Australian
ALZHEIMER'S
RESEARCH
Foundation

2022
Annual Report

Year in Review

Australian Alzheimer's Research Foundation is the largest non-government, non-profit funder of specialist Alzheimer's disease research in Australia.

Since 2000, we have been a leader in the fight against Alzheimer's disease, pioneering new scientific research and innovative initiatives aimed at reducing the impact of Alzheimer's disease.

Our specialist research is only possible due to the commitment of the community who give generously to ensure our research continues and knowledge is advanced.

At the core of our mission is the pursuit of excellence in research, which we believe is essential for achieving our ultimate goal of improving the lives of millions of people affected by this devastating disease.

Our values of collaboration, passion, and sustainability are all anchored by our commitment to excellence in research.

Acknowledgement of Country

In the spirit of reconciliation, the Australian Alzheimer's Research Foundation acknowledges the Traditional Custodians of the country throughout Australia and their connections to land, sea and community.

We pay our respect to their Elders past and present and extend that respect to all Aboriginal and Torres Strait Islander peoples today.

OUR

TABLE OF CONTENTS

> **I am immensely proud of the innovation and dedication of the team at the Australian Alzheimer's Research Foundation and collaborating universities. We are leaders in the fight against Alzheimer's disease, pioneering new research and educating the community. Our scientists pave the way for future discoveries by advancing knowledge through deeper understanding.**
>
> *PROF RALPH MARTINS*

OUR
BOARD OF DIRECTORS

Graeme Prior - Chair
Chief Executive Officer - Hall & Prior Aged Care Group

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

Rod O'Dea - Treasurer
Director - Ellann Finance

Professor Ralph Martins AO - Director of Research
Professor of Neurobiology - Macquarie University
Foundation Chair of Aging and Alzheimer's disease - Edith Cowan University

Professor Colin Masters AO - Board Member
Laureate Professor of Dementia Research - The Florey Institute and The University of Melbourne

Enzo Sirna AM - Board Member
Deputy Chief Executive Officer - National Trust of Western Australia

Tim Andrew - Board Member
Head of UBS Perth

Rob Davies - Board Member
Accountant - Mine Site Construction Services

BOARD ATTENDENCE

BOARD MEMBER	*MEETINGS ATTENDED*	*MEETINGS HELD*
Graeme Prior	5	5
Dr Terry Bayliss	5	5
Rod O'Dea	4	5
Professor Ralph Martins AO	3	5
Professor Colin Masters AO	5	5
Enzo Sirna AM	4	5
Tim Andrew	5	5
Rob Davies	5	5

OUR
BOARD COMMITTEES

FINANCE, AUDIT & RISK COMMITTEE
Rod O'Dea - Chair
Graeme Prior
Tim Andrew
Rob Davies
Liza Dunne

INVESTMENT COMMITTEE
Rod O'Dea - Chair
Jemma Sanderson *Director - Cooper Partners*
John Cunningham *Fellow - CPA Australia*
Mark Hewitt *Director of Hewitt & Jones*

CLINICAL RESEARCH GOVERNANCE COMMITTEE
Professor Colin Masters - Chair
Dr Terry Bayliss
A/Professor Roger Clarnette
Liza Dunne

NOMINATION COMMITTEE
Tim Andrew - Chair
Graeme Prior
Dr Terry Bayliss
Professor Ralph Martins
Liza Dunne

FACILITIES COMMITTEE
Enzo Sirna - Chair
Graeme Prior
Rod O'Dea
Professor Ralph Martins
Tim Andrew
Liza Dunne

FUNDRAISING & COMMUNICATIONS COMMITTEE
Rod O'Dea - Chair
Professor Ralph Martins
Liza Dunne
A/Professor Stephanie Rainey-Smith

A MESSAGE FROM OUR
CHAIR

I am pleased to report that 2022 was a strong year for the Australian Alzheimer's Research Foundation (AARF) from both a financial perspective and the significant progress in research.

As you will read in the pages of this Annual Report, many of our long-established research programs are now providing valuable data and information to a global audience of research networks. Our commitment to advancing knowledge of Alzheimer's disease, particularly in areas such as early diagnosis and prevention, has positioned us as a leading institution on the global stage.

The global EDoN and AU-ARROW networks, along with the international collaborations they foster, showcase the potential impact of cross-border cooperation in advancing scientific knowledge.

The studies focusing on the gut-brain connection, together with ongoing efforts in the field of sleep research and prevention strategies, further highlight the breadth and depth of the work being undertaken.

By leveraging our expanding knowledge, we are poised to make even greater contributions to the scientific community and improve outcomes for individuals worldwide.

I am proud to acknowledge the continued success of the financial management of AARF. Through careful planning and prudent decision-making, we have maintained a strong financial position and ensured the steady growth of our balance sheet.

Our commitment to financial stability remains unwavering, as we strive to create a solid foundation for our organization's long-term success.

Furthermore, I am pleased to inform you that we are diligently managing our allocation of funding to administration and overheads. We recognize the importance of utilizing our resources efficiently and effectively, ensuring that every dollar spent contributes to our mission and goals.

In line with our commitment to growth and progress, the Board has agreed to include additional members, with the hope of welcoming them at the upcoming Annual General Meeting. The inclusion of new members will bring fresh perspectives, diverse experiences, and valuable expertise to our organization. By broadening the composition of our Board, we enhance our decision-making processes and strengthen our ability to address our evolving needs.

