

Australian  
**ALZHEIMER'S  
RESEARCH**  
Foundation



**2021**  
**Annual Report**

Year in Review

# 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.

Leading cause of death  
of women



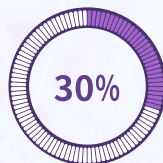
Females account for 64.5% of all dementia-related deaths and it remains the leading cause of death among Australian females.

487,500 Australians  
are living with dementia



Without a medical breakthrough, the number of people living with dementia is expected to increase to 1.1m by 2058.

30% of people over  
85 have dementia



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

Two thirds of aged  
care residents



More than two-thirds of aged care residents have moderate to severe cognitive impairment.

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.



**There is no cure**



## TABLE OF CONTENTS

### INTRODUCTION

<i>Chair Report</i>	3
<i>The Board</i>	4
<i>CEO Report</i>	5
<i>Financial Snapshot</i>	6
<i>Celebrating 21 Years</i>	7

### RESEARCH

<i>Research Report</i>	9-11
<i>WA Memory Study</i>	12-14
<i>Charlies Collaboration</i>	15
<i>Sleep</i>	16-17
<i>ADNeT</i>	19
<i>Blood-based Biomarkers</i>	20
<i>Genetics and Alzheimer's</i>	21
<i>AIBL</i>	22
<i>Student Spotlights</i>	23-24
<i>Testosterone Study</i>	25
<i>Childhood Dementia</i>	26-27
<i>DIAN &amp; D-CAA</i>	28
<i>Nutrition &amp; Alzheimer's</i>	29
<i>Personality Traits &amp; Dementia</i>	30
<i>Coffee &amp; Alzheimer's Disease</i>	31
<i>AU-ARROW Study</i>	32-33

### CLINICAL TRIALS DIVISION 34-37

### IN THE COMMUNITY 38-45

### SCIENTIFIC PUBLICATIONS 46-48

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 and conduct Alzheimer's disease research.

# Chair Report

GRAEME PRIOR



**2021 brought hope to those with Alzheimer's disease or at risk of developing the disease. We saw the first treatment for Alzheimer's approved by the US Food and Drug Administration (FDA) in almost twenty years, and significant progress on developing a blood test to detect the very early signs of the disease.**

The announcement by the FDA has brought renewed interest in potential treatments for Alzheimer's, and with Western Australia being largely COVID free during 2021, the Foundation experienced a significant increase in the activity of clinical trials for new therapies. With the prospect of a diagnostic test that can detect Alzheimer's before symptoms appear, we are now seeing research into treatments that may work at the very early stage of the disease before significant damage occurs in the brain.

This gives us all cause for optimism. A vision of the early diagnosis, prevention, treatment and cure of Alzheimer's disease is potentially within our grasp. The prospect of ageing well, living independently and enjoying our senior years must remain our steadfast goal.

In 2021, the Foundation was invited to be a part of a national initiative led by Dementia Australia, looking at the potential role of comprehensive dementia centres in each state; a centre where people can receive a rapid diagnosis of the disease, access treatment and connect with research opportunities to improve their outcome. Additionally, the centre will provide training to increase capacity in the sector of skilled health care workers in dementia diagnosis, treatment and care. The challenges today for people to obtain a timely diagnosis is evident and only delays the opportunity to intervene early. Likewise, the more rapid translation of research outcomes into clinical practice to provide better outcomes for people as they age is critical.

2021 also saw the release of the Final Report of the Royal Commission into Aged Care Quality and Safety. The Commissioners brought further focus on the care of people with dementia, with specific recommendations around dementia training, design for dementia and the need for specialist dementia care services. These recommendations once again place dementia research and care back at the forefront of the Commonwealth's social policy agenda.

Dementia is the second leading cause of death in Australia and the single greatest cause of disability in older Australians. Dementia, including Alzheimer's disease, has been described as the chronic disease of the 21st century. It must be elevated as a sense of urgency across all sectors of our society and within government. Increased investment into research is paramount if we are going to achieve the results we need.

The Foundation is enormously grateful to those who have provided it with philanthropic support, which enables the Foundation to provide state of the art research facilities, other direct and indirect research support, and scholarships for aspiring dementia researchers. The work commenced in 2020 to investigate transitioning to a Medical Research Institute continued in 2021. We believe the breadth of services and support the Foundation provides is in keeping with a Medical Research Institute and enables researchers to focus on what's important - their research.

I would like to thank the AARF Board members and external advisors for their support, time and expertise to provide the necessary and essential governance and oversight of the Foundation. A special thank you to Jenny Day, who resigned from the Board in 2021. Jenny was instrumental in several key initiatives, and funding opportunities during her 11-year tenure with the Foundation and her input into the success of the Foundation is greatly appreciated. I would also like to extend my thanks and encouragement to the CEO and staff at the Foundation, and the many researchers focused on developing a cure for Alzheimer's. We are indebted to you.

**Graeme Prior**

Chairperson

# THE BOARD



**Graeme Prior**  
Chair



**Dr Terry Bayliss**  
Deputy Chair



**Rod O'Dea**  
Treasurer  
Chair Fundraising Committee  
Chair Future Fund Committee



**Prof. Ralph Martins AO**  
Director of Research



**Prof. Colin Masters AO**  
Chair Scientific Advisory Committee  
Chair Clinical Research  
Governance Committee



**Enzo Sirna AM**  
Board Member



**Tim Andrew**  
Board Member



**Rob Davies**  
Board Member



**Jenny Day**  
Board Member  
(Resigned May 2021)

## Board Committees

### EXECUTIVE COMMITTEE

**Graeme Prior**

CEO - Hall & Prior Aged Care Group

**Dr Terry Bayliss**

Coordinator Development Projects & Research  
- Ramsay Health Care

**Professor Ralph Martins AO**

Professor of Neurobiology - Macquarie University,  
Foundation Chair of Aging and Alzheimer's  
disease - Edith Cowan University

**Rod O'Dea**

Director - Ellann Finance

**Liza Dunne**

CEO - Australian Alzheimer's Research Foundation

### FUTURE FUND COMMITTEE

**Rod O'Dea**

Director - Ellann 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**

Coordinator Development Projects & Research  
- 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 - Macquarie University,  
Foundation Chair of Aging and Alzheimer's disease  
- Edith Cowan University

**Professor Roger Chung**

Professor of Neurobiology and Neurochemistry,  
Deputy Dean Research and Innovation - Macquarie  
Medical School, Macquarie University

**Professor Lars Ittner**

Director, Dementia Research Centre - Macquarie  
University

**Professor Sharon Naismith**

Professor of Clinical Neuropsychologist -  
University of Sydney

BOARD MEMBER	NUMBER OF MEETINGS ATTENDED	NUMBER OF MEETINGS HELD
Mr Graeme Prior	6	6
Dr Terry Bayliss	6	6
Mr Rod O'Dea	6	6
Prof. Ralph Martins AO	5	6
Prof. Colin Masters AO	6	6
Mr Enzo Sirna AM	3	6
Mr Tim Andrew	4	6
Mr Rob Davies	6	6
Ms Jenny Day (Resigned May 2021)	2	2

# CEO Report

L I Z A D U N N E



## I am pleased to report on the activities at the Australian Alzheimer's Research Foundation in 2021.

We are incredibly grateful for the philanthropic support we receive from across the community, including corporate supporters, community businesses and individuals who may have been touched by Alzheimer's disease. As the second leading cause of death in Australia, dementia has touched most of us.

Alzheimer's disease is the primary cause of dementia and supporting research that makes Alzheimer's disease treatable and preventable is our mission.

The Foundation celebrated 21 years since its formation in 2021 and published a booklet and video celebrating our achievements over this time. These can be found on our website if you have not had the opportunity to see these.

We are proud of the progress over these years under the leadership of the Director of Research, Professor Ralph Martins AO. Research supported by the Foundation into biomarkers for the early detection of the disease has been a focus area and is showing excellent promise. These include blood biomarkers and retinal imaging markers that have the potential to identify Alzheimer's disease up to 20 years before noticeable symptoms develop. The detection of Alzheimer's as early as possible is key to the effectiveness of potential treatments and risk reduction strategies.

The Foundation is continuing its research program into the potential role of Testosterone in Alzheimer's disease in both Western Australia and New South Wales. Interruptions due to COVID-19 resulted in slower progress than planned in 2021, but the trial is moving forward again in 2022. If a positive outcome is shown, this treatment could be relatively quickly made available as it is already an approved drug for other conditions.

Research programs into Alzheimer's prevention and risk reduction are also a major focus of the work the Foundation is supporting. Research into prevention has identified the significant impact modifiable risks can have on Alzheimer's disease, including the important roles of exercise, diet and sleep.

The Foundation provides a broad range of support services and funding for Alzheimer's research which include funding researcher salaries, providing research scholarships, providing clinical and laboratory research facilities, and providing accounting, insurance and administrative support for research programs. These activities come at a considerable cost but enable the researchers to focus on research and to find solutions that deliver a better outcome for us all as we age.

The Foundation's Clinical Trials Division moved into larger premises in 2021 to accommodate the increase in the pharmaceutical clinical trials we are engaged in. These trials provide opportunities for people with early symptoms of Alzheimer's and those who are pre-symptomatic but at risk of developing the disease to access potential treatments being researched internationally.

The Foundation has been involved in the clinical trials for the Biogen drug Aducanumab which gained approval from the US Food and Drug Administration (FDA) in June 2021. This represented the first Alzheimer's therapy to gain approval that targets the underlying disease process of Alzheimer's, rather than treating symptoms. The approval was not without its detractors but has renewed momentum in the industry for Alzheimer's treatment solutions.

With no government funding, we are indebted to the financial support of the community to conduct the research required to prevent and treat Alzheimer's disease. Thank you to everyone who has supported the Foundation, including those who have supported our fundraising activities and those who generously give their time to be involved in our research programs.

Thank you also to the hard work and commitment of the Foundation's board, researchers and staff, who are committed to bringing us closer to an Alzheimer's free world.

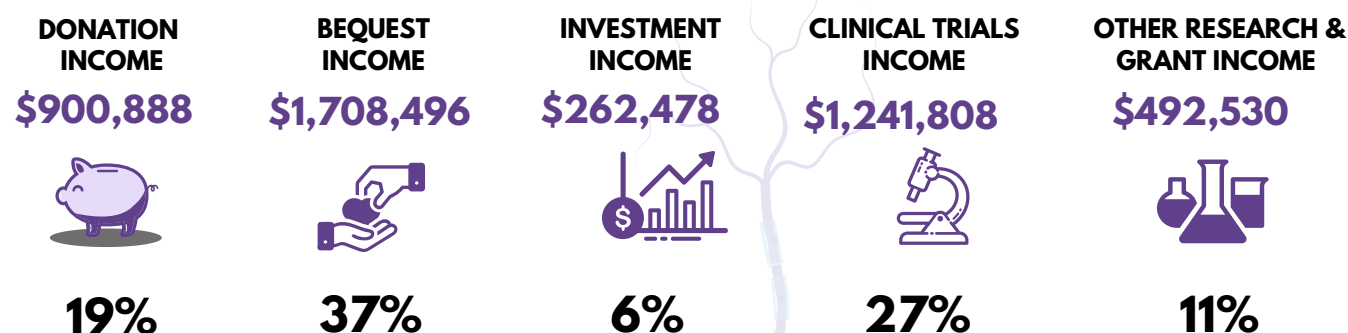
A handwritten signature in dark ink that reads "L Dunne". The signature is fluid and cursive.

**Liza Dunne**

CEO

# 2021 FINANCIAL SNAPSHOT

## INCOME 2021 - \$4.6 MILLION



## EXPENSES 2021 - \$3.5 MILLION

### PHILANTHROPIC SUPPORT

Philanthropic support, including donations and bequests, is the Foundation's primary source of income.

### CLINICAL TRIALS INCOME

The Foundation earns income from researching potential new pharmaceutical treatments for Alzheimer's disease.

### OTHER RESEARCH & GRANT INCOME

Other research and grant income includes funds received in prior years but recognised as income in 2021, as the funds were tied to projects conducted in 2021.

### DIRECT RESEARCH COSTS

Direct research 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

Indirect costs are vital services that enable research work to continue. These include information technology, finance, communications, fundraising, human resource management, research governance, risk management and insurance. Indirect costs also included expenditure on the strategic initiatives of becoming a Medical Research Institute in the future and joining the National Network of Comprehensive Dementia Centres.

### DIRECT RESEARCH COSTS

\$2,834,766



81%

### INDIRECT COSTS

\$655,151



19%

Through the generosity of our donors, the Australian Alzheimer's Research Foundation is one of the nation's largest non-government funders of research into Alzheimer's disease.

**Note:** The financial summary has been extracted from the audited Special Purpose Financial Statements of the Australian Alzheimer's Research Foundation. The audited special purpose financial report can be obtained through the ACNC website.





*Celebrating*  
**21 YEARS**

proudly supporting Alzheimer's research to bring us one step closer to an  
Alzheimer's free world

**In 2021, the Australian Alzheimer's Research Foundation  
celebrated 21 years of making a difference.**

**Thank you to everyone who has supported this journey.**

Over the past 21 years, the Australian Alzheimer's Research Foundation has evolved from a small research team to an internationally recognised Alzheimer's research and advocacy group.

We have a much greater understanding of the disease than we did 21 years ago, leading to better ways to diagnose, prevent, and treat the disease.

Thank you to everyone who has been part of our journey – our staff, researchers, donors, and the community.

*As a result of the hard work and community support  
of the last 21 years, we are on the cusp of several  
major developments in Alzheimer's research.*

**- Professor Ralph Martins**

# 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.**

The Australian Alzheimer's Research Foundation Foyer

# Research Report

PROFESSOR RALPH MARTINS AO



**I am delighted to report that our team has continued to make major progress with our ongoing projects these last 12 months and have also embarked on exciting new projects during this time.**

We continue to be focused on research on understanding, preventing, diagnosing, and treating Alzheimer's and other causes of dementia. The most recent developments are childhood dementia research led by Dr Prashant Bharadwaj and partnering with the major Alzheimer's organisation in the United Kingdom, namely Alzheimer's Research UK, to utilise digital technology to develop "fingerprints" for the early diagnosis of Alzheimer's and Dementia.

## Early Diagnosis

In my report last year, I wrote about the exciting work that my team are undertaking to diagnose Alzheimer's early, well before the onset of symptoms, using blood biomarkers and retinal imaging.

The retinal imaging work is now making significant progress with the recent recruitment of a very talented PhD student Purna Poudel who has joined our retinal imaging team led by Dr Eugene Hone to develop methods to accurately measure the changes in the retina captured by the state-of-the-art hyperspectral camera kindly donated by the Lions Alzheimer's Foundation. The changes in the retina reflect changes in the Alzheimer brain and thus offer the promise of a non-invasive, relatively inexpensive early diagnosis. This research is conducted at the Australian Alzheimer's Research Foundation (AARF) in close collaboration with Dr Shaun Frost from CSIRO and with Macquarie researcher Dr Tejal Shah and her team, who have one of only two other hyperspectral cameras in Australia.

