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Vale Professor Don Iverson

It is with great sadness that we mourn the loss of IHMRI’s Founding Executive Director, Professor Don Iverson, who has died of cancer.

Described by University of Wollongong Vice-Chancellor, Professor Paul Wellings CBE, as a “visionary academic who saw the big picture”, Professor Iverson joined the UOW in 2001 as Dean of Health and Behavioural Sciences, later serving as Executive Dean of Health and Behavioural Sciences, Pro Vice-Chancellor (Health), Executive Dean of the Faculty of Science, Medicine and Health, and Executive Director of IHMRI.

The Canadian-born academic leaves behind the legacy of the UOW’s Medical School which broke new ground in the training of doctors for rural, regional and remote areas of Australia, and IHMRI, which brings academic and clinician researchers together to address regional health issues. Both represent a significant contribution to the Illawarra community.

Professor Iverson served on a number of high-level health and medical research boards and was known to go to great lengths to offer advice and provide the most up-to-date treatment information for friends, colleagues and even strangers who had just received a diagnosis of cancer.

In 2008, the National Breast Cancer Foundation honoured him for his role in establishing a national breast cancer research program. He also led a review of Australia’s priorities for breast cancer research in 2003, which resulted in the development of a national research plan.

In 2011, Professor Iverson was appointed to the NSW Health and Medical Research Strategic Review Committee, which developed the state’s first long-term plan to future-proof the sector.

After almost 13 years he left the UOW in 2014 to join Swinburne University in Melbourne as Executive Dean of the Faculty of Health, Arts and Design. At his farewell function in Wollongong he noted, “My whole career has been unplanned (but) Wollongong is the institution I have remained the longest in my career and so far the most comfortable I’ve been anywhere. The greatest gift has been the friendships and relationships I have been able to have. There have been so many people here who did things to make my life better and richer.”

Our thoughts are with his wife Lynne and daughter Amelia.
A breakthrough in our understanding of Motor Neurone Disease (MND) will lead to the development of a new genetic test for the fatal disorder thanks to the efforts of a 70-strong research team including IHMRI MND expert, Dr Justin Yerbury.

As recently reported to the journal *Nature Communications* the team, led by Associate Professor Ian Blair from Macquarie University’s Australian School of Advanced Medicine, linked a gene called CCNF to MND and Frontotemporal dementia (FTD) for the first time.

Ten per cent of people who contract MND are able to trace it to a family member. Of this familial cohort, around 70 per cent have mutations in genes previously linked to MND such as SOD1, TDP43, FUS and C9ORF72, meaning that individuals and family members can be tested for the presence of these mutations.

However, for the remaining 30 per cent without these gene mutations, tests are either inconclusive or unavailable.

According to Dr Yerbury, a founding member of the IHMRI-based Proteostasis and Disease Research Centre, the fact that the CCNF gene mutation has been found is a very strong indicator that it is dysfunctional in MND patients.

"As a result, new genetic testing will be developed and specialist clinicians may soon be able to screen embryos for these mutations so that children from these families are not born with the devastating disease," he said.

"It also represents another piece of the MND puzzle, adding to a body of evidence suggesting that protein degradation is going to be a very important drug target for MND and FTD in the future."

The research began over four years ago after A/Prof Blair identified the CCNF gene mutation in a single Australian family. He went on to test the hypothesis with international cohorts, with Dr Yerbury and Research Assistant Natalie Farrawell using IHMRI’s state-of-the-art laboratories to examine cells with normal CCNF and those with mutations.

"One of the functions of CCNF is to identify and tag old, worn-out and potentially dangerous proteins with ubiquitin [a regulatory protein] to signal their degradation and prevent a dangerous build-up of these proteins within cells," explained Dr Yerbury.

"We liken this process to a garbage disposal unit which chops up household waste for easier disposal. If that unit breaks down, the waste builds up. That’s exactly what we found in our cellular experiments; that mutations in CCNF cause junk protein to accumulate in cells."

In collaboration with IHMRI drug delivery expert Dr Kara Perrow, Dr Yerbury is already using the information to design preclinical gene therapy trials aimed at boosting the cell’s capacity to degrade dangerous proteins.

*The Nature Communications paper (2016) is entitled: ‘CCNF mutations in amyotrophic lateral sclerosis and frontotemporal dementia’.*
Last year a crew member from a tourist boat moored in the Whitsunday Islands off north Queensland was walking barefoot in the shallows when he stepped on a cone snail which shot a potent cocktail of bioactive venom into his foot, causing his respiratory system to start shutting down. The man survived but told reporters that the pain was excruciating.

Given this, it is ironic to think that marine cone snail venom is being developed as a potent pain killer. In fact, it is showing so much promise that it is even being touted as a possible replacement for morphine which, as we know, is highly addictive.

Leading efforts to harness the potential of the analgesic peptides (mini proteins) found in cone snail venom is IHMRI Executive Director, Professor David Adams, who first learned about the cone snails when he joined the University of Queensland (UQ) as Chair of Physiology in the mid-nineties.

“At the time, researchers in the Centre for Drug Design and Development were discovering powerful peptides in the venom, but they didn’t have the capacity to study the function of these peptides, so I started collaborating with them,” he told Research Matters.

