven research organisations.



#### PROGRAM OF WORK

The consumer advocates, jointly funded by the Consumer and Community Health Research Network and the partner organisations supported by a team of staff within the Network, will deliver a comprehensive program of work and services that are supported by the following six core components:

#### **ADVOCACY AND ADVICE:**

A face-to face service provided to researchers, students, consumers and community members to support and advise on implementing involvement activities. A dedicated **website** houses a range of resources, publications, topical issues, training opportunities and events

#### AN EVIDENCE BASE:

Evidence for the impact and value of consumer and community involvement is key to the success of the Network. Audits of existing involvement activities will be undertaken in 2017 using a tool developed and implemented in 2010 and 2013 in collaboration with researchers and community members.

#### **CONSUMER AND COMMUNITY NETWORKS:**

A database of over 1000 consumers and community members, known as the *Involvement Network*, provides access to a diverse range of people interested in research. Opportunities for involvement in research are advertised through the Network's website and social media.

#### **GOVERNANCE:**

Community oversight is an integral aspect of the Consumer and Community Health Research Network. A range of strategic level committees and advisory groups has been established since 2006 to enhance the quality and relevance of research activities. Strong collaborations with national and state consumer peak bodies such as Consumers Health Forum and Health Consumers Council WA provide a further level of community oversight to the work of the Network.

#### **METHODS FOR INVOLVEMENT:**

Tried and tested methods for involving consumers and community members in research are available for researchers to implement involvement activities in their research. A 'one size does not fit all' philosophy means that any of these methods can be modified to suit a diverse range of projects. This resulted in 369 community members serving on 43 research and organisational committees in 2016.

#### **TEACHING AND TRAINING:**

Training is a core platform of the Network. Responding to requests from researchers and community members for training, a range of bespoke workshops are now available. Over 960 researchers, students, clinicians, administrators, consumers and community members from across Australia have attended 65 workshops on the 'how and why' of implementing consumer and community involvement in research. These workshops are one-of-a-kind in Australia and have been developed in collaboration with a UK consultant. An evaluation of the researcher workshops was published in 2016.

#### THE FUTURE

Our goal over the coming three years is to further expand the Network to offer our services across the Western Australian Health Translation Network. Funding, dedicated staff, engaged and involved consumers, community members and researchers supported by a comprehensive program of work will ensure the Network has the right 'mix' to continue delivering opportunities for consumers and community members to use their lived experiences to guide and influence research priorities, policy and practice components.









Providing consumers and community the opportunity to have a VOICE in health research #communityfunding



magine receiving treatment without swallowing a pill or having an injection. A treatment that instead works by implanting a miniaturised electronic device, smaller than a grain of rice, into your body. It sounds like science fiction, but research into bioelectronic medicine is happening now.

It's a new scientific field that has the potential to revolutionise the way chronic illness like asthma, arthritis, inflammatory bowel disease, hypertension and diabetes are treated.

These devices would be programmed to read and modify electrical signals that pass along nerves in the body, including irregular or altered impulses that occur in a broad range of diseases. The hope is that these devices could allow the treatment of these diseases with greater precision and fewer side effects than with conventional medicines.

Treatment of medical conditions with electrical impulses has been used in the past – from cardiac pacemakers to deep brain stimulation in parkinson's. However existing devices target large areas of tissue indiscriminately, rather than honing in on a specific group of neurons within circuits.

GSK believes that recent scientific advances have made it possible to control specific sets of neurons, which create the potential to develop more precise bioelectronic treatments. These treatments will regulate the neural impulses controlling the body, repair lost function and restore health.

They could, for example, coax insulin from cells to treat diabetes, regulate food intake to treat obesity and correct balances in smooth-muscle tone to treat hypertension and pulmonary diseases.

#### SO HOW WILL ALL THIS COME ABOUT?

This will need a truly cross functional industry approach with disease biologists working with neuroscientists to map circuits and with bioinformaticians to identify the action-potential signatures of diseases. To develop treatment devices, bioengineers designing biocompatible interfaces will need to collaborate with electrical engineers to develop microchips for real-time signal processing; with nanotechnologists to create energy sources; and with neurosurgeons to ensure that these designs can be implanted and connected. Researchers will need to embrace the languages and tools of other fields, and perhaps even dream differently: much of the challenge lies in translating biological understanding into engineering specifications.

