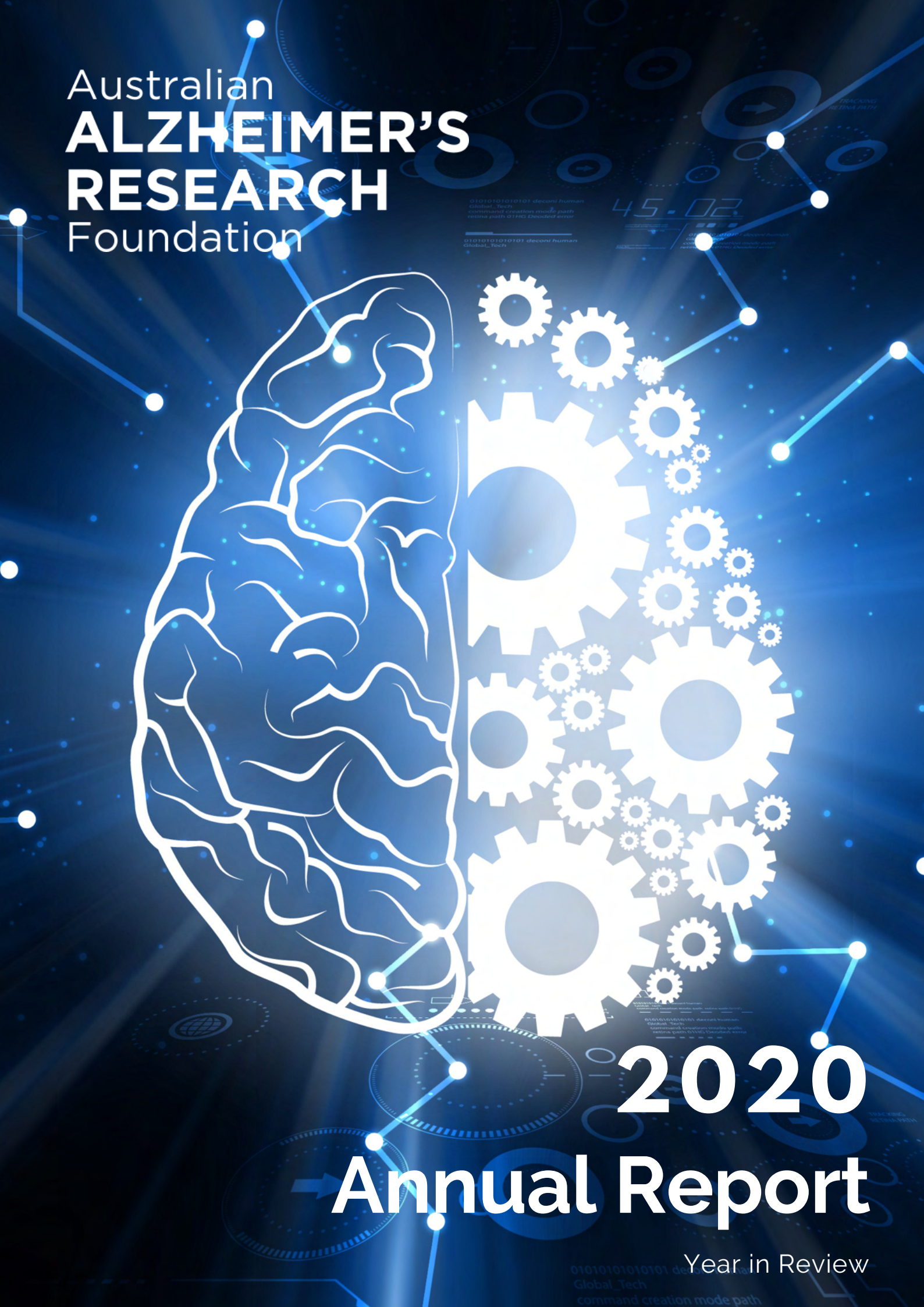
Australian
ALZHEIMER'S
RESEARCH
Foundation



2020 Annual Report

Year in Review

Dementia including Alzheimer's disease is the second leading cause of death in Australia and the single greatest cause of disability in Australians aged 65 and over. It is estimated to cost the nation more than $15 billion annually. Together with our supporters, we remain committed to continue our fight for memories and to our vision, mission, objectives and values.

Our Vision

A world in which Alzheimer's disease no longer exists.

Our Mission

To support research that makes Alzheimer's disease treatable and preventable.

Our Objective

The Australian Alzheimer's Research Foundation becomes a self-sustaining Foundation that raises funds to support Alzheimer's disease research.

Our Values

For our stakeholders and customers we will always focus on supporting Alzheimer's disease research; act with integrity; be transparent in everything we do; and celebrate our achievements.

Our key pillars are:

- Research focused on understanding, preventing, diagnosing and treating Alzheimer's and other neurodegenerative diseases.
- Revenue sustainability through diversification of funding support, fundraising, grants and research fee-for-service activity, including industry supported clinical trials.
- Community engagement related to education and awareness.
- Strengthening partnerships and national presence.

To ensure our continued operations and sustainability we will always have a clear and shared understanding of our risk appetite and have mechanisms in place to ensure we operate within this; ensure appropriate policies and procedures are in place and complied with; maintain strict financial discipline; and refuse to compromise on quality and competence in anything we do and represent.

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Dementia and Alzheimer's
Key Facts

Alzheimer's is the main cause of dementia

Alzheimer's disease is the most common form of dementia, affecting up to 70% of all people with dementia.

250 people are diagnosed with dementia each day

Currently, an estimated 250 people are joining the population with dementia each day in Australia. The number of new cases of dementia is expected to increase to an estimated 318 people per day by 2025 and more than 650 people per day by 2056.

Leading cause of death of women

Females account for 64.5% of all dementia related deaths and it remains the leading cause of death among Australian females.

472,000 Australians are living with dementia

Without a medical breakthrough, the number of people with dementia is expected to increase to an estimated 590,000 by 2028 and 1,076,000 by 2058.

30% of people over 85 have dementia

Three in 10 people over the age of 85 and almost one in 10 people over 65 have dementia.

2nd leading cause of death

Dementia is the second leading cause of death of Australians contributing to 5.8% of all deaths in males and 11.3% of all deaths in females each year.

Every 3 seconds someone in the world develops dementia.

There is no cure.

Australian Bureau of Statistics (2018) Causes of Death, Australia, 2017 (cat. No. 3303.0).
The National Centre for Social and Economic Modelling NATSEM (2016) Economic Cost of Dementia in Australia 2016–2056.
Dementia Australia (2018) Dementia Prevalence Data 2018-2058, commissioned research undertaken by NATSEM, University of Canberra.

Chairman's Report

GRAEME PRIOR

I would like to thank the Board and Members for the opportunity to become Chair of the Australian Alzheimer's Research Foundation (AARF) in June 2020.

On behalf of myself and the Board, my sincere thanks to the prior Chair, Mr Enzo Sirna AM for his careful stewardship of the organisation which he has chaired since 2013 and also for his contribution to the Foundation since he joined the Board in 2000.

I would also like to acknowledge the very sad passing of Dr Michael Quinlan AO in October 2020. Dr Quinlan was an AARF Board Member since 2014 and a staunch advocate for the critical importance of Alzheimer's disease research. His wisdom is greatly missed.

The COVID-19 pandemic certainly presented some challenges in 2020, in both fundraising and conducting research. The Foundation was extremely grateful to receive several bequests during the year and the continued support of Wesfarmers for which we are incredibly grateful. Fundraising and Sponsorship are the primary source of income for the Foundation and growth in this area is critical if we are to meet the growing demands of research into Alzheimer's disease.

I would like to acknowledge and thank the CEO, Ms Liza Dunne and the team for ensuring the Foundation and all staff were well supported during this difficult period and the necessary measures were implemented across our three research sites to minimise the COVID-19 related risks for staff and the public.

Thank you to Rod O'Dea (Chair) and all members of the Future Fund for their contribution throughout 2020. The Future Fund Committee met quarterly during 2020, which was a particularly challenging year in the financial markets with considerable uncertainty and the collapse in interest rates. New sources of income must be explored and I have suggested the establishment of an IP Committee to review the income opportunities of research activities and assets which enables us to fund ongoing Alzheimer's disease research.

Supporting the research lead by Prof Ralph Martins AO continues to be a primary focus of the Foundation. 2021 represents the Foundation's 21 years since its establishment and on behalf of myself and the rest of the Board, I would like to thank Prof Martins for the outstanding research he has led over this time.

I would like to particularly acknowledge the role Prof Martins has played in taking Perth and the Foundation into the national dementia research stage and the international world of dementia research.

The Foundation's pharmaceutical clinical trials continued through 2020 and the staff are to be congratulated for providing an environment that the public had confidence in through the pandemic. On behalf of myself and the Board, I would like to thank Dr Roger Clarnette for his leadership of the Clinical Trials Division and contribution to the Foundation.

As you will see from reading this report, the Australian Alzheimer's Research Foundation operates unlike many other Foundations and probably more like a Medical Research Institute. The Foundation engages in research into understanding Alzheimer's disease, supports the development of biomarkers for diagnosis, and researchers interventions to prevent and treat the disease. In 2020, the Foundation commenced a review of the opportunity to formally become a Medical Research Institute and this review will continue in 2021.

The Foundation provides world-class research facilities, employs research personnel, undertakes the insurance associated with conducting medical research, provides the accounting and HR support for a range of clinical trials and provides the governance structure required for conducting medical research.

We were delighted that Prof Colin Masters AO joined the Board in late 2020 bringing his wealth of knowledge in the field of Alzheimer's research to AARF. We'd like to thank Prof Masters for agreeing to Chair the Foundation's Scientific Advisory Committee and Research Governance Committee.

I would finally like to thank the Board, staff, researchers and the broader community who support the Foundation and the vital work we are doing into Alzheimer's disease research. We must continue to work collaboratively to find answers to this crippling disease and the Foundation is absolutely committed to do its part in supporting Alzheimer's research, whilst being financially prudent and having strong governance.

Graeme Prior
Chairman

The Board

GRAEME PRIOR

Chairman (Jul - Dec 2020)

DR TERRY BAYLISS

Deputy Chair

ROD O'DEA

Treasurer
Chair of the Future Fund Committee

ENZO SIRNA AM

Chairman (Jan - Jul 2020)

PROF COLIN MASTERS AO

Chair of the Scientific Advisory Committee and Clinical Research Governance Committee
(Oct - Dec 2020)

PROF RALPH MARTINS AO

Director of Research

JENNY DAY

Board Member

DR MICHAEL QUINLAN AO

Board Member (Jan - Oct 2020)

ROB DAVIES

Board Member

TIM ANDREW

Board Member

Vale Professor Michael Quinlan AO

On October 2nd, 2020 the Australian Alzheimer's Research Foundation lost a colleague, a leader and a friend.

Professor Michael Quinlan's considerable clinical, scientific and research experience was invaluable, and he will be greatly missed by his friends at the Foundation, both past and present.

Professor Michael Quinlan was a leading and highly respected Australian physician and educator who was deeply committed to the advancement of medicine, education, and healthcare. He was as a man of great integrity, knowledge, skill, and energy who had a sustained commitment to his profession.

Professor Michael Quinlan joined the Australian Alzheimer's Research Foundation Board in 2014 and will always be remembered for his kindness, intellect and passion for furthering research into Alzheimer's disease to improve the lives of future generations.

Michael's passing is a very sad loss of a kind, generous and intelligent human being and his invaluable contribution to the Foundation will always be remembered.