The Board has set a strategic intent to further invest in research and explore the possibility of transforming our organization into a Medical Research Institute (MRI). This expansion will allow us to deepen our commitment to scientific discovery and contribute to ground-breaking advancements in research. By establishing ourselves as an MRI, we will enhance our capacity to secure financial support, as well as expand the opportunities to collaborate with leading experts.

We will also be exploring the commencement of treatment programs for individuals suffering from dementia, Alzheimer's disease, or Mild Cognitive Impairment (MCI). This expansion into treatment programs reflects our dedication to making a tangible difference in the lives of those affected by these conditions.

In line with our ambitious plans, we will be actively establishing deeper and better relationships in Perth, throughout Australia and internationally, in both research and treatment sectors. By fostering collaborative partnerships, we can pool our expertise, share resources, and collectively contribute to the advancement of Alzheimer's research and treatment.

Your continued support is instrumental in driving our success and achieving our strategic goals. Together, we will make significant strides in research, expand our treatment capabilities, and positively impact the lives of individuals affected by neurodegenerative diseases.

I would like to close by thanking the staff, Board and researchers who have contributed to the 2022 results and most particularly to the public who have made a decision to support Alzheimer's research with a shared vision of an Alzheimer's free world.

Graeme Prior
Chairperson

A MESSAGE FROM OUR
CHIEF EXECUTIVE OFFICER

I am pleased to report on the activities at the Australian Alzheimer's Research Foundation in 2022.

Alzheimer's disease remains the primary cause of dementia, is the leading cause for women in Australia and is the 2nd leading cause of death for all Australians. Today, 1 in 6 Australians are aged 65 and over (16%). By 2066, it is expected that 22% of the Australian population will be over 65. With an ageing society, dementia presents an unprecedented challenge for all Australians.

The cost of dementia in Australia in 2016 was $ 15 billion and is expected to increase to $ 26 billion by 2036 in today's dollars. 40% of the cost is indirect costs through lost productivity of both persons with dementia and their family and carers needing to reduce their working hours. Approximately 25% of the Australian workforce is currently over the age of 55 and finding opportunities to live productive happy healthy lives as we age is of paramount importance.

Research into strategies to reduce the risk and potentially prevent the onset of dementia is a major research theme at the Foundation. This is not only important to us individually, but as a whole society. We all have a responsibility to be involved in working towards a better future and reducing the impact of this disease.

The impact of many chronic diseases is decreasing in Australia due to research that has delivered better treatment and prevention programs. However, the impact of Alzheimer's disease continues to increase. Across Australia, only 10% of medical research grants are fully funded, leaving a heavy reliance on philanthropic and corporate support to fund the research required.

We are incredibly grateful to everyone who has provided philanthropic support to AARF in 2022. You are critical to enabling us to continue the vital research work that is required to have the impact we must deliver. We are supporting a wide range of research projects outlined in the following pages. One of the highlights for the year was progress made in biomarkers with the aim of developing an affordable blood test to diagnose Alzheimer's.

Evidence shows the brain is affected by Alzheimer's disease many years before symptoms appears. The earlier it can be detected the earlier risk reduction strategies can be implemented, or new treatments started, providing significant opportunities to reduce the impact of this disease.

In late 2022, a second pharmaceutical treatment was approved in the United States by the U.S. Food and Drug Administration (FDA) showing a reduction in brain amyloid and improved cognition. We are excited to be conducting clinical trials into this and other potential treatments for Alzheimer's disease and look forward to approval of these treatments for use in Australia. With the arrival of new treatments, the need for a blood biomarker to diagnose the disease at the earliest possible time is critical. It is a core focus of the research funding provided by the Foundation.

AARF's commitment to research excellence has been further reinforced in the past year by the support of our members and supporters. Through their generous donations, we have been able to provide funding to support new research projects and expand existing research initiatives. These projects are aimed at advancing our understanding of Alzheimer's disease and developing effective treatments and preventative measures.

In conclusion, I am proud to report that AARF has demonstrated strength and resilience in the face of unprecedented challenges in funding and the COVID pandemic in recent years. We remain steadfast in our commitment to support research aimed at finding a cure for Alzheimer's disease, and we are grateful for the ongoing support of our members and supporters.

Liza Dunne
Chief Executive Officer

OUR
FINANCIALS

As a non-profit organisation dedicated to advancing research into Alzheimer's disease, we rely on philanthropic support to ensure vital research into this disease continues. We are tremendously thankful for those people in the community that share our vision. A summary of our income and expenses is provided below.

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

Investment and Other Income
Investment and other income includes income received from facilities owned or leased by the Foundation, the sale of shares and other investment returns.

Clinical Trials
The Foundation earns income from conducting clinical trials for potential new pharmaceutical treatments for Alzheimer's disease.

Research & Grant Income
Other research and grant income includes funds received in prior years but recognised as income in 2022, as the funds were tied to projects conducted in 2022.

Direct Research Costs
Direct research costs include researcher salaries, PhD scholarships, research facilities, research consumables, maintenance and depreciation of research equipment, research consultants, service providers (for example, brain imaging services) and costs associated with 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, insurance and strategic projects.

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

INCOME 2022 - $5.6 MILLION

12%	DONATION INCOME $687,475	
27%	BEQUEST INCOME $1,524,309	
18%	INVESTMENT & OTHER INCOME $1,019,420	
22%	CLINICAL TRIALS INCOME $1,244,479	
21%	RESEARCH & GRANT INCOME $1,149,394	

EXPENSES 2022 - $4.0 MILLION

82%	DIRECT RESEARCH COSTS $3,279,626	
18%	INDIRECT COSTS $736,462	

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.