The researchers established a team to successfully apply for a series of Australian Research Council (ARC) and National Health and Medical Research Council (NHMRC) grants, allowing them to examine more than 50 species of marine cone snails, with Professor Adams developing new electrophysiological and fluorescence imaging techniques to understand how these peptides act against ion channels and other membrane receptors involved in pain pathways.
Among the key candidates for drug development is α-conotoxin Vc1.1, a peptide from the species Conus victoriae (pictured) which has been shown to be highly efficacious for the treatment of neuropathic pain without side effects. The researchers have since published several important papers on α-conotoxin Vc1.1 and synthetic analogues of the peptide have been developed.

In the prestigious journal Gut, the team recently reported that they had been able to use α-conotoxin Vc1.1 to manage chronic pain associated with Irritable Bowel Syndrome (IBS) for which few analgesic therapies are available.

They showed how Vc1.1 acts as a potent agonist (a compound which initiates a physiological response when it binds to its receptor) against the human γ-aminobutyric acid B receptor (GABA_B) to reduce pain signalling from the colon to the spinal cord in animal models. This suggests that it is, indeed, a novel candidate for the treatment of chronic visceral pain associated with IBS.

While continuing to advance the Institute’s research agenda, Professor Adams is building a new laboratory in IHMRI’s headquarters to further the development of novel peptides for the treatment of chronic and visceral pain.

He is a Chief Investigator on an NHMRC Program Grant (2015-2019) examining ‘Ion channel modulators of pain pathways’ and an ARC Discovery Grant (2015-2019) investigating ‘Nicotinic receptor structure and function probed by conotoxins and synthetic analogues’.

This research will not only raise the profile of biomedical research at IHMRI, but attract talented young researchers to the University of Wollongong.

We expect to publish more on this research soon.

In a landmark proof-of-concept experiment, researchers in the Australian Research Council Centre of Excellence for Electromaterials Science (ACES) recently collaborated with a team at St Vincent’s Hospital Melbourne to create a hand-held 3D printing pen capable of drawing human stem cells in freeform patterns with extremely high survival rates.

The BioPen device allows surgeons to sculpt customised cartilage implants during surgery and uses a hydrogel-based bio-ink to carry and support living human stem cells. A low-powered light source solidifies the ink, enabling the pen to deliver a cell survival rate in excess of 97 per cent.

Three-dimensional bio-printers have the potential to revolutionise tissue engineering as they can be used to print cells, layer-by-layer, to build up artificial tissues for implantation. However, in some applications, such as cartilage repair, the exact geometry of an implant cannot be precisely known prior to surgery. This makes it extremely difficult to pre-prepare artificial cartilage for implantation.

The BioPen can be held in the surgeon’s hand, giving him or her unprecedented control in treating defects by filling them with bespoke scaffolds.

Professor Peter Choong, Director of Orthopaedics at St Vincent’s Hospital, developed the concept with ACES Director and IHMRI-affiliated researcher, Professor Gordon Wallace.

“The development of this type of technology is only possible with interactions between scientists and clinicians - clinicians to identify the problem and scientists to develop a solution,” said Professor Choong.

The team designed the BioPen with the practical constraints of surgery in mind and fabricated it using 3D printed medical-grade plastic and titanium. The device is small, lightweight, ergonomic and sterilisable and has a low-powered light source fixed to it to solidify the ink.

“The BioPen project highlights both the challenges and exciting opportunities in multidisciplinary research,” said Professor Wallace.

“When we get it right we can make extraordinary progress at a rapid rate.”

The work was recently published in the journal Biofabrication.

Design expertise and fabrication of the BioPen was supported by the Materials Node of the Australian National Fabrication Facility.
Review of regional birth cohort studies reveals opportunities

If you really want to know about the factors that lead to health and wellbeing over the long-term, you need time - and plenty of it. Around the world, dozens of large-scale longitudinal birth cohort studies are underway and many are providing powerful insights on how infant and childhood development affects health into adulthood. While the results can have a major impact on public health policy and practice, these kinds of studies are obviously complex and expensive to run.

To determine the feasibility of running such a study in the Illawarra, an IHMRI-based team recently completed a study with 41 local families. Data from the Illawarra Born cross-generational health study is currently being analysed to support journal articles and grant applications which will hopefully result in the study being extended to involve 1,000 local residents for a period of 21 years.

As part of their initial investigations into Australian and New Zealand birth cohort studies, the Illawarra Born team, led by Professor Brin Grenyer, found that the last systematic review had been conducted more than a decade ago, so they decided to embark upon a new one. As reported to the prestigious journal PLOS ONE, they found that there had been significant growth in the number of Australian and New Zealand studies, up from 13 in 2004 to 23 in 2015.

Among the most well-known studies are the Dunedin Multidisciplinary Health and Development Study (NZ) which has been running for more than 41 years, the Christchurch Health and Development Study (NZ), the Mater University of Queensland Study of Pregnancy, the Raine Study (Western Australia) and the Aboriginal Birth Cohort Study (NT).

By reviewing 772 papers from a total of 23 studies which met the team’s eligibility criteria, they were able to assess the quality and productivity of these studies, as well as their scientific and policy contribution and scope.

All studies included a physical assessment and most collected data on mental health and nutrition, as well as biological samples to conduct genetic research and test for environmental exposures.

While most studies focussed on the newborn child and their journey through childhood, adolescence and adulthood, some studies followed up with the mothers longer-term. Less than half of the studies collected data on at least one occasion from fathers.