The blood biomarker work led by Macquarie University's Dr Pratishtha Chatterjee in collaboration with Edith Cowan University's (ECU's) Steve Pedrini has gone to new heights with the published findings from the KARVIAH study replicated in the much larger Australian Imaging Biomarkers Lifestyle Study of Ageing that many of our wonderful volunteers in Perth have played an important role as regular participants. I am happy to announce that this work will be published in the prestigious journal Alzheimer's and Dementia.

AARF played a vital role in providing the expensive kits needed for this latter study and supporting some of the laboratory facilities to enable this work and is providing researcher salary support in 2022. Thanks to the Lions Alzheimer's Foundation, who have provided the state-of-the-art Simoa HD-X Analyser and the outstanding work of Dr Chatterjee and Mr Pedrini, we are now being approached by research organisations throughout the country to measure blood biomarkers in their cohorts. This includes the NHMRC funded national Alzheimer's Disease Network to screen high-risk individuals from their memory clinics with blood biomarkers. If the latter is successful, it will be a significant step toward making population screening a reality in the near future.

We are also embarking on an exciting, innovative approach for the early detection of Alzheimer's and Dementia with a substantial grant from The Alzheimer's Drug Discovery Foundation (ADDF), a U.S. based venture philanthropy to fund the Early Diagnosis of Neurodegenerative diseases (EDoN) that Alzheimer's Research UK has been awarded with ECU. The significance of our blood biomarkers will be evaluated in EDoN.

EDoN is an ambitious project spearheaded by Alzheimer's Research UK, the UK's leading dementia research charity. It brings together global experts in data science, digital technology and neurodegeneration to use measures such as sleep, fine motor control, heart rate, speech and brain activity to develop digital 'fingerprints' of early disease that could transform dementia research efforts in the future. Associate Professor Stephanie Rainey-Smith and Associate Professor Hamid Sohrabi will play a leading role in this global partnership with Alzheimer's Research UK. I am most grateful for the loyal support of our WA Memory Study (WAMS) participants at the Australian Alzheimer's Research Foundation who have participated in WAMS for over two decades which has resulted in this major global initiative, recognizing the importance of WAMS. Thank you also to the Charlies Research Foundation's support which has enabled important brain imaging of WAMS participants and their clinical assessment with collaborators at Sir Charles Gairdner Hospital, further assisting with the biomarker project. Thank you all so much for your outstanding support.

## Childhood Dementia

I am proud to announce that our team are undertaking a new initiative to investigate childhood dementia with the aim of applying the knowledge we have gained from our research into Alzheimer's to benefit children with this devastating neurological disease. In particular, our major achievements and expertise with blood biomarkers for Alzheimer's can now be applied to develop blood biomarkers for the early detection and progression of childhood dementia. This work will be led by Dr Prashant Bharadwaj who completed his PhD under my supervision at ECU less than six years ago.

The project aims to identify specific changes in proteins in the blood and urine from children with various types of childhood dementia that could be used to monitor the progression of their disease. These relatively non-invasive markers could be very useful tools to measure response to new treatments in clinical trials. In addition, this project will add to the knowledge base about these diseases and may uncover new approaches to treatment. This research will be conducted at the laboratory facilities provided by AARF and ECU. We are seeking funding to develop therapeutic approaches to childhood dementia and will be applying knowledge gained from our work on Alzheimer's to effectively slow the onset of this devastating disease focusing initially on dietary interventions.

### Without researchers, there is no research

Funding for research is increasingly challenging, especially throughout the COVID pandemic which has brought significant financial hardship to universities. Without researchers, the critical research into Alzheimer's disease and other causes of dementia will simply come to an end. The support provided by the Australian Alzheimer's Research Foundation in funding key researcher positions and providing research facilities and support activities is absolutely invaluable, thanks to the generosity of all our supporters. Support from the Lion's Alzheimer's Foundation has also been considerable during this period, and I thank them for their support.

Dr Bharadwaj represents just one of a number of our outstanding researchers that need to be supported to conduct their groundbreaking research. Dr Bharadwaj has opened a new field in childhood dementia that has recently attracted the support of the health minister, Hon. Greg Hunt who has provided a \$3million Medical Research Future Fund (MRFF) funding opportunity for childhood dementia. We are hopeful that Dr Bharadwaj and myself will be successful in being awarded some of this MRFF funding to investigate diet-based intervention strategies for arresting and stabilizing the cognitive decline in children affected by dementia and related genetic disorders.

Scholarships for PhD candidates in another important initiative to support aspiring Alzheimer's researchers. Capacity building within this sector is critical to ensure the best and brightest talent are supported and focus on this disease. Thank you to the Foundation for their support in this area.

## Continuing Programs of Work

Prevention continues to be a strong theme of research conducted at the Foundation's clinical research facilities. Work has continued in 2021 with the **Sleep Improvement Study** to assess whether improving sleep patterns can help older Australians retain their cognitive capacity and prevent or delay the onset of dementia. Sleep is now being recognised globally as a significant modifiable risk factor in the onset and progress of dementia.

On the theme of prevention and risk reduction, the **AU-ARROW Study** is focused on lifestyle interventions to reduce the risk of dementia. Sleep, exercise, diet, and general physical and psychological health are regularly assessed for both observational and interventional arms of the study. The aim is to identify the potential benefits of life style interventions and contribute to the development of blood biomarkers and retinal imaging biomarkers.

We are proud to be a partner in the **Australian Dementia Network (ADNeT)**, a network of leading scientists and researchers from across 15 institutions in Australia working on shared Alzheimer's research objectives. ADNeT provides the opportunity for people to register their interest in participating in Alzheimer's research and be screened for clinical trials. ADNeT is also developing best practice guidelines on the diagnosis and treatment of dementia and is facilitating the development of new therapies.

The **Australian Imaging, Biomarker & Lifestyle Flagship Study of Ageing (AIBL)**, conducted at the Florey Institute in Melbourne and the Australian Alzheimer's Research Foundation's facilities in Western Australia, is the largest study of its kind in Australia with over 1000 participants involved in this longitudinal study of cognition. 2021 marked 15 years since the AIBL study commenced with a seminal publication outlining the AIBL study's achievements and contribution to improving patient outcomes over these years. AIBL has provided significant insight into the disease and the nature and magnitude of cognitive changes caused by Alzheimer's disease, and the diagnostic importance of amyloid-beta imaging in identifying opportunities for early intervention.



In 2021, we commenced work on the collaboration with colleagues at the Leiden University in The Netherlands. The project is called Track D-CAA (Dutch type-cerebral amyloid angiopathy). The project aims to understand the relationship between a build-up of beta-amyloid in the lining of the blood vessels in the brain causing stroke and cognitive decline. A better understanding and more accurate diagnosis of cerebral amyloid angiopathy may allow the identification of novel treatment targets for CAA with the potential to benefit patients at risk of stroke and Alzheimer's disease.

The **Testosterone Study** is investigating the specific benefits the naturally occurring hormone testosterone can have on cognition in men as they age and has the potential to be a treatment immediately available should the results demonstrate a positive outcome. The study has had a challenging few years with COVID, but work is now ramping up with the aim of completing recruitment into the study in 2022. The study is conducted in NSW and Western Australia and is fully sponsored by the Foundation and its supporters.

#### **Thank you to our volunteers, donors and entire team**

I would like to take this opportunity to express my gratitude to our wonderful volunteers and their families and generous donors, without which our research would not be possible.

I am fortunate to have the support of an outstanding team and particularly wish to acknowledge Kevin Taddei, my deputy, who plays a central role in ensuring our research programs receive tremendous ongoing support to achieve excellence, Professor Roger Clarnette who generously donates his time to oversee the clinical aspects of our projects, and Associate Professor Stephanie Rainey Smith and Associate Professor Hamid Sohrabi for their outstanding work in leading the Sleep Intervention Study and the WA Memory Study respectively and working with me and Dr Binosha Fernando to supervise several postgraduate students.

Thank you also to the supporters of the Australian Alzheimer's Research Foundation, without which these programs could not continue. As a result of the philanthropic support the Foundation receives, it is able to provide financial support for Kevin Taddei to manage the research programs, provide funding for Alzheimer's researchers and clinical trial staff, and provide research facilities and other research supporting activities that are needed. This enables our researchers to focus on their important research work to improve the outcomes for people at risk of developing Alzheimer's disease and provide hope that we can all age gracefully without this disease.



**Professor Ralph Martin AO**

Director of Research

**Pictured (L-R):** A/Prof Hamid Sohrabi, Prof Ralph Martins AO, A/Prof Stephanie Rainey-Smith and Mr Kevin Taddei.



# THE WA MEMORY STUDY

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

Have you ever walked past someone in the street, and despite not knowing them, the smell of their perfume or aftershave brought back a lifetime of memories of young love, or an experience from your past?

Have you ever wondered just how that works? How a smell can trigger your brain to be right back in the moment, with memories as strong as if it was mere moments ago?

Well, wonder no more! It's called *olfactory memory*, and a group of West Australians, as part of the Western Australian Memory Study, are helping Associate Professor Hamid Sohrabi, the Director of the Centre for Healthy Ageing at Murdoch University, understand this fascinating phenomenon better.

*"I've always been very interested in how memory works," Hamid says. "I'm interested in how it may actually change over time, what the consequences of these changes are for people in their daily lives, and how as a clinical psychologist I can help people to improve it."*

The Western Australian Memory Study was initiated in 1996 by Professor Ralph Martins, and was originally funded by the National Health and Medical Research Council (NHMRC). Recent funding and facilities have been provided by the Australian Alzheimer's Research Foundation. The study has included more than 1100 people living in WA, testing many of them at 18-month intervals to better understand changes to memory across the ageing process.

What you may not know is that many individuals with dementia develop changes in their memory well before other signs and symptoms of dementia become clinically identifiable. The changes, however, are small, and highly specialised and very sensitive techniques are required to be able to clearly identify the changes and monitor them in older Australians.



The WA Memory Study has developed three important tools to better understand memory decline:

The **WA Prospective Memory Test** is a unique and non-invasive way to assess prospective memory abilities. Prospective memory is the ability to remember and execute a task in the future. For example, have you ever walked into a room and completely forgotten why you entered in the first place? Prospective memory declines with age, and Hamid and his research team have developed this test to assess this. The team has collected data for 200 participants. This data also suggests that sleep disruption may contribute to age-related prospective memory deficits.

The **WA Olfactory Memory Test** is a unique assessment which is a very useful way to identify people who may be at a higher risk of developing dementia. There is now a lot of evidence that olfactory memory goes down very quickly in the earlier stages of dementia.

The **McCusker Subjective Cognitive Decline Inventory** or McSCI is a questionnaire to be completed by someone with concerns about their memory and by someone close to them like a spouse or sibling or GP. The McSCI assesses things like language, memory and attention. A cut-off score means the test differentiates between people who need to be investigated further and those who experience changes that are a normal part of the ageing process.

The WA Memory Study has been supported by the Australian Alzheimer's Research Foundation (AARF), who have helped Hamid and Ralph build critical research capacity to undertake this world-class study on memory decline as an indicator of dementia risk.

The study has also provided a platform for the development of some of Western Australia's leaders in dementia research and clinical trials, including Hamid, Professor Simon Laws (Director, Centre for Precision Health, Edith Cowan University) and A/Professor Roger Clarnette (Geriatrician, Fremantle Hospital; Head of AARF's Clinical Trials Division).

The next steps for the WA Memory Study are peer-reviewed publications of the tools that have been developed and then the essential process of independently validating the three tools so they can benefit people across Australia and beyond.

Professor Martins says, "the people participating in the WA Memory Study have had incredible benefits. We have identified many people who have changes in their memory and referred them for early clinical intervention. These research studies have had a huge impact on people's quality of life. Our goal is to give back to the community. Independent validation is a critical step to maximising the impact of the WA Memory Study and the tools we have developed and will continue to refine and advance."

Associate Professor Hamid Sohrabi, PhD



## THE NEXT GENERATION



In 2021, there were eight Honour Students and Graduate Diploma Students working on the WA Memory Study who completed their university studies.

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

The Foundation is proud to be providing students who have an interest in dementia with access to research opportunities to better understand the condition, its diagnosis and risk factors.

### Honour Students 2021

*Germaine Gregory  
Laura Jeanes  
Paula St Lawrence*

### Graduate Diploma Students 2021

*Jayne Pennington  
Charlotte Wheeler  
Lindsay Roberts  
Josh Beanie  
Olivia Calleri*

*Congratulations*



# THE WA MEMORY STUDY STUDENT PROFILES

## LISA BELL STUDENT PROFILE

**Supervisor:**  
A/Prof Hamid Sohrabi, Murdoch University

My work with Hamid and the WA Memory Study researched the relationship between subjective cognitive decline (SCD) and brain functioning as measured using FDG-PET. SCD refers to a person's self-perception of a worsening of their mental ability despite performing within the normal range on objective cognitive tests. SCD is believed to be the first clinical symptom of Alzheimer's disease. However, SCD is complex and is also associated with depression, certain personality traits, and other medical conditions. It is therefore important for research to establish the characteristics of SCD that are associated with Alzheimer's-related neuropathology and those that are not. Our study thus aimed to establish whether multiple cognitive domains of SCD (for example, language, memory, executive functioning, attention etc.) were related to glucose metabolism in various brain regions. As rates of dementia increase, so too are the number of people seeking help for worries about their mental ability. This information will potentially be useful for assisting medical professionals in assessing individuals with SCD when deciding who should be referred for expensive neuroimaging and who should first be screened for other factors which may be causing the SCD, like depression.

## LAURA JEANES STUDENT PROFILE

**Supervisors:**  
A/Prof Hamid Sohrabi, Murdoch University  
A/Prof Helen Correia: Australian College of Applied Professions

My work on the WA Memory Study is to research the impact of COVID-19 lockdown on the mental health and activity levels of community-dwelling older adults. This could potentially help us understand how individuals have adapted to life following enforced social distancing and stay-at-home measures, as well as address important focus areas for intervention in older adults, particularly as we move through the COVID-19 pandemic.

## JOANNE SCOTNEY STUDENT PROFILE

**Supervisors:**  
A/Prof Hamid Sohrabi, Murdoch University  
A/Prof Belinda Brown, Murdoch University  
A/Prof Stephanie Rainey-Smith, Murdoch University  
Prof Ralph Martins, Edith Cowan University  
Prof Paul Maruff, Cogstate Ltd

My work on the WA Memory Study is to add new knowledge and understanding of 'functional resilience' and the mechanisms that can contribute to this resilience. This could help us to understand why some people are able to maintain their quality of life and independent activities of daily living compared to others displaying similar cognitive decline or Alzheimer's disease pathologies. Identifying individuals who are asymptomatic but at risk of developing Alzheimer's disease is a current knowledge gap that may represent the potential for future interventional trials, which in turn may assist in delaying the onset of dementia.