OUR 2022 IMPACT

Visits

3,000

Over 3,000 people visited our state of the art research facilities in 2022, giving their valuable time to Alzheimer's research.

Citations

33,363

The total number of times Prof Ralph Martins' publications have been referenced by other researchers.

Collaborators

215

We are global partners with colleges, research groups and universities.

Trials

15

We conducted 15 pharmaceutical trials into the treatment of Alzheimer's disease.

Publications

39

We published 39 research papers, reviews and articles, adding to the global body of knowledge on Alzheimer's disease.

Scopus H-index

91

Prof Ralph Martin's h-index* of 91 ranks him among the world's top researchers.

Brain Scans

320

Brain imaging is the gold standard assessment of Alzheimer's disease and vital to research to combat this disease.

Students

34

The future of research is in good hands. In 2022, 34 students worked on Alzheimer's research at AARF, including 25 PhD candidates.

Appointments

1,157

Clinical trials into new drug treatments are critical if we are to find effective treatments. We had 1,157 visits from people participating in these treatment trials.

Countries

15

Our researchers worked with collaborators in 15 countries around the world in 2022.

Registrations

463

People want to learn everything they can about Alzheimer's disease. We had 463 people attend our information events in 2022.

*The h-index reflects a researcher's productivity and impact.

OUR
COLLABORATIONS

The pursuit of knowledge transcends borders and unites scientists from every corner of the globe. It is through true collaboration and engagement with other leaders, educators and experts that innovation can occur. Some of our collaborators are listed below.

36 Europe

83 North America

Asia 13

2 South America

81 Australia & New Zealand
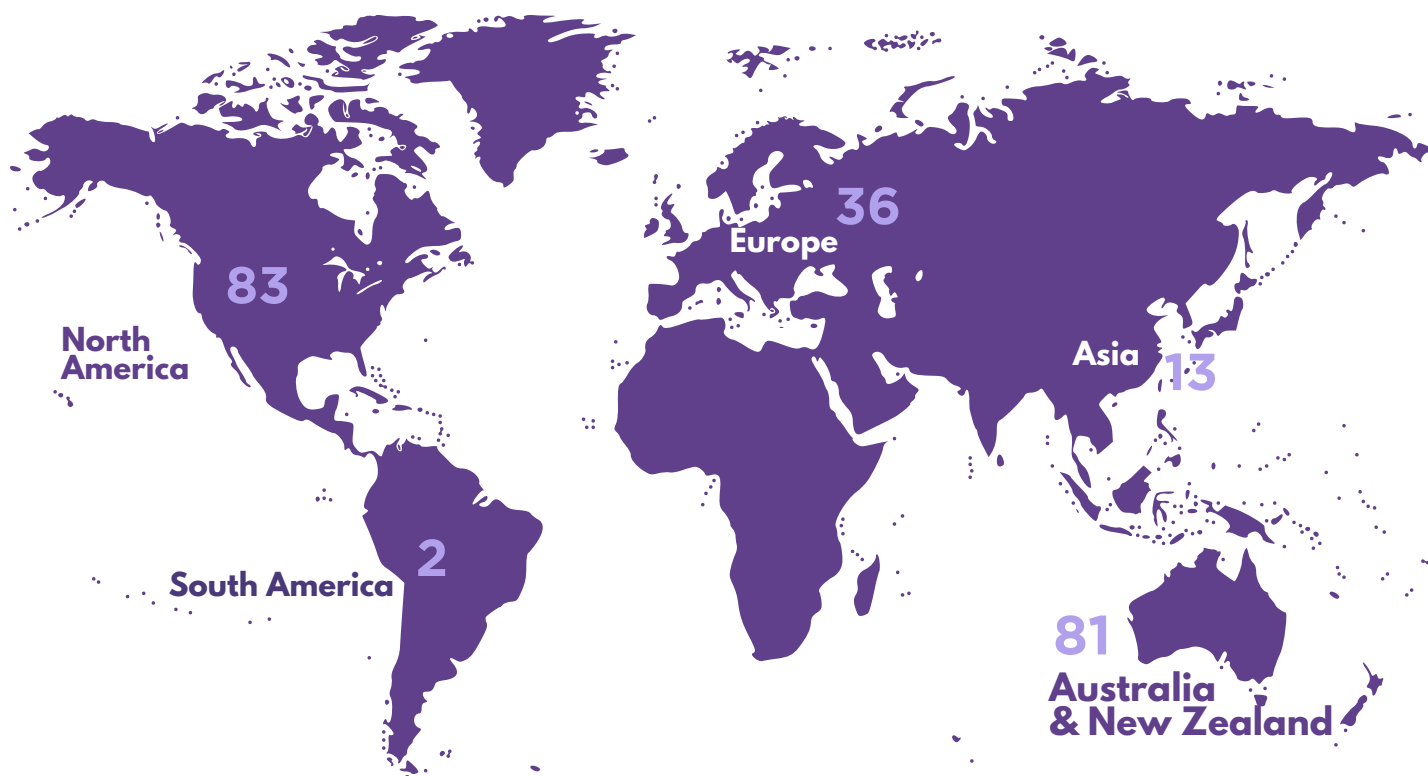
EUROPE

- Institute for Stroke and Dementia Research
- King's College London
- Leiden University
- Lund University
- UK Dementia Research Institute
- University College London
- University of Barcelona
- University of Exeter
- University of Gothenburg
- University Munich
- University of Tübingen