Several studies, including the Illawarra Born Study, have taken on a broader intergenerational focus to investigate human development through the framework of the family unit whose environment, genetics and behaviours all have a lasting legacy on the child.

Overall, the team found that these Australian and New Zealand studies had made a significant contribution to the understanding of human development over time. They provided examples of how specific studies had influenced public health policy (i.e. effects of passive smoking on children) and highlighted how many also had a direct and positive impact on health service provision.

The success of some studies meant that the original objectives were met, so in the paper they suggested that broader aims may be required to justify long-term investment. They also identified opportunities to reduce costs by pooling data and made a case for open access to data to maximise the impact of these types of studies.

It was also suggested that studies which were conducted in small or specific geographic regions (microclimates) offered a useful avenue to address funding and resource issues, as it was less expensive to recruit and retain participants and made it easier to translate findings into improved service provision.

The biggest areas of opportunity were using advances in the fields of genetics and epigenetics to expand current knowledge on the interplay between genes and environment on outcomes in a cost effective way.

‘Longitudinal Intergenerational Birth Cohort Designs: A Systematic Review of Australian and New Zealand Studies’ was published by Illawarra Born team members: Dr Michelle Townsend, Dr Angelique Riepsamen, A/Prof Christos Georgiou, Professor Vicky Flood, A/Prof Peter Coputi, Professor Ian Wright, Dr Warren Davis, Professor Alison Jones, Dr Theresa Larkin, A/Prof Moira Williamson and Professor Brin Grenyer.
An increasing body of evidence suggests that it is important to eat fruits and vegetables with vibrant colours, as each colour carries its own set of disease-fighting chemicals.

Over the past two years, a group of IHMRI-affiliated researchers led by Associate Professor Karen Charlton and including PhD candidate Katherine Kent, A/Prof Steven Roodenrys, A/Prof Victoria Traynor and Professor Jan Potter, have been investigating the health benefits of anthocyanins; naturally-occurring compounds which give fruits such as strawberries, blueberries and plums their rich, deep colours and contain powerful antioxidants.

The first phase of their research involved cherries, with a 12-week study investigating the association between the consumption of cherry juice and improved cognitive function in older adults with moderate to severe dementia. The positive findings have been published and presented at international conferences.

Now the team have turned their attention to the Queen Garnet plum – known affectionately as the “royal lady of plums”. Accidentally bred by Queensland government scientists over a decade ago, Queen Garnets have more than double the anthocyanin concentration of common plums.

With a University Research Council partnership grant (secured with Nutrafruit Pty Ltd), the team recently conducted an acute feeding study to better understand the metabolism of plum anthocyanins in order to determine how much plum juice would be needed in trials designed to investigate their effect on blood pressure and memory in humans.

The study, coordinated by PhD candidate Ezinne Igwe, was carried out in 24 healthy participants (12 people aged 18 to 45 and 12 aged over 65) who visited IHMRI’s Clinical Research and Trials Unit twice to consume, in random order, either a single dose (300ml) of juice or a triple dose (3 x100ml).

The results showed that the Queen Garnet plum juice exerted impressive blood pressure-lowering effects in the 24-hour period following consumption. “This effect was more evident in the older age group, who had higher baseline blood pressure levels compared to the younger group,” said A/Prof Charlton.

“There was no acute effect of the Queen Garnet plum juice on cognition both in the young and older adults.”

The researchers also took urine samples at regular intervals to determine how quickly the bioactive compounds were being metabolised by the body.

“We were surprised to find that, unlike the cherry juice study, it didn’t make any difference if a large glass of juice was gulped down in one go, or whether the same amount was taken in smaller sips over a longer period,” added A/Prof Charlton.

“This is probably explained by the larger quantity of anthocyanins in the Queen Garnet plum juice which overcame the threshold required for uptake.”

Prior to this study, the team believed that anthocyanins acted solely as antioxidants by reducing inflammation in the body and scavenging free radicals to fight disease.

“But recent research has shown that these compounds have the potential to improve learning and memory by reaching the brain through the blood system and increasing blood flow to the brain,” concluded A/Prof Charlton.

“It is very exciting to work with a fruit with such potential. It also tastes delicious and is only grown in Australia.”

The researchers have now submitted several external grant applications to fund randomised clinical trials on the role of the Queen Garnet plum on memory and cognition in older adults.
Suicide prevention program

Suicide deaths in Australia are now more than twice the national road toll, with the latest figures from the Australian Bureau of Statistics showing that 2,864 people died from suicide in 2014, up from 2,335 in 2009, equating to a 13.5 per cent increase.

According to IHMRI-affiliated researcher, Dr Coralie Wilson, around three-quarters of those who died were male, making intentional self-harm the tenth leading cause of death for men in Australia.

“The tragic thing is, suicide is preventable,” she said.

“To bring these unacceptable suicide rates down, we need to provide support and education to men in the community and in the workforce. Of course, we need excellent crisis care and mental health institutions, but we can’t afford to wait until people are in crisis to help them, as the chances of catching them at this point are greatly reduced.”

Dr Wilson recently formed a partnership with the OzHelp Foundation to undertake suicide science and service development research. The foundation was established in 2015 to support men in the workplace by boosting resilience and confidence in meeting life’s challenges. Around 33,000 men across Australia are now accessing the service.