## Student Spotlight

### RACHEL XIAO STUDENT PROFILE

**Supervisor:**  
A/Prof Hamid Sohrabi, Murdoch University

Personality factors, such as neuroticism and conscientiousness, are the early indicators of subjective cognitive decline (SCD) and dementia. I am working on the WA Memory Study to research if there is a difference in SCD between cognitively healthy older individuals with different personality factors. Also, we are looking at if there is a difference in the level of self-reported decline in specific domains of cognitive capacities between people with different personality factors; for instance, language, orientation, attention, memory, executive functions, and visuospatial abilities. This project will use subjective measures that are based on self-reported complaints made by older individuals regarding those cognitive domains. This could potentially help us to better understand the mutual relations between subjective cognitive decline and the future onset of dementia in older individuals. It is hoped that this research will facilitate the early detection of cognitive decline and dementia in older individuals through the use of subjective measures.

### HADEEL TARAWNEH STUDENT PROFILE

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

There has been a strong association between auditory function and cognitive function. Changes in the way the brain processes sound have been tied to changes in cognitive function that are associated with Alzheimer's disease. 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, has been proposed as a possible screening tool for preclinical Alzheimer's disease.

In order to evaluate the currently available literature and identify any gaps in the knowledge, we reviewed full-length publications investigating objective auditory measures in older adults diagnosed with Alzheimer's disease and those at higher risk of developing Alzheimer's disease, i.e., mild cognitive impairment and subjective cognitive decline. Following a detailed literature search, 1,076 publications were screened against strict eligibility criteria, from those, 74 articles met the full inclusion criteria and were included in the systematic review, and 47 articles were included in the statistical analyses.

Findings from this systematic review and meta-analyses indicate that some objective measures of auditory function may be valuable biomarkers of Alzheimer's disease. In conjunction with currently available clinical and neuropsychological assessments, auditory electrophysiological measures may aid in detecting cognitive impairment associated with Alzheimer's disease.



# CHARLIES FOUNDATION FOR RESEARCH - COLLABORATION

The Charlies Foundation for Research and the Australian Alzheimer's Research Foundation are collaborating on a research project to investigate biomarkers to identify the early stages of Alzheimer's disease working with the WA Memory Study research team and study participants.

The biological changes that result in the diagnosis of Alzheimer's disease are thought to commence at least 2 decades before the clinical manifestation of dementia and an early diagnosis could have a significant impact on patient outcomes.

We believe that Alzheimer's disease-related biomarkers can be detected in older adults who report concerns and changes in their memory, language, working memory, executive function abilities as well as behaviour and personality.

Individuals with self-reported concerns, namely the subjective cognitive decliners, who are at higher risk of Alzheimer's disease, usually perform normally on actual neuropsychological assessments and can live an independent life for years before showing signs of dementia. **If we can identify biomarkers of Alzheimer's disease in such individuals, then we will be able to introduce preventive measures that can help them to halt or delay the neurodegenerative changes resulting in Alzheimer's disease.**

The study is now well underway utilising the WA Memory Study, led by Prof Ralph Martins and A/Prof Hamid Sohrabi. Professor Charles Inderjeeth, Consultant Physician and Dr Chris Lind, Consultant Neurosurgeon at Sir Charles Gairdner Hospital together with Adjunct A/Prof Nick Carrigan from ECU are collaborating on this project providing the clinical assessment and oversight of all participants in the study.

Both blood biomarkers and cerebral spinal fluid biomarkers of Alzheimer's disease are being investigated. The project will have significant implications for understanding the underlying causes of Alzheimer's disease, its early diagnosis and enabling preventive approaches to be implemented early.

The Australian Alzheimer's Research Foundation is delighted to be partnering with the Charlies Foundation for Research to support important research into this disease that affects so many Australians.



Australian  
**ALZHEIMER'S  
RESEARCH**  
Foundation



Professor Ralph Martins AO, PhD and Associate Professor Hamid Sohrabi, PhD

# TURNING GOOD SLEEP INTO GREAT BRAIN HEALTH FOR OLDER AUSTRALIANS

Associate Professor and NHMRC Emerging Leader Fellow in the Centre for Healthy Ageing (Murdoch University), Stephanie Rainey-Smith, knows that sleep is more than just a chance to rest our weary bones at the end of the day – it’s actually when our brains rest, reset and rejuvenate.

“While we are busy dreaming,” Stephanie explains “our brains are recharging, consolidating memories and clearing toxins that build up during the day.”

Poor sleep doesn’t just leave us feeling tired and irritable – it may increase our risk of dementia in our later years!

Sleeping well is an essential part of living well, but despite this, many Australians, and alarmingly, 60 percent of older Australians, struggle with disrupted and disordered sleep.

## **Sleep and cognitive decline – cause or consequence?**

An abundance of research describes that how we live in our younger years increases our risk of cognitive decline. Obesity, diabetes and even being sedentary increases our risk of dementia in our later years.

For years, scientists and doctors had described the relationship between people with cognitive decline (dementia and Alzheimer’s) and poor sleep behaviours, but Stephanie found herself wondering if, in fact, poor sleep was a risk factor for the onset of disease?

Her current study, the *Sleep Improvement Study*, aims to understand exactly this – whether improving sleep patterns can help older Australians retain their cognitive capacity, and fight off the earliest signs of dementia?

The Sleep Improvement Study is being conducted at the clinical research facilities at the Australian Alzheimer’s Research Foundation.

Stephanie recruits older Australians who are cognitively normal but may describe that their memory “isn’t as good as it used to be.” As part of her research study, the research participants undergo behavioural training (cognitive behavioural therapy, or CBT) to learn to improve their sleep.

Associate Professor Stephanie Rainey-Smith, PhD



“We are empowering them to improve their own sleep,” Stephanie says. “This is really important, because the effects are much longer-lasting. I liken it to that old adage about teaching an individual to fish. The skills are for life.”

Prior to, and following the training, the research participants are also put through a range of tests to measure their memory, language and recognition skills (cognitive ability). Stephanie hopes the study will show that training people to improve their sleep behaviours will result in better brain health and help to prevent the onset of dementia.

## **THE POTENTIAL FOR IMPACT**

Stephanie is excited by the possibility of such a simple, safe and non-invasive intervention to protect Australians from dementia in their later years, and her study is likely to reveal results in one to two years. She’s working with a range of health care professionals to train them to deliver the sleep training. She’s hopeful that should the results of her study show better sleep improves brain health long term, this style of sleep intervention could be recognised globally and used to protect everyone’s brain against the effects of ageing.

**The Australian Alzheimer’s Research Foundation (AARF) – supporting people, and research, from the ground up!**

Stephanie attributes her early success, growing roots and establishing her research career in Australia to a chance interaction with AARF's Director of Research, Professor Ralph Martins. After almost eleven years, and many successes, this partnership is still going strong. Stephanie is continuing to collaborate with Ralph and AARF, despite having now forged a highly successful independent career.

"We've built some amazing relationships, and done some really impactful work together," Stephanie says. I feel privileged to have had the support of AARF for the last decade and am really looking forward to seeing what's possible for the next decade!"

AARF have helped Stephanie establish new research relationships, showcase her research to the local community, and has helped her build capacity through the financial support of her team.

"They've supported me to grow the next generation of young scientists," Stephanie says, "and that's a long-term investment with an excellent return. We're training people who can work in the space for a long time to come. After all, the next wave of preventative strategies and treatments for dementia will be led by them."

It's clear that Stephanie is working to create a brighter future; not only for the next generation of emerging researchers, but critically for everyone who stands to benefit from her new discoveries for healthy ageing and long-term brain health.

## SLEEP RELATED STUDENT RESEARCH

### LOUISE PIVAC STUDENT PROFILE

#### Supervisors:

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

Louise is investigating the effect of sleep on memory and thinking, and markers of brain health assessed using neuroimaging. Her most recent work has been focused on understanding the relationship of sleep to the accumulation of the Alzheimer's hallmark, A $\beta$ -amyloid, in the brain.

Using data from the Australian Imaging, Biomarkers and Lifestyle (AIBL) Study, Louise has shown that the amount of sleep, and the efficiency of that sleep (time spent in bed, asleep), are particularly important for the accumulation of A $\beta$ -amyloid in the brain. Individuals with shorter and/or poorer sleep had faster rates of A $\beta$ -amyloid accumulation compared to those with longer and/or better sleep.

Importantly, these results were seen in individuals with 'normal' memory and thinking. This adds further support to the idea that improving sleep could have an important role to play in slowing the rates at which A $\beta$ -amyloid is accumulating in the brain, thus delaying the onset of Alzheimer's disease symptoms. Louise was recently awarded a Travel Fellowship to enable her to present these findings at the 2022 Alzheimer's Association International Conference.

**Congratulations, Louise!**

*The Australian Alzheimer's Research Foundation is providing Louise with a 50% PhD scholarship to support her research.*

### ALEXANDER MLADENOVIC STUDENT PROFILE

#### Supervisors:

A/Prof Michael Weinborn, University of Western Australia  
Dr Stephanie Rainey-Smith, Edith Cowan University  
Prof Romola Bucks, University of Western Australia

Alex commenced his PhD at the University of Western Australia in 2018 and undertook his Masters in Clinical Neuropsychology the following year. His research interests are sleep, cognitive ageing, neurodegeneration, and the interaction between these factors. Alex will graduate from the combined MPsych/PhD program in Clinical Neuropsychology in 2022. Alex's thesis entitled "Beyond Averages: Exploring the Relationship between Sleep Intraindividual Variability, Cognition, and Brain Pathology in Community-Dwelling Older Adults", is in its final stage of completion and will be submitted in April 2022.

Results from the research studies included in his thesis provide novel insights into how certain patterns of sleep over time relate to changes in cognition and brain pathology, namely, beta-amyloid (A $\beta$ ). Specifically, individuals with more variable sleep patterns performed worse on measures of episodic memory and had a greater brain A $\beta$  burden across visits compared to those with less sleep variability. Collectively, these results suggest that higher night-to-night sleep variability might be a risk factor for subsequent Alzheimer's disease. These findings also indicated that individuals who slept excessively had a greater A $\beta$  burden across visits. Recognising highly variable or prolonged sleep could assist in identifying those who may benefit greatly from sleep improvement interventions, which may help preserve cognitive function in older adults.

**Congratulations, Alex!**



Dementia is diagnosed  
**EVERY 3 SECONDS**  
around the world.

---

# ADNET – AUSTRALIAN DEMENTIA NETWORK

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

The Australian Alzheimer's Research Foundation is delighted to be lending its support to the ADNeT initiative in Western Australia.

**ADNeT was announced by the Federal government in July 2018 as a major new initiative in Alzheimer's diagnosis, clinical trial enrolment and patient care.**

15 institutions across Australia are involved in the ADNeT program, which has 3 core aims:

## REGISTRY

Establishing the first dementia clinical quality registry to track, benchmark, and report on the clinical care of people with dementia.

## MEMORY CLINICS

Establishing consistent best practice guidelines for the diagnosis and treatment of dementia.

## SCREENING & TRIALS

Facilitating the development of effective therapies by providing detailed dementia screening of patients suitable for participation in clinical trials.

Prof Ralph Martins from Edith Cowan University is an ADNeT Chief Investigator and part of the National ADNeT Management Team.

AARF is supporting the ADNeT program in Western Australia in a variety of ways, including providing clinical neuropsychologists and the facilities for the program.

One of the key outcomes in 2021 was the launch of the first national **Memory and Cognition Clinic Guidelines**. These Guidelines were developed in collaboration with Australian health professionals, leading academics and researchers, and people with a lived experience of dementia and their care partners.

The Guidelines seek to bring together an agreed approach in the clinical practices and procedures of Australian Memory and Cognition Clinics. The Guidelines include best-practice standards across 14 areas, including:

- the pre-assessment process,
- clinical interview and diagnostic work-up, and
- the post-diagnostic care pathway.

The Guidelines promote consistent, evidence-based and high-quality assessments to all clients, regardless of where they live. The Guidelines also offer an overarching view to supporting continuity of care, enhancing patient outcomes, and improving the quality of life for those diagnosed with dementia and their care partners.

Accompanying the Guidelines is a **Client Guide**. This was developed for current and future clients of Memory and Cognition Clinics. The Client Guide outlines the functions of a Memory and Cognition Clinic and summarises important points from the Guidelines, such as how to access a clinic, recommended waiting times, what to expect before the assessment and when receiving a diagnosis, and what post-diagnostic care may include.

The Memory Clinics Initiative also published an online map of Memory Clinics across the Country enabling the general public and health professionals to view more than 135 services across Australia.



Australian  
Dementia Network  
REGISTRY. CLINICS. TRIALS.

## CUTTING-EDGE, COST-FREE SPECIALIST DIAGNOSTICS

The ADNeT Screening and Trials initiative is creating opportunities for Australians living with dementia to access new therapies.

The initiative provides clinicians with cutting-edge specialist diagnostic techniques at no cost to the patient, with the aim of facilitating recruitment into intervention trials across Australia.

Eligible patients will undergo brain imaging and neuropsychological assessments.

Results are provided to referring clinicians to assist with diagnosis and patient management.

### INTERESTED?

**PLEASE CONTACT MARK RODRIGUES  
ON (08) 6457 0266 OR EMAIL  
M.RODRIGUES@ECU.EDU.AU**

# A BLOOD TEST FOR ALZHEIMER'S DISEASE WOULD BE A GAME-CHANGER

Prof Ralph Martins AO, PhD  
Dr Pratishtha Chatterjee, PhD  
Mr Steve Pedrini, MSc

With no effective treatment for Alzheimer's disease, prevention and risk reduction are key strategies of current Alzheimer's research.

**Identifying those at greater risk of Alzheimer's disease paramount and developing a low-cost and accessible blood biomarker for Alzheimer's disease is a critical step in this process.**

Building on our previously published study (listed at the back of this report) looking at the presence of blood glial fibrillary acidic protein (GFAP) in cognitively unimpaired older adults at risk of Alzheimer's disease, we have studied other potential blood biomarkers, including total-tau and phosphorylated-tau 181 and 231 (t-tau, p-tau181, p-tau 231) and neurofilament light (NFL).

Blood glial fibrillary acidic protein (GFAP), total-tau and phosphorylated-tau 181 and 231 (t-tau, p-tau181, p-tau 231) and neurofilament light (NFL) levels are higher in Alzheimer's disease and it has been suggested that these proteins could serve as potential blood-biomarkers for the disease, given that they reflect Alzheimer's disease-related neuropathological processes.

Our recent study, published in *Alzheimer's and Dementia*, (listed at the back of this report) carried out a parallel investigation of plasma GFAP, tau (including t-tau, p-tau181 and p-tau231) and NFL in people with preclinical Alzheimer's disease, by comparing the circulating levels of these proteins between cognitively unimpaired older adults with an absence of brain amyloidosis (A $\beta$ -) and cognitively unimpaired older adults who were classified as being within the preclinical stage of the disease, characterised by the presence of brain amyloidosis (A $\beta$ +).

We found elevated blood GFAP, p-tau181 and p-tau231 levels in the A $\beta$ + group compared with the A $\beta$ - group that were consistent 12 months apart, suggesting that the plasma protein differences observed are potentially reliable candidate markers for the diagnosis of preclinical Alzheimer's disease.