Board Committees

EXECUTIVE COMMITTEE

Graeme Prior
CEO - Hall & Prior Aged Care Group

Dr Terry Bayliss
Development Projects & Research Coordinator - Ramsay Health Care

Professor Ralph Martins AO
Professor of Neurobiology at Macquarie University, Foundation Chair of Aging and Alzheimer's disease at Edith Cowan University

Enzo Sirna AM
Deputy CEO - National Trust of WA

Rod O'Dea
Director - Insignia Finance

Liza Dunne
CEO - Australian Alzheimer's Research Foundation

FUTURE FUND COMMITTEE

Rod O'Dea
Director - Insignia Finance

Jemma Sanderson
Director - Cooper Partners

John Cunningham AO
Fellow - CPA Australia

Mark Hewitt
Director of Hewitt & Jones

CLINICAL RESEARCH GOVERNANCE COMMITTEE

Professor Colin Masters AO
Head of Department Neuropathology and Neurodegeneration - The Florey Institute

Dr Terry Bayliss
Development Projects & Research Coordinator - Ramsay Health Care

A/Professor Roger Clarnette
Consultant Geriatrician - Fremantle Hospital

Liza Dunne
CEO - Australian Alzheimer's Research Foundation

SCIENTIFIC ADVISORY COMMITTEE

Professor Colin Masters AO
Head of Department Neuropathology and Neurodegeneration - The Florey Institute

A/Professor Roger Clarnette
Consultant Geriatrician - Fremantle Hospital

Professor Ralph Martins AO
Professor of Neurobiology at Macquarie University, Foundation Chair of Aging and Alzheimer's disease at Edith Cowan University

Professor Roger Chung
Professor of Neuroscience - Macquarie University

Professor Melinda Fitzgerald
Professor of Neurotrauma - Curtin University

Professor Lars Ittner
Director, Dementia Research Centre - Macquarie University

CEO's Report

LIZA DUNNE

As the second leading cause of death in Australia, Dementia including Alzheimer's disease is an enormous challenge for our community. Whilst research continues into a cure, great strides are being made into developing low cost early diagnostics for Alzheimer's disease and risk reduction strategies that have the potential to significantly reduce the impact of this disease.

I am delighted to provide an update on the activities at the Australian Alzheimer's Research Foundation during 2020.

There is no doubt we must continue to support medical research into understanding this disease, how it can be diagnosed, treated and prevented. Alzheimer's disease is the most common cause of dementia accounting for approximately 70% of dementia cases. It is a progressive neurodegenerative disorder characterised by an unrelenting decline in cognition that ultimately results in death. Alzheimer's disease is the single greatest cause of disability in Australians aged over 65 with 1,800 new cases of dementia diagnosed each week in Australia.

We are proud of the work we are doing to support research into this insidious disease and we must do more. The Foundation receives no government funding and our ability to support Alzheimer's research relies on philanthropic support, corporate sponsors and income derived from conducting clinical trials with pharmaceutical companies.

We are indebted to the generosity of our many supporters, including corporations, small businesses, families and individuals. Our community supports us in so many ways – by participating in our research, fundraising, and advocating for what we do.

In 2020, the COVID pandemic presented some challenges. Understandably, many people directed their philanthropy to COVID-19 projects and events were cancelled. We were however, thrilled and humbled to receive several significant bequests in memory of people who have sadly experienced the decline brought about by Alzheimer's disease. Our sincere thank you to those families.

The Foundation is also indebted to Wesfarmers for their support, which was particularly important given the uncertainties presented in 2020 by COVID-19.

The cost of conducting medical research is significant. Whilst some direct costs such as researcher salaries may be funded by research grants, many other costs associated with conducting medical research are funded by the Foundation enabling researchers to focus on doing great research. Unlike many other Foundations, AARF funds a broad range of costs associated with Alzheimer's research including everything from keeping the lights on to ensuring facilities are research appropriate and world-class.

In addition to providing research facilities, our support extends to providing information technology, human resources management, risk management, insurance, finance, research governance, equipment and salaries. The Foundation currently employs 21 staff of which 17 are involved in direct research activities. The Foundation also contributes to the salaries of researchers employed at several universities.

The Foundation is also supporting the development of bright young minds in the field of Alzheimer's research by providing PhD scholarships and funding research programs that enable students to investigate their research hypotheses and publish their results. This directly assists their success in gaining future grant funding to forward their research endeavours.

The COVID pandemic also presented challenges to many of our research activities. Working with older people in the more at risk population for COVID-19, the immediate priority was the safety of our study participants and several research programs were put on hold for several months. Once research programs recommenced vigorous processes were implemented at each of our sites in compliance with health department guidelines to ensure the health and safety of our research participants and staff.

The Foundation also conducts clinical trials into new therapies in development for people who are diagnosed with early Alzheimer's disease, under the leadership of Dr Roger Clarnette. Thirteen pharmaceutical clinical trials were conducted at the Foundation in 2020 with most aimed at achieving cognitive improvements for people diagnosed with early Alzheimer's disease.

Evidence suggests that the changes within the brain begin years before clinical symptoms become evident. The scientific community has therefore shifted its focus to target patients earlier in the course of the disease with the belief those patients are more likely to benefit from therapy. This work not only provides an important income source for the Foundation but also contributes to the international research into a cure and enables people in Western Australia to participate in research into new therapies.

Professor Ralph Martins, the Foundation's Director of Research lead a team of exceptional researchers in 2020. There is a strong focus in the team on researching preventative strategies which complements the publication in The Lancet in 2020 which identified 12 modifiable risk factors which may prevent or delay up to 40% of dementias. It is never too early or late to focus on prevention. Some of these projects are summarised in this Annual Report.

I would like to thank our Board Members who volunteer their time and talents for the good governance and strategic leadership of the Foundation. In June 2020, Mr Enzo Sirna AM resigned as Chairman of the Foundation having served in the role for the last 7 years. Enzo's leadership, friendship and tireless commitment to the Foundation is greatly appreciated.

In 2020, the Foundation welcomed Mr Graeme Prior as Chairman who brings an incredible depth of knowledge in Alzheimer's disease research within Australia and internationally. Graeme is co-founder and CEO of Hall & Prior, a national aged care provider. Graeme is currently the President of the International Federation on Ageing and Deputy Chairman of the Commonwealth Government sponsored CRC for Mental Health. Graeme is also a Director of the Australian Aged Care Workforce Industry Council and a Committee Member of the Commonwealth Department of Health's Aged Care Sector Committee (Ministerial Appointment).

Most importantly, I would like to thank the researchers and support staff for their tireless work and support during a challenging 2020. Your work is contributing to the global knowledge of this disease and bringing us closer to an Alzheimer's free world. Thank you for the commitment you show every day.

Liza Dunne
CEO

We are indebted to the generosity of our many supporters, including corporations, small businesses, families and individuals. Our community supports us in so many ways – by participating in our research, fundraising, and advocating for what we do.

Financial Snapshot

TOTAL INCOME $4.2 M

15%	DONATIONS & SPONSORSHIP	$642,394
28%	BEQUESTS	$1,174,671
17%	CLINICAL TRIALS INCOME	$736,125
4%	RESEARCH & GRANT INCOME	$174,314
15%	RESEARCH PROJECT INCOME	$629,881
5%	INVESTMENT INCOME	$188,198
16%	OTHER INCOME (INCLUDING JOBKEEPER AND COVID STIMULUS)	$679,774

In 2020, 81% of the Foundation's expenditure was for direct research costs including researcher salaries, research facilities, research equipment and third party research services.

The audited financial statements are available on request.

TOTAL EXPENSES $2.9 M

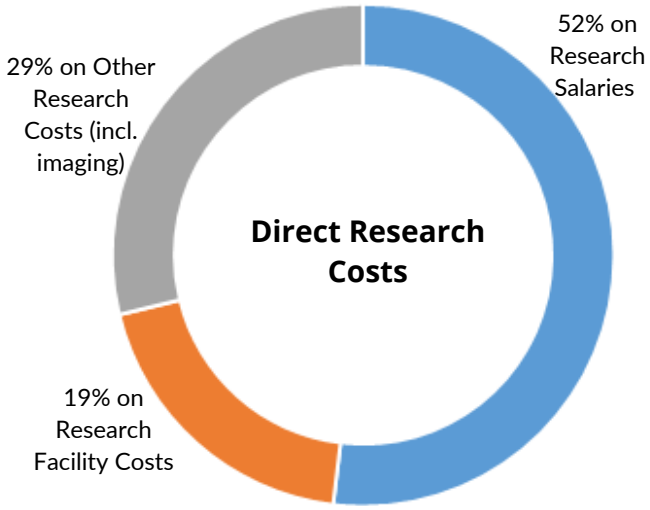
81%	DIRECT RESEARCH COSTS	$2,352,450
19%	INDIRECT COSTS	$568,922

Philanthropic support including donations, sponsorships and bequests are the Foundation's primary source of income. Additionally, the Foundation receives income from researching potential **new pharmaceutical treatments** for Alzheimer's disease.

Research project income includes funds received in prior years but recognised as income in 2020, as the funds were tied to specific projects conducted in 2020.

Direct costs include research salaries, scholarships, research facilities, research consumables, maintenance and depreciation of research equipment, external research consultants, service providers (for example brain imaging) and conducting clinical trials.

Indirect costs are vital services provided to enable research work to continue. These include information technology, finance, communications, fundraising, human resource management, research governance, risk management and insurance.



THE RESEARCH

The Australian Alzheimer's Research Foundation has a long history of providing support for vital research into Alzheimer's disease.

We provide world class research facilities and funding support for a broad range of Alzheimer's disease research programs under the leadership of Professor Ralph Martins.

Research Report

PROFESSOR RALPH MARTINS AO

My team and I have made considerable progress on our major research programs focussed on early diagnosis and prevention of Alzheimer's disease in 2020. This has only been possible due to the Foundation's longstanding supporters and the public for which we are deeply grateful.

Over the last 12 months we have been challenged by COVID disrupting our research activities. Nevertheless my amazing team and our wonderful participants regrouped and our work moved forward with exciting new developments which include cutting edge early diagnosis of Alzheimer's disease using blood biomarkers and retinal imaging biomarkers and being the only research group in Australia to undertake a lifestyle intervention program for the prevention of Alzheimer's in close collaboration. Our ongoing studies particularly the Sleep Improvement Study and the WA Memory Study have seen substantial growth thanks to the efforts of the team leaders who I will mention in detail below under their respective research programs.

This growth and advances in our research is only achievable with the tremendous support of our study participants, our donors and the Australian Alzheimer's Research Foundation (AARF) which provides state of the art facilities for our team and participants to work in, as well as essential support by providing doctors to assist in all our clinical studies. I am particularly grateful to Dr Roger Clarnette who has most generously given of his time to oversee the clinical aspects of our studies.

WA Memory Study and Centre of Healthy Ageing

In 1996 I had the privilege of establishing the WA Memory Study (WAMS) which has assessed over 2000 people over this time including those who are concerned about their memory. This assessment of memory and cognition is a free service provided by WAMS. This has helped many people identify memory problems and if requested, we are happy to send a report of the results to the participant's General Practitioner so follow-up with a Medical Specialist can be arranged. The findings from WAMS supported the PhDs of a number of prominent medical researchers including Dr Roger Clarnette and A/Prof Hamid Sohrabi. During the last 10 years A/Prof Sohrabi has played a leading role in WAMS and under his leadership WAMS has diversified and supported a number of our major research programs.

These include the Sleep Improvement Study, Hearing and Memory Loss Study, the internationally recognised AIBL study of ageing and more recently the major national NHMRC study called ADNeT (Australian Dementia Network) which screens people for their eligibility to enter clinical trials. These studies have led to a number of high impact publications of which A/Prof Sohrabi has played a central role. Last year he was appointed as an Associate Professor at Murdoch University and became the Director of the Centre of Healthy Ageing where he will establish his own team of researchers and students but will continue to be an integral member of my team supported by AARF. A/Prof Sohrabi represents members of my team who have grown to take up leadership roles in their own right but are committed to continue to working closely together to ensure we have a strong united front to combat Alzheimer's disease. In the last 12 months A/Prof Sohrabi has received several accolades and has been awarded grants. A major grant that Hamid is playing an important role in is to study the trajectory of cognitive change in large cohorts across the globe. This is a prestigious National Institute of Health funded study led by Professor Colin Masters.