“A long-range blueprint for outcomes from the partnership has been developed, with OzHelp currently supporting two innovative student projects,” said Dr Wilson.

“It has also recently funded UOW research assistance for the analysis of the mental and medical health data of over 7,000 service participants.

“It’s exciting to be involved in this kind of research, as the results will directly inform advances in suicide science and play a role in improving the kinds of services that OzHelp can deliver to vulnerable men.”

Iron deficiency is a common complication of Inflammatory Bowel Disease (IBD), a group of disorders in which the small and large intestines become inflamed, causing symptoms such as chronic pain, diarrhoea, weight loss, fever, joint pain and loss of appetite.

While iron replacement therapy (IRT) is recommended for IBS patients, it is thought that taking iron tablets orally may exacerbate symptoms by upsetting the bacterial community in the gut. Therefore intravenous (IV) administration may be preferable.

To test this, IHMRI-affiliated researcher and Illawarra Shoalhaven Local Health District gastroenterologist, Dr Thomas Lee, recently collaborated with researchers in Canada and Germany on a clinical trial comparing how the intestinal microbiota responded to oral versus IV iron treatment.

The study included 72 patients with Crohn’s disease, ulcerative colitis and anaemia. Over a period of three months, half the subjects took iron sulphate orally, while the other half received iron sucrose intravenously. Mass spectroscopy techniques were used to examine stool samples taken from the patients before and after therapy.

The findings, recently published in the prestigious journal Gut, showed that while both oral and IV treatments led to improved iron balance, the bacterial community was substantially altered depending on the route of administration.

Crohn’s disease patients with an unstable intestinal flora particularly benefited from IV treatment. However, the change in the intestinal microbiota did not influence disease activity during the study period, leading the team to conclude that short-term therapy does not exacerbate bowel disease but may increase the risk of disease flare ups due to an unstable bacterial ecosystem.

Dr Lee said, “It is pleasing to be able to provide new clinical evidence on this topic, as it has been confusing for specialists to know what to do. Hopefully, this resolves the question for now.”

The paper is entitled: ‘Oral versus intravenous iron replacement therapy distinctly alters the gut microbiota and metabolome in patients with IBD’.
Study highlights role of GPs in reducing polypharmacy

For older Australians, the single most common cause of adverse drug events is the co-administration of multiple drugs. A recent survey of 4,500 community-dwelling Australians over the age of 65 found that almost 50 per cent reported taking five or more medications and more than 10 per cent reported using 10 or more. In the medical world, this is known as polypharmacy, which is defined as the concomitant use of five or more medications.

For the residents of long-term care facilities (LTCFs) such as nursing homes, nursing facilities and assisted living facilities, the average number of prescribed medications is estimated to be seven to 10 medications per resident, suggesting that polypharmacy is occurring in up to 95 per cent of LTCF residents, placing this vulnerable population group at greater risk of adverse drug reactions and hospitalisation.

With collaborators at the George Institute for Global Health at the University of Sydney including polypharmacy expert, Professor Richard Lindley, IHMRI-affiliated researcher, Professor Jan Potter, recently conducted a first-of-its-kind study called RELEASE which looked at perceptions of medication use in the Illawarra and the concept of deprescribing - the process of withdrawing inappropriate medications under the supervision of a healthcare professional.

As reported to the journal BMC Geriatrics, the RELEASE study involved focus groups and interviews with GPs, pharmacists and nursing staff, as well as residents and their relatives within three local LTCFs. While study participants acknowledged the burden of too many medications, many also displayed passivity towards medication reduction. Residents and relatives also lacked an understanding of medicine indications and potential harms; hence their willingness to initiate and accept medication change was dependent on the advice of their GPs.

While GPs emerged as central trusted figures, the study also found that GPs often chose “the path of least resistance” in reducing their patients’ medications, citing systems barriers (i.e., poor uniformity of LTCF medical records, limited trained LTCF personnel), time constraints and the organisation of care (i.e., collaborating with LTCF staff, pharmacists and prescribing specialists) as obstacles to deprescribing.

The study team concluded that a targeted intervention addressing these barriers within LTCFs was vital, as was strong engagement with GPs to raise awareness of the risks of polypharmacy and ensure they played a more active role in deprescribing initiatives.

The paper is entitled: ‘Barricades and brickwalls – a qualitative study exploring perceptions of medication use and deprescribing in long-term care.’
Removing barriers to exercise for women after breast cancer surgery

Given that physical activity has been linked to improved cancer survival rates, it is vital that barriers to exercise and activity are addressed says IHMRI-affiliated researcher, Dr Deirdre McGhee.

Dr McGhee is a Sports Physiotherapist, a Senior Lecturer in the UOW’s Faculty of Science, Medicine and Health (SMAH) and a founding member of the internationally-recognised UOW-based centre, Breast Research Australia, which seeks to decrease breast-related discomfort and injury so that women can comfortably participate in activities of daily life.

Dr McGhee recently attracted a Small Project Grant from SMAH to investigate musculoskeletal barriers to physical activity incurred by women post-breast reconstruction.

"Many women experience pain and dysfunction beyond those caused by their mastectomy," she explained.

"The symptoms, which are local to the implant or autograph site, as well as donor sites used to harvest tissue, include loss of shoulder range (motion and strength), lower back and abdominal pain, reduced trunk strength, breast pain and difficulty achieving sufficient breast support. If severe enough, these symptoms prevent breast reconstruction patients from performing common tasks or participating in physical activity."