Dr Daniel Chew, Head of Neural Interfacing Group at GSK is currently running an experiment in his Stevenage laboratory to implant miniaturised electrodes in order to drive low current through specific organs. "We're looking at stimulating very specific nerves in the neck to provide fine control to organs such as the heart and lungs— which could eventually translate to treatment for asthma sufferers for example."

If his work goes to plan, diabetics and people with a host of other diseases may one day no longer need to inject themselves or take pills.

They are not working alone. From the headquarters at Stevenage, GSK is funding and coordinating more than 30 research projects worldwide among academics and



institutions. "We're not only working on producing proof of principle - we want to create a landscape for development of bioelectronic medicine and we know we can't do it alone."

GSK's researchers are also developing cutting-edge materials combined with wireless technology on a miniature scale: the implants will be smaller than a grain of rice. "I like the idea of making obscure concepts a reality," says Chew. "I believe we will enable many people to have a better lifestyle."

So how soon does Chew expect this revolutionary treatment to be available? A severe arthritis sufferer has already benefited from similar treatment: an implant in the vagus nerve improved the pain and swelling they felt in their fingers and toes in a matter of weeks. "But we're talking early days with this," says Chew. It's never been done before. We'd like this to be available for human trial within five to 10 years."



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GSK doesn't believe they can succeed in this field alone, they recognise that experts across a range of disciplines need to work together. Unlike more traditional areas of science, bioelectronics requires the combined skills of world-leading physiologists, engineers, neuroscientists and informatics experts. That's why they are seeking to grow and integrate a research network that will become a new bioelectronics community.

The research currently being undertaken in bioelectronics is like learning a new language - the electrical language of the body. Through learning to read and write the electrical signals that travel between the brain and the body's organs, GSK believe they can open up a whole new frontier in treating disease. It may sound like science fiction, but they're edging closer to a future where precision electronic therapies sit alongside the medicines and vaccines used today.

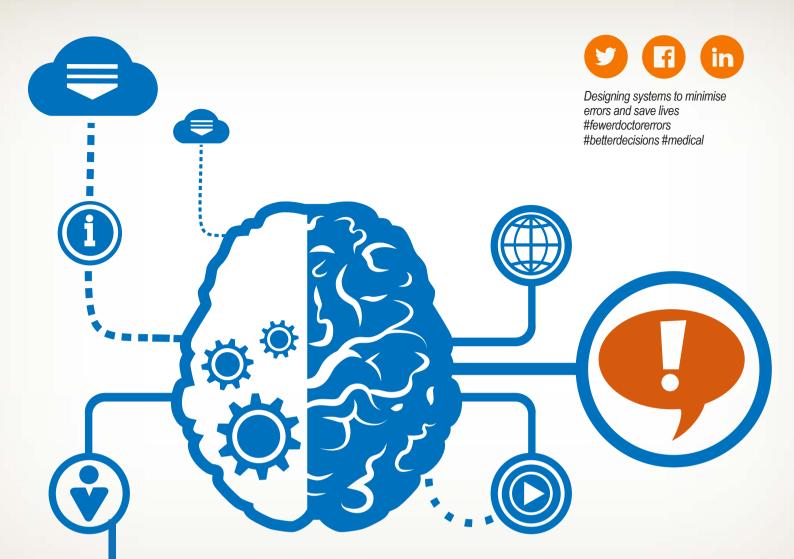
Australian researchers interested in this field should submit their project ideas to GSK's global team. Submit your ideas today, simply email bioelectronics.







Bioelectronics: The future of medicine is electric #bioelectronics



## DESIGNING SYSTEMS TO MINIMISE ERRORS AND SYSTEM TO THE TENTH TO THE TE

by clinicians and support them in making decisions requires an understanding of how people interact with, and respond to, technology. It's harder than it sounds.