Improving Sleep to Help Prevent Alzheimer's Disease

Another example of a member of my team "coming of age" is A/Prof Stephanie Rainey-Smith. She is playing a leading role driving her own research program and has made important advances in our understanding why good sleep is important for a healthy brain and has identified a unique genetic risk factor that impacts negatively on sleep leading to the build up of beta amyloid in the brain. She is currently undertaking a clinical trial to enhance good sleep to reduce the risk of Alzheimer's.

I am proud to announce that Stephanie has recently been appointed an Associate Professor at Murdoch University. While she continues to be a key member of my team, she will be working within Murdoch's Centre for Healthy Ageing with Hamid and Dr Belinda Brown. A/Prof Rainey-Smith should be doubly congratulated as she has also been awarded a prestigious 5-year Emerging Leader Investigator Grant which is funded by the National Health and Medical Research Council (NHMRC). Stephanie's Investigator Grant supports a program of research which will examine the relationship of sleep to cognition and markers of brain health. The research program will also explore whether interventions to improve sleep can prevent, or decrease the risk of, unhealthy brain ageing and cognitive decline.

The ongoing Sleep Improvement Study (SIS), for which recruitment is underway, and of which Stephanie is the lead investigator, forms part of this research program.

Stephanie was also successful in the 2020 'CogSleep Seed Funding Round', through which she was awarded a small grant for a project titled "Examining the impact of intensive lifestyle modification on sleep, cognition and dementia biomarkers". This research will be conducted as part of the AU-ARROW study, in collaboration with Professor Sharon Naismith (University of Sydney) and myself. AU-ARROW-Sleep will test whether intensive lifestyle modification (diet, exercise, and cardiovascular risk reduction) can improve sleep disordered breathing, sleep fragmentation, duration and other objective measures of sleep quality in older adults at-risk for cognitive decline and dementia, and will examine whether intervention-related improvements in cardiometabolic health and sleep predict 12-month improvements in cognitive function, and are associated with better dementia biomarker profiles.

After the COVID related delays, the last quarter of 2020 finally saw the commencement of the Early Detection of Alzheimer's Disease Subtypes (EDADS) Consortium; a multinational research project on personalised medicine for neurodegenerative diseases. This work is co-funded by the EU Joint Programme – Neurodegenerative Disease Research (JPND) and the NHMRC, and Stephanie is the Australian Research Lead (by invitation) examining the contribution of modifiable risk factors. More to follow as this research gains momentum.

Over the last twelve months she has successfully built her team of PhD students, with five of them achieving Confirmation of Candidature and four students publishing the first manuscripts of their studies.

Blood Based Biomarkers for the Early Diagnosis of Alzheimer's Disease

Over the last 25 years I have been chasing a blood test for Alzheimer's disease. Many researchers in our field thought this was not possible but I persevered with my team and I am happy to report that over the last 2 years promising candidate blood biomarkers have been identified with one candidate biomarker in particular showing the most promise in our studies. Our recent study published in Translational Psychiatry showed that a particular protein (glial fibrillary acidic protein or GFAP) was increased in the blood in cognitively unimpaired older adults at risk for Alzheimer's disease. GFAP is present in brain cells, known as astrocytes that provide nourishment to neurons. Under disease conditions GFAP is overexpressed in the astrocytes and leaks into the blood.

Our future studies will validate our findings in the much larger AIBL cohort as well as examine GFAP along with a panel of other potential blood-based makers (such as the phosphorylated forms of the protein tau, a major component of the Alzheimer's disease brain pathology called neurofibrillary tangles) to develop an accurate blood test for Alzheimer's.

While it has taken several years to reach this point I am confident a blood test for Alzheimer's disease is imminent. However, it must be noted that a number of factors were essential to take us to this point including the use of a highly characterised cohort. Together with adjunct A/Prof Kathryn Goozee, I established the KARVIAH cohort in 2013, which was supported by AARF and funded by Anglicare, which provided a grant of $2 million to enable 100 older people to be brain scanned for beta amyloid at two time points and to be extensively memory tested. This cohort has been invaluable for our blood biomarker work with 11 publications over the last 12 months including our recent GFAP paper, which has attracted international attention.

I am indebted to the Lions Alzheimer's Foundation who raised $300,000 to purchase a Simoa HD-X Analyser platform which enables us to accurately measure GFAP and other brain proteins in blood. The Simoa is the only equipment of its kind in WA and the only one in Australia dedicated to Alzheimer's disease research. I am also grateful to AARF for providing $100,000 from a generous donor to allow us to purchase the kits needed to perform the measurement of these proteins in blood. We need continued funding support for our blood biomarker work in order to build on our current findings for a successful conclusion. I need to acknowledge Dr Pratishtha Chatterjee from Macquarie University who has played a major role working tirelessly on this blood biomarker project in close collaboration with my PhD student Steve Pedrini.

PhD completions

I am proud to announce that two of our PhD students completed their theses with flying colours. Dr Sherilyn Tan from UWA investigated the role of testosterone on memory and cognition in men and published a major review article evaluating the work done globally to support the importance of testosterone treatment for the prevention of Alzheimer's. Dr Tan's work dovetails nicely with the world first testosterone clinical trial that is funded and sponsored by AARF at the Sarich Neuroscience Institute in Perth and at Macquarie University in Sydney. Dr Pamoda Jayatunga is from ECU and her research topic was entitled "Investigation of selected nutraceuticals to protect against mitochondrial dysfunction". Mitochondria are the powerhouses of the cells in our bodies that are essential for maintaining our normal activities. Pamoda identified known compounds like Curcumin and the omega3 DHA as well as some novel agents that together had a synergistic effect on protecting neurons.

I have tried to highlight some of our exciting projects but unfortunately have not done justice to many members of my team. They are all amazing and doing great work. They include Dr Belinda Brown, Dr Prashant Bharadwaj, Dr Eugene Hone, Dr Samantha Gardener, Dr Binosha Fernando and Dr Ian Martins as well as several research assistants who play key roles in the success of all our projects. I am indebted to Kevin Taddei who has given so much of himself to oversee all our projects and is the reason why our team has been so successful.

I am grateful to Enzo Sirna AM the recent past Chair of AARF and Graeme Prior the current Chair and all the AARF Board and Liza Dunne and her staff who are committed to supporting my team to work together towards our vison to END Alzheimer's.

Lastly, but most importantly a very big thank you is extended to all our donors, past and present, small and large. Your continued interest, friendship and support are critical to the outcomes we are striving for to successfully combat Alzheimer's disease.

Ralph Martins AO
Director of Research

WA Memory Study (WAMS)

Prof Ralph Martins, PhD
A/Prof Hamid Sohrabi, PhD
Mr Kevin Taddei, MSc
A/Prof Michael Weinborn, PhD
A/Prof Stephanie Rainey-Smith, PhD

Our longitudinal flagship study, the WA Memory Study (WAMS) started in 1996 and has been endeavouring to achieve the following aims:

- **To identify factors influencing cognitive functions in ageing;**
- **To follow up the longitudinal trajectory of cognitive change in ageing;**
- **To identify biological and clinical changes that can be used for screening those at higher risk of Alzheimer's disease.**

The WAMS also provides an invaluable platform for affiliated researchers, their students and volunteers to collect data, to observe and learn clinical and neuropsychological assessments and to investigate new hypotheses on cognitive ageing and future risk of dementia. The WAMS is also a service to the community by providing clinical and neuropsychological assessments to those who have been referred to us from community sources and clinical settings.

WAMS Study Team

Pictured above (L-R): Jo Shaw, Kevin Taddei, Prof Ralph Martins, A/Prof Hamid Sohrabi, A/Prof Stephanie Rainey-Smith, Dr Nick Carrigan

The WAMS has approximately 276 active participants and we are very grateful to our study participants, donors, volunteers and students for their critical contribution to this study.

WAMS is also developing several novel measures of subjective memory decline:

- McSCI – for screening those at risk of future dementia.
- WA Prospective Memory Test - potential use in the differential diagnosis of dementia.
- WA Olfactory Memory Test – assesses olfactory memory abilities that are uniquely affected in different types of dementia.

The first round of data collection has been completed for these novel measures and validation work is in progress.

In 2020, the WAMS was awarded research support from the Charlies Foundation to validate some of its assessment tools using specialized clinical assessments and lumber puncture. Through lumber puncture we will collect samples from cerebrospinal fluid and will analyse them for different biomarkers related to Alzheimer's disease. Our sincere thanks to the Charlies Foundation for providing these funds to further Alzheimer's research and enable this collaboration between the Australian Alzheimer's Research Foundation and clinicians at Sir Charles Gairdner Hospital.

The WAMS has also received WA Government funding to the Murdoch University Centre for Healthy Ageing to examine the effects of COVID-19 pandemic on the mental health of older adults here in Western Australia. This is a big step towards future national and international collaborations.

There are currently two active PhD students involved in the WAMS, including Miss Rasangi Seneviratne and Miss Hadeel Tarawneh.

Finally, we have published several papers using data from the WAMS or in collaboration with WAMS investigators, which are listed at the back of the Annual Report.

WAMS STUDENT PROFILES

At the Australian Alzheimer's Research Foundation, we are committed to training the next generation of Alzheimer's researchers.

HADEEL TARAWNEH

STUDENT PROFILE

Supervisors:
Dr Dona Jayakody, ESIA
A/Prof Wilhelmina Mulders, University of Western Australia
Prof Ralph Martins, Edith Cowan University
A/Prof Hamid Sohrabi, Murdoch University

HER RESEARCH

Cognitive decline has been shown to be strongly associated with hearing loss and changes in auditory processing skills. In fact, untreated hearing loss has been identified as a modifiable risk factor for developing dementia. Objectively investigating auditory functions in populations at risk of developing Alzheimer's disease using auditory electrophysiological measurements, the measure of the brain's electrical responses to sound, can potentially be a screening measure for pre-clinical Alzheimer's disease. Previous research conducted on auditory electrophysiological measures has focused on participants with Alzheimer's disease at different severities and participants with mild cognitive impairment. However, to date no auditory electrophysiological research has been conducted on people with subjective cognitive decline (SCD) in comparison to healthy controls. Individuals with SCD, i.e., self-reported decline in cognitive function without impairment on cognitive measures, are considered at higher risk of developing AD. My PhD project aims to bridge the knowledge gap by investigating the association of objective measures of hearing function with comprehensive neuropsychological data, an array of Alzheimer's disease related blood markers and neuroimaging biomarkers in people with and without SCD. Through this research we are better able to establish whether using these objective measures of auditory function can be used as a quick, non-invasive, and inexpensive screening tool for early Alzheimer's disease.

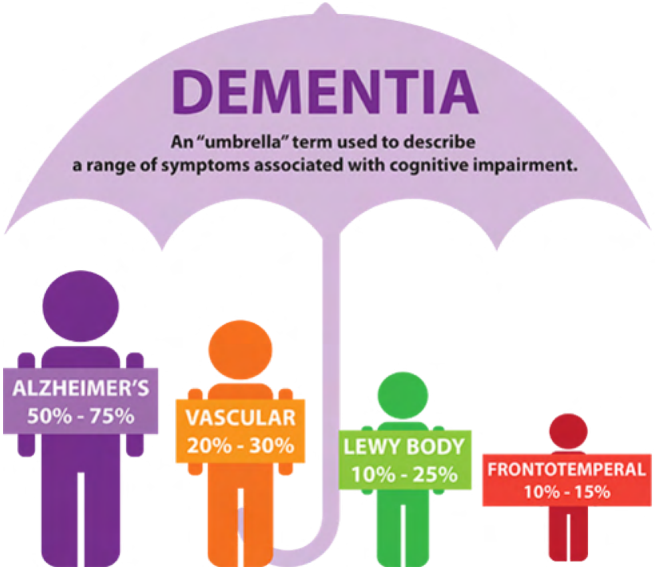
RASANGI SENEVIRATNE

STUDENT PROFILE

Supervisors:
A/Prof Michael Weinborn, University of Western Australia
A/Prof Hamid Sohrabi, Murdoch University
Prof David Badcock, University of Western Australia
Prof Ralph Martins, Edith Cowan University

HER RESEARCH

My research is looking at how your ability to learn and remember smells can help detect early signs of cognitive problems before a diagnosis of Alzheimer's disease. Subtle changes in our memory for smells could be an early sign of dementia. So, can we develop a comprehensive smell memory test that can be easily used by clinicians? Our results showed that the newly designed Western Australia Olfactory Memory Test (WAOMT) was an accurate and reliable measure of smell memory, especially in people with below-average to very high smell memory abilities. We also found that the WAOMT predicted brain health after 18-months in areas that are vulnerable to ageing and dementia. These results are important, as the WAOMT could predict early signs of Alzheimer's disease even before problems are noticed on tests of general memory skills (such as learning and remembering words), or smell naming abilities.