She says that these issues can be addressed through rehabilitation, education and exercise, however, most women are not referred and left to struggle with these issues on their own.

Dr McGhee will use the grant to collect stakeholder information on the musculoskeletal issues experienced by women post-reconstruction and the extent to which they restrict their physical activity and function. She will also collate information on current intervention strategies that people find helpful, as well as those they would avoid. The aim is to develop evidence-based rehabilitation and education strategies to alleviate these symptoms and barriers to physical activity.

The pilot data will also be used to support a National Health and Medical Research Council Translating Research into Practice Fellowship application.

Clinical PhD Scholarship Program expands

In 2014, the Illawarra Shoalhaven Local Health District launched the first-ever ISLHD/UOW Clinical PhD Scholarship Program to support ISLHD clinicians or UOW Higher Degree Research students to undertake PhDs “with direct clinical relevance”.

The initiative, which received strong support from ISLHD clinicians, is well underway with four students looking at topics as diverse as chemotherapy-induced fatigue (Sina Ameli), the use of the drug Liraglutide for the treatment of schizophrenia (Ilijana Babic), an assessment of a program seeking to improve older people’s balance through exercise (Maryam Ghahramani) and links between end-stage kidney disease and cognitive impairment (Kelly Lambert).

Now, the ISLHD has introduced a new Graduate Clinical Fellowship to give graduates from nursing, medicine or allied health the opportunity to undertake PhDs within a clinical setting while consolidating their clinical skills. The program is funded by the ISLHD Cancer Care Centre and the University of Wollongong’s Australian Postgraduate Award.

Emily Hazzard, a graduate dietitian working in oncology, has been awarded a fellowship to explore the prevalence, impact and interdisciplinary management of dehydration among patients with head, neck and upper gastrointestinal cancers under the supervision of Honorary Clinical Associate Professor Marianna Milosavljevic and Professor Andrew Miller (Wollongong Hospital) as well as Associate Professor Karen Walton, Senior Professor Linda Tapsell and Dr Anne McMahon (UOW).

We look forward to hearing more about the outcomes of these projects.
Does where you live make you fat?

The Australian government has invested billions in health promotion campaigns to prevent obesity in Australia, yet the population keeps getting fatter.

IHMRI-affiliated researcher Associate Professor Karen Charlton says that, over the past two decades, the prevalence of obesity in Australian adults has risen from 19 per cent to 28 per cent, while the proportion of overweight adults has remained similar, at around 38 per cent.

“What this means is that two thirds of Australian adults are now either overweight or obese,” she said.

With Abhijeet Ghosh, Senior Epidemiologist at COORDINARE (South Eastern NSW Primary Health Network) and A/Prof Marijka Batterham, Director of the Statistical Consulting Centre associated with the UOW’s School of Mathematics and Applied Statistics, A/Prof Charlton recently published a paper in BMJ Open showing a strong link between obesity and socioeconomic disadvantage in the Illawarra-Shoalhaven region. The findings are likely to have national implications.

To make the link, the team analysed a subset of COORDINARE’s Sentinel Practices Data Sourcing Project’s phase 1 database, consisting of 118,794 adult patient-doctor interactions collected from 17 General Practices in the region between September 2011 and September 2013.

They then looked at the Australian Bureau of Statistics’ Socio-Economic Indexes for Areas Index of Relative Socio-Economic Disadvantage scores of patients’ residential statistical local area to assess levels of overweight and obesity in areas of high and low socioeconomic disadvantage. From this, they were able to determine that those living in areas of high socioeconomic disadvantage are at much greater risk of obesity than those living in wealthier areas.

“In men, the odds of being overweight were lowest in areas of highest socioeconomic disadvantage,” said A/Prof Charlton.

“However, no statistically significant association with the socioeconomic score was found for women. Overall, for both genders, obesity was associated with 29 per cent higher odds for those living in areas of high socioeconomic disadvantage.”

The authors argue that the study highlights a need for preventive health initiatives to be gender specific and for them to take into account the socioeconomic attributes of the target population.

“The study provides new insights for population health planning in the local area,” said A/Prof Charlton.

“In areas of high socioeconomic disadvantage, for example, primary care providers could have a more streamlined approach to linking obese patients to existing weight loss program such as the free, government-funded Get Healthy information and coaching service.

“Conversely, in areas of low socioeconomic disadvantage, efforts could be focused on preventing further weight gain in adults who are in the overweight range.”

The authors also argue that a simple but effective strategy in this regard may be to routinely weigh patients every time they visit their GP. This has been demonstrated by IHMRI and Illawarra and Southern Practice Research Network researchers who recently presented data on the positive impact of regularly weighing patients in General Practices. Marketing materials are now being distributed around the region to raise awareness of this among doctors and patients.

“In the coming months, the Sentinel Practices Data Sourcing project will be rolled out to the entire South Eastern NSW region in order to establish a GP-based sentinel site surveillance system to monitor chronic disease,” said A/Prof Charlton.

“This will allow closer monitoring of weight status between communities within each of the NSW’s Primary Health Networks and thereby allow for more directed planning of population health and primary care services.”
Cancer researchers take their seat at the table

IHMRI-affiliated cancer researchers, Professor Marie Ranson and Dr Kara Perrow, are active members on the organising committee for the fifth Sydney Cancer Conference (SCC), to be held at the Australian Technology Park in Sydney from 22 to 23 September this year.