If a car alarm goes off in your street, do you look out the window to see if a crime is in progress? Or do you just shrug and hope it stops soon? Do you even notice? If it's the first time you have heard an alarm, you will probably pay attention. But if the alarm tends to be triggered regularly for no apparent reason, it's more likely you'll ignore it.

Like that car alarm, a clinical information system can succeed or fail at warning clinicians of a potential danger depending on the expectations and experience of the people using it, and on the reliability of the alert system.

At Macquarie University, the Australian Institute of Health Innovation (AIHI) is engaged in human factors research on clinical information systems. Human factors is the science which studies the interactions between people and the systems and environments they work with, with the aim of finding out how to improve those interactions so systems don't fail. Dr Melissa Baysari, of the Centre for Health Systems has been trying to understand the fit between doctors and IT, and in particular, computerised decision support. That is, information provided to doctors as they make prescribing decisions, particularly the computerised alerts, online resource material and pre-populated orders included in electronic prescribing systems.

Dr Baysari said decision support could be very poorly designed. "It is a deceptively simple concept, but it is difficult to put in place effective decision support."

In one of her research projects, she spent 60 hours observing doctors on their ward rounds to see how they used decision-support when prescribing medications. The results showed that assumptions about how electronic systems work in clinical practice could be seriously off target.

Nearly half the prescriptions triggered an alert, which doctors tended to overlook. Only 17% of alerts were read.

"This is alert fatigue, where as a consequence of being bombarded with too many alerts, doctors learn to ignore all the alerts – even those which are useful."

In addition, the doctors responsible for making the prescribing decisions – senior doctors – rarely used the electronic system. The research team concluded that decision support is of limited value when the users of the system – mainly junior doctors – are not the decision makers. Current AIHI research is focusing on how to design much more effective decision support. For example, projects include determining which alert types are most effective in changing prescribing behaviours, how best to design computerised alert interfaces (text, colour, etc), and determining how many alerts to include in a clinical information system before alert fatigue sets in.

Clinical processes and guidelines that have been developed based on an ideal system may not work at all when put into the busy world of frontline healthcare. AlHI undertakes innovative observational studies in hospital wards and clinics to reveal how systems really work, and to adapt clinical processes and guidelines to make them more effective and user-friendly.

In a recent study, AIHI collaborated with hospital clinicians and managers to implement a new traffic light system for improving access to an Intensive Care Unit for fragile patients undergoing elective surgery. The new process better met clinical and patient needs, resulting in fewer elective surgery cancellations due to unavailability of beds.

Any difference between theory and practice can have major implications when things go wrong. The AIHI's Dr Robyn Clay-Williams explains "Our mental models of how we view an error will affect how we try to fix it. This means that we try to put fixes in place to stop a particular error from happening based on how we think a system works. However, we may introduce new processes that make other errors possible."

Over time, as different errors occur and multiple fixes are introduced, earlier ones are forgotten or ignored, like band-aids layered endlessly over problems. This makes the system more complex, and more error-prone.

To break this impasse a new approach is needed, to expand our thinking to focus on a systems approach to problems, rather than focusing on each problem in isolation. Unlike 'protective safety', which constantly scrutinises what has gone wrong, the new 'productive safety' (or Safety-II) seeks to understand why most things go right. A resilient system adapts and keeps functioning even in the event of a disturbance in ways that avoid, or circumvent, errors that might otherwise put patient safety at risk. The constituent elements of productive safety and how healthcare systems build resilience are a major focus of AIHI research.

A new approach is needed, to expand our thinking to focus on a systems approach to problems, rather than focusing on each problem in isolation.



>> Pictured above Dr Melissa Baysari, Senior Research Fellow and Dr Robyn Clay-Williams, Research Fellow, both of the Australian Institute of Health Innovation, Macquarie University.

#### HARNESSING COMMUNITY ENGAGEMENT

he Ingham Institute's pioneering research into using liquid biopsy to detect circulating tumour cells and circulating tumour DNA can change the way we treat cancer, and is reliant on the willingness of existing cancer patients to help future generations.