NORTH & SOUTH AMERICA

- Alzheimer's Association
- Argentina Institute for Neurological Research
- Brown University
- Columbia University
- Duke University
- Harvard Medical School
- Icahn School of Medicine
- Indiana University
- Northern California Institute for Research and Education
- University of California
- University of Pennsylvania
- University of Pittsburgh
- University of Southern California
- University of Texas
- University of Toronto
- Washington University

AUSTRALASIA

- Austin Health
- Busselton Population Medical Research Institute
- Curtin University
- Deakin University
- Edith Cowan University
- KaRa Institute of Neurological Diseases
- Kolling Institute of Medical Research
- Macquarie University
- Massey University
- Monash University
- Murdoch University
- National Ageing Research Institute
- The Australian e-Health Research Centre
- University New South Wales
- University of Melbourne
- University of Newcastle
- University of Otago
- University of Queensland
- University of Sydney
- University of Tasmania
- University of Western Australia

ASIA

- Fudan University
- Niigata University
- Osaka City University
- Osaka Metropolitan University
- University of Singapore
- University of Tokyo
- University of Ulsan College of Medicine

A MESSAGE FROM OUR
DIRECTOR OF RESEARCH

It has been an exciting year for our team, as we have made significant progress on various projects thanks to everyone's outstanding effort, working in collaboration with national and international partners.

Highlights of 2022 include the role of music in reducing neuropsychiatric symptoms led by Professor Hamid Sohrabi; developing biomarkers in childhood dementia led by Dr Prashant Bharadwaj; and using digital technology to develop "fingerprints" for the early diagnosis of Alzheimer's and dementia led by Associate Professor Stephanie Rainey-Smith and Professor Sohrabi.

I am delighted to share what will be the first study examining how personalised music listening influences the quality of life of people living with dementia. The role of music in dementia is an area of research that is rapidly gaining importance. As dementia progresses, older adults with reduced cognitive capacity and communication abilities are particularly susceptible to the benefits of music. Listening to music is potentially a highly effective, low-cost, and non-invasive tool for improving psychological well-being, reducing drug consumption, and reducing hospitalisations.

Our team will investigate different aspects of personalised music intervention in a randomised clinical trial, the results of which will inform a unified protocol that can be utilised as a part of the daily care plans in nursing homes. This study is possible through funding from The Lindsay & Heather Payne Medical Research Charitable Foundation (Perpetual Grant), and in-kind support of the Rotary Club of Freshwater Bay, the Elderbloom Community Care Centre and Koh-I-Noor Contemporary Care.

Dr Bharadwaj is leading an investigation into the rare genetic disease Childhood Dementia using the extensive knowledge we have gained from our own work on Alzheimer's disease. This project aims to identify specific changes in proteins in the blood and urine of children with various types of childhood dementia. As well as adding to the knowledge base, this project may uncover new treatment approaches for these diseases.

In collaboration with Dr Isaac Canals (Lund University, Sweden), Dr Bharadwaj has established a stem cell lab to investigate disease mechanisms and develop new treatment strategies. Dr Bharadwaj works closely with clinicians across Perth and various neurologists. He also collaborates with the Children's Dementia Initiative and doctors from the Queensland Children's Hospital and Royal Melbourne Hospital.

Our team has launched an innovative approach to early detection of Alzheimer's and dementia by employing wearable digital tools, which have the potential to develop non-invasive digital 'fingerprints' of early neurological changes associated with dementia. Alzheimer's Research UK has been awarded this grant with ECU to fund the Early Diagnosis of Neurodegenerative Diseases (EDoN), thanks to a substantial grant from The Alzheimer's Drug Discovery Foundation, a U.S.-based venture philanthropy.

As part of this project, we will be collecting data on behalf of Alzheimer's Research UK at two sites in Australia, one at our own Western Australia Memory Study in Perth and the other at the University of Sydney. The data will be analysed by the Big Data Institute at the University of Oxford and the Alan Turing Institute at the University of London.

A/Prof Rainey-Smith and Prof Sohrabi are playing a leading role in this global partnership, which demonstrates what a powerful resource the Western Australian Memory Study has become over the past 20 years.

With the support of the Charlies Research Foundation and clinicians from Sir Charles Gairdner Hospital, the Western Australian Memory Study participants underwent brain imaging and clinical assessments in order to contribute to the biomarker study for early diagnosis. I would like to thank our team, clinical collaborators, the Alzheimer's Drug Discovery Foundation and the Charlies Foundation for their outstanding support which has enabled us to make considerable progress for early diagnosis of Alzheimer's and dementia.

I am excited about a new study that is highly innovative and will hopefully provide novel insights into our understanding of this devastating disease. This project, led by Dr Binosha Fernando, will examine the relationship between the gut and Alzheimer's disease.

It has been shown that the gut microorganisms (gut microbiota) in Alzheimer's patients differs from that of healthy controls. Moreover, changes in the gut microbiota can contribute to increased amyloid-β deposits, tau phosphorylation, neuroinflammation, metabolic dysfunctions, and chronic oxidative stress which collectively contributes to Alzheimer's disease progression.

These findings suggest that faecal microbiota profiles can serve to provide valuable insight into disease pathogenesis as well as biomarkers for Alzheimer's disease. As part of Dr Fernando's current research, she utilises a variety of

techniques to study the imbalance of gut bacteria in patients with mild cognitive impairment and Alzheimer's disease to determine the key bacteria contributing to the Alzheimer's pathology.