The purpose of the conference is to support future generations of cancer researchers and provide them with a national forum to share ideas and highlight areas of research strength in NSW. The theme of this year’s event - Bridging research and practice - reflects cancer research along the translational research continuum from basic biomedical research to public health, clinical and psychosocial research.

The IHMRI and UOW representation is significant given that, for the first time, the event is being co-hosted by the major NSW universities, including the University of Sydney, UNSW Australia, Macquarie University and Newcastle University.

Professor Ranson, who is Chief Investigator on the state-wide Centre for Oncology Education and Research Translation (CONCERT) initiative, was also recently elected Co-Chair of the 2018 Gordon Research Conference on Plasminogen Activation and Extracellular Proteolysis, to be held in Ventura, California.

"Participation in high profile events such as these brings us face-to-face with potential collaborators and showcases the depth and breadth of cancer research being conducted in the Illawarra," said Professor Ranson.

Regional leadership in suicide prevention

On the eve of World Suicide Prevention Day last year, members of the newly-formed Illawarra Shoalhaven Suicide Prevention Collaborative met for the first time at IHMRI to discuss how they could tackle the region’s stubbornly high rates of suicide.

Initiated through a partnership between IHMRI and senior representatives from regional health, education and community organisations, the project has since gathered significant pace with the Mental Health Manager of Grand Pacific Health, Dr Alex Hains, about to take up a full-time role coordinating the initiative thanks to funding from the Illawarra Shoalhaven Local Health District (ISLHD) and COORDINARE (Primary Health Network).

In April, regional stakeholders met in Kiama to workshop practical ways of improving services by firstly identifying gaps and opportunities.

"The workshop was a great success," said Dr Hains.

"More than 70 people from 20 organisations representing a broad range of services, including the police and local councils, attended. We had a great discussion and came up with some innovative ideas on how we could advance the collaborative’s aims."

The insights gathered from this meeting will be used for a tender application for the Illawarra-Shoalhaven to be one of four pilot sites dedicated to addressing the strategies highlighted in the Suicide Prevention Framework for NSW, prepared recently by the Mental Health Commission, National Health and Medical Research Council and the Black Dog Institute.

“We really want to ensure we keep our momentum and we are thrilled that so many regional stakeholders have chosen to get involved," added Dr Hains.

Among these organisations are the ISLHD, IHMRI, the UOW, Illawarra Shoalhaven Partners in Recovery, Grand Pacific Health, Lifeline South Coast, the Illawarra and Shoalhaven Suicide Prevention and Awareness Networks, the Salvation Army, Illawarra Mercury, Department of Education and Communities, Independent Schools, Illawarra Institute of Mental Health, Catholic Education Office, Lifeline Foundation and South Coast Aboriginal Medical Service.

We look forward to bringing you updates on this project, and the research associated with it.
Research raises questions on the cause of Alzheimer’s disease

Conventional wisdom on the cause of Alzheimer’s disease (AD) and current thinking on treatment strategies may be called into question by the publication of a paper suggesting that the real culprit may be slow changes to plaque in the brain that simply happen with time.

As reported to the journal *Analytical Chemistry* recently, IHMRI-affiliated researchers working in collaboration with scientists at the Save Sight Institute, applied their knowledge and expertise of other diseases of ageing, such as cataract to examine changes to the composition of proteins in the human brain.

The link between eye health and AD relates to the fact that the human lens contains the highest concentration of proteins of any tissue in the body and altered proteins are associated with a range of age-related pathologies including cataract and AD.

According to the paper’s lead author Professor Roger Truscott, plaque, which is the key diagnostic feature of AD, forms when the amyloid precursor protein (APP) is cut by enzymes to create smaller fragments called amyloid beta (Aβ) peptides which are sticky and form clumps that are toxic to brain cells.

To date, researchers and drug companies have focused most of their efforts on clearing two toxic variants - Aβ 1-40 and Aβ 1-42 - but Professor Truscott says that the vast majority of plaque in the human brain is not Aβ 1-40 or Aβ 1-42 per se, but highly degraded or modified versions of these peptides, meaning that current strategies which seek to clear them from the brain may be ineffective.

“These peptides may have been deposited initially, but almost all of them have undergone a large number of changes which make it very difficult for the body’s normal enzymes to break down and dispose of modified Aβ 1-40 or Aβ 1-42,” he said.

“In this paper we show that all of these modifications are due to spontaneous processes; i.e. no enzymes are required. These are simply slow chemical reactions that just depend on time and they can all be reproduced in the test tube.”

One conclusion that can be drawn from this study is that the vast majority of peptides within plaque are long-lived, a discovery which could help to explain why many people past middle age have plaque in the brain but seem to suffer no cognitive ill effects.

“It is possible that plaque needs time to become toxic,” said Professor Truscott. With this knowledge he suggests that researchers should now investigate the composition of plaque as a function of age in normal human donors, as well as in AD patients.

“The majority of AD studies underway are animal studies. What we really need to do is look at how the peptides that make up plaque alter with age and ask if they are different in normal elderly people compared to AD patients and also if they are different in different regions of the brain.

“The next stage of the AD work is to perform these investigations together with research on the toxicity of the modified forms of Aβ 1-40 or Aβ 1-42.”