In this study, we also report for the first time that the combination of the Alzheimer's disease risk factors (age, sex and Apolipoprotein gene  $\epsilon$ 4 carrier status) and GFAP in a statistical model had the highest accuracy (86%) for identifying A $\beta$ + versus A $\beta$ -, compared with the combination of the Alzheimer's disease risk factors with any of the other proteins investigated in the study.

Additionally, our study also shows for the first time that GFAP and p-tau181 levels increased with time in the A $\beta$ + group over 12-months, suggesting that GFAP and p-tau181 may have the potential in serving as longitudinal monitoring markers and outcome measures for relatively shorter clinical trials conducted in preclinical Alzheimer's disease populations.

These results are very promising and further validation will ultimately lead to the development of a blood test to identify people at risk for Alzheimer's disease.



Mr Steve Pedrini, Research Fellow, Edith Cowan University



# GENETICS AND ALZHEIMER'S DISEASE

Through the generous support from the Pinnacle Charitable Foundation and Spheria Asset Management, the Australian Alzheimer's Research Foundation is delighted to be supporting a genetics project led by Professor Simon Laws, to understand how our genes contribute to the development of Alzheimer's disease.

**Whilst Age is the biggest risk factor for Alzheimer's disease, genetics plays a significant role.**

Whilst a rare genetic mutation will result in a definitive progression to Alzheimer's disease at a relatively young age, other gene mutations increase the risk of developing the disease.

The project aims to develop a clearer picture of how an important mechanism called DNA methylation (that affects how gene activity is adjusted during life), is altered at the earliest stages of Alzheimer's disease. Understanding the implications of genetic variations has the potential to provide more avenues for the development of therapeutic interventions.

This research is using state of the art assessment of blood samples and will assess the differences in the levels of DNA methylation between individuals at greatest risk of Alzheimer's disease or showing the greatest rate of decline in memory or accumulation of brain changes. Through ongoing analysis of these differences, a better understanding of what biological pathways are being altered with Alzheimer's, which will then be prime targets for the development of new treatment strategies.

So far, the research team has found that a particular combination of methylation signals, which allows the construction of an individual's "biological age", results in an association with hippocampal volume. Those individuals with a higher biological age than their actual age (i.e. fast agers) have a reduced hippocampal volume compared to those with a lower biological age (i.e. slow agers).

The research is using samples from the Australian Imaging, Biomarkers and Lifestyle (AIBL) Study which undergo a methylation analysis to gain an understanding of how components of the DNA may change over time as the disease progresses.



Professor Simon Laws - Professor of Translational Genomics and the Director of the Centre for Precision Health, a Strategic Research Centre, at Edith Cowan University

## LIDIJA MILICIC STUDENT PROFILE

### **Supervisors:**

Prof Simon Laws, Edith Cowan University  
Dr Tenielle Porter, Edith Cowan University  
Dr Michael Vacher, CSIRO

**The Foundation is delighted to provide a PhD scholarship top-up to ECU student Lidija Milicic, who is working on a genetics project titled: Investigating changes in DNA Methylation age in Alzheimer's disease.**

The project aims to investigate whether the likelihood of developing Alzheimer's disease may be predicted by discrepancies between chronological and DNA methylation ages to improve the diagnostic processes; and will aim to investigate DNA methylation age in the context of Alzheimer's disease to provide an alternative way in which samples could be stratified for clinical trials.

# AIBL STUDY

## The Australian Imaging, Biomarkers and Lifestyle Study

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

**In 2021, as AIBL entered its fifteenth year, we published a manuscript that summarises the incredible achievements of this study to date. This manuscript clearly highlights that AIBL is at the forefront of Alzheimer's research, globally.**

AIBL data have contributed to the development of new diagnostic criteria for Alzheimer's that permit earlier and more accurate diagnosis, and to the design of early intervention trials aimed at preventing the development of dementia from Alzheimer's disease. AIBL has also united Alzheimer's researchers across Australia and greatly increased Australian collaboration with international Alzheimer's research groups.

As we continue to collect data from participants, further refinement, and validation of blood biomarkers for Alzheimer's disease will be undertaken, genetic contributions and profiles for onset and progression will be developed, lifestyle influences on cognition and Alzheimer's disease will be prospectively tracked, and more early intervention studies will be launched - including AU-ARROW, commencing in 2022.

The AIBL study framework has been responsible for training researchers and clinicians of the future, by supporting multiple Honours and MSc projects, more than 25 PhD projects, as well as over 15 clinical placement students, at the time of writing. Moreover, with over 340 publications to date and 2500 citations per year, the increasing value, impact, and productivity of AIBL with time is apparent, as is the increasing value of accumulating longitudinal data.

We thank all participants, past and current, without whom these achievements would not have been possible.

Associate Professor Stephanie Rainey-Smith, PhD and Mr Kevin Taddei, MSc



## Student Spotlight

### KELSEY SEWELL STUDENT PROFILE

#### **Supervisors:**

A/Prof Stephanie Rainey-Smith, Murdoch University  
A/Prof Belinda Brown, Murdoch University  
A/Prof Hamid Sohrabi, Murdoch University  
A/Prof Jeremiah Peiffer, Murdoch University  
A/Prof Kirk Erickson, University of Pittsburgh

Physical activity and exercise can improve cognitive function and reduce the risk for dementia. Other lifestyle factors, including sleep, are associated with cognitive function and dementia risk, and exercise is an effective therapeutic strategy for improving sleep. Based on these associations, it has been hypothesised that sleep might be an important mediator of the effects of exercise on cognition.

We reviewed the current literature to evaluate whether sleep and physical activity are independently or jointly associated with cognitive function. The result were published in a paper listed at the back of this report. The extant literature in this area is minimal, and the causal relationships between physical activity, sleep and cognition have not been examined.

We found some evidence that physical activity may compensate for the effects poor sleep has on cognitive function, and that physical activity may improve sleep, which may, in turn, improve cognition. However, further research in this area is required to fully understand these pathways and their underlying mechanisms. Further research may enable the development of individually tailored intervention programs to result in the greatest cognitive benefit, ultimately delaying the onset of Alzheimer's disease. For now, the message is clear, move well and sleep well!

### RACHAEL MUMME STUDENT PROFILE

#### **Supervisors:**

A/Prof Michael Weinborn, University of Western Australia  
Prof Romola Bucks, University of Western Australia  
A/Prof Stephanie Rainey-Smith, Murdoch University  
Prof Paul Maruff, Cogstate Ltd

In 2018 Rachael commenced her PhD and Masters of Clinical Neuropsychology at The University of Western Australia. In late 2021 she completed her studies, including the acceptance of her thesis titled 'Cognitive Variability and the Onset of Alzheimer's disease.'

This thesis focused on in-session variability in neuropsychological testing as a marker of Alzheimer's disease risk. Overall, the works found that this variability, also called Intra-individual variability, is a reliable predictor of future dementia status or cognitive decline. This included findings that more complex tasks show greater promise in predicting Alzheimer's disease by showing early differences between those who develop the disease and those who do not. An improved understanding of early Alzheimer's disease markers, such as these, may play an important role in early disease identification and provide greater scope for clinical research around disease prevention and treatment.

**Congratulations, Rachael!**





## Student Spotlight

### SHAUN MARKOVIC STUDENT PROFILE

**Supervisors:**

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

The Australian Alzheimer's Research Foundation is delighted to be providing Shaun with an annual top-up scholarship to support his PhD research.

Shaun commenced his PhD in 2019 with a focus on traumatic brain injury (concussions) specifically examining, how concussions impact the ageing brain. While also investigating if any lifestyle-based strategies could promote recovery and long-term health outcomes for older adults who have experienced concussions.

Shaun had originally planned to study a group of older adults who had been recently exposed to a mild concussion for 12 months following their injury. However, due to ongoing COVID 19 implications, the study was unable to proceed. Fortunately, Shaun was able to work with pre-collected data, where it was concluded that a history of concussion was linked to changes in later-life brain volume in a sample of older adults.

After analysing this data, Shaun published a comprehensive review of the current evidence for lifestyle factors as an important element of post-concussion rehabilitation. Current evidence suggests that physical activity is important during recovery, even if it's just brief periods of low intensity.

In 2021, Shaun had the opportunity to collaborate with a team of researchers from the Curtin Neuroscience Laboratory, where he took part in a project conducting an Australia-wide survey of community members' concussion-related experiences. This survey aimed to evaluate peoples' post-concussion exercise habits while also examining exercises' role in self-reported recovery. The results from this survey are soon to be published!

Shaun will be submitting his thesis in 2022.



## Student Spotlight

### NATALIE FROST STUDENT PROFILE

**Supervisors:**

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

Dr Natalie Frost completed her PhD in early 2021 under the supervision of Dr Belinda Brown, Associate Professor Michael Weinborn, and Associate Professor Gilles Gignac. Natalie holds a Bachelor of Psychological Science with Honours from Edith Cowan University and a Masters and PhD in Clinical Neuropsychology from the University of Western Australia.

Natalie's research involved the Intense Physical Activity and Cognition (IPAC) study undertaken as a collaboration between Murdoch University and the Australian Alzheimer's Research Foundation.

The focus of Natalie's PhD research investigated whether there was an optimal exercise intensity level to promote the maintenance of executive functions in older adults. She examined the interrelationships between exercise intensity, cardiorespiratory fitness, executive function, and frontal lobe grey matter volume in older adults. Encouragingly, the results of her research showed that an experimentally induced increase in cardiorespiratory fitness is associated with better performance in some executive function subdomains, as well as increased grey matter volume in several frontal lobe regions for certain individuals.

Now that she has completed her PhD and clinical training, Natalie has moved to the opposite end of the lifespan, working as a Paediatric Clinical Neuropsychologist Registrar. She provides a neuropsychological assessment of complex cognitive and psychiatric cases, with a particular interest in drug and alcohol and trauma-induced cognitive presentations, as well as assessment of neurodevelopmental disorders (Fetal Alcohol Spectrum Disorder, ADHD, Autism Spectrum Disorder, Intellectual Disability, Specific Learning Disorder). Natalie provides diagnostic assessments across the metro, regional, remote, and criminal justice settings. However, she still maintains a strong interest in research related to the benefits of regular exercise on cognitive function across the lifespan and plans to remain actively engaged in research alongside her clinical work.

**Congratulations Natalie!**

# TESTOSTERONE STUDY

Age remains the most important known risk factor for Alzheimer's disease.

**Testosterone levels decline in men as they age, and low levels of sex hormones could be associated with worse cognitive function.**

It is known that sex hormones positively affect brain function but the effect on cognition is less well known. The Foundation is undertaking a large study to understand what effect testosterone can have on brain amyloid levels and cognition.

Previous studies have demonstrated that Alzheimer's disease is caused by the abnormal build-up of a protein called *amyloid* in brain cells. This build-up is then connected to the brain cells functioning in an abnormal way, and the cognitive signs and symptoms of Alzheimer's disease.

Earlier work was focused on the safety of giving testosterone to men. This was followed up with lab-based studies where the team led by Prof Martins learned and reported for the first time, that treatment with the male sex hormone testosterone decreased the build-up (or accumulation) of amyloid in their model, a breakthrough discovery.

This was a huge moment for the team, recognising that a solution as simple as a naturally occurring hormone could be used to halt the progression of cognitive decline in Alzheimer's disease. The excitement of this discovery has fuelled the now 20 years of research culminating in the current testosterone clinical trial in Australian men, **to identify if testosterone supplements can prevent the increase in the amyloid protein, which eventually leads to Alzheimer's disease.**

## *A personal experience...*

"I was part of the study until I was diagnosed with cancer last year.

Actually, it was one of the routine blood tests whilst on the study that alerted one of the doctors to contact me and let me know.

Luckily it was caught while still not too aggressive and I was treated and my PSA is down. I was so sorry I had to leave the study because the team were such lovely, caring people doing a wonderful job".

The study involves an initial brain scan to look at amyloid levels in the brain. Participants then receive 13 months of testosterone treatment, and some memory testing, before a final brain scan to see if the testosterone treatment has prevented the build-up of amyloid protein in the brain. Men aged 60-80 with lower-than-average testosterone levels are eligible for the study.

The Foundation is hoping to complete the study in the next couple of years, and the results show promising signs for future, larger and longer studies. It's an ambitious goal, which has been well supported by the Australian Alzheimer's Research Foundation (AARF).

*"We are lucky to have funding from AARF to do this important trial," says Prof Martins. "These trials are expensive, and so the support from the Foundation means that we can better understand whether testosterone is an effective drug at suppressing Alzheimer's onset in men."*

If you would like to learn more about the testosterone study, please contact the team at [trial@alzheimers.com.au](mailto:trial@alzheimers.com.au) or call (08) 6304 3966. The study is being conducted in NSW and Western Australia.

The participants in the study are under the care of doctors and nurses who closely monitor them throughout the study. "We take great care of our study participants and get to know them very well", said Dr Christina Di Camillo, one of the doctors working on the study, "and we are extremely grateful to everyone who chooses to take part in this important research".



**T E R R Y**  
T R I A L P A R T I C I P A N T

# CHILDHOOD DEMENTIA

Dr Prashant Bharadwaj, PhD

**Dementia is usually considered an ageing disorder and cognitive decline in children has received little attention.**

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

This equates to 129 births in Australia each year. Childhood dementia is clinically characterized by severe degeneration of the central nervous system with a learning disorder and associated behavioural abnormalities. The symptoms generally start between 2 and 6 years of age with a life expectancy of 10 to 20 years.

Because of its rarity, there is a lack of awareness of the disorder which has a significant burden on the public health system. The total economic cost of childhood dementia in Australia between 2021 to 2030 is estimated to be \$3.9 billion. While this may be considered low in comparison to other childhood conditions, there are two attributing factors that must be considered: childhood dementias confer only a short life expectancy and given the lack of treatment options across the 70 identified conditions, the burden of care is disproportionately met by the affected families themselves, support services and carers.

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. Currently there are no effective treatment options or ways to measure disease progression and response to treatment.

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 lysosomal storage disorders predominantly features an accumulation of lipid, cholesterol, or sugar molecules.



Dr Prashant Bharadwaj, Research Fellow, Edith Cowan University

In 2021, Dr Bharadwaj was awarded a \$250,000 grant by the WA Child Research Fund (WACRF) for a 2-year project to discover biomarkers for childhood dementia. The project aims to identify specific changes in proteins in the blood and urine of children with various types of childhood dementia that could be used to monitor the progression of their disease. These relatively non-invasive markers could be very useful tools to measure response to new treatments in clinical trials. In addition, this project will add to the knowledge base about these diseases and may uncover new treatment approaches.

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. The correlation of blood and urine biomarkers to clinical pathology will be assessed to identify prognostic biomarkers that inform disease severity and progression.