Prevention is a major theme of the clinical research conducted at the Foundation and we had several preventative programs ongoing in 2022.

Adopting a healthy diet, exercising regularly, staying socially active, and undergoing brain training exercises have all been shown to improve brain function, and/or slow its decline. Our team is part of the AU-ARROW study which is investigating the role lifestyle modifications may play in reducing the risk of Alzheimer's disease. We are currently undertaking an extensive media campaign to recruit 600 participants for both the NSW and WA arms of the study.

The AU-ARROW study is a member of a global collaboration called World-Wide FINGERS, and is primarily funded by a Medical Research Future Fund (MRFF) grant, a US Alzheimer's Association grant, and funding from Alzheimer's WA, the Lions Alzheimer's Foundation, Macquarie University and Edith Cowan University. In addition to direct research funding, AARF is also providing funding and the research facilities for the conduct of the WA arm of the study.

Collaborating with colleagues at Leiden University in the Netherlands, we began working on the Track D-CAA (Dutch type-cerebral amyloid angiopathy) study in mid-2022. In these families, there is a rare and specific genetic mutation in one of the Alzheimer genes that results in bleeding in the brain. AARF will host the Perth arm of the collaboration between the Netherlands and Australia. A better understanding and accurate diagnosis of cerebral amyloid angiopathy (CAA) will potentially benefit both stroke and Alzheimer's patients.

Our team is a proud partner of the Australian Dementia Network (ADNeT), a unique dementia network that draws together the expertise of leading researchers and clinicians from 17 Australian institutions working on Alzheimer's research. Since its inception in 2018, ADNeT has established Australia's first Clinical Quality Registry, launched national quality guidelines for memory clinics and increased access to diagnostic scans, blood tests, and clinical trials. This powerful collaboration is paving the way for better and more equitable dementia prevention, diagnosis, treatment, care, and cure.

Thank you to our volunteers, donors and the entire team.

My heartfelt gratitude goes out to our amazing study participants and their families as well as the generous donors, without whom our research would not be possible.

Your continued generosity enables us to achieve the milestones I have shared with you and make the necessary advances to eventually lead to a world without Alzheimer's and dementia.

I would also like to thank the supporters of AARF who make all these programs possible. The philanthropic support received enables us to provide funding for researchers, clinical trial staff, provide world class facilities, and other research-supporting activities, as well as financial support to manage the research programs.

Prof Ralph Martins AO
Director of Research

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.

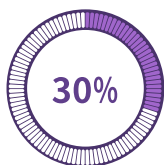### Leading cause of death of women

Females account for 64.5% of all dementia-related deaths and it is 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 800,000 by 2058.

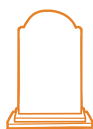### 30% of people over 85 have dementia

30%

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

UNDERSTANDING ALZHEIMER'S

Our research helps unravel the complex interplay of factors contributing to the disease. Ultimately, understanding Alzheimer's disease is the first step on the path towards finding a cure.

OUR RESEARCH STARTS WITH YOU

"The more people I speak to about my father's battle with Alzheimer's disease, unfortunately I discover the more common this story is."

Peter Bedford, from Bacchus Marsh in Victoria, has been racing the toughest roads in Australia to honour his late father, Chris Bedford.

Peter said, "Although dad was unable to talk or communicate for five and a half of his last years, he still continued to teach me life lessons. The biggest of all was, 'you don't know what's coming around the corner, so if it makes you happy, then do it!'"

Chris was diagnosed with early onset Alzheimer's disease when he was only 59 years old. Peter made the difficult decision to put his dad in a dementia ward in a nursing home. "For seven years I watched him slowly deteriorate through the stages of the disease."

He said knowing that his dad never got to enjoy retirement or tick off a bucket list, made him determined to seize every opportunity in life. With this in mind, he entered the 2022 Finke Desert Race to ride in tribute of his dad.

The "Finke" is an annual offroad two-day race through 460km of tough desert country from Alice Springs to the small Aputula community (formerly known as Finke). The race has the reputation of being one of the most difficult and remote offroad courses in the world.

Peter used the race to raise funds for the Australian Alzheimer's Research Foundation and raised an astonishing $31,785. He finished 339th out of 530 participants, which is very impressive for a first-time racer!

"The Foundation is trying to stop, stall, prevent or find a way to predict the disease," said Peter. "It's probably too late for me, but if I can in any way help my kids or future grandkids from having to experience what I had to with my dad then it's worth it."

"I want my kids to take on the life lesson to follow their dreams."

WA MEMORY STUDY

Prof Ralph Martins, Macquarie University and Edith Cowan University
Prof Hamid Sohrabi, Murdoch University
Mr Kevin Taddei, MSc, Edith Cowan University
A/Prof Michael Weinborn, University of Western Australia
A/Prof Stephanie Rainey-Smith, Murdoch University

The success of the ongoing WA Memory Study (WAMS) continues, with another 120 participants taking part in this important study, which is cited in research across the globe.

In 2022, approximately 120 participants visited the Nedands facility of AARF to undergo clinical and memory assessments, blood sample collection for Alzheimer's plasma-based biomarkers analysis and brain imaging.

Since the study's inception in 1996, more than 1200 people have been tested at 18-month intervals for the purpose of better understanding memory changes across the ageing process. WAMS was initially established by Prof Ralph Martins with funding from the National Health and Medical Research Council (NHMRC). More recently, funding support and facilities have been provided by AARF.