The Ingham Institute is at the cutting edge of liquid biopsy research and its clinical use for enhancing personalised oncology. One of the most pressing challenges for this work however, is also an extraordinary opportunity: that in this type of translational medical research, we require the generosity and active participation of patients in our research. Without their valuable contribution of blood and tissue samples it would be difficult to make the journey toward clinical practice a reality.

Every headline-grabbing announcement of a breakthrough in medical science brings many seeking a cure, irrespective of the months and years yet required for the "breakthrough" to be translated into clinical treatment. That frustration for everyone concerned aside, the community awareness these announcements raise is highly valuable, especially when it comes to enlisting public support for medical research and the impact that it can potentially have on the quality of medical treatments and care available to all Australians.

As I write, our *Circulating Tumour Cell* (CTC) team's research continues using samples that come from patients from our partner hospitals who are living with cancers that are significantly impacting their lives. Yet the majority stress they wouldn't even need to be asked for their cells to be used in our research, despite their suffering and cognisance of their own mortality in facing a disease that may not be curable. There is this altruistic understanding that their participation may help find that cure for someone else, if not for themselves.

All of us in the medical research community live by the understanding that any new medical discovery or diagnostic test requires a rigorous process of validation.

Without the many patients that need to be recruited in order for our work to progress, new techniques such as the Ingham Institute's liquid biopsy diagnostics would never see the light of day.

Arguably the most important role of an initiative like our upcoming CTC Cancer Research Appeal is to encourage more people to understand how our research is performed and how this can ultimately assist people living with the conditions we are investigating.

Another way we have been able to achieve this has been through partnering with local organisations to invest in elements of the research. For example, Liverpool Catholic Club's three-year funding of a PhD student to work on a CTC project has had a dual purpose of communicating its importance and progress to our community as well as supporting the future career of talented young researchers.

#### TRANSLATIONAL MEDICAL RESEARCH

We're able to do what we do largely due to the close collaboration between our research and clinical teams across the Ingham Institute and patient care facilities, most notably Liverpool Hospital.



All of us across this mix of researchers and clinicians agree that an informed and inspired community leads to better health outcomes across the board. The pride that this calibre of research is happening in my hospital, that I am a part of that, and that I'm automatically invested in the process and outcome... our experience is that regardless of background or education, awareness of research contributes to treatment and even encourages clinicians to do better.

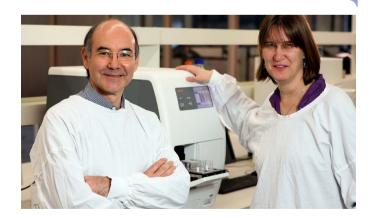
This again speaks to the selflessness we see week in, week out from patients who know the fruits of any contribution they make to our research may not appear until years later.

#### **ADOPTION**

The work we're doing now to bring people with us on the journey toward implementing liquid biopsy diagnostics into clinical practice is an investment. That awareness we're fostering today, as more people find out about and request their doctors and specialists consider the methodology, will contribute to the adoption of next-generation diagnostic and therapeutic practices.

Apart from this, and especially considering that the majority of funding for medical research is from the public purse, people deserve to know where that money is going and what it'll achieve for their health, and the health of their children.

As medical researchers, we have a responsibility to bring the public with us as we step toward the discoveries and developments that will solve the health riddles of current and future generations.



>> Pictured above Ingham Institute's A/Professor of Medical Oncology, Kevin Spring PhD with Ingham Institute Circulating Tumour Cell Program Leader, A/Professor Therese Becker.

Article by Kevin Spring PhD, Associate Professor of Medical Oncology, Ingham Institute and Liverpool Hospital: Liverpool Clinical School, Western Sydney **University (WSU): CONCERT Centre Fellow: Conjoint Associate Professor UNSW** 

### research gathers momemtum and launches

#### **FELLOWSHIP GRANTS**



PKD Australia are offering enabling and Fellowship grants to PKD researchers. In 2015, the Foundation provided funding for enabling projects examining epigenetic therapies, heart disease, stem cell modelling and research outcomes based on patient, family and health professional priorities. In partnership with the PKD Foundation US, they are now also co-funding an early-career Fellowship Grant.

olycystic Kidney Disease (PKD) is one of the most common, life-threatening genetic diseases, often resulting in kidney failure and death. Currently, the only available treatments for PKD are dialysis or a kidney transplant. The PKD Foundation of Australia was established in 2014 to find a cure for PKD. Their vision is to do this through raising funds for research specifically to find a cure and for the treatment of PKD, connecting and supporting Australians and their families affected by PKD and providing education and information to people impacted by PKD.