Additionally, Dr Bharadwaj has initiated a national childhood dementia biomarker study in collaboration with Queensland Children's hospital (Dr Anita Inwood and Dr Matthew Lynch) and Sydney Children's health network (Dr Michelle Farrar and Dr Kaustuv Bhattacharya). This study will be an extension of the WACRF study and aims to involve more than 7 rare LSDs that cause severe neurodegeneration in children. A PhD student, Mr Ray Adisa enrolled at Edith Cowan University has been recruited for this project and will be working with Dr Bharadwaj, Dr Fernando and Prof Martins.

Dr Bharadwaj is an expert in autophagy and Alzheimer's disease and has 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.

Dr Bharadwaj has established a neural stem cell line in collaboration with Lund University, Sweden (Dr Isaac canals) for investigating Sanfilippo syndrome, one of the LSD that causes childhood dementia. A masters student Ms Amrita Das from the University of Western Australia, was recruited for this project.

Ms Das received a high distinction for her thesis and her findings have provided novel insight into the autophagy-lysosomal pathways involved in the disease pathogenesis of Sanfilippo syndrome. Further analysis is being undertaken to characterize autophagy-lysosomal defects and assess the effects of pharmaceutical modulators on autophagy in this disease model.

This is an extremely exciting step forward for families affected by childhood dementia and a project the Australian Alzheimer's Research Foundation is delighted to be supporting. Ongoing additional funding for the research is needed and the Foundation would welcome contributions focused on this important research into childhood dementia.

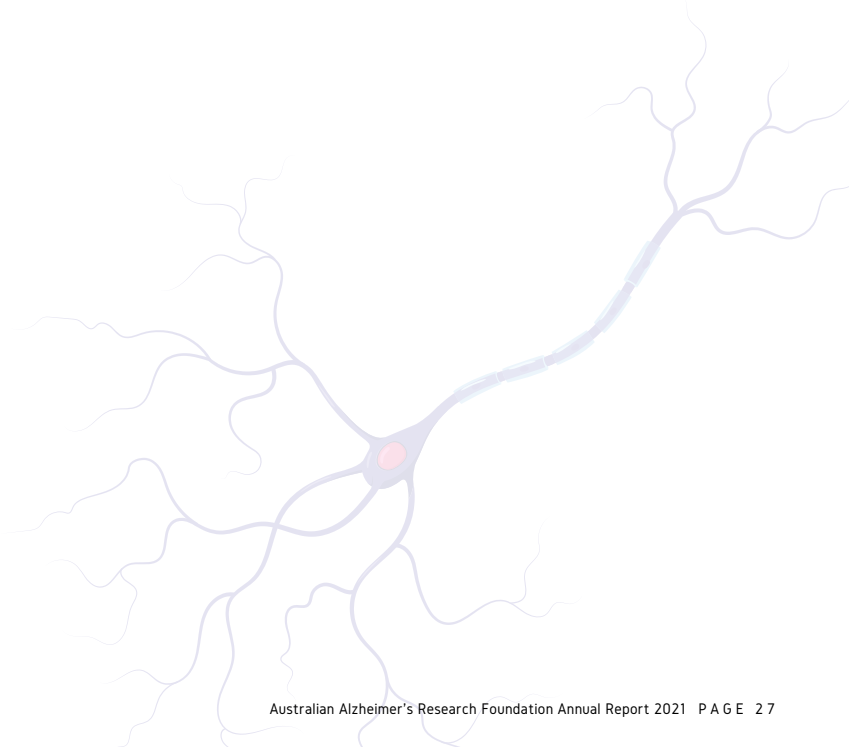
## GLOBALLY, EVERY 11 MINUTES, A CHILD DIES FROM CHILDHOOD DEMENTIA. 48,300 DIE EACH YEAR



**AROUND 1 IN EVERY 100 PEOPLE  
DIAGNOSED WITH DEMENTIA  
ARE KIDS**



**700,000 PEOPLE ARE  
ESTIMATED TO BE LIVING WITH  
CHILDHOOD DEMENTIA TODAY**



# DIAN STUDY

## The Dominantly Inherited Alzheimer's Network

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

The DIAN study is an international, multi-site collaboration led by Washington University, aiming to identify the biological changes that occur in the development of Alzheimer's disease to improve early diagnosis and track the 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.

At the end of 2021, the Perth site had 25 DIAN participants enrolled in the DIAN Observational Study undergoing week-long assessments every two years with a remote visit in the interim year. Whilst some visits were unable to proceed with study participants residing in Queensland and South Australia and unable to enter Western Australia due to COVID-19 restrictions, the research on data previously collected was ongoing throughout 2021 and led to numerous publications in journals with significant international reputations. These publications aimed to compare blood levels of biomarkers in mutation carriers and non-carriers to identify a panel of biomarkers for the diagnosis of pre-symptomatic cerebral amyloid angiopathy.

The DIAN Study is conducted at the Australian Alzheimer's Research Foundation facilities.

---

## A TRIAL RUN-IN STUDY (TRACK D-CAA)

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

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

In 2020, the team announced the commencement of the Track D-CAA Study, researching a group of individuals with a mutation that causes haemorrhagic stroke, which is a stroke caused by a break in the wall of a blood vessel in the brain. The mutation causes an accumulation of beta-amyloid in the brain blood vessels, which is commonly associated with Alzheimer's disease. The genetic mutation is called **Dutch-Type Cerebral Amyloid Angiopathy or D-CAA**.

The project is a collaboration with Leiden University Medical Centre in The Netherlands and is being conducted at the clinical research facilities at the Australian Alzheimer's Research Foundation in Western Australia.

Due to the COVID-19 pandemic, the start of participant assessments was deferred until 2022. In 2021 the team concentrated on informing potential study participants of the importance of the study, as well as the procedures involved over the 2-year study. The research team held two meetings for potential participants in Perth and Albany. These meetings were well received, and the team now has a list of nearly 25 participants ready to commence the study in 2022.

We are aiming to recruit 50 participants for the study, so if you have a Dutch heritage and you know of strokes in family members, please email our study coordinator, Samantha Gardener, at [s.gardener@ecu.edu.au](mailto:s.gardener@ecu.edu.au).

Findings are likely to be of great importance to the much larger group of older adults who develop cerebral amyloid angiopathy later in life, causing a stroke.

In 2021, the team was also successful in their bid to host the 8th International Cerebral Amyloid Angiopathy Conference in November 2022 (<https://icaaconference.org>) with support from the Australian Alzheimer's Research Foundation and other funders. The conference will present the highest quality research and knowledge on the diagnosis, prevention and treatment of Cerebral Amyloid Angiopathy. The 2022 Conference is the first to be held outside North America and Europe and will connect internationally renowned scientists and clinicians from all Cerebral Amyloid Angiopathy research pathways - bench to bedside.



# NUTRITION AND ALZHEIMER'S

Dr Binosha Fernando, PhD

Is it possible to eat particular foods or follow a particular diet that could delay or prevent Alzheimer's disease?

The good news is that we have observed and identified a variety of dietary factors that improve the health of the brain in older adults who may develop Alzheimer's disease.

Given the prevalence of Alzheimer's disease, which accounts for approximately 70% of dementia, and the lack of treatment options, the need for the identification of Alzheimer's disease prevention strategies is appealing.

## EFFECT OF DIETARY PROTEIN AND DIETARY FIBRE

Research on dietary protein and fibre suggests that consuming a high protein and high fibre diet may protect against Alzheimer's disease. Low and medium protein or fibre intakes are associated with significantly lower cognition levels, indicating that the more protein and fibre consumed, the lower the likelihood of low executive functions, language, or attention.

Additionally, low protein intake has been associated with poorer executive function performance among Apolipoprotein E (APOE) carriers. APOE is the genetic risk factor for Alzheimer's disease and carriers of the APOE e4 allele are at higher risk of age-related cognitive decline and Alzheimer's disease than non e4 carriers.

Low fibre intake was strongly associated with lower performance in language among APOE carriers and non-APOE carriers. Using data from the Australian Imaging, Biomarker & Lifestyle Flagship Study of Ageing (AIBL) conducted in Melbourne and at the Australian Alzheimer's Research Foundation in Western Australia, we have also identified additional associations between dietary protein and fibre intake and age, gender, and apolipoprotein E allele. Apolipoprotein E was found to influence the consumption of protein in female older adults, whereas fibre intake was unaffected by Apolipoprotein E. There were also greater chances of having high levels of brain amyloid if protein intake fell below a certain threshold.

We are currently exploring the relationship between diet and depression using these results, as well as the relationship between diet and imaging biomarkers of brain health, and the relationship between diet and blood-based biomarkers of brain health.



Dr. Binosha Fernando, Research Fellow, Edith Cowan University

## EFFECT OF GUT ORGANISMS

The diet is considered the most important factor that influences the microorganisms in the human gut. The availability of different types of nutrients (from the diet) determines the abundance and function of certain microorganisms. A recent study suggests that gut microbiota regulate immunity in a significant way. In the gut, microbes produce a wide range of physiologically important products, such as short-chain fatty acids. Our research indicates that short-chain fatty acids, specifically butyrate, could reduce the toxicity of amyloid-beta. Thus, we suggest that butyrate should be further studied as a potential therapeutic agent to treat cognitive deficits associated with Alzheimer's disease. Intake of dietary fibre helps to grow bacteria that could produce short-chain fatty acids in the human gut. Currently, we are investigating how the bacterial population influences neuroinflammation, senile plaque formation, and neurofibrillary tangle accumulation in Alzheimer's disease patients and patients with subjective memory complaints.

## EFFECT OF POLYPHENOLS

Fruits and vegetables have naturally occurring bioactive components such as polyphenols. Polyphenols are the most abundant antioxidant in the human diet. Natural polyphenols (PPs) target multiple Alzheimer's disease related pathways such as protecting the brain from beta-amyloid and tau neurotoxicity, ameliorating oxidative damage and mitochondrial dysfunction. Among natural products, the cereal crop sorghum, grape seed, goji berries and sea buckthorn have some unique features. A broad range of polyphenols, including phenolic acids, flavonoids, and condensed tannins are present in these including some classes that are rarely found in other plants. Higher antioxidant activity potentially makes their consumption beneficial through oxidative stress reduction and thus the prevention and treatment of neurodegenerative diseases. Our work has shown that polyphenols from sorghum, goji berries and sea buckthorn could reduce the amyloid-beta, tau levels and oxidative stress at the cellular level.

# PERSONALITY TRAITS AND DEMENTIA

At the Foundation's Public Lecture in September 2021, a keynote address by **Associate Professor Hamid Sohrabi**, Director, Murdoch University Centre of Healthy Ageing, captured great attention.

A/Prof Sohrabi and his collaborators studied individuals from two studies: the WA Memory Study and the Karviah Study in NSW, which have both been supported by the Australian Alzheimer's Research Foundation and other funding groups.

**Personality factors have long been associated with Alzheimer's disease and dementia**, but they have not been examined to ascertain a specific link with brain imaging that reflects Alzheimer's disease.

Imaging of the brain's glucose metabolism provides an assessment of neuronal function in the brain and is closely associated with Alzheimer's disease. A type of brain imaging called FDG-PET has the unique ability to estimate the local cerebral metabolic rate of glucose consumption. This provides information on neuronal death and synapse dysfunction, as synapse dysfunction and loss induce a reduction in neuronal energy demand that results in decreased glucose metabolism.

So is there a relationship between personality factors and the brain's use of glucose shown in brain imaging?

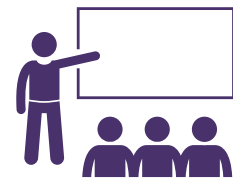
Which is the chicken, and which is the egg?

Could personality factors be a potential early sign of dementia?

And could interventions into personality factors reduce the risk of dementia?

The study did not attempt to answer all these questions. But the study was designed to investigate the relationships between personality factors and glucose metabolism in neural regions more susceptible to Alzheimer's disease. The personality factors investigated were neuroticism, extraversion, openness/intellect, agreeableness and conscientiousness. The group studied were cognitively healthy community-dwelling older adults.

**The research found significant relationships between personality factors and glucose metabolism in neural regions more susceptible to Alzheimer's disease.**



Higher neuroticism and lower scores on extraversion and conscientiousness were significantly associated with decreased glucose metabolism in brain regions typically affected by Alzheimer's disease. Openness and agreeableness were not significantly related to brain functions.

The individual with the highest score on neuroticism showed significantly lower glucose metabolism in regions of the brain affected by Alzheimer's disease, while the individuals with the highest scores on conscientiousness and extraversion showed higher glucose metabolisms in these regions. **This may imply that some personality traits may be a risk or protective factor for the future development of Alzheimer's disease.**

Finally, the research team observed that women scored higher on the neuroticism scale. It is important to note that depression is one of the primary facets of neuroticism and is more common in women. **Depression is also an established risk factor for Alzheimer's disease and cognitive decline.** Given that women are disproportionately at higher risk of Alzheimer's disease, further research is warranted to examine the implications of this finding for dementia risk and gender contribution later in life.

In summary,

- There is a significant relationship between cognition, brain function and personality factors.
- There is compelling evidence for a specific personality profile to predict a higher risk of dementia.
- Some evidence exists that in-born personality factors may result in a higher risk of dementia.
- Longitudinal studies may solve the 'chicken and egg' dilemma?

Further research will inform whether personality factors can be used to screen those at higher risk of neurodegeneration and whether psychological intervention towards moderating personality factors may minimise or delay the risk of Alzheimer's disease.



# COFFEE AND ALZHEIMER'S DISEASE

Dr Samantha Gardener, PhD

**Good news for coffee drinkers - higher coffee consumption is associated with a slower decline in memory and thinking abilities and slower accumulation of the toxic amyloid-beta protein.**

**Worldwide, coffee is one of the most popular beverages consumed.**

Several studies have suggested a protective role of coffee against various conditions, including stroke, heart failure, cancers, diabetes, and Parkinson's disease. Research also shows that coffee reduces the risk of Alzheimer's disease, however, there is limited data looking at coffee intake and decline in memory and thinking abilities over time, and exactly how coffee affects these abilities.

Researchers at Edith Cowan and Murdoch Universities investigated usual coffee intake using a questionnaire, and decline in memory and thinking abilities in 227 older adults from the Australian Imaging, Biomarkers, and Lifestyle (AIBL) study. This study was conducted at the Australian Alzheimer's Research Foundation over 10 years.

Research Fellow Dr Samantha Gardener said the study also investigated the relationship of usual coffee intake to the change in brain volume over time, and the accumulation of the toxic brain protein amyloid-beta which is linked to a greater risk of Alzheimer's disease.



Dr Samantha Gardener, Research Fellow, Edith Cowan University

"We found that those who drank more coffee had a slower decline in executive function and attention. Executive functioning helps a person complete tasks and includes skills like managing time, switching focus, planning and organising, remembering details, and multi-tasking," Dr Gardener said. "Those who drank more coffee also had a slower accumulation of the toxic brain protein, amyloid-beta." There were no associations between the amount of coffee drunk and brain volume.

"Our results suggest that if the average cup of coffee made at home is 240 grams, increasing intake from one to two cups per day could provide up to eight per cent decrease in executive function decline over an 18-month period, and up to five per cent decrease in toxic brain amyloid-beta protein accumulation over the same time period."