WAMS aims to find out what factors may influence memory change and also to follow the longitudinal trajectory of cognitive change and see who will, or will not, develop dementia. The study hopes to identify what characteristics are specifically associated with Alzheimer's disease in order to pinpoint individuals who are at a higher than average risk of developing dementia. This is enabling new screening tests to be developed to identify people who may have the very early symptoms of Alzheimer's disease.

People in the WAMS study are asked to do various memory tasks including identifying common smells, remembering lists of words, recalling details of brief narratives, and spacial recognition tests.

As well as memory assessment, many participants had cerebrospinal fluid samples collected through lumber punctures. Cerebrospinal fluid analysis is currently the gold standard for identifying changes in brain chemistry that may predict the future risk of dementia. This exciting element of the study was accomplished with the generous support of the Charlies Foundation for Research and was made possible thanks to collaboration with specialists from Sir Charles Gairdner Hospital. AARF would like to thank the Charlies Foundation for Research for supporting this project.

The WAMS has also been successful in publishing important papers, including one on the WA Olfactory Memory Test (WAOMT) by Dr Rasangi Seneviratne, who completed this work as part of her PhD thesis at AARF, supervised by A/Prof Weinborn, Profs Sohrabi and Martins.

The newly-published WAOMT has proven to meet the need for a comprehensive test that measures olfactory episodic memory for clinical and research applications. Prior research has shown that losing the ability to identify smells is a way of reliably predicting the progression from normal aging to neurodegenerative disorders. More than 200 volunteers were tested, and retested, smelling odour samples and taking brain memory examinations.

Additionally, a paper was published by Miss Hadeel Tarawneh, a PhD student at UWA supervised by A/Prof Mulders, Prof Sohrabi, Prof Martins and Dr Jayakody. This review examined the compelling relationship between age-related hearing loss and Alzheimer's disease. Age-related hearing loss is the most prevalent health condition that affects older adults worldwide and evidence suggests that even mild hearing loss may increase the long-term risk of cognitive decline and dementia.

Another assessment tool being developed in WAMS is the WA Prospective Memory Test, which collected data from 200 participants and aims to test and assess the ability to remember a task to be completed in the future. Prospective memory declines as we age and may be an early warning sign for dementia.

The McCusker Subjective Cognitive Decline Inventory (McSCI) is a questionnaire which has been developed to help with the diagnosis of someone with concerns about their memory, and looks at elements such as language, memory and attention.

CHARLIES FOUNDATION COLLABORATION

Prof Ralph Martins, Macquarie University and Edith Cowan University
Prof Hamid Sohrabi, Murdoch University
Prof Charles Inderjeeth, University of WA
Prof Christopher Lind, University of WA

A productive collaboration between AARF and Charlies Foundation for Research has allowed the two organisations to work together, sharing knowledge and experience in a project that has significant implications towards understanding the underlying cause of Alzheimer's disease.

The Charlies Foundation for Research contributed a substantial research grant of $100,000 towards this ground-breaking work and allowed the team to investigate biomarkers in blood, cerebral spinal fluid and brain imaging.

Prof Ralph Martins, Director of Research at AARF, said, "The generous grant greatly contributed to a novel aspect of our research that has not been so far achieved due to funding restrictions."

Prof Charles Inderjeeth, Consultant Physician, and Prof Chris Lind, Consultant Neurosurgeon at Sir Charles Gairdner Hospital, provided the clinical assessment and oversight of all participants in the study. The study also utilises the cohort of the WA Memory Study (WAMS) at AARF, led by Prof Martins and Prof Dr Hamid Sohrabi.

> WAMS has access to a unique group of individuals with self-reported concerns over their cognitive decline who were readily recruited for the study.
>
> - Prof Martins

"These individuals are already fully phenotyped through WAMS, which included plasma collection, neuropsychological and hearing assessments, brain glucose metabolism, and olfactory memory measures as well as many other tests."

The Charlies Foundation funding went towards lumbar punctures to collect the cerebral spinal fluid, clinical assessments by Prof Inderjeeth, and the analysis of biomarkers by the team under Prof Martins.

"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 the disease," Prof Martins said.

Furthermore, specific biomarkers would provide insight into the molecular causes of Alzheimer's disease, which in turn has the potential for development of drug targets, he said.

During the study, 153 participants aged between 52-90 years old were recruited and assessed. All of the participants — 54 men and 99 women — underwent a clinical assessment and donated a blood sample, and 141 have undergone amyloid brain imaging. In addition, 53 (35%) of the total 153 participants consented to the optional lumbar puncture and a cerebrospinal fluid sample was collected.

Preliminary analysis of the data indicates some exciting results, but a more thorough analysis is being conducted to prepare the findings for publication. Once published, the results will be available to researchers worldwide.

Clinical
assessments
153
VOLUNTEERS TOOK PART
IN THIS STUDY

HADEEL TARAWNEH
STUDENT PROFILE

Supervisors:
A/Prof Wilhelmina Mulders, University of Western Australia
Dr Dona Jayakody, Ear Science Institute Australia
Prof Hamid Sohrabi, Murdoch University
Prof Ralph Martins, Macquarie University, ECU

I have been investigating if the use of auditory electrophysiological measurements (the measure of the brain's electrical responses to sound) can potentially be a screening measure for pre-clinical Alzheimer's disease. In 2022, I had papers published in the Journal of Alzheimer's Disease Reports and the journal Frontiers in Neurology.