The research also has significant implications for the development of therapeutics to treat AD, as current strategies focus on the use of monoclonal antibodies to clear plaque from the brain.

“Monoclonal antibodies are very specific tools that target certain sites on Aβ. They may not work as well on target proteins that have been highly modified,” concluded Professor Truscott.

*The paper is entitled: ‘Amyloid Plaque in the Human Brain Can Decompose from A(1-40/1-42) by Spontaneous Nonenzymatic Processes’.*
For premature babies, it’s all about oxygen

Premature babies require supplementary oxygen to support their breathing and ensure they have adequate oxygen saturation in the blood to support their growth and development.

Until recently, neonatal paediatricians aimed to keep this haemoglobin saturation within a range of 85 to 95 per cent; a fairly imprecise target when you consider that going above or below this range risks eye damage, disability - even death.

To provide doctors and nurses with better information on safer levels of blood oxygen, the BOOST-II (Benefits of Oxygen Saturation Targeting, Trial II) study was launched in 2005 with the aim of ascertaining which of two oxygen saturation ranges (85 to 89 per cent and 91 to 95 per cent) is better for very premature babies.

The study, led in Australia by University of Sydney Professor William Tarnow-Mordi and involving IHMRI-affiliated researcher and Wollongong Hospital paediatrician Professor Ian Wright, was coordinated through the National Health and Medical Research Council’s Clinical Trials Centre.

As recently reported to the New England Journal of Medicine, the research team combined BOOST-II Australian data with BOOST-II British data, representing a total of 2,108 infants, to deliver new clinical evidence on safer levels. They found that targeting oxygen saturation below 90 per cent in extremely preterm infants was associated with a higher risk of death, but not of disability.

The risk of death or disability at the age of two among infants born before 28 weeks’ gestation was five per cent higher if they had been allocated a lower targeted oxygen saturation (85 to 89 per cent) than a higher targeted oxygen saturation (91 to 95 per cent).

“We now have clearer evidence that the higher concentration of oxygen is superior, increasing survival without an associated increase in disability,” said Professor Tarnow-Mordi.

“If confirmed when combined with the results of three similar trials in the US, Canada and New Zealand, it will help to prevent a great many deaths worldwide every year.”

Professor Wright, who is also the region’s Chair of Paediatrics and Child Health Research said: “Studies like this, to ‘fine tune’ the care of our sick and premature infants, take many years to complete and involve collaboration between researchers, clinicians and parents across the world. They are, however, the best way to answer difficult questions that affect the lives of many families.”
It's Time2bHealthy for pre-schoolers

PhD candidate Megan Hammersley is running the Time2bHealthy trial to help parents improve their child’s eating habits and levels of physical activity, screen time and sleep.

Research shows that only five per cent of Australian pre-schoolers are eating enough fruit and vegetables. Up to a third of their energy comes from foods such as biscuits, cakes and other energy-dense snacks.

Megan Hammersley, an Accredited Practising Dietitian who is currently undertaking a PhD, says rapid growth in the number of convenience and fast food stores, coupled with the fact that parents have less time to prepare healthy meals, means we have created an environment conducive to childhood obesity.

To arm parents with better tools and resources on how to improve their child’s eating habits and levels of physical activity, screen time and sleep, Megan is conducting an innovative healthy lifestyle program.

Believed to be the first in Australia to target pre-schoolers, the Time2bHealthy trial is being run under the auspices of the IHMRI-affiliated Early Start Research Institute.

Following some initial visits to IHMRI’s Clinical Research and Trials Unit for measurements (of their children) and consultations, participating parents complete a series of online modules on topics such as healthy eating, physical activity, screen time and sleep. Parents are encouraged to read up on these topics, watch videos, complete activities and set goals while the children wear activity monitors to track their energy expenditure.

The control group receives fortnightly emails linking them to similar information (they will be provided with full access to the program at a later date) and the children have their measurements taken at regular intervals.

"Early childhood is a critical time for the development of healthy lifestyle practices which are not only important for physical health, but also for cognitive development and social and emotional wellbeing," said Megan.

"As children get older, it becomes harder to change unhealthy behaviours, so the influence of parents in early childhood is vitally important and why this program is parent-focussed".

Interested in this study? Contact Megan on 0403 233 875 or mlh965@uowmail.edu.au.

IHMRI students set to fly

Since IHMRI’s headquarters were completed in 2010, the building has been home to dozens of talented PhD candidates who have enjoyed a supportive environment, direct access to IHMRI’s state-of-the art laboratories and opportunities to exchange ideas with their supervisors and peers.

Several of these students are now being offered postdoctoral positions and gaining recognition for their research excellence.

Fabian Kreilau, who started at IHMRI in 2011 during his honours year, was recently awarded his PhD and offered a position in the laboratory of Senior Research Fellow, Professor Brett Garner, where he will continue promising research on Vitamin B12 and Alzheimer’s disease.

Under the supervision of Senior Professor Mark Wilson, Daniel Whiten recently submitted his thesis on the role of clusterin in Motor Neurone Disease and the molecular mechanism of its action. Based on the excellence of his research, he has been offered a postdoctoral position in the laboratory of Professor David Klenerman, a British researcher best known for his contribution to the field of next-generation sequencing of DNA.