AIBL Study

Prof Ralph Martins, PhD
A/Prof Hamid Sohrabi, PhD
Mr Kevin Taddei, MSc
A/Prof Stephanie Rainey-Smith, PhD
Prof Simon Laws, PhD
A/Prof Michael Weinborn
Dr Samantha Gardener

The AIBL Study has collected up to 9 timepoints of data at 18-month intervals in over 2500 participants, yielding a current database of more than 8600 person-contact years.

The multicentre, multidisciplinary approach and engagement of Aβ-amyloid imaging from the outset has enabled AIBL researchers to make world-class contributions to understanding the natural history of Alzheimer's disease progression.

Using data from the AIBL cohort, the very slow accumulation rate of Alzheimer's-related pathologic change has been calculated, the diagnostic and prognostic utility of Aβ-amyloid imaging have been confirmed, and a wide window of opportunity for prevention trials has been identified. This vital, new knowledge has been translated to the design and implementation of trials to prevent progression to dementia, including the AU-ARROW Study which will enrol its first participants in 2021.

Whilst the events of 2020 saw the disruption of AIBL's normal activities in both Perth, and to a greater extent, Melbourne, participants continued to undertake their 144-month assessments and some new participants were enrolled into the study. The break from usual activities provided an excellent opportunity to quality control existing data and to write a comprehensive manuscript summarising the achievements of AIBL over the past 15 years. This manuscript has now been accepted for publication in the Journal of Alzheimer's Disease Reports.

See a full list of the AIBL 2020 publications at the back of this report.

The AIBL Study is internationally recognised for its significant contribution to the global understanding of Alzheimer's disease.

AIBL Study Team

Pictured above (L-R): Lucy Lim, Kelsey West, Mark Rodrigues, Dr Nick Carrigan, Kevin Taddei, Prof Ralph Martins, A/Prof Stephanie Rainey-Smith, A/Prof Hamid Sohrabi, Samuel Rocchi, Dr Samantha Gardener, Magdalene Soh

ADNeT

Prof Ralph Martins, PhD
A/Prof Hamid Sohrabi, PhD
Mr Kevin Taddei, MSc
A/Prof Stephanie Rainey-Smith, PhD
Dr Samantha Gardener

Australian Dementia Network
REGISTRY. CLINICS. TRIALS.

The Australian Dementia Network (ADNeT) is the largest single research program funded to date through the NHMRC's $200 million Boosting Dementia Research Initiative, receiving $18 million in funding with $2 million additional support from philanthropic organisations, the Wicking Trust and the Yulgilbar Foundation.

Dementia is the second leading cause of death in Australians and remains the single greatest cause of disability in Australians aged 65 and over. It is estimated to cost the nation more than $15 billion annually.

The Australian Dementia Network of leading scientists and researchers from across 15 institutions, are working together with the aim of:

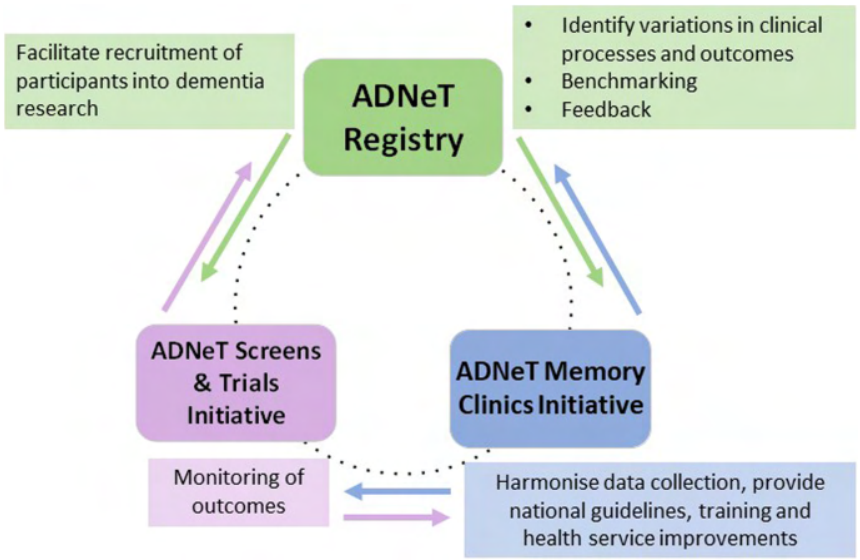
- establishing the first dementia clinical quality registry to track, benchmark, and report on the clinical care of people with dementia (Registry);
- establishing consistent best practice guidelines for the diagnosis and treatment of dementia (Memory Clinics);
- facilitating the development of effective therapies by providing detailed dementia screening of patients suitable for participation in clinical trials (Screening and Trials).

Led by Professor Chris Rowe nationally, ADNeT is comprised of 25 investigators, 12 institutions and a broad spectrum of government, clinicians and consumer advisors. ADNeT is supported by the National Health and Medical Research Council (NHMRC), The Wicking Trust, The Yulgilbar Foundation, Dementia Australia, and Neuroscience Research Australia (NeuRA).

Professor Ralph Martins and his team at Edith Cowan University, lead the ADNeT site in Western Australia at AARF contributing to two key initiatives:

- ADNeT-Clinics to improve diagnosis of dementia via a national network of memory clinics with close links to primary care; and
- ADNeT-Trials to develop a large, highly-characterised cohort of people with dementia, or at increased risk of dementia, to populate a Trials-Ready Cohort for participation in cutting-edge clinical trials.

2020, saw the establishment of the ***Perth ADNeT-Trials*** site within the clinical research facility of the **Australian Alzheimer's Research Foundation**, on the ground Floor of the Sarich Neuroscience Research Institute building on the QEII medical campus. The Perth site has received more than 40 referrals from specialists and commenced screening, with patients getting free access to amyloid PET brain scans amongst other tests. Further information about ADNeT can be obtained by visiting the website: australiandementianetwork.org.au



"The ADNeT screening and trials initiative will give more West Australians access to the latest potential therapies to prevent or treat dementia through participation in clinical trials".

Professor Ralph Martins

The Personal Impact

Anne is one of our generous supporters and is learning to live with Alzheimer's disease in her family right now. This is Anne's story:

In a way, mum was a self-fulfilling prophecy. From my early teens I remember her saying, 'I hope I don't end up like my mother'. Grandma was a quiet and gentle but very withdrawn lady. Looking at photos of her, her eyes seem empty. This was in the 1950s and the word we used was 'senility'.

Over the years the fear of being like her mother grew and as mum reached her 60s the signs were there. It was a strange time for the family as dad was in denial and thought I was wrong. I wish I had been. We never discussed it with mum or anyone else, we just fumbled through. So I have no idea how mum felt in those early years of dementia. I do recall her rummaging and organising her wardrobe and drawers. Now I suspect she was depressed.

A few years after dad died, mum went into a care home. It was in the city where she was brought up and still had friends and ex-neighbours who visited regularly. As her memory of more recent events disappeared, she seemed to construct a life based on a remembered past, of a time that made sense of her current situation. Of course, there was no place for me, my brother, or, sadly, her grandchildren – none of us had been born in the period in which she thought she was living. But while that was hard for us, she appeared to be content.

There was one occasion when my husband Tony and I visited her. We chatted for a while and suddenly she addressed me, 'I can't remember your name, but have you met my friend Tony'. We managed to conceal our shock tinged with amusement and the conversation moved on. We had to accept that was how things were and be glad she was enjoying having visitors.

I am lucky so far. I have outlived mum and show no signs of having memory loss, or not that I recall anyone telling me! By being part of one of the research studies at the Australian Alzheimer's Research Foundation called AIBL, **I can help in a small way to enable research into Alzheimer's disease to continue**. There is much more information available about Alzheimer's disease than there was for my grandma and mum, but how much more satisfying it is to think I am contributing to finding a cure.

Sincerely,

Anne

AU - ARROW

Prof Ralph Martins, PhD
Dr Samantha Gardener, PhD
Mr Kevin Taddei, MSc
A/Prof Stephanie Rainey-Smith, PhD
Dr Belinda Brown, PhD
A/Prof Hamid Sohrabi, PhD

The AU-ARROW clinical trial is a collaboration of over 30 Australian scientists, as well as being a member of the world-wide collaboration, World-Wide FINGERS.

WW-FINGERS has developed rapidly following the success of the original FINGER study (Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability), with the same four lifestyle domains, physical activity, diet, cognitive activity and medical monitoring, which will be implemented in AU-ARROW. The AU-ARROW study protocol will follow closely that of the US-POINTER study (also a member of WW-FINGERS), to enable data sharing and greater international collaboration.

The study will recruit 450 participants (150 in Perth) aged 60 - 79 clinically assessed to be at increased risk of cognitive decline and dementia in later life. Participants will be randomly allocated to either the intervention (Multidomain Lifestyle Intervention) or control (Health Education and Coaching only) group. The study is a two-year intervention that will be conducted across two sites in Australia: the Macquarie University Health Clinics, Sydney, NSW, and the Australian Alzheimer's Research Foundation, Perth, WA.

In the past year, AU-ARROW has appointed two study coordinators, Dr Samantha Gardener (Perth site coordinator) and Dr Stephanie Fuller (Sydney site coordinator), and a principal dietitian, Dr Juliana Cheng, and exercise physiologist, Dr Belinda Thompson. The study clinicians have also been appointed, Dr Andrew Gleason and Dr Catriona Ireland in Sydney, and Dr Roger Clarnette in Perth.

The study received ethical approval at both sites in December 2020 through Macquarie University and Ramsay Health Care. The setup of the study is well underway with gyms being sought for the exercise intervention, necessary equipment purchases, and data sharing agreements being finalised. Recruitment is expected to commence mid-2021, once all procedures are in place and the sites and facilities are ready.

The AU-ARROW Study has received full stipend support from the Australian Alzheimer's Research Foundation for a PhD student to undertake their research program at Murdoch University under A/Prof Hamid Sohrabi, A/Prof Stephanie Rainey-Smith and Dr Belinda Brown using the AU-ARROW data.

The AU-ARROW clinical trial brings Australia into the international initiative for dementia risk reduction and optimising cognitive function across the ageing lifespan.

WW-FINGERS-SARS-COV-2 SURVEY

The WW-FINGERS network has developed a COVID-19 questionnaire which is being undertaken worldwide by the countries participating in the network. As seniors represent the group most severely affected by the COVID-19 pandemic in terms of higher morbidity and mortality, the main aim of the survey is to collect information to better understand the direct and indirect consequences of the pandemic on the lifestyle, health and wellbeing of seniors. This will help to develop strategies to mitigate negative effects of the current or future pandemics on populations, especially seniors, who are the most vulnerable.

AU-ARROW

WORLD WIDE FINGERS
alzheimer's association

https://www.alz.org/wwfingers/overview.asp

The Dominantly Inherited Alzheimer's Network (DIAN) Observational Study

Prof Ralph Martins, PhD
A/Prof Hamid Sohrabi, PhD
Mr Kevin Taddei, MSc
Dr Samantha Gardener, PhD
Dr Pratishtha Chatterjee , PhD

The DIAN study in an international, multi-site collaboration aiming to identify the biological changes that occur in the development of Alzheimer's disease to improve early diagnosis and to track progression of the disease. This study specifically collects biological information from adults who have parents with a known inheritable, genetic mutation for Alzheimer's disease causing a young onset, familial type of the disease.