My research aimed to bridge the knowledge gap by investigating auditory electrophysiological assessment measures in relation to biological markers, such as brain amyloid burden, in those at high risk of Alzheimer's disease. Data revealed that amyloid-positive participants had delayed auditory responses when compared to amyloid-negative participants. These results suggest that this auditory response may be a useful tool to identify individuals at higher risk of developing measurable cognitive decline. Further research is needed to draw any final conclusions.

MEHRANE MEHRAMIZ
STUDENT PROFILE

Supervisors:
Prof Simon Laws, Edith Cowan University
A/Prof Stephanie Rainey-Smith, Murdoch University
Dr Eleanor O'Brien, Edith Cowan University
Dr Tenielle Porter, Edith Cowan University

My PhD investigates the impact of the interaction between a particular gene (SIRT1) and lifestyle factors on Alzheimer's disease risk and related phenotypes. This project integrates cross-sectional and longitudinal data from the Australian Imaging, Biomarkers, and Lifestyle (AIBL) Study to explore genetic and early epigenetic biomarkers for dementia disorders related to lifestyle factors, before the onset of the disease.

This ground-breaking study aims to explore the SIRT1 gene's relationship with lifestyle factors and age, and how this relates to Alzheimer's disease at various biological levels over a long period of time. The achievements of this thesis include preparing seven papers, of which one has been published, one has been accepted and the others are under review.

BHARGAV TALLAPRAGADA
STUDENT PROFILE

Supervisors:
Prof Hamid Sohrabi, Murdoch University
A/Prof Belinda Brown, Murdoch University
Prof Paul Maruff, Cog State Ltd
Dr Rosita Shishegar, CSIRO
Dr Shaun Markovic, Murdoch University

My project focuses on developing 'cognitive-composites' using machine-learning approaches. These approaches can detect patterns in composite and biomarker data and predict a person's risk for developing Alzheimer's disease up to 10 – 15 years before any clinical symptoms appear. Such data-driven composites have the potential to be a cost-effective and non-invasive screening tool for physicians and a useful outcome measure for researchers.

The results of my project could inform more precise and targeted approaches to Alzheimer's prevention trials, ultimately helping in the early and accurate diagnosis of dementia syndromes.

EDON

A/Prof Stephanie Rainey-Smith, Murdoch University
Prof Ralph Martins, Macquarie University and Edith Cowan University
Mr Kevin Taddei, MSc, Edith Cowan University
Prof Hamid Sohrabi, Murdoch University
Study Co-ordinator: Ms Jo Shaw

A big problem requires big thinking — and you can't get bigger than EDoN.

The Early Detection of Neurodegenerative diseases (EDoN) is the largest initiative in the world to collect, share and analyse clinical and digital health data to detect diseases like Alzheimer's disease.

Spearheaded by Alzheimer's Research UK and partnered with global leaders including Bill Gates, EDoN is an ambitious project which aims to develop an innovative approach to detect dementia years before the onset of symptoms, using a wealth of digital data which is at our fingertips.

The project is funded by the Alzheimer's Drug Discovery Foundation via a grant awarded to Alzheimer's Research UK on which A/Prof Stephanie Rainey-Smith and Prof Ralph Martins are named investigators.

Currently, by the time someone receives a dementia diagnosis, the disease may have already progressed too far for interventions to assist.

> " It is crucial to detect dementia-causing diseases as early as possible.
> - Prof Ralph Martins

The EDoN initiative aims to detect conditions such as Alzheimer's disease by investigating a range of very subtle behavioural changes that emerge years before problems like memory loss start to affect a person's day-to-day life. Certain biomarkers such as heart rate, sleep patterns, gait, mood, and some cognitive functions may be affected by underlying neurodegenerative processes.

By capturing this type of information using non-invasive, readily available, direct to consumer technologies such as wearable digital tools, these biomarkers have potential value in reflecting the earliest brain changes in dementia-causing diseases. This may help predict an individual's risk of developing dementia long before the onset of symptoms.

The EDoN Study takes an efficient approach, using a 'digital toolkit' comprising a combination of commercially available digital tools, including active and passive smartphone-based assessments and passive data collection from wearable devices.

Perth researchers recruit from the Western Australia Memory Study (WAMS), a study supported by AARF. "The EDoN award demonstrates what a powerful resource WAMS has become. The funding awarded is US$874,000 [$1.3million AUD] over three years and the grant will be administered through Edith Cowan University," said A/Prof Rainey-Smith.

She thanked the Australian Alzheimer's Research Foundation for its support in funding WAMS over the previous four years. She said, "As a result of this award, the funding provided will enable us to directly sustain WAMS from 30 June 2022 for the ensuing three years.

"While we are thrilled to receive this grant, we are also appreciative of the continued support AARF provides to our research team and the facilities for the WAMS and EDoN studies," said A/Prof Rainey-Smith.

A/Prof Rainey-Smith said the project involved collecting data on behalf of Alzheimer's Research UK. The other Australian data collection site is the University of Sydney. Data will be analysed by the Big Data Institute, University of Oxford and the Alan Turing Institute, UK on behalf of the EDoN initiative.

Funding
$1.3m
Awarded

DIAN STUDY
The Dominantly Inherited Alzheimer Network

Prof Ralph Martins, Macquarie University and Edith Cowan University
Prof Hamid Sohrabi, Murdoch University
Mr Kevin Taddei, MSc, Edith Cowan University
Dr Samantha Gardener, Edith Cowan University
Dr Pratishtha Chatterjee, Macquarie University

A network of researchers that stretches around the world, all working towards a common goal. This is the reality of the Dominantly Inherited Alzheimer Network (DIAN) Observational Study.