In 2015, and in only their second year of operation, the Foundation provided funding for four projects. These grants were awarded to:

**Dr. Cherie Stayner** from the University of Otago, New Zealand to study tissue specific targeting of an epigenetic therapy for PKD. Epigenetic modification is a type of gene regulation, with drugs that block epigenetic modifications having been shown to slow cyst formation in animal models of PKD. This projects aims modify epigenetic inhibitors in order to target them to the kidneys.

Professor Jacqueline Phillips from Macquarie University, Sydney was awarded funding to study PKD, heart disease and the sympathetic nervous system. The sympathetic nervous system acts as a driver of heart disease in PKD sufferers, however, when and where this process begins is not known. This research identified whether the sympathetic nervous system is implicated in the development of heart disease in PKD with the hope it will lead to early-intervention treatment strategies.

Associate Professor Sharon Ricardo and her team from Monash University Melbourne were awarded funding to study how pluripotent Stem Cells from Patients with PKD could be used for disease modelling and drug screening. Using stem cell lines made from the skin cells of patients with PKD they aim to compare the genetic differences in PKD cells leading to cyst formation, paving the way for more patient-specific stem cell options and, in the long term allowing for correction of the genetic defect identified in these cells.

Associate Professor Allison Tong from the University of Sydney was awarded funding for her project 'Standardised Outcomes in Nephrology – Polycystic Kidney Disease' (SONG-PKD), which aims to establish core outcomes for PKD research based on the shared priorities of patients with PKD, their family and health professionals. Her goal is to ensure that meaningful and important outcomes are consistently measured and reported in research for patients living with PKD.

In 2017, the Foundation will again be supporting four Enabling Grants. These \$15,000 enabling (or seed) grants will be awarded to the most progressive and innovative researchers from across Australia and New Zealand in the following areas:

- Basic research, being fundamental in nature, aims to understand the genetic, biological and mechanistic processes leading to PKD and the overall disease presentation and is not necessarily with an obvious clinical endpoint;
- Clinical research, studying specific clinical problems in humans and/or animal models;
- Translational research, which is orientates for translation into clinical practice, e.g.:, the development of treatments and interventions, testing the effectiveness of treatments; population studies; outcome studies and:
- Patient focused research, which aims to improve patient care and or enable the transfer of research into policy and practice.

PKD Australia is also interested in the emerging field of genetics and welcomed submissions related to this area.

The Foundation are also very excited to announce a Fellowship Grant is being offered for the first time in 2017 in partnership with their American counterpart, the PKD Foundation US. This co-funded two-year US\$100,000 grant will support world-leading and recognised scientific research into PKD. Each organisation is investing US\$25,000 per year in 2017 and 2018 to support an early-career scientist whose achievements and potential identify them as the part of the next generation of scientific leaders in PKD research. Early-career PKD researchers around the world, and specifically from Australia, are encouraged to apply. Applications are due March 1, 2017.

Mr. Robert Gardos, Chair of PKD Australia said that "We are confident that this is only the start of a program of collaboration between our two patient-focused organizations in our drive to find a cure for this condition that affects 12 million people globally" and US PKD Foundation Chief Scientific Officer Dr. David Baron agrees this is an important partnership "The PKD Foundation is fortunate to be able to co-fund research with Australia –these partnerships allow our research funding to increase its already international scope and facilitate collaboration around the globe," said Baron.

Article prepared by Sarah Metcalf (General Manager, PKD Australia) and Prof Jacqueline Phillips (BVSc Hons PhD, Professor of Neurophysiology, Macquarie University)

>> Pictured left Professor Jacqueline Phillips, Macquarie University, Recipient of an inaugural PKD Foundation Enabling Grant in 2015 for her work on PKD, heart disease and the sympathetic nervous system.