Prof Martins leads the Perth DIAN site, one of 13 DIAN sites around the world, and with the support of the Australian Alzheimer's Research Foundation has contributed to a long list of achievements recognised worldwide. These including the first blood based biomarkers panel to identify those at higher risk of developing the disease and DIAN has begun clinical trials of drugs to see if they can prevent the onset of Alzheimer's disease symptoms in family members who are at risk. The Australian Alzheimer's Research Foundation Clinical Trials Division is participating in the DIAN-TU trials for these new therapies.

The Perth site has 27 active DIAN participants enrolled in the DIAN Observational Study undergoing week-long assessments every two years with a remote visit in the interim year. The COVID-19 pandemic provided many challenges in 2020 and we are lucky to have managed to continue seeing our participants as required throughout the year. COVID has led to the inclusion of telehealth appointments (by videoconference) which will revolutionise the conduct of studies in the future and ensure that at least a minimum of data can continue to be collected.

DIAN
Dominantly Inherited Alzheimer Network

Track D-CAA Study

Tracking the Natural History of Dutch-type Hereditary Cerebral Amyloid Angiopathy.

Within the DIAN study larger cohort, we have a very unique group of individuals with a mutation that causes haemorrhagic stroke. It is known as the Dutch-type hereditary cerebral amyloid angiopathy (D-CAA).

Prof Martins' Lab and a team in the Netherlands are the only groups worldwide with such a group of D-CAA participants. In 2016, A/Prof Sohrabi attended a conference on CAA in London that was organised by Prof Steve Greenberg (Boston General Hospital, USA) and Prof Mark van Buchem (Leiden University Medical Centre, the Netherlands). His meeting with these two leading CAA researchers resulted in further collaborative work aimed at future clinical trials for this condition. To further the collaboration, Prof Martins, A/Prof Sohrabi and Mr Taddei visited the Lab in the Netherlands and discussed the potential of a clinical study on these individuals with an international team of scientists who gathered in Leiden to discuss the design of this trial.

Australian Alzheimer's Research Foundation Head Office, Perth, where the DIAN and Dutch-CAA studies are conducted.

In 2020, the international team of scientists formed an alliance (called the D-CAA Consortium) to design a study referred to as TRACK D-CAA. This collaboration will see 50 participants in Perth from families carrying the mutation for D-CAA assessed over two years, with a further 50 participants in Leiden, the Netherlands. This hereditary abnormality causes a protein related to Alzheimer's disease (amyloid beta) to accumulate in the blood vessel wall, which makes it more vulnerable. During the course of the disease, small brain bleeds and larger bleeding may occur, as well as various complaints such as epileptic seizures, headaches and memory problems. The study will investigate which complaints people develop and how the disease progresses.

D-CAA is the young onset version of a similar condition that is more prevalent in the elderly population and is considered a silent cause of stroke. Identifying a young onset group with this condition is likely to be of great importance to the much larger group of older adults who may develop this condition. Following this two-year study, it is hoped a clinical trial with possible treatments for these individuals will commence. The study will be conducted at the Australian Alzheimer's Research Foundation in Perth.

In 2020 an important manuscript using data from our DIAN participants was published, led by Dr Pratishtha Chatterjee at Macquarie University, Sydney NSW. This manuscript investigated alterations in the blood of participants carrying the mutation that causes the D-CAA compared with non-carriers of the mutation.

Of the 275 molecules measured, 22 had lower levels in the mutation carriers, and these molecules have the potential to serve as a blood marker for CAA before symptoms are seen. The molecules observed to have altered levels in the blood have previously been reported to be associated with processes associated with Alzheimer's disease including oxidative stress and inflammation.

TRACK D-CAA is currently in the initial stages of being set up with protocols being written and ethical approval application. We hope to commence recruitment in July 2021 and have 50 participants recruited by the end of June 2022. The Australian Alzheimer's Research Foundation will be the sponsor of this international collaboration and will contribute to the advancement of knowledge and hopefully to a clinical trial aimed at prevention of the D-CAA.

A/Prof Hamid Sohrabi with Prof Ralph Martins and colleagues from the Netherlands collaborating on the D-CAA Study.

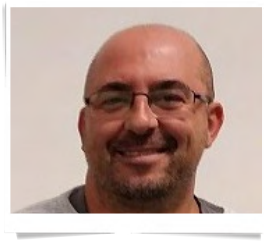
Blood-based Biomarkers

Currently, there is no cure or effective treatment for Alzheimer's disease despite all scientific efforts and therefore, more recent clinical trials are focussing on prevention programs for Alzheimer's disease, thereby making the identification of populations at risk of Alzheimer's disease paramount.

The existing markers to identify populations at risk are expensive and unfriendly for high throughput screening or are invasive in nature, restricting the implementation of these markers for standard clinical practice and as screening tools in clinical trials. In contrast, the cost effective and less invasive nature of blood-based biomarkers will serve as attractive surrogate markers for initial clinical diagnostic testing and screening for clinical trials.

Our recent study published in Translational Psychiatry showed that a particular structural protein (glial fibrillary acidic protein or GFAP) present in the type of brain cells that provide nourishment (astrocytes) to the brain cells responsible for transmitting information to other nerve cells (neurons) was higher (≈ 60%) in the blood in cognitively unimpaired older adults at risk for Alzheimer's disease. Additionally, GFAP along with the known risk factors for Alzheimer's disease, namely, age, gender and apolipoproteinE ε4 carrier status, provided a sensitivity = 85% and specificity = 80% to identify cognitively unimpaired older adults at risk for Alzheimer's disease.

These observations could be attributed to a compromised blood-brain barrier along with a process called "astrogliosis" (i.e. the proliferation of astrocytes) occurring within the 20-30 year preclinical phase of Alzheimer's disease, however, further validation studies are required. Studies in the future also need to examine GFAP along with a panel of other potential blood-based makers (such as the phosphorylated forms of the protein tau) to increase the detection sensitivity of this potential blood-based marker for individuals at risk for Alzheimer's disease and specificity against other neurodegenerative diseases.



Mr Steve Pedrini
Senior Research Fellow and PhD Candidate, Edith Cowan University

Dr Pratishtha Chatterjee , PhD
Senior Research Fellow, Macquarie University

We have also analysed the involvement of high-density lipoprotein (HDL) in Alzheimer's disease, as previous studies have suggested that high levels of cholesterol might be a risk factor for the disease. The carriage of cholesterol and lipids through the body is mediated via lipoproteins, and HDL is regarded as a "good" lipid complex due to its ability to clear the excess cholesterol via 'cholesterol reverse transport'. During its maturation, HDL particles range from the newly formed small HDL, to much larger HDL. Our study published in the Journal of Alzheimer's Disease showed that small HDL is overall reduced in Alzheimer's disease patients and that lower levels of small HDL are associated with reduced cognitive performance.

Further studies will determine at what stage of Alzheimer's disease these alterations to small HDL occur and how they are involved in the progression of the disease. However, these data support the notion that patients with Alzheimer's disease exhibit alterations in their plasma lipoprotein profile, suggesting another area of interest with regards to blood-based biomarkers.

The Australian Alzheimer's Research Foundation supports a number of clinical trials from which the data has been used in these findings. This includes the provision of research facilities for the AIBL and DIAN studies in Western Australia.

Retinal Imaging

The diagnosis of Alzheimer's disease, the most common type of dementia facing our ageing population, is highly challenging for healthcare professionals.

There are currently no quick low cost screening tests that can reliably identify affected individuals, or those at risk of developing the disease. There are promising brain imaging methods being researched that are based on a technique known as Positron Emission Tomography (PET imaging). Their main advantage is there is no requirement for highly invasive procedures and are considered by many researchers to be the de facto standard for measurement of brain amyloid. However, brain imaging for Alzheimer's disease is not readily available, is expensive and is not standardised for clinical use.

Dr Hone, based at the Sarich Neuroscience Institute in Perth, and Dr Shah from Macquarie University in Sydney are currently testing a prototype retinal imager for feasibility as a non-invasive screening tool to help identify individuals with high brain amyloid.

The camera uses hyperspectral imaging techniques, which were first developed for mining and geology. Early studies of these techniques in animal models have shown encouraging results. Because the eye presents as an external surface of the body and shares many neural and vascular resources with the brain, it could offer a window into brain amyloid status. The retinal imager fits on a desk no larger than what you would find at the optometrist. This could lend itself to being a relatively inexpensive biomarker for Alzheimer's disease which can potentially be implemented widely.

Dr Eugene Hone, PhD
Senior Research Fellow, Edith Cowan University

Dr Tejal Shah, PhD
Research Fellow, Macquarie University

In the Perth arm of the Retinal Imaging Study, eligible volunteers are recruited from existing cohorts of other studies. To date, approximately 80 individuals have been imaged. We have also begun to develop machine learning algorithms for image analysis. This is needed due to the large volumes of data captured in each image. The study is still in its infancy and the algorithms require a much larger dataset to be trained for accuracy.

Professor Ralph Martins, Australian Alzheimer's Research Foundation

> ***Thank you to the Lions Alzheimer's Foundation who provided the Optina Hyperspectral Retinal Camera for this research***
>
> ***- Professor Martins***

Childhood Dementia

Dementia is usually considered an ageing disorder and cognitive decline in children has received little attention. However, it is estimated that one in every 2,800 babies is born with a genetic condition that leads to childhood dementia.

Childhood dementia is mostly caused by a group of 70 rare genetic diseases (called autophagy-lysosomal storage disorders (LSDs)), that result in deficiency of an enzyme leading to the accumulation of un-degraded or partially degraded material.

Because of its rarity, there is a lack of understanding of the molecular neuropathology and awareness of the disorder and currently there are no effective treatment options or ways to measure disease progression and response to treatment (1).

The autophagy-lysosomal pathway is a waste removal process that clears unwanted proteins, lipids, sugars and damaged organelles, and evidence indicates that impairment in this pathway is a central mechanism in Alzheimer's disease. Alzheimer's disease is associated with a build-up of aggregated proteins including beta amyloid and tau, whereas LSDs predominantly features accumulation of lipid, cholesterol, or sugar molecules.

Dr Bharadwaj, an expert in autophagy and Alzheimer's disease, has recently initiated a lab-based and clinical biomarker study in childhood dementia, with the long-term aim of establishing a stem cell lab for human derived neuron cell models to investigate novel treatment strategies for LSDs and for developing prognostic biomarkers to measure disease progression.

For the lab-based research project, Dr Bharadwaj is collaborating with the stem cell lab at Lund University, Sweden (Dr Isaac canals), autophagy and neuronal trafficking experts Prof Subhojit Roy (University of California San Diego) and Prof Wai Haung (Ho) Yu (Centre for Addiction and Mental Health (CAMH) Toronto, Canada.

Dr Prashant Bharadwaj, PhD
Research Fellow, Edith Cowan University

Dr Bharadwaj has recently established a neural stem cell line investigating Sanfilippo syndrome that causes childhood dementia. Further analysis is being undertaken to characterize autophagy-lysosomal defects in this disease model. A masters student Ms Amrita Das from University of Western Australia has been recruited for this project and will be working under Dr Bharadwaj and Prof Martins.

For the biomarker study, Dr Bharadwaj is working closely with clinicians across Perth including Dr Maina Kava (Consultant Paediatrician, Perth Children's Hospital) and neurologists to recruit families affected by childhood dementia. This study will use blood and urine samples collected from children affected by LSDs. Plasma will be analysed for protein biomarkers using the ultra-sensitive Simoa® HD-1 Analyzer recently established in Prof Martins' lab. This technology will be combined with the mass spectrometric expertise at Prof Maria Fuller's lab in South Australia for lipid and sugar analysis in urine. Correlation of blood and urine biomarkers to clinical pathology will be assessed to identify prognostic biomarkers that inform disease severity and progression.