Dr Gardener said the results further support the hypothesis that coffee intake may be a protective factor against Alzheimer's disease, with increased coffee consumption potentially reducing the decline in memory and thinking abilities by slowing the accumulation of the toxic amyloid-beta protein in the brain, and thus reducing the brain cell death this protein causes.

"Further investigation is required to evaluate whether coffee intake could be incorporated as a modifiable lifestyle factor aimed at delaying Alzheimer's onset," she said.

The research, published in 'Frontiers of Aging Neuroscience' in November 2021, attracted more than 430 media mentions across 30 countries, reaching an audience of approximately 420 million people, highlighting the relevance of the research.

You can read the full article at this website:

[doi.org/10.3389/fnagi.2021.744872](https://doi.org/10.3389/fnagi.2021.744872)

"Those who drank more coffee had a slower accumulation of the toxic brain protein that causes Alzheimer's disease"

# THE AU-ARROW STUDY

The **AU**stralian-Multidomain **A**pproach to **R**educe dementia Risk by **p**rotecting brain health **W**ith lifestyle intervention study.

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

**The AU-ARROW study is researching the potential role of lifestyle modifications to reduce the risk of developing Alzheimer's disease.**

Lifestyle modifications that include adopting a healthy diet, carrying out regular aerobic exercise, staying socially active and undergoing brain training exercises have all been shown to improve brain function, and/or slow the deterioration of brain function.

The AU-ARROW project is primarily funded by a Medical Research Future Fund (MRFF) grant and the US Alzheimer's Association. Macquarie University in NSW is sponsoring the study, with Macquarie University and the Australian Alzheimer's Research Foundation in Western Australia being the two sites involved in the study. The Australian Alzheimer's Research Foundation is providing additional funding for the project, together with the research facilities for the conduct of the study.

The AU-ARROW study is a member of the worldwide collaboration, called World-Wide FINGERS and closely follows the protocol of the US-POINTER study (also a member of WW-FINGERS) to enable data sharing and greater international collaboration.

There are also several aspects that are novel to the Australian study. One such example is the sleep component.

In 2021 the team received funding from the US Alzheimer's Association to purchase WatchPAT™ 300 devices which will be worn for two nights at baseline, 12-, and 24-month assessments by as many participants as possible. They enable continuous overnight measurement of oxygen desaturation, pulse tonometry, and heart rate using finger pulse oximetry. The main aims of the sleep component of AU-ARROW are to:

## ONE

Investigate whether the lifestyle intervention improves nocturnal hypoxemia (low blood oxygen) and sleep fragmentation.

## TWO

Assess the degree to which longitudinal and intervention effects on sleep (hypoxemia, fragmentation, duration, efficiency and other objective measures) predict changes in cognitive trajectory.

## THREE

Assess the degree to which longitudinal and intervention effects on sleep predict dementia biomarker profiles in the blood and brain.

Another novel aspect of the AU-ARROW study is a Mindfulness questionnaire completed at baseline, 12- and 24-months assessments to investigate the effects of a structured multidomain lifestyle intervention versus a healthy lifestyle education intervention on Mindfulness.

Mindfulness represents an underexplored yet promising non-pharmacological strategy for the prevention of cognitive decline. The practice of Mindfulness has been associated with enhanced cognition and increased hippocampal grey matter density in young adults.

Following some delays in 2021 due to COVID restrictions, the Study has now commenced in Perth, with the aim to recruit over 200 participants to take part in the AU-ARROW study, aged between 60 and 79 years of age, who have a relatively sedentary lifestyle. If you are interested in taking part in this two-year lifestyle intervention study please email the study coordinator, Samantha Gardener ([s.gardener@ecu.edu.au](mailto:s.gardener@ecu.edu.au)) or call the AU-ARROW study staff at (08) 6304 3966.



# WELCOME

## TO THE AU-ARROW TEAM

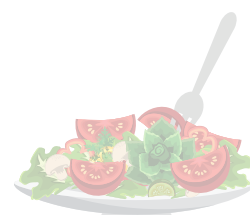
### KIRSTY WOODS

AU-ARROW Exercise Physiologist

"I am a passionate Exercise Physiologist excited to apply and expand my experience in the research sector, particularly in regard to holistic management of common conditions such as Alzheimer's. I completed my Bachelor of Exercise Rehabilitation at the University of Western Australia in June 2011.

In the AU-ARROW trial, I will be guiding participants through a combined gym-based program in conjunction with activity education to explore the impact of exercise on at-risk individuals seeking to prevent Alzheimer's. Some potential mechanisms by which exercise can help include increases in BDNF (Brain-Derived Neurotrophic Factor) and insulin sensitivity.

I strongly believe that the upcoming trial can help advance the understanding of Alzheimer's development and optimise management in years to come."



### TRISTAN SCHWARTZKOPFF

AU-ARROW Dietitian

"I am an Accredited Practising Dietitian who completed my Master's in Nutrition and Dietetics from Edith Cowan University in 2018. Since graduating, I have worked in both private practice and clinical roles, specialising in gastroenterology, surgical, oncology, general weight management and general healthy eating.

As part of the upcoming AU-ARROW Study, I will be guiding participants through the MIND (Mediterranean-DASH Intervention for Neurodegenerative Delay) diet and its benefits for cognitive performance. The MIND diet promotes the consumption of berries, green leafy vegetable, fish and olive oil, whilst reducing intake of fried/fast foods, red and processed meats, saturated fats, and high sugar foods and drinks. These dietary components have been linked to lower blood pressure, better blood lipid profiles, better blood glucose control and weight loss, all of which can reduce the risk of cardiovascular disease, diabetes type II and hypertension, conditions which are risk factors for dementia, including Alzheimer's disease."



# CLINICAL TRIALS DIVISION

A hand is shown holding a glowing lightbulb. Inside the lightbulb, there is a white outline of a human brain. The background of the lightbulb is a warm, orange-gold color with a grid of small, bright white stars. At the base of the lightbulb, several black gears are visible, suggesting a connection between research and technology.

**The Australian  
Alzheimer's Research  
Foundation conducts  
clinical trials into new  
investigational  
pharmaceutical 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 of those diagnosed with Alzheimer's disease or at risk of developing the disease.

# CLINICAL TRIALS DIVISION

Clinical trials are a vital part of the development of new medical treatments.

**A clinical trial aims to determine whether new medicines or interventions are safe and effective, and they are essential for the development of new medical treatments.**

The Foundation's Clinical Trials Division (CTD) has a dedicated multi-disciplinary team consisting of clinicians and clinical trial staff. The CTD works collaboratively with major pharmaceutical companies to examine new potential treatments to delay and prevent the progression of Alzheimer's disease.

Despite the continuing COVID related challenges of 2021, the team continued to secure and start new clinical trials. At the end of 2021, the team reached a peak of 15 active interventional trials.

Recruitment of new patients to clinical trials remained open throughout 2021, ensuring that as many people as possible still had access to potential new treatments. The pandemic continued to highlight the necessity for clinical trial research across all fields of medicine and the critical role that Australia, and indeed Western Australia plays internationally.

In May 2021, the team moved into larger premises at the Hollywood Specialist Centre. The move positions the team for growth while still under the same roof as other allied health services, providing a one-stop shop for their patients.

**The following few pages summarise some of the current trials being conducted at the Foundation's Clinical Trials Division.**

## A personal experience.....

*"Fifteen years ago, my family and I were stunned when my Mum was diagnosed with Alzheimer's disease, although it may have been blindingly obvious to some.*

*After seeing a TV advert seeking participants for a research study targeting the early detection of Alzheimer's disease, I signed up. Three years into the trial, I was diagnosed with early-onset Alzheimer's disease.*

*I felt disturbed, distressed, and was overthinking everything.*

*Due to my diagnosis, I was no longer eligible to take part in the early detection study, however, I was directed to the Foundation's Clinical Trial Unit.*

*The Unit ran trials that offered potential treatments for those who, like me, had a diagnosis of Alzheimer's disease. From the beginning, the Clinical Trials team did not attempt to give me false hope.*

*The level of care and balanced approach in my journey has been most rewarding with positive results.*

*My daughters thank you for giving them their old Dad back.*

*The only downside is that it took a little time to get the team to leave the teabag in the cup so that one could not see the bottom of the cup on drinking the tea."*

*John*

CLINICAL TRIAL PARTICIPANT



**“OVER THE PAST THREE YEARS, THE AUSTRALIAN ALZHEIMER'S RESEARCH FOUNDATION HAS BEEN AN IMPORTANT PART OF MY AND MY FAMILY'S LIFE AND WILL BE FOR SOME TIME YET, THANK GOODNESS.”**

## 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 AD. Iron chelators are used in the treatment of conditions such as haemochromatosis and thalassemia, where abnormal iron accumulation is present. In AD iron accumulates in affected brain regions causing neurotoxicity.



## ATHIRA ATH1017-AD-0202/0203 (PHASE 2)

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

- Hepatocyte growth factor (HGF) signalling agonist

This is a Phase 2 multicentre, randomized, double-blind, placebo-controlled, parallel-group, a 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 AD. All participants are now enrolled in the open-label extension of the study.



## BIOGEN EMBARK 221AD304 (PHASE 3)

*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*

- A human monoclonal antibody that recognizes aggregated forms of  $\beta$ -amyloid ( $A\beta$ ) (Aducanumab)

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



## GREENVALLEYPHARMA GREEN MEMORY GV971-007 (PHASE 3)

*A Phase 3, multi-centre, randomized, double-blind, parallel-group, placebo-controlled clinical trial to evaluate the efficacy and safety of sodium oligomannate (GV-971) in the treatment of mild to moderate Alzheimer's disease*

- A mixture of linear, acidic oligosaccharides originally derived from seaweed (GV-971)

The study medication targets gut bacteria in the hope of reducing inflammation in the body, which is believed to be related to brain deterioration. This is a phase 3 study, and eligible participants are between 50 to 85 years old with mild to moderate AD.



## ROCHE GRADUATE/POSTGRADUATE WN29922/WN42171 (PHASE 3/3B)

*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*

- Human monoclonal antibody targeting fibrils, and plaques (Gantenerumab)

This study aims to evaluate the ongoing safety and efficacy of gantenerumab, which is proposed to work by binding to aggregated target fibrillary and oligomeric forms of amyloid. It is administered as a subcutaneous injection fortnightly and is expected to clear amyloid plaque from the brain to improve the memory problems associated with AD. The two-year Open-Label Extension Phase commenced in 2021 and is ongoing.



## EISAI CLARITYAD BAN2401-G000-301 (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.*

- A humanized IgG1 monoclonal antibody binding to soluble  $A\beta$  aggregates (BAN2401/Lecanemab).

This double-blind study investigates the efficacy of lecanemab with early AD participants. The study medication aims to remove insoluble amyloid plaques and potentially reduce the toxic amyloid that is known to contribute to neuronal degradation in AD. The Open-Label Extension Phase will commence at our site this year.



## JANSSEN AUTONOMY 63733657ALZ2002 (PHASE 2)

*A Randomized, Double-blind, Placebo-controlled, Parallel-group, Multicenter Study to Assess the Efficacy and Safety of JNJ-63733657, an Anti-tau Monoclonal Antibody, in Participants with Early Alzheimer's Disease*

- A humanized immunoglobulin G (IgG)1/k monoclonal anti-tau antibody (JNJ-63733657)

The autonomy trial investigates the efficacy of JNJ-63733657 in participants with mild cognitive impairment or early-stage AD aged 55 to 80. The drug is administered by monthly infusion and is proposed to prevent tau collection in the brain, a known hallmark of AD. Eligible participants are tested for plasma tau levels in blood and tau pathology via brain scan.



## PRECLINICAL STUDIES – CURRENTLY RECRUITING

The following two studies recruit participants who currently have no symptoms of Alzheimer's disease (AD) but are interested in learning if they are at risk based on blood sampling and brain scans.

### EISAI AHEAD3-45 (PHASE 3)

*AHEAD 3-45 Study: A Placebo-Controlled, Double-Blind, Parallel-Treatment Arm, 216 Week Study to Evaluate Efficacy and Safety of Treatment with BAN2401 in Subjects With Preclinical AD and Elevated Amyloid (A45 Trial) and in Subjects With Early Preclinical AD and Intermediate Amyloid (A3 Trial)*

- A humanised IgG1 monoclonal antibody binding to soluble amyloid-beta (A $\beta$ ) aggregates BAN2401/Lecanemab).

The AHEAD3-45 trial targets participants with established brain amyloid but no current memory impairment to examine whether the removal of amyloid will delay the onset of cognitive decline. This 4.5 year study will assess the hypothesis that fortnightly or monthly infusions of the study drug will delay or prevent the development of AD.



### ROCHE SKYLINE WN42444 (PHASE 3)

*SKYLINE: A phase III, multicenter, randomized, parallel-group, double-blind, placebo-controlled study to evaluate the efficacy and safety of gantenerumab in participants at risk for or at the earliest stages of Alzheimer's disease*

- Human monoclonal antibody targeting fibrils, and plaques (Gantenerumab)

This phase 3 study aims to evaluate the efficacy of Gantenerumab on participants with risk factors for AD, but no current symptoms. Eligible participants are aged between 60 to 80 and have evidence of AD pathology assessed via a blood test and brain scans. Throughout the 4 years of the trial, participants receive weekly or fortnightly Gantenerumab injections to determine if it delays or prevents the onset of AD.



## ALZHEIMER'S DISEASE STUDIES – UPCOMING AND CURRENTLY RECRUITING IN 2022

The following studies recruit participants diagnosed with mild cognitive impairment due to Alzheimer's disease or Alzheimer's disease.

### NOVO NORDISK EVOKE/+ (PHASE 3A)

*A randomised double-blind placebo-controlled clinical trial investigating the effect and safety of oral semaglutide in subjects with early AD*

- Peptide-1 receptor agonist (Semaglutide)

Semaglutide, sold under the brand names Ozempic and Rybelsus, is used for the treatment of type 2 diabetes. Recent clinical data has shown that this medication reduces the risk of dementia, lowering brain inflammation. This phase 3 study aims to determine the safety and the impact of oral semaglutide on cognitive function in participants with early-stage AD.

### INMUNEBIO XPRO-AD-02 (PHASE 2)

*A Randomized, Placebo-Controlled, Double-Blind Study of XPro™ in Patients with Mild AD with Biomarkers of Inflammation*

- Antagonist of Soluble Tumor Necrosis Factor (sTNF) (XPRO)

The elevated level of TNF is one of the common characteristics associated with AD aetiology. XPro™ inhibits the bioactivity of TNF to reduce neuroinflammation and AD progression. This phase 2 double-blind study evaluates the effectiveness of XPro™ with mild AD patients. It is administered by subcutaneous injection once a week for 6 months. Eligible participants are 60 to 85 years old and assessed for amyloid positivity and inflammatory biomarkers. After completion of 6 months of treatment, participants will have the option to enrol in a 12 months extension study.

**The Clinical Trials Division has been selected for more studies in the first quarter of 2022.**

If you would like more information about any of the above trials and how you can be involved, please contact the team at [aarfctd@alzheimers.com.au](mailto:aarfctd@alzheimers.com.au) or call (08) 9389 6433.