# Making Maddie's Some Frue

n July 2016, Maddie Riewoldt's Vision (MRV), a charity with a mission to find a cure for Bone Marrow Failure, selected Dr Wayne Crismani of St Vincent's Institute of Medical Research (SVI) in Melbourne as their inaugural MRV Fellow.

Nick Riewoldt, Deputy Chair of MRV, made the announcement at SVI on behalf of his family, who founded MRV to find new treatments for bone marrow failure. At the event, Nick said, "My sister Maddie died in February 2015 with one wish, that no-one ever has to experience what she did. That wish has underpinned Maddie's Vision's mission to urgently find new treatments for Bone Marrow Failure Syndromes and this award highlights our progress in achieving this goal," said Nick, Maddie's older brother and former Captain of the St Kilda Football Team.

During his 3 year Fellowship, Wayne will be working with Dr Andrew Deans in SVI's Genome Stability Unit. Researchers in the Unit focus on a rare disease called *Fanconi Anaemia* – a heritable disorder where bone marrow failure occurs on average at 7 years old and is the major cause of death at around age 16. One of the genes responsible for preventing *Fanconi Anaemia* is FANCM – which was the subject of Wayne's previous work.

"I'm incredibly honoured to work with and have the support of Maddie's Vision and the Snowdome Foundation," said Wayne. "It is my hope that in the next 3 years we can gain a better understanding of what triggers bone marrow failure, and use that knowledge to further our research into how to prevent it from occurring.

"Philanthropy is incredibly important for research into 'rare conditions' because there are a number of diseases that get a lot of airtime, but bone marrow failure is as serious as it gets and research in the area is desperately underfunded."

Prior to his arrival at SVI in April 2016, Wayne had spent most of his scientific career examining the complex genomes of agricultural crops. While describing his post-doctoral studies, he reveals, almost proudly, that a wheat cell contains more than five times as much DNA as a human cell. Furthermore, wheat cells contain six copies of each of their chromosomes, compared to the paltry two copies present in human cells.

This means that when the pairs of chromosomes of a wheat cell divide to allow reproduction, the process is complicated and highly choreographed. If it goes awry, the resulting cells end up with the wrong number of chromosomes. In humans, this type of error during cell division leads to conditions such as Down Syndrome.



To add a level of complexity, in addition to divvying up the chromosomes (a process called *meiosis*), an exchange of genetic information also occurs between maternal and paternal chromosomes. Wayne explains that this is why human siblings are not identical - we don't get just one set of chromosomes from our father and one from our mother, but instead sets of unique chromosomes derived from maternal and paternal sections of chromosomes that have 'crossed over' with each other.

After doing his PhD at the University of Adelaide, Wayne moved to Versailles, France, where he identified that a gene, called FANCM, limits the number of 'crossings' that chromosomes can make with their partner chromosome. Controlling crossing over - the speed at which genetic diversity is generated - means that new plant varieties can be produced faster. This is important because if a serious new crop pest surfaces, and a new resistant plant variety is needed, it would take 10-15 years to develop the variety. Controlling the rate of crossing over could allow quicker response times.

After his postdoc, Wayne himself 'crossed over' to industry, when he was recruited to work for the agricultural biotechnology giant DuPont Pioneer in Iowa, to commercialise his research for the improvement of crop breeding. He enjoyed the time in the USA and gained a lot of experience away from academia, but in 2015 he decided that the time was ripe to return to Australia and turn his attention to human diseases. Strange as it may sound, many human diseases are underpinned by the same biological processes that Wayne was deciphering in plants.

Wayne says, "It's been quite a journey - from researching agricultural crops to bone marrow failure in human beings - but at the end of the day both lead to outcomes that could have positive, significant impact on people around the world. I'm hopeful our research will take us closer to making Maddie's wish come true."

>>Pictured above Dr Wayne Crismani, SVI and Nick Riewoldt, **Deputy Chair MRV** 

Find out more information on bone marrow failure and the work being conducted at St Vincent's Institute of Medical Research.

RESEARCH AUSTRALIA MEMBERS MAGAZINE