It is estimated that one in every 2,800 babies is born with a genetic condition that leads to childhood dementia

(1) Bharadwaj, P, Martins, R, "Autophagy and Lysosomal Storage Disorder in Late-Onset Alzheimer's and Childhood Dementias", *Dementia: A Global Approach*, 2nd Edition (in press)

Nutrition & Alzheimer's disease

Our understanding of dietary influences on Alzheimer's disease is in its infancy; however, a growing number of work shows a strong relationship between nutrition and Alzheimer's disease.

Whilst saturated fats and high serum cholesterol is associated with an increased risk of Alzheimer's disease, we identified the consumption of short chain fatty acids and antioxidants rich compounds appear to lower risk.

Our work with mouse models of Alzheimer's disease reported that short chain fatty acid butyrate had significant effects on beta-amyloid peptide (Aβ) levels and associative learning and cognitive functioning. There was a 40% reduction in brain Aβ and a 25% increase in fear response in both the cued and contextual testing. These findings propose that sodium butyrate warrants further investigation as a potential therapeutic agent of Alzheimer's disease.

Consequently, we investigated the ability of sodium butyrate to attenuate toxicity of amyloid-beta in an in-vitro cell model. Our results indicated that sodium butyrate had profound effects on Aβ levels in M17 (neuroblastoma cells) cells by reducing the Aβ toxicity in cells. While the precise mechanism by which amyloid pathology is impaired by butyrate remains to be elucidated, we identified that when the cells were treated with butyrate, a 10-fold reduction in both load and surface stiffness was observed following nanoindentation.

Even though these results are preliminary, it will be interesting to find out the influence of M17 cells becoming soft at the presence of butyrate and how the interaction between Aβ and cells can be altered. Currently we are seeking funding to explore further to what extent these alterations in adhesion, cohesion, elastic and viscous properties of neuronal cells at the presence of butyrate can reduce the damage from Aβ and to initiate a clinical trial.

With industry support I am also investigating the effect of polyphenols from sorghum (PhD student, Nasim Rezaee), sea buckthorn (Dr Kevin Dong) and grape seed (MSc, Lahiru Ranepura) to reduce the toxicity of amyloid beta at cellular levels. The results so far demonstrated the significant effect of polyphenolic extract on the attenuation of Aβ-induced oxidative stress which is one of the main hallmarks of Alzheimer's disease.

Dr Binosha Fernando
Research Fellow, Edith Cowan University

Natural polyphenols could protect the brain from Aβ and tau neurotoxicity, ameliorating the oxidative damage and mitochondrial dysfunction.

- Sorghum is an underutilized grain that grows widely in Australia, where it is primarily used as feed for farm animals. It is rich with phenolic acids, flavonoids, and condensed tannins. Pigmented varieties of sorghum have the highest polyphenolic content and antioxidant activity which potentially makes them beneficial for human health, particularly for the prevention and treatment of neurodegenerative diseases.

- Sea buckthorn is a yellowish or orange berry, mainly growing in China, Mongolia, Russia, Northern Europe and Canada, and is popular for its high nutritional value and health benefits. Sea buckthorn is a rich source of vitamins, minerals, polyphenols, carotenoids, flavonoids and essential fatty acids.

- In the winery and grape juice industries, grape seeds waste is generated as a by-product. Grape seed extract is considered as a powerful antioxidant source because it has polyphenols such as gallic acid, resveratrol, flavonoids, including the monomeric flavan-3-ols catechin, epicatechin, gallocatechin, epigallocatechin, and epigallocatechin gallate, and procyanidin.

The 2020 publications related to this research are at the back of this report.

Genetic risk and resilience factors in Alzheimer's disease

One of the major research programs within the Centre for Precision Health, an Edith Cowan University Strategic Research Centre, involves developing a greater understanding of the biological pathways that underpin the earliest changes on the path to Alzheimer's disease. Understanding the basic pathological processes that contribute to disease is crucial for the design of targeted treatments and/or prevention techniques.

One major study is focused on the identification of epigenetic patterns and, in turn, novel biological pathways that are altered at the earliest stages of the disease process. This study will contribute new knowledge about the underlying causes of Alzheimer's disease, how it develops and progresses, particularly at the earliest stages of the disease where it is critical that interventions are implemented.

Currently therapeutic interventions for Alzheimer's disease have failed and one potential reason for this is that current treatments are not directed at the right targets. This study therefor has the potential to also provide improved avenues for the development of therapeutic interventions.

The longer-term impact of this study will be the ability to leverage the initial findings to support larger studies of gene expression to identify whether biological pathways are disproportionately altered as Alzheimer's disease progression advances. Doing so will provide strong evidence to prioritise pathways that are undergoing dynamic changes that track with disease progression and thus are the most optimal for targeting with pharmacological intervention. This is likely to result in the most effective treatment of the disease as it can be targeted at the earliest stages of the disease process.

Prof Simon Laws, Associate Dean, Medical and Exercise Sciences, Edith Cowan University,

The project was initially funded by two NHMRC grants but has been provided with added impetus through funding from the Australian Alzheimer's Research Foundation as a result of generous donations from Pinnacle Charitable Foundation and Spheria Asset Management. This funding has been integral to allowing the research to develop one of the world largest and most characterised longitudinal epigenetic datasets related to Alzheimer's disease.

From a technical perspective, this work will involve looking at the longitudinal levels of DNA methylation (an important epigenetic mechanism that sees the attachment of molecules to DNA) across the genome. This will allow us to assess the functional implications of these epigenetic variations to identify biological pathways that are altered at the very earliest part of the disease process and the mechanisms driving these alterations, particularly the integral role of an individual's interaction with their environment. We are hoping to have the initial results available through 2021.

PhD student Ms Lidija Milicic is working on this project and an outline of her research thesis is below.

LIDIJA MILICIC

STUDENT PROFILE

Supervisors:
Prof Simon Laws, Edith Cowan University
Dr Tenielle Porter , Edith Cowan University
Dr Michael Vacher, University of Western Australia

The overarching focus of Lidija's PhD work is the identification of markers of DNA methylation and their association with both risk for Alzheimer's disease development and related clinical and pathological changes that occur as the disease progresses. These changes include memory performance and changes in the brain, such as shrinking (atrophy) of brain regions as well as deposition of the key protein, beta-amyloid. Lidija is currently in the process of drafting a manuscript based on the results of the first study of her PhD, which has used specific methylation data to determine an individual's biological age in comparison to how old they are. This comparison allows the assessment of the relationship between advancing biological age, i.e. someone who is biologically older than their actual age, and Alzheimer's disease. Further work to be covered in Lidija's PhD will study methylation across the genome to identify individual markers and combinations of markers that are associated with Alzheimer's disease risk and related clinical and pathological changes.

Lidija has also recently been awarded a small grant from the Centre of Precision Health, one of Edith Cowan University's new Strategic Research Centres, for a project complementary to her PhD work, which aims to look at further markers of ageing in combination with advancing biological age in the context of Alzheimer's disease.

Exercise

There is compelling evidence that more physical activity is good for the brain in older adulthood.

However, for physical activity and exercise to be widely implemented as a prevention strategy for dementia, more evidence from rigorous research is needed. Our team uses different types of research studies and designs to understand the best parameters of exercise for brain health, and how the brain benefits from physical activity.

Our team has recently completed the **Intense Physical Activity and Cognition** (IPAC) study, undertaken as a collaboration between Murdoch University and AARF. The study commenced in 2017 and we recruited 99 individuals to undertake either six month high-intensity exercise or moderate-intensity exercise (or to enter a no exercise control group), and evaluated the effect of exercise on memory and thinking and indicators of brain health from brain scans.

We have just reported our primary findings in the journal *Alzheimer's Research and Therapy*: we did not find any differences in memory and thinking performance from before to after the exercise intervention between our groups. Nevertheless, we did find that **individuals that experienced the biggest improvements in cardiorespiratory fitness gained the greatest benefits in terms of improvement on tasks assessing memory and executive functio**n (organisational thinking and planning skills).

Dr Belinda Brown
Senior Research Fellow, Murdoch University

We also noted some influence of genetics on these associations, where we were more likely to observe a relationship between fitness and memory in individuals of certain genetic make-ups. This type of research pertains to a long-term research aim of ours, where we aim to gather sufficient evidence to be able to provide individually tailored exercise, based on genetic factors.

Although work from our team, and others, indicates that exercise can improve brain health and reduce dementia risk, we know that participants tend to stop exercising once an intervention finished. In 2019, our team was awarded a Dementia Collaborative Research Centre/Dementia Australia grant, that we will use to investigate the effect of high-intensity exercise on the brain, this time with the aim of creating a long-term behaviour change toward exercise. Our intervention will include ongoing education regarding exercise, and various behavioural change techniques. This study was delayed due to COVID-19 research restrictions; however, we plan to commence this work mid-2021.

NATALIE FROST
STUDENT PROFILE

Supervisors:
A/Prof Mike Weinborn, University of Western Australia
Dr Belinda Brown, Murdoch University

HER RESEARCH

Advancing age is commonly associated with neurocognitive decline, and heightened risk of dementia. These effects are most notable within the frontal lobes of the brain and associated executive functions. There is extensive literature supporting regular physical exercise as a protective factor against age-related neurocognitive decline. Although there is some observational data indicating an exercise intensity level beyond which neurocognitive benefits optimise, little interventional research systematically assesses intensity level in the relationship between exercise and neurocognitive health. To address this limitation, my doctoral research investigated whether there was an optimal exercise intensity level to promote maintenance of executive functions in older adults. To do this, I examined the interrelationships between exercise intensity, cardiorespiratory fitness, executive function, and frontal lobe grey matter volume in cognitively normal older adults. The results of my research did not provide evidence for a differential role of intensity in the relationship between exercise and neurocognitive health at a group level. However, it is possible that individual differences in experimentally induced changes in cardiorespiratory fitness may be associated with changes some executive function subdomains, as well increased grey matter volume in some frontal lobe regions. Future interventional studies should assess the role of inter-individual variance in neurocognitive response to exercise-induced cardiorespiratory fitness.

SHAUN MARKOVIC
STUDENT PROFILE

Supervisors:
Dr Belinda Brown , Murdoch University
Prof Melinda Fitzgerald, Curtin University
A/Prof Jeremiah Peiffer, Murdoch University
Dr Brendan Scott, Murdoch University

HIS RESEARCH

Shaun's PhD looks at how concussions affects the cognition and brain health of older adults in both its acute and chronic stages. Additionally, his project also aims to better understand how exercise and physical activity habits following concussion could improve recovery and reduce longer-term neurocognitive dysfunction. COVID-19 presented a significant challenge in 2020 and it was determined that, given the time constraints of a PhD, it was no longer feasible to continue the project as it was initially structured. The project originally required collecting face-to-face cognitive and biological data from older adults who had sustained a recent concussion at several time points over a 12-month period. Consequently, the project was changed to incorporate pre-collected data from the Intense Physical Activity and Cognition (IPAC) study and the UK Biobank. Furthermore, Shaun was also able to incorporate some of his research aims into a study run by Dr. Melinda Fitzgerald (external supervisor) which involved an online national survey of participants' experiences and self-reported factors contributing to improved or slowed recovery.

Sleep Improvement Study

The Sleep Improvement Study (SIS) is an intervention study which aims to assess whether memory and thinking (cognition) and neuroimaging biomarkers of brain health are improved following a cognitive behavioural therapy intervention targeted at improving sleep.

Compelling evidence indicates that sleep is a critical contributor both to cognitive health and to neurobiological changes in the ageing brain. Yet this study fills an important knowledge gap by being one of only a few to explore the utility of interventions to improve sleep as a preventative approach to decrease Alzheimer's disease risk.

Despite the COVID-related challenges of 2020, SIS continued to make steady progress with the intervention sessions delivered via telehealth instead of face-to-face. This ensured existing participants could continue their involvement in the study without disruption. Some newly enrolled individuals did however have to wait until restrictions had lifted before they could undergo their baseline sleep, cognitive and brain imaging assessments.

To date, more than 70 of the target of 90 participants have been enrolled in the study, with 2020 seeing the first wave complete their 18-month follow-up assessments, which mark the end of the study. Feedback from this first group was overwhelmingly positive with comments made such as "life changing" and "the best thing I ever did".