# Thank You

## TO OUR SUPPORTERS

**We are incredibly indebted to the community of donors and supporters who share a deep commitment to supporting Alzheimer's disease research and our vision of an Alzheimer's free world.**

We very much appreciate their support and simply could not do what we do without it.

**In 2021 we welcomed Perrigo Australia as a corporate sponsor.**

*"Each year Perrigo Australia pledges to donate \$10,000 to charity. One of our employees, Michelle Burton, nominated the Foundation as she has a connection to your charity."*

*Thanks to Michelle's nomination and the support from the whole of Perrigo Australia I am extremely pleased and excited to advise that the Australian Alzheimer's Research Foundation is one of the recipients for 2021."*

**Leanne Brydon, General Manager**

**Perrigo**  
Australia



# THANK YOU FOR YOUR SUPPORT

As one of Australia's largest non-government funders of Alzheimer's disease research, we rely greatly on donations from our many supporters.

In 2021 donations and bequests made up 57% percent of our funding. We are very grateful for the help of our supporters, donors, fundraisers, research volunteers, and corporate and government partners who share our vision and enable us to continue the work we do.

In 2021 the Foundation's fundraising revenue totalled \$2,609,383 and we were delighted to welcome 757 new supporters in 2021.

A significant portion of our fundraising income in 2021 was from bequests. It is a great honour to receive these funds and the Foundation's careful stewardship of the bequests will enable the long term support of Alzheimer's research.

The Foundation's fundraising initiatives continue to evolve and innovate. We receive support through Gifts in Wills, regular monthly gifts, participation in community fundraising activities, and corporate partnerships.

## IN 2021:

- WELCOMED MORE THAN 11 NEW REGULAR DONORS
- RECEIVED \$1.7 MILLION IN BEQUESTS
- ACQUIRED 757 NEW DONORS
- INCREASED DIRECT MAIL INCOME BY 16 PERCENT
- GREW OUR WORKPLACE GIVING INCOME BY 76%
- ACKNOWLEDGED THE GENEROUS CONTRIBUTIONS OF CLOSE TO 1,260 INDIVIDUALS AND ORGANISATIONS

## BEQUESTS

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.

*Desmond Bowes, Elizabeth June Magee, James Joseph Kennedy and John Henry Carol*

all provided a bequest to the Australian Alzheimer's Research Foundation in 2021 to enable us to work towards a better future for us all.

*Thank you.*

*Thank you to all who have been inspired to leave a legacy in their Will.*

*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 to enable the long term support of Alzheimer's research.*

# IN THE COMMUNITY 2021 HIGHLIGHTS

Our community fundraising initiatives empower friends, families, workplaces and communities to come together to raise funds to support our programs and initiatives. We thank everyone for their tremendous support.



## CommBank Staff Foundation

A huge thank you to the CommBank Staff Foundation for the \$10,000 the Australian Alzheimer's Research Foundation received in 2021 as part of their Community Grants Giving Program.

These funds will allow us to continue to support vital research programs that we hope will bring us one step closer to an Alzheimer's free future.

Thank you to the generous staff at the Commonwealth Bank who participate in the workplace giving program, this grant wouldn't be possible without you!

## Swimming for Memories!

A huge thank you to the Stadium Masters Swimming Club that held their annual fundraiser in July 2021.

The event raised more than \$5,000. Thank you to everyone who took part!

An especially big shout out to Barry Green for his tireless effort in organising these annual events. We are so grateful for the ongoing support.



## World Alzheimer's Month

The 2021 annual public lecture provided a wonderful opportunity to celebrate the Foundation's 21st anniversary.

Director of Research, Professor Ralph Martins AO, provided the opening address and expressed his sincerest thanks to everyone who has supported him, the Foundation, and the various research projects over the years.

From the feedback we received, everyone thoroughly enjoyed the morning, where topics included: Understanding Dementia, 12 ways to reduce your risk, Research into a blood test for Alzheimer's, Personality traits and dementia, and Childhood dementia.



# IN THE COMMUNITY 2021 HIGHLIGHTS

Our community fundraising initiatives empower friends, families, workplaces and communities to come together to raise funds to support our programs and initiatives. We thank everyone for their tremendous support.



## The Rotary Club of Palm Beach WA

The Rotary Club of Palm Beach WA Inc put on an amazing event in 2021, the Rockingham Beach Cup.

It is an iconic event to showcase Rockingham's natural attractions and provide economic development for the local community. With the support of the City of Rockingham, generous sponsors and partner Channel 7, they delivered a fabulous showcase of entertainment that was enjoyed by all in attendance.

The Foundation is very grateful to be a beneficiary of the Rotary Club of Palm Beach WA and appreciates the support they provide through the Rockingham Beach Cup event.

## IGA Community Chest

In 2021 we were extremely grateful to be presented with a \$3,000 cheque from Taylor Road IGA as part of their Community Chest program.

A big thank you to everyone at Taylor Road IGA and everyone who purchased a product with the IGA Community Chest logo printed on the label.

The IGA Community Chest program has raised well over \$96m to help local communities, and we were extremely grateful to be a chosen charity!



## Sun Run & Cole Classic

A huge thank you to Jo McLellan, who completed the Sun Run & Cole Classic in 2021.

After losing her father to Alzheimer's, Jo wanted to raise money for the Australian Alzheimer's Research Foundation to help bring us closer to our vision of an Alzheimer's free world.

Jo finished the race in just over an hour, and was the 14th female to finish and 43rd finisher out of 308 swimmers overall! Jo raised an incredible \$1,300 for the Foundation!

# IN THE COMMUNITY 2021 HIGHLIGHTS

Our community fundraising initiatives empower friends, families, workplaces and communities to come together to raise funds to support our Alzheimer's disease programs and initiatives. We thank everyone for their tremendous support.



## Vision Blinds and Shutters

In early 2021, Vision Blinds and Shutters kindly pledged to donate \$1 for every square metre of plantation shutters sold in 2021.

Despite challenging times, they reached their fundraising goal and presented the Foundation's Director of Research, Professor Ralph Martins AO, with a cheque for \$10,000!

A big thank you to the team at Vision Blinds and Shutters. We are so grateful for your incredible contribution.

## Mighty Marathon Runners!

A massive shout to our mighty marathon fundraisers!

- Erica Morgan, who completed the Newport Wales
- Rachel Pinchbeck, who completed the Los Angeles Marathon
- Team Orbitel, who completed the McLaren Vale Marathon

Collectively, these events raised over \$6,000 for the Foundation, and we are so appreciative!



## The Canberra Times Marathon Festival

After a year-long hiatus due to COVID-19 restrictions, it would take a lot more than freezing temperatures and strong winds to keep Canberra's keenest runners away.

Thousands took to pounding the pavement around some of Canberra's most recognisable sites on April 11 as part of The Canberra Times Marathon Festival. A contingent of more than 8000 people lined up to take part in the event, including Stephanie Symons.

Stephanie has seen first-hand the devastating effects of Alzheimer's disease and managed to raise just over \$1,300 for the Foundation! Thank you Stephanie, for not only raising much-needed funds but also bringing awareness to this devastating disease.



# THE PERSONAL IMPACT

Kirstin Dunn is the Director of Semple Property Group in Perth, Western Australia. Kirstin's dedication to supporting the Australian Alzheimer's Research Foundation comes from personal experience.

In 2019 Kirstin's beloved grandmother Shirley was diagnosed with Alzheimer's disease. Like many people, Kirstin was shocked to discover the lack of treatment available for Alzheimer's disease.

## This is her story:

*"My Nanna Shirley is a firecracker. She has vibrant strawberry blonde hair, loves dressing up in her best, loves shopping, darts, outings and her family. In 2019 I learned of my nanna's Alzheimer's diagnosis. It absolutely flayed and devastated our family as Nanna was a fiercely independent, strong woman and the quick deterioration of her was shocking and confronting.*

*I think that the worst part was the lack of ANY form of treatment or cure. There was just nothing. We watched a woman who lived a rich and vibrant life lose the ability to brush her teeth and dress herself. By March 2020 she could no longer safely live at home and we moved her into a nursing home. This was another devastating blow to our family as she became severely depressed and cried often, wishing for her old life, a life that she loved.*

*I think one of the hardest things to see is the lack of joy she has now. Her quality of life has been taken from her by this disease. Her ability to enjoy my visits has gone. Her sparkle has left her. This disease has left her anxious and scared of everything. She is also tormented by horrible nightmares that affect her sleep so much she often needs to sleep during the day. These nightmares are so real that she cannot differentiate them from real life.*

*I know that eventually she will forget me, and that day haunts me. Until then I will spend my time with her, be patient with her when she is angry or upset and allow her to feel how she is feeling."*

*Kirstin*



**With community support for their movie fundraiser event pictured below and generous donations from local businesses, Kirstin Dunn and the Semple Property team raised just over \$16,000 for the Foundation.**

Sadly, Shirley lost her battle with Alzheimer's in February 2022.



# WINE & HORSES

Dedicated supporter Maryanne Phillips has raised over \$200,000 for Alzheimer's disease charities over the past ten years.

In 2021, Maryanne raised almost \$40,000 for the Australian Alzheimer's Research Foundation.

Maryanne's unwavering dedication to supporting Alzheimer's disease comes from personal experience. "My father in law, who came to live with us from Melbourne, was diagnosed with Alzheimer's disease. Although we had been speaking with him regularly on the phone, we had not detected any anomalies. He had become a master at hiding his condition."

Upon her father-in-law's diagnosis, Maryanne was astonished to learn there is no known cure for Alzheimer's disease. She was saddened to see the effect a diagnosis can have on the person and their family and friends. "I felt that there is a lot of support for other conditions, such as cancer or various disabilities, which are, of course, worthy causes; however, at the time, I couldn't find any other organisations that we're fundraising for this cause, and yet it is so widespread."

Maryanne's fundraising event is a horse ride from Clackline to Northam following the CY O'Connor Pipeline. "We have just held our 7th event last October and raised approximately \$40,000 for the Alzheimer's Alzheimer's Research Foundation."

With an extensive amount of work and commitment behind the scenes, Maryanne has decided to run her event bi-annually, making the next event October 2023.



Thank you to the sponsors, small and large, who support this event.

We really appreciate everyone's support in making the event such a success.



# SPONSORS & PARTNERS

Our corporate partnerships provide vital support to the Australian Alzheimer's Research Foundation, both financially and through the building of professional networks that empower us to share our programs.

We thank all our corporate supporters for their ongoing commitment to the Foundation and Alzheimer's disease research.



## THANK YOU WESFARMERS

Thank you Wesfarmers for your support of Alzheimer's research and for helping us deliver impactful outcomes for a better future.

Over many years, Wesfarmers' has contributed significant funding to the Foundation, which has enabled the continuation of several Alzheimer's disease research programs and the provision of world-class research facilities that include consulting rooms for cognitive assessment, treatment rooms, laboratories and a freezer farm. As research funding often does not include the cost of the facilities and equipment required to conduct the research, the support of Wesfarmers has had a direct and significant impact on the Foundation and our research objectives and enabled the researchers to focus on their important work.

We are especially indebted to the continuation of support from Wesfarmers throughout the COVID pandemic when fundraising activities were limited.

## THANK YOU PINNACLE CHARITABLE FOUNDATION AND PARTNERS

Thank you Pinnacle Charitable Foundation and their partners, Spheria Asset Management and Resolution Capital, for your support and encouragement.

Together they have provided significant support to several Alzheimer's research programs aimed at understanding the cell biology and very early-stage changes at the onset of Alzheimer's disease, especially around gene mutation. They are also supporting research focused on developing a blood biomarker for Alzheimer's disease, which has the potential to detect the presence of the disease well before symptoms appear. Their commitment to supporting Alzheimer's research to explore advances in diagnosis and treatment, and ultimately find a cure for this debilitating disease is very much appreciated.

## WORKPLACE GIVING

Workplace Giving is one of the most effective ways for working Australians to support a charity.

We are extremely grateful to work with several loyal, committed corporate partners and their staff through the workplace giving program. These include National Australia Bank | Google | Microsoft | Juniper | Visa | Findex | Westpac | PWC | Citi Australia | Toyota | Stockland | Suncorp | Pinnacle | Vita | Australia Post | Thermo Fisher | Equifax.

# SCIENTIFIC PUBLICATIONS





# SCIENTIFIC PUBLICATIONS

## GENETICS AND ALZHEIMER'S DISEASE

Nabais MF, Laws SM, Lin T, Vallerga CL, Armstrong NJ, Blair IP, Kwok JB, Mather KA, Mellick GD, Sachdev PS, Wallace L, Henders AK, Zwamborn RAJ, Hop PJ, Lunnon K, Pishva E, Roubroeks JAY, Soininen H, Tsolaki M, Mecocci P, Lovestone S, Kłoszewska I, Vellas B; Australian Imaging Biomarkers and Lifestyle study; Alzheimer's Disease Neuroimaging Initiative, Furlong S, Garton FC, Henderson RD, Mathers S, McCombe PA, Needham M, Ngo ST, Nicholson G, Pamphlett R, Rowe DB, Steyn FJ, Williams KL, Anderson TJ, Bentley SR, Dalrymple-Alford J, Fowder J, Gratten J, Halliday G, Hickie IB, Kennedy M, Lewis SJG, Montgomery GW, Pearson J, Pitcher TL, Silburn P, Zhang F, Visscher PM, Yang J, Stevenson AJ, Hillary RF, Marioni RE, Harris SE, Deary IJ, Jones AR, Shatunov A, Iacoangeli A, van Rheenen W, van den Berg LH, Shaw PJ, Shaw CE, Morrison KE, Al-Chalabi A, Veldink JH, Hannon E, Mill J, Wray NR, McRae AF. *Meta-analysis of genome-wide DNA methylation identifies shared associations across neurodegenerative disorders*. Genome Biol. 2021 22(1):90. doi: 10.1186/s13059-021-02275-5.PMID: 33771206

## BIOMARKERS

Chatterjee, P., Pedrini, S., Stoops, E., Goozee, K., Villemagne, V., Asih, P., Verberk, I., Dave, P., Taddei, K., Sohrabi, H., Zetterberg, H., Blennow, K., Teunissen, C., Vanderstichele, H., Martins, R. (2021). *Plasma glial fibrillary acidic protein is elevated in cognitively normal older adults at risk of Alzheimer's disease*. Translational Psychiatry, 11(June 2021), Article number 27.

Chatterjee, P., Pedrini, S., Ashton, N., Tegg, M., Goozee, K., Singh, A., Karikari, T., Simrén, J., Vanmechelen, E., Armstrong, N., Hone, E., Asih, P., Taddei, K., Doré, V., Villemagne, V., Sohrabi, H., Zetterberg, H., Masters, C., Blennow, K., Martins, R. (2021). *Diagnostic and prognostic plasma biomarkers for preclinical Alzheimer's disease*. Alzheimer's and Dementia, 2021(Article in Press), 14p.