In April, another IHMRI student, Danielle Camer, was conferred with a PhD and an Examiners’ Commendation for Outstanding Thesis at the UOW’s graduation ceremony. Danielle’s research, conducted under the supervision of Senior Professor Xu-Feng Huang from the IHMRI-based Centre for Translational Neuroscience, focused on the use of bardoxolone methyl, a drug derived from a naturally-occurring chemical called oleanolic acid, as a novel therapeutic for the prevention of obesity and obesity-induced complications such as cognitive deficits, insulin resistance and organ damage in mice fed a high-fat diet.

Danielle has presented this research at several national and international conferences and she is listed as an author on papers published in over eight international peer-reviewed journals.

We look forward to hearing more about our students’ success.
The International College of Neuropsychopharmacology (CINP) has recognised two young IHMRI researchers with prestigious awards. Dr Jiamei Lian, a postdoctoral researcher in Professor Chao Deng’s Antipsychotic Research Laboratory, won the CINP Rafaelsen Young Investigator Award for 2016, while Centre for Translational Neuroscience PhD student, Jeremy Lum, won both the Student Encouragement and CINP Mentor/Mentee awards.

The Rafaelsen Young Investigator Award is conferred by an international scientific jury. It will enable Dr Lian to travel to the CINP World Congress in Seoul, Korea, in July 2016, where she will receive her award and present her research on the obesity side effects of antipsychotic drugs. This is not the first time Dr Lian has been recognised. In 2014, she was awarded a Highest Ranked Non-clinical Abstract Award at the Biological Psychiatry Australia Conference and in 2015 she won a coveted National Health and Medical Research Council Project Grant as a Chief Investigator (B). This latest award recognises her outstanding achievements at an international level and is testament to the high quality of research being conducted in Professor Deng’s laboratory. Two PhD students from the laboratory, Bo Pan and Michael De Santis, will also present their research at the congress.

After winning both the Student Encouragement and CINP Mentor/Mentee awards, Jeremy will also attend the congress, where he will present research on novel antipsychotics in the treatment of schizophrenia, undertaken under the supervision of Dr Kelly Newell, Senior Professor Xu-Feng Huang and Dr Lezanne Ooi.

The CINP awards are highly competitive, so both researchers have done exceptionally well to win.

CMRP student success
Being offered a full-time position as a Medical Physics Registrar in one of our leading hospitals is no easy feat as such appointments are always highly competitive.

It is with delight then that we announce that two IHMRI-affiliated PhD students from the Centre for Medical Radiation Physics (CMRP) were recently offered Medical Physics registrar positions.

Ryan Brown, who has been studying High-Z Nanostructured Ceramics in radiotherapy under the supervision of Associate Professor Michael Lerch, will soon take up a position at St George Hospital in Kogarah while Sally McKinnon, who has been developing Monte Carlo radiation transport simulations for studying novel aspects of proton therapy and synchrotron X-ray therapy under the supervision of Dr Susanna Guatelli, will take up a position at the Tamworth Hospital.

The students acknowledge the successful collaboration between the CMRP, Australian Institute for Innovative Materials and Prince of Wales Hospital. Well done all.

IHMRI students shine
At the Kioloa Neuroscience Colloquium, held at the Australian National University’s Kioloa Coastal Campus in April, second-year PhD candidate Rachelle Balez won Best Student Presentation for her talk entitled: ‘Alzheimer’s next top model: Investigating disease pathogenesis using induced pluripotent stem cells’.

The annual colloquium brings some of Australia’s top neuroscientists and students together to network and share the latest research in a relaxed and informal setting.

IHMRI was well-represented this year with Executive Director, Professor David Adams giving a plenary talk.

“Given that this was Rachelle’s first conference presentation as a PhD student, and that she was competing with candidates from some of Australia’s leading universities, she did remarkably well to take out the top prize,” he said.

Professor Adams also congratulated Jeremy Lum and Ashleigh Osborne who gave oral presentations, as well as Ilijana Babic, Dr Henry Li, Samuel Millard, Marta Ramos and Rebecca Webby who did poster presentations.

Radiotherapy workshop
In April, more than 80 national and international experts visited Wollongong to participate in the 3rd Geant4 School and Monte Carlo Workshop for Radiotherapy, Imaging and Radiation Protection.

Hosted by the IHMRI-affiliated Centre for Medical Radiation Physics (CMRP) and chaired by CMRP researcher, Dr Susanna Guatelli, the event focused on the use of, and improvements to, Monte Carlo simulation software tools used in medical physics to verify and improve clinical radiotherapy treatment, as well as the development of novel technologies associated with these techniques.

According to Dr Guatelli, there has been a 30 per cent increase in the total number of workshop participants compared to the previous event in 2013, with international participation increasing from around 15 to 35 per cent.

The workshop provided fertile ground for ideas exchange and provided opportunities for collaboration. The most significant scientific contributions to the workshop will be published in a dedicated Focus Issue of the international, peer-reviewed journal Physica Medica.

The event clearly demonstrates that the CMRP is becoming a leading international centre for Monte Carlo-based studies for medical physics.

Research Matters is a publication of the Illawarra Health and Medical Research Institute, a joint initiative of the Illawarra Shoalhaven Local Health District and University of Wollongong.

IHMRI’s purpose is to build a regionally relevant, but internationally and nationally recognised centre of health and medical research, targeting health improvements through novel treatments, better clinical practice and preventative health.