A/Prof Stephanie Rainey-Smith
Associate Professor, Murdoch University

Last year was also positive for the SIS team with two new PhD students (Louise Pivac and Nadia Soh) beginning their postgraduate studies. Louise and Nadia work on different aspects of SIS and will use data from the study in their PhD theses. Moreover, SIS lead investigator A/Prof Stephanie Rainey-Smith was awarded a 5-year Investigator Grant funded by the National Health and Medical Research Council (NHMRC). The NHMRC is the primary agency of the Australian Government responsible for medical and public health research. The Investigator Grant supports a program of research which will examine the relationship of sleep to memory and thinking (cognition), and markers of brain health. The research program will also explore whether interventions to improve sleep can prevent, or decrease risk of, unhealthy brain ageing and cognitive decline, with SIS forming part of this research program.

Sleep Improvement Study Team

Pictured above (L-R): Fatemeh Kamalinejad, Lucy Lim, Jo Shaw, Kevin Taddei, Prof Ralph Martins, A/Prof Stephanie Rainey-Smith, A/Prof Hamid Sohrabi, Louise Pivac

SLEEP IMPROVEMENT STUDY STUDENT PROFILES

Nadia Soh and Louise Pivac are two postgraduate students working at the Australian Alzheimer's Research Foundation on the Sleep Improvement Study.

NADIA SOH

STUDENT PROFILE

Supervisors:
A/Prof Stephanie Rainey-Smith, Murdoch University
A/Prof Michael Weinborn, University of Western Australia
Dr Melissa Ree, University of Western Australia

HER RESEARCH

With the ultimate aim of improving overall quality of life, and reducing the risk of Alzheimer's disease, Nadia's research will examine an important yet relatively unexplored area of poor sleep – the discrepancy between self-report and objective sleep measurements, and an individual's level of distress about their own sleep, both of which are commonly found in insomnia. Specifically, Nadia's research will explore the relationships of sleep discrepancy and sleep distress to brain health and cognitive function, and the underlying neurophysiological mechanisms behind these relationships.

As part of the Sleep Improvement Study, Nadia has been helping to coordinate the cognitive behavioural therapy booster sessions and conducting neuropsychological assessments for study participants. Nadia's PhD confirmation of candidature was approved in March 2021.

LOUISE PIVAC

STUDENT PROFILE

Supervisors:
A/Prof Stephanie Rainey-Smith, Murdoch University
A/Prof Michael Weinborn, University of Western Australia
Dr Belinda Brown, Murdoch University
A/Prof Hamid Sohrabi, Murdoch university
Dr Samantha Gardener, Edith Cowan University

HER RESEARCH

After gaining valuable research experience at the Australian Alzheimer's Research Foundation as a research volunteer, Louise began her PhD studies in 2020. Louise is the recipient of a research scholarship which is co-funded by the Foundation and Murdoch University. She is involved in the Sleep Improvement Study, conducting neuropsychological tests and performing quality control checks on the research data. Ultimately, she will use these data to investigate whether those individuals with improvement in sleep, following a sleep-specific cognitive behavioural therapy program, gain observable improvement in cognition and biomarkers of brain health. This research has the potential to provide a cost-effective standard therapy for a significant proportion of the population at risk of cognitive decline due to poor sleep.

Recently, Louise successfully obtained Confirmation of Candidature from Murdoch University; a process which involves examination of two substantial pieces of writing and a presentation of the proposed research project to faculty and students alike. She is now analysing data and commencing the write up of her first manuscript.

A personal experience .....

Jan is a Sleep Improvement Study participant at the Australian Alzheimer's Research Foundation

"I have recently finished the Sleep Study and I got far more than I expected to. I thought it would be interesting but it was a real eye opener.

One of the benefits was the workshops when we got together in small groups. Listening to the other people in our group meetings was very interesting and hearing how they are feeling. They were stressed and cross about the same things I was, especially related to our sleep and cognitive behaviour.

We had occasional gatherings for workshops, completed workbooks and had time in a sleep laboratory. We also did some memory testing. The hearing tests were also very interesting especially to learn about the association between hearing and cognition.

I heard about the Sleep Study when I attended an information session held by the Australian Alzheimer's Research Foundation at the WA Library in September 2019. There is not really Alzheimer's in my family, except perhaps my grandfather, but I have a very close friend with dementia.

It was a very good experience and I would thoroughly recommend getting involved if you have the opportunity to."

JAN ROSE
SLEEP STUDY PARTICIPANT

Testosterone Supplementation Study Update

The Foundation is conducting a study into the role of testosterone supplementation on cognitive decline in older men and in the pathology associated with Alzheimer's disease. One of the proposed reasons for cognitive decline and Alzheimer's disease in men is the age-related decline in the testosterone hormone.

Recent studies have indicated that a decrease in testosterone is related to an increase in amyloid build up in the brain and testosterone replacement reduces beta amyloid levels in both the blood and the fluid that surrounds the brain (cerebrospinal fluid). This suggests that the reduction in testosterone during ageing could contribute to the development and underlying causes of Alzheimer's disease.

An increasing body of literature also suggests a positive, neuroprotective effect for testosterone on cognition in older men.

This information has guided the development of the Foundation's testosterone trial, a ground-breaking study to assess the effect of testosterone supplementation on brain amyloid and cognition in men over 60 years of age.

During 2020 the study was unfortunately placed on hold for several months due to the COVID-19 pandemic. Those people who were in the study at the time, had telehealth appointments with our research doctors and continued to have their blood levels checked for safety assessments. We are very glad the study is now back up and running after this delay.

The study is a significant commitment by the Foundation, who is sponsoring and funding this study. However, the study has the potential to have an enormous impact on people at risk of Alzheimer's disease. Testosterone is already an approved therapy so the regulatory requirements to potentially expand its clinical indication would not be as time consuming and costly as new drugs in development.

Hormones are chemical messengers that travel in the bloodstream and regulate complex processes including growth, metabolism, appetite and reproduction. They are also very important for brain function, for example facilitating neuronal (brain cell) connections to allow memory processing, consolidation and retrieval and protect the brain from inflammation or oxidative stress.

The study commenced in 2018 and to date 54 men have participated. We are aiming to recruit 200 men across the two sites in Perth and at Macquarie University in NSW.

The study is suitable for men aged 60-80 who have testosterone levels at the low end of normal. Eligible participants will receive 13 months of treatment (placebo or testosterone). Participants attend regular visits for blood tests, testosterone or placebo treatment and safety assessments. To measure the effect of the treatment interventions, participants will be required to have brain scans and memory tests before and after entering a 56 week treatment period.

TESTSTERONE STUDY STUDENT PROFILE

SHERILYN TAN

Supervisors:
A/Prof Michael Weinborn, University of Western Australia
A/Prof Hamid Sohrabi, Murdoch University
Prof Ralph Martins AO, Edith Cowan University

My postgraduate journey has given me many valuable experiences and I remain passionate about older adult mental health, changes in cognition associated with ageing and dementia. I hopes to be able to continue this work across both a research and clinical setting.

- PhD Student, Sherilyn Tan

HER RESEARCH

Sherilyn commenced her PhD in 2016 with a scholarship from the Australian Alzheimer's Research Foundation and undertook her Masters in Clinical Neuropsychology in the following year. Sherilyn will graduate from her PhD/Masters in Clinical Neuropsychology in June 2021. Sherilyn's completed and accepted thesis entitled "**Understanding the Relationship Between Testosterone and Cognition in Cognitively Healthy Older Men: An Examination of Potential Mediating and Moderating Factors**", was passed earlier this year.

Overall, findings across various research studies included in her thesis, provides further support that testosterone supplementation could be a preventative measure against cognitive decline in older men. Thesis findings also identified that genetic variations in the androgen receptor gene and levels of physical activity, are factors that can influence the relationship between testosterone and cognition in older men. Identifying these moderating and mediating factors can help inform ongoing clinical trials that are examining the potential for testosterone supplementation to be a preventative measure against cognitive decline in older men.

A/Prof Hamid Sohrabi and Senior Research Assistant Lucy Lim at the Australian Alzheimer's Research Foundation laboratory.

CLINICAL TRIALS DIVISION

The Australian Alzheimer's Research Foundation conducts clinical trials into new investigational therapies for Alzheimer's disease.

Under the leadership of Dr Roger Clarnette, the Foundation is working with international pharmaceutical companies, trialling new drugs that may ease the suffering for those diagnosed with Alzheimer's disease.

Pictured above (L-R) Shima Motooka, Vivian Ngo, Dr Sarah Binns, A/Prof Roger Clarnette, Ron Pensini, Paula Mather and Dr Cate Mansfield.

Clinical Trials Division

The Foundation's Clinical Trials Division conducts clinical trials with some of the world's leading pharmaceutical companies to test potential treatments for people at risk of, or diagnosed with, Alzheimer's disease.

The Foundation is a vital part of the search for new treatments to slow the progression of, and treat Alzheimer's disease. These trials offer hope for many people and an opportunity to help researchers find better treatments for others in the future. They also provide an opportunity for people to access the latest therapies being researched internationally for Alzheimer's disease.

Based at the Hollywood Specialist Centre in Nedlands, the Foundation's Clinical Trials Division is staffed by medical practitioners, study coordinators and nurses. The unit is supervised by Associate Professor Roger Clarnette, a senior specialist physician at Fremantle Hospital who has a particular interest in memory loss and Alzheimer's disease.

During the 2020 COVID pandemic, the safety of our study participants was absolutely paramount. We worked with our collaborators to adopt new processes, which included home visits and telephone appointments where possible. All participants chose to continue with their participation in the clinical trials, motivated to explore a potential therapy to assist their diagnosis.

The Foundation conducted 13 clinical trials for Alzheimer's disease in 2020. Most of the therapies under investigation are aiming to slow disease progression and the cognitive impairment in people with early Alzheimer's disease. Many therapies target the build-up of beta-amyloid (Aβ) peptides in the brain and neurofibrillary tangles containing tau protein, which are hallmarks of Alzheimer's disease. Brain imaging conducted in the studies may also explore brain volume over the course of the treatment.

The Foundation has also embarked on a new trial exploring the role of biological metals in the Alzheimer's disease process and whether lowering brain iron burden will slow cognitive decline in patients with mild Alzheimer's disease.

The Foundation is involved in Phase 1, Phase 2 and Phase 3 clinical trials.

A snapshot of the therapeutic trials the Clinical Trials Division was involved in throughout 2020 are summarised on the following pages.

Current medications provide only modest symptomatic benefit. There are currently no therapies that modify the course of Alzheimer's disease.

ABBVIE AWARE M15-566 (PHASE 2)

A Phase 2 Multiple Dose, Multicenter, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate the Efficacy and Safety of ABBV-8E12 in Subjects with Early Alzheimer's Disease

- Humanized immunoglobulin G4 (IgG4) monoclonal antibody against human microtubule-associated protein tau (ABBV-8E12)

Approximately 400 participants worldwide with early Alzheimer's disease between 55 to 85 years of age were eligible to participate in the study. Upon completion of screening and baseline procedures, eligible subjects were randomized to one of the three ABBV-8E12 dose arms (300 mg, 1000 mg or 2000 mg) or placebo in a 1:1:1:1 ratio. Doses are administered every 4 weeks via IV infusion.

Aware

ABBVIE AWARE EXTENSION M15-570 (PHASE 2)

Open Label Extension Study for Patients with Early Alzheimer's Disease (AD) Enrolled in Study ABBV-8E12

- Humanized immunoglobulin G4 (IgG4) monoclonal antibody against human microtubule-associated protein tau (ABBV-8E12)

Participants that complete the AbbVie AWARE M15-566 study have the opportunity to enrol in the extension study.