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.

An international, multi-site collaboration project led by Washington University since 2008, the DIAN study aims 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. There are 23 sites worldwide, with two Australian sites; one in Sydney and one at the Australian Alzheimer's Research Foundation, based in Perth.

Dr Samantha Gardener, Research Fellow and DIAN study coordinator, said, "At the end of 2022, the Perth site had 16 DIAN participants undergoing week-long assessments every two years, with a remote visit in the interim year."

Across the world, several manuscripts were published using the study data in 2022. Participants for the DIAN study live in Queensland, Tasmania, South Australia, Canada, and Libya, as well as Western Australia. Hybrid visits were introduced following the COVID-19 pandemic and these have allowed completion of some parts of the assessments via phone.

"Whilst this means in-person assessments like the brain imaging and lumbar puncture are not completed, minimal data is still able to be collected including memory testing," Dr Gardener said.

Dominantly inherited Alzheimer's disease represents less than 1% of all cases of Alzheimer's disease, but it is an important model for study because the responsible mutations have known biochemical consequences.

Genetic testing can identify those who carry the gene, and researchers around the world monitor and identify changes in those people. Research suggests that brain changes may occur years before actual Alzheimer's symptoms are detected.

> By observing the complex interrelated biological changes that occur in gene carriers well before symptoms appear, scientists will obtain invaluable insight into how and why this disease develops.
>
> – Dr Samantha Gardener

Participants undergo genetic testing, brain imaging, and provide blood and spinal fluid samples. Among other things, researchers measure the amount of abnormal amyloid in the brain and spinal fluid, changes in brain size (e.g. shrinkage), and brain metabolism (energy processing). They compare the changes that occur in participants with and without mild Alzheimer's symptoms, who may or may not have an Alzheimer's genetic mutation.

All results are stored in the DIAN Central Archive, an international database that allows qualified researchers to access and analyse the information.

AARF is pleased to be supporting the DIAN project by providing the clinical research facilities for participants to visit for their regular assessments.

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

Prof Ralph Martins, Macquarie University and Edith Cowan University
Prof Hamid Sohrabi, Murdoch University
Mr Kevin Taddei, MSc, Edith Cowan University
Dr Samantha Gardener, Edith Cowan University

People looking back into their family's history are often searching for the origins of handed-down stories, and to preserve the paths and choices of their ancestors.

As well as finding family stories, looking back through family records also holds the secrets to hereditary conditions. In some cases, family history can be a vital tool in medical research.

One hereditary condition is cerebral amyloid angiopathy (CAA), which causes a build-up of protein clumps called amyloid deposits in blood vessels in the brain, causing vascular disease (angiopathy). People with hereditary CAA often have cognitive decline in mid-adulthood, and the condition is usually fatal in one's 60s. Currently, there are no disease-modifying treatments available.

There are many different types of CAA, which are named after the regions where they were first diagnosed, including Flemish, Italian and Icelandic. The different types are distinguished by their genetic cause, and the signs and symptoms that occur.

The Dutch type of hereditary CAA is the most common form. Stroke is frequently the first sign of the Dutch type, and those who are affected often develop dementia and have recurrent strokes.

The Tracking the Natural History of Dutch-type Hereditary Cerebral Amyloid Angiopathy (TRACK D-CAA) study commenced in mid-2022 with 15 participants recruited by the end of 2022. Due to the extremely rare nature of this disease, these participants were recruited from just two families.

The weeklong assessments for these participants include a PET brain scan, MRI imaging, blood test, memory testing, clinical assessment, and a lumbar puncture — the most important procedure to collect the valuable cerebrospinal fluid that flows around the brain and spinal cord.

These families have a mutation in their genes that results in haemorrhagic stroke, or brain bleeding, which is a stroke following a break in the wall of a blood vessel in the brain.

To try and find other families in Australia carrying this mutation, a national advertising campaign was run in all the major state newspapers, looking for Dutch Australians with a history of stroke in their family. After 140 responses, this was narrowed down to nine that could potentially be gene mutation carrying families. Those families are currently undergoing genetic testing.

While the TRACK D-CAA study is based on a small portion of the population, the study findings will increase the understanding of the interplay between neurodegenerative and vascular diseases, which has the potential to lead to improvements in the treatment and prevention of Alzheimer's disease.

International Conference

The TRACK D-CAA Study is conducted at the Australian Alzheimer's Research Foundation facilities.

The 8th International Cerebral Amyloid Angiopathy (CAA) Conference was hosted in Perth over three days in November 2022, with AARF as the primary sponsor.

Reporting on the research and knowledge on the diagnosis, prevention and treatment of CAA, the conference was an opportunity for international collaboration.

Research Fellow Dr Samantha Gardener said one of the highlights of the conference was a public forum where, for the first time, researchers and patient advocates from three continents (Australia, USA and Europe) came together to discuss CAA and Dutch CAA.

HILAL AL SHAMSI
STUDENT PROFILE

Supervisors:
Dr Binosha Fernando, Edith Cowan University
Dr Samantha Gardener, Edith Cowan University
A/Prof Stephanie Rainey-Smith, Murdoch University
Prof Hamid Sohrabi, Murdoch University
Prof Ralph Martins, Macquarie University