Chatterjee, P., Cheong, Y., Bhatnagar, A., Goozee, K., Wu, Y., McKay, M., Martins, I., Lim, F., Pedrini, S., Tegg, M., Villemagne, V., Asih, P., Dave, P., Shah, T., Dias, C., Fuller, S., Hillebrandt, H., Gupta, S., Hone, E., Taddei, K., Zetterberg, H., Blennow, K., Sohrabi, H., Martins, R. (2021). *Plasma metabolites associated with biomarker evidence of neurodegeneration in cognitively normal older adults*. Journal of Neurochemistry, 159(2), 389-402.

Doecke, J., Francois, C., Fowler, C., Stoops, E., Bourgeat, P., Rainey-Smith, S., Li, Q., Masters, C., Martins, R., Villemagne, V., Collins, S., Vanderstichele, H. (2021). *Core Alzheimer's disease cerebrospinal fluid biomarker assays are not affected by aspiration or gravity drip extraction methods*. Alzheimer's Research and Therapy, 13(December 2021), Article number 79.

Fagan, A., Henson, R., Li, Y., Boerwinkle, A., Xiong, C., Bateman, R., Goate, A., Ances, B., Doran, E., Christian, B., Lai, F., Rosas, H., Schupf, N., Krinsky-McHale, S., Silverman, W., Lee, J., Klunk, W., Handen, B., Allegri, R., Chhatwal, J., Day, G., Graff-Radford, N., Jucker, M., Levin, J., Martins, R., Masters, C., Mori, H., Mummery, C., Niimi, Y., Ringman, J., Salloway, S., Schofield, P., Shoji, M., Lott, I. (2021). *Comparison of CSF biomarkers in Down syndrome and autosomal dominant Alzheimer's disease: a cross-sectional study*. Lancet Neurology, 20(8), 615-626.

## NUTRITION AND ALZHEIMER'S DISEASE

Fernando, B., Dong, K., Durham, R., Stockmann, R., Jayasena, V. (2021). *Effect of goji berry on the formation of extracellular senile plaques of Alzheimer's disease*. Nutrition and Healthy Aging, 6(2), 105-116.

Dona Pamoda W. Jayatunga, Eugene Hone, Harjot Khaira, Taciana Lunelli, Harjinder Singh, Gilles J. Guillemain, Binosha Fernando, Manohar L. Garg, Giuseppe Verdile and Ralph N. Martins, 2021, *Therapeutic Potential of Mitophagy-Inducing Microflora Metabolite, Urolithin A for Alzheimer's Disease*. Nutrients 13, 3744. <https://doi.org/10.3390/nu13113744>

Nasim Rezaee, Binosha Fernando, Eugene Honea, Hamid Sohrabi, Stuart Johnson, Stuart Gunzburg, Ralph N. Martins, 2021, *Potential of sorghum polyphenols to prevent and treat Alzheimer's disease: A review article* - Frontiers in Aging Neuroscience, <https://doi.org/10.3389/fnagi.2021.729949>

Ke Dong, WMAD Binosha Fernando, Rosalie Durham, Regine Stockman and Vijay Jayasena, 2021, *Nutritional value, food application and health-promoting benefits of sea buckthorn*. Food reviews international- <https://doi.org/10.1080/87559129.2021.1943429>

Rezaee, N., Fernando, B., Hone, E., Sohrabi, H., Johnson, S., Gunzburg, S., Martins, R. (2021). *Potential of sorghum polyphenols to prevent and treat Alzheimer's disease*. Frontiers in Aging Neuroscience, 2021 (Article in Press), 24p.

## DIAN

Keret, O., Staffaroni, A., Ringman, J., Cobigo, Y., Goh, S., Wolf, A., Allen, I., Salloway, S., Chhatwal, J., Brickman, A., Reyes-Dumeyer, D., Bateman, R., Benzinger, T., Morris, J., Ances, B., Joseph-Mathurin, N., Perrin, R., Gordon, B., Levin, J., Voglein, J., Jucker, M., Fougere, C., Martins, R., Sohrabi, H., Taddei, K., Villemagne, V., Schofield, P., Brooks, W., Fulham, M., Masters, C., Ghetti, B., Saykin, A., Jack, C., Graff-Radford, N., Weiner, M., Cash, D., Allegri, R., Chrem, P., Yi, S., Miller, B., Rabinovici, G., Rosen, H. (2021). *Pattern and degree of individual brain atrophy predicts dementia onset in dominantly inherited Alzheimer's disease*. Alzheimer's and Dementia: Diagnosis, Assessment and Disease Monitoring, 13(1), Article Number 12197.

Ewers, M., Luan, Y., Frontzkowski, L., Neitzel, J., Rubinski, A., Dichgans, M., Hassenstab, J., Gordon, B., Chhatwal, J., Levin, J., Schofield, P., Benzinger, T., Morris, J., Goate, A., Karch, C., Fagan, A., McDade, E., Allegri, R., Berman, S., Chui, H., Cruchaga, C., Farlow, M., Graff-Radford, N., Jucker, M., Lee, J., Martins, R., Mori, H., Perrin, R., Xiong, C., Rossor, M., Fox, N., O'Connor, A., Salloway, S., Danek, A., Buerger, K., Bateman, R., Habeck, C., Stern, Y., Franzmeier, N. (2021). *Segregation of functional networks is associated with cognitive resilience in Alzheimer's disease*. Brain: a journal of neurology, 144(7), 2176-2185.

## TESTOSTERONE

Tan, S., Porter, T., Bucks, R., Weinborn, M., Milicic, L., Brown, A., Rainey-Smith, S., Taddei, K., Ames, D., Masters, C., Maruff, P., Savage, G., Rowe, C., Villemagne, V., Brown, B., Sohrabi, H., Laws, S., Martins, R. (2021). *Androgen receptor CAG repeat length as a moderator of the relationship between free testosterone levels and cognition*. Hormones and Behaviour, 131(May 2021), Article number 104966.

# SCIENTIFIC PUBLICATIONS

## AIBL

Fowler, C., Rainey-Smith, S., Bird, S., Bomke, J., Bourgeat, P., Brown, B., Burnham, S., Bush, A., Chadunow, C., Collins, S., Doecke, J., Dore, V., Ellis, K., Evered, L., Fazlollahi, A., Fripp, J., Kirby, S., Gibson, S., Grenfell, R., Harrison, E., Head, R., Jin, L., Kamer, A., Lamb, F., Lautenschlager, N., Laws, S., Li, Q., Lim, L., Lim, Y., Louey, A., Macaulay, L., Mackintosh, L., Martins, R., Maruff, P., Masters, C., McBride, S., Milicic, L., Peretti, M., Pertile, K., Porter, T., Radler, M., Rembach, A., Robertson, J., Rodriguez, M., Rowe, C., Rumble, R., Salvado, O., Savage, G., Silbert, B., Soh, M., Sohrabi, H., Taddei, K., Taddei, T., Thai, C., Trounson, B., Tyrell, R., Vacher, M., Varghese, S., Villemagne, V., Weinborn, M., Woodward, M., Xia, Y., Ames, D. (2021). *Fifteen years of the Australian Imaging, Biomarkers and Lifestyle (AIBL) Study: Progress and observations from 2,359 older adults spanning the spectrum from cognitive normality to Alzheimer's disease*. Journal of Alzheimer's Disease Reports, 5(1), 443-468. <https://doi.org/10.3233/ADR-210005>.

Kirby, S., Rainey-Smith, S., Villemagne, V., Fripp, J., Dore, V., Bourgeat, P., Taddei, K., Fowler, C., Masters, C., Maruff, P., Rowe, C., Ames, D., Martins, R. (2021). *Higher coffee consumption is associated with slower cognitive decline and less cerebral A $\beta$ -Amyloid accumulation over 126 months: Data from the Australian Imaging, Biomarkers, and Lifestyle Study*. Frontiers in Aging Neuroscience, 13(19 November 2021), Article number 744872. <https://doi.org/10.3389/fnagi.2021.744872>.

Chong TWH, You E, Ellis KA, Cox KL, Harrington KD, Rainey-Smith SR, Ames D, Lautenschlager NT; AIBL Research Group. *The Support Person's Preferences and Perspectives of Physical Activity Programs for Older Adults With Cognitive Impairment*. Front Public Health. 2021 Sep 23;9:704561. doi: 10.3389/fpubh.2021.704561.

Tan, S., Porter, T., Bucks, R., Weinborn, M., Milicic, L., Brown, A., Rainey-Smith, S., Taddei, K., Ames, D., Masters, C., Maruff, P., Savage, G., Rowe, C., Villemagne, V., Brown, B., Sohrabi, H., Laws, S., Martins, R. (2021). *Androgen receptor CAG repeat length as a moderator of the relationship between free testosterone levels and cognition*. Hormones and Behaviour, 131(May 2021), Article number 104966. <https://doi.org/10.1016/j.yhbeh.2021.104966>.

Doecke, J., Francois, C., Fowler, C., Stoops, E., Bourgeat, P., Rainey-Smith, S., Li, Q., Masters, C., Martins, R., Villemagne, V., Collins, S., Vanderstichele, H. (2021). *Core Alzheimer's disease cerebrospinal fluid biomarker assays are not affected by aspiration or gravity drip extraction methods*. Alzheimer's Research and Therapy, 13(December 2021), Article number 79. <https://doi.org/10.1186/s13195-021-00812-9>.

Fernandez, S., Burnham, S., Milicic, L., Savage, G., Maruff, P., Peretti, M., Sohrabi, H., Lam, Y., Weinborn, M., Ames, D., Masters, C., Martins, R., Rainey-Smith, S., Rowe, C., Salvado, O., Groth, D., Verdile, G., Villemagne, V., Porter, T., Laws, S. (2021). *SPON1 Is Associated with Amyloid- $\beta$  and APOE  $\epsilon$ 4-Related Cognitive Decline in Cognitively Normal Adults*. Alzheimer's Disease Reports, 5(1), 111-120. <https://doi.org/10.3233/ADR-200246>

Van Der Kall, L., Truong, T., Burnham, S., Dore, V., Mulligan, R., Bozinovski, S., Lamb, F., Bourgeat, P., Fripp, J., Schultz, S., Lim, Y., Laws, S., Ames, D., Fowler, C., Rainey-Smith, S., Martins, R., Salvado, O., Robertson, J., Maruff, P., Masters, C., Villemagne, V., Rowe, C. (2021). *Association of  $\beta$ -amyloid level, clinical progression and longitudinal cognitive change in normal older individuals*. Neurology, 96(5), e662 -e670. <https://doi.org/https://doi.org/10.1212/WNL.0000000000011222>.

Bradfield, N., Ellis, K., Savage, G., Maruff, P., Burnham, S., Darby, D., Lautenschlager, N., Martins, R., Masters, C., Rainey-Smith, S., Robertson, J., Rowe, C., Woodward, M., Ames, D. (2021). *Aggregation of Abnormal Memory Scores and Risk of Incident Alzheimer's Disease Dementia: A Measure of Objective Memory Impairment in Amnesic Mild Cognitive Impairment*. Journal of the International Neuropsychological Society, 27(2), 146-157. <https://doi.org/10.1017/S135561772000079X>.

Kirby, S., Weinborn, M., Sohrabi, H., Doecke, J., Bourgeat, P., Rainey-Smith, S., Shen, K., Fripp, J., Taddei, K., Maruff, P., Salvado, O., Savage, G., Ames, D., Masters, C., Rowe, C., Martins, R. (2021). *Longitudinal Trajectories in Cortical Thickness and Volume Atrophy: Superior Cognitive Performance Does Not Protect Against Brain Atrophy in Older Adults*. Journal of Alzheimer's Disease, 81(3), 1039-1052. <https://doi.org/10.3233/JAD-201243>.

Moussavi Nik, S., Porter, T., Newman, M., Bartlett, B., Khan, I., Sabale, M., Eccles, M., Woodfield, A., Groth, D., Dore, V., Villemagne, V., Masters, C., Martins, R., Laws, S., Lardelli, M., Verdile, G. (2021). *Relevance of a truncated PRESENILIN 2 Transcript to Alzheimer's disease and neurodegeneration*. Journal of Alzheimer's Disease, 80(4), 1479-1489.

## SLEEP AND EXERCISE

Markovic, S., Fitzgerald, M., Peiffer, J., Scott, B., Rainey-Smith, S., Sohrabi, H., Brown, B., (2021). *The impact of exercise, sleep, and diet on neurocognitive recovery from mild traumatic brain injury in older adults: A narrative review*. Ageing Research Reviews, 68, , pages 101322 -.

Sewell, K.R., Erickson, K.I., Rainey-Smith, S.R., Peiffer, J.J., Sohrabi, H.R. and Brown, B.M. (2021) *Relationships between physical activity, sleep and cognitive function: A narrative review*. Neuroscience & Biobehavioral Reviews, 130 . pp. 369-378.

Parker, D., Bucks, R., Rainey-Smith, S., Hodgson, E., Fine, L., Sohrabi, H., Martins, R., Weinborn, M. (2021). *Sleep Mediates Age-Related Executive Function for Older Adults with Limited Cognitive Reserve*. Journal of the International Neuropsychological Society, 27(7), 711-721.

Brown, B., Frost, N., Rainey-Smith, S., Doecke, J., Markovic, S., Gordon, N., Weinborn, M., Sohrabi, H., Laws, S., Martins, R., Erickson, K., Peiffer, J. (2021). *High intensity exercise and cognitive function in cognitively normal older adults: a pilot randomised clinical trial*. Alzheimer's Research and Therapy, 13(December 2021), Article number 33.

Frost, N., Weinborn, M., Gignac, G., Xia, Y., Dore, V., Rainey-Smith, S., Markovic, S., Gordon, N., Sohrabi, H., Laws, S., Martins, R., Peiffer, J., Brown, B. (2021). *The effect of self-paced exercise intensity and cardiorespiratory fitness on frontal grey matter volume in cognitively normal older adults: A randomised controlled trial*. Journal of the International Neuropsychological Society, 2021(Article in Press), 1-14.

Frost, N., Weinborn, M., Gignac, G., Rainey-Smith, S., Markovic, S., Gordon, N., Sohrabi, H., Laws, S., Martins, R., Peiffer, J., Brown, B. (2021). *A Randomized Controlled Trial of High-Intensity Exercise and Executive Functioning in Cognitively Normal Older Adults*. American Journal of Geriatric Psychiatry, 29(2), 129-140.



Australian  
**ALZHEIMER'S  
RESEARCH**  
Foundation

**HEAD OFFICE**

8 Verdun Street, Nedlands WA 6009  
Telephone: (08) 6457 0253  
Facsimile: (08) 6457 0270  
PO Box: 963, Nedlands WA 6909  
Email: [info@alzheimers.com.au](mailto:info@alzheimers.com.au)



[www.alzheimers.com.au](http://www.alzheimers.com.au)

The Australia Alzheimer's Research Foundation is a registered charity and accredited to carry the Australian Charities and Not-for-profit Commission (ACNC) Deductible Gift Recipient number 900 487 245.

ABN: 34 575 647 667.