ANAVEX2-73-AD-004 (PHASE 2B/3)

A Phase 2b/3, Double-Blind, Randomized, Placebo-Controlled 48-week Safety and Efficacy trial of ANAVEX2-73 for the Treatment of Early Alzheimer's Disease

- Sigma-1 (σ1R) and muscarinic receptors agonist (ANAVEX2-73)

In addition to evaluating the effects on cognition and functioning, ANAVEX also explores sleep outcomes, behavioural and psychological symptoms, changes in daily functioning of participants and changes in caregiver burden. Safety assessments include pharmacokinetic (PK) assessments and blood markers of Alzheimer's disease pathophysiology before and after treatment.

anavex LIFE SCIENCES Corp.

ANAVEX2-73-AD-004 EP (PHASE 2B/3)

Open Label Extension Study for Patients with Early Alzheimer's Disease (AD) Enrolled in Study ANAVEX2-73-AD-004

Participants that complete the ANAVEX2-73-AD-004 study have the opportunity to enrol in the extension study.

NTA THE 3D STUDY DEF-001 (PHASE 2)

Deferiprone to Delay Dementia (The 3D Study): A clinical proof of concept study

- Iron chelator (Deferiprone)

The 3D study investigates whether an iron chelator medication, Deferiprone, delays dementia progression in the early stages of Alzheimer's disease. Iron chelators are used in the treatment of conditions such as haemochromatosis and thalassemia, where abnormal iron accumulation is present. In Alzheimer's disease iron accumulates in affected brain regions causing neurotoxicity.

The 3D Study
Deferiprone to Delay Dementia

BIOGEN EMBARK 221AD304 (PHASE 3B)

Phase 3b Open-Label, Multicenter, Safety Study of BIIB037 (aducanumab) in Subjects with Alzheimer's disease Who Had Previously Participated in the Aducanumab Studies 221AD103, 221AD301, 221AD302 and 221AD205

- Human monoclonal antibody that recognizes aggregated forms of β-amyloid (Aβ) (Aducanumab)

This open-label, single arm clinical study is being conducted to assess the long-term safety and efficacy of aducanumab in participants with Alzheimer's disease who were actively participating in previous aducanumab studies. It is a two-year study involving monthly infusions of aducanumab.

Biogen

ROCHE GRADUATE WN29922 (PHASE 3)

A phase III, multicenter, randomized, double-blind, placebo-controlled, parallel-group, efficacy, and safety study of Gantenerumab in patients with early (prodromal to mild) Alzheimer's disease

- Fully human monoclonal antibody targeting fibrils, and plaques (Gantenerumab)

This study aims to evaluate the ongoing safety and efficacy of gantenerumab administered as a subcutaneous injection over a 24-month period.

Roche

EISAI CLARITY BAN2401 (PHASE 3)

A Placebo-Controlled, Double-Blind, Parallel-Group, 18-Month Study With an Open-Label Extension Phase to Confirm Safety and Efficacy of BAN2401 in Subjects With Early Alzheimer's Disease

- BAN2401 is a humanized IgG1 monoclonal antibody that binds to soluble Aβ aggregates.

Approximately 245 sites around the world will be involved in this study.

Eisai

INMUNEBIO XPRO-1595 (PHASE 1B)

Phase 1b Open-Label, Dose-Identification Study of XPro1595 in Patients With Mild to Moderate Alzheimer's Disease With Elevated High Sensitivity C-reactive Protein in Blood.

The primary objective of the study is to evaluate the safety and tolerability of XPro1595 given as a subcutaneous injection once a week for 12 weeks.

The study originally closed in 2020, however due to the COVID-19 pandemic our site was approached to reopen to assist with reaching the Australian recruitment target. After completion of 12 weeks of treatment, patients will have the option to enrol in a 9-month extension study if the investigator believes they are benefiting from treatment.

ATH-1017 - ACT-AD (PHASE 2)

A randomised, Placebo-Controlled, Translational Study of ATH-1017 in Subjects with Mild to Moderate Alzheimer's disease.

This is a Phase 2 multicentre, randomized, double-blind, placebo-controlled, parallel-group, dose-ranging study comparing ATH-1017 40 mg/day and ATH-1017 70 mg/day with placebo in subjects with a clinical diagnosis of mild to moderate Alzheimer's disease.

The study will be conducted at approximately 12 centres in Australia and the US. All eligible subjects will be tested for apolipoprotein E (ApoE) genotype. Eligible participants must be between the ages of 55 to 85 years.

A personal experience .....

Caroline is a clinical trial participant at the Australian Alzheimer's Research Foundation. A former nurse who, during her career, used to take care of people with Alzheimer's disease.

"The Foundation has been most supportive of myself and my partner.

"They have been compassionate, attentive, understanding, given me time, explained things thoroughly, provided coping strategies and given me inspiration and hope."

CAROLINE
CLINICAL TRIAL PARTICIPANT

THANK YOU TO OUR SUPPORTERS

Our community of donors and supporters come in all sorts of shapes and sizes – individuals and families, foundations, corporates and community groups.

They all share a deep commitment to support vital research into Alzheimer's disease.
We appreciate their support very much and simply could not do what we do without it.

In 2020 we welcomed Alternative Surfaces as a corporate sponsor.

"As a family run business, we are very proud to be supporting a cause that's so close to our families' hearts. We have experienced first-hand the devastating effects of Alzheimer's disease and are committed to helping the Australian Alzheimer's Research Foundation in their fight to find a cure so that we can save memories and lives around the world".

Laura Di Bartolo, Marketing Manager

Alt.

Our Supporters

We very much appreciate the contribution of all our supporters and simply could not do what we do without them.

Throughout these pages, every day on our website and through social media you will find examples of research that often started through a simple gesture – an act of generosity and philanthropy.

Whether you are an employee of one of our corporate partners, made a personal donation or took part in a community event and raised funds for us, you have made a difference and we thank you for your support.

Donors and Fundraisers
We are always touched by the number of people who donate to, or fundraise for, the Foundation. We wish to thank all those individuals who have given to the Foundation through regular giving, one of our appeals, or through one of our fundraising programs.

Major Giving
We greatly value the wonderful contributions by our major donors and sponsors in helping us achieve our mission to supporting research that makes Alzheimer's disease treatable and preventable.

In Memoriam
To everyone who chose to honour a loved one by making a donation to the Australian Alzheimer's Research Foundation in their memory, our sincerest thanks. Your generous gift will enable us to continue supporting leading edge research.

In Celebration
The Foundation would like to give recognition to everyone who invited their family and friends to make a donation to assist our cause rather than receive presents. What a generous spirit!

Volunteers
Delivering our programs and events would not be possible without the contribution of our wonderful volunteers. We thank our volunteers who have given their time, skills and energy in helping us throughout the year, including taking part in our research programs.

Bequests
The Gift in Wills/Bequest program provides information and resources to people considering leaving a gift in their Will or those who have already included a gift.

Gifts included in Wills are critical in funding our work and provide important certainty that enables us to plan future programs.

It's with respect and gratitude that we recognise those who gave a lasting gift to the Australian Alzheimer's Research Foundation via a gift in their Will. Their kindness enables us to fund research that we hope brings us one step closer to an Alzheimer's free world.

Peter Frederick Roberts
In 2011, Peter was sadly diagnosed with Alzheimer's disease, and after an 8 year battle, Peter passed away peacefully on the 9 July 2019, at 83 years. We are extremely grateful to the Roberts family for their incredible generosity in support of Alzheimer's research.

Pat Kidson
The Foundation was very grateful to receive a bequest from Barrie Kidson in memory of his beloved wife, Pat Kidson. This funding has assisted in the purchase of state of the art equipment (Simoa HD-X-Analyser) and consumables for the development of a blood diagnostic for Alzheimer's disease.

Thank you also to Thelma Criddle, Doreen Taylor and Elaine Bobbin who provided a bequest to the Australian Alzheimer's Research Foundation in 2020 to enable us to work towards a better future for us all.

We are thankful to all who have been inspired to leave a legacy in their Wills. Such gestures are very much appreciated and we acknowledge with gratitude those who have bequeathed part of their estate to the Australian Alzheimer's Research Foundation.

Sponsors & Partners

Our corporate sponsors and partners are incredibly important and their continued support helps raise awareness of Alzheimer's disease with their employees while providing support for Alzheimer's research. THANK YOU.

Workplace Giving
We would also like to acknowledge those employees who continue to support the Australian Alzheimer's Research Foundation through regular workplace giving and their employers who make it possible.

Workplace giving is a powerful and simple way to make regular donations to Alzheimer's disease research. Sometimes, the employer offers matched giving effectively doubling the contribution.

IN THE COMMUNITY
2020 HIGHLIGHTS

Community activities to raise funds for the Foundation and bring greater awareness and understanding of the disease are greatly appreciated. We thank everyone for their tremendous support. Whilst many community activities were cancelled in 2020, people still founds ways to support us.

Etching for Moi

Internationally acclaimed artist Leon Pericles produced a beautiful etching called "Etching for Moi" dedicated to his wife Moira in 2019 with all funds donated to the Foundation to support Alzheimer's research. All 150 limited edition etchings were quickly sold.

We were delighted when Leon made reproductions available enabling people to enjoy this beautiful art, with funds continuing to come to the Foundation in 2020.

We would like to thank Leon, his family, the Linton & Kay Gallery and everyone behind the scenes for their tremendous support.

Michael Symon Yoga

We know it is important to keep up physical activity, as it is crucial for cognitive health. The challenges of 2020 made it harder than ever to stay active.

Throughout 2020, Michael from Michael Symon Yoga provided free yoga classes via Facebook and encouraged all participants to donate to Australian Alzheimer's Research Foundation.

Exercise reduces the risk of high blood pressure, obesity, diabetes and high cholesterol, which are associated with an increased risk of cognitive decline and dementia.

Thank you Michael!

HBF Run

Although cancelled due to the COVID-19 pandemic, HBF kindly donated the $400,000 of unspent event funds amongst 170 health charities, including the Australian Alzheimer's Research Foundation.

We were extremely grateful for this support in a challenging year.

IN THE COMMUNITY
2020 HIGHLIGHTS

Community activities to raise funds for the Foundation and bring greater awareness and understanding of the disease are greatly appreciated. We thank everyone for their tremendous support.

Containers for change

In late 2020, Containers for Change was launched in Western Australia. Containers for Change is a new state-wide container deposit scheme that enables eligible containers to be cashed in for 10 cents each. In WA, we use more than 1.3 billion eligible containers each year.

The Australian Alzheimer's Research Foundation is very pleased to be part of this change in support of our environment. When you take your containers to one of the donation points, by selecting the Foundation's Scheme ID C10339406, the value of the refund is transferred directly to the Foundation. This is a great initiative to reduce the ecological footprint through recycling and also support Alzheimer's research.

World Alzheimer's Month Webinars

During September, World Alzheimer's Month, the Australian Alzheimer's Research Foundation provides free public lectures to bring awareness to Alzheimer's disease and the research work that will hopefully provide a better future for those at risk of developing the disease. As the second leading cause of death in Australia, dementia, including Alzheimer's disease, is a significant issue for all Australians.

To ensure everyone's safety during the COVID-19 pandemic, we delivered our public lectures online in 2020, as webinars. These webinars still gave all attendees an opportunity to ask questions and each session was recorded, and are available to be view at any time on our website.

Saracen Minerals and Wine & Horses

Although the Wine & Horses Annual Charity Ride was cancelled due to the pandemic, we had the opportunity to invite some of the key organisers and supporters, including Saracen Minerals, to our research facility at the Ralph and Patricia Neuroscience Research Institute.

This provided everyone in attendance an opportunity to hear from some of our researchers and discuss the significant impact Alzheimer's has on many people in our community. They were given an overview of current research into the diagnosis and treatment of the disease and risk reduction strategies.

SCIENTIFIC PUBLICATIONS

Scientific Publications

Some publications are repeated under multiple headings

WAMS

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Fine, L., Weinborn, M., Ng, A., Loft, S., Li, Y., Hodgson, E., Parker, D., Rainey-Smith, S., Sohrabi, H., Brown, B., Martins, R., Bucks, R., (2019), Sleep disruption explains age-related prospective memory deficits: implications for cognitive aging and intervention. *Aging, Neuropsychology, and Cognition*, 26(4), 621-636. https://doi.org/10.1080/13825585.2018.1513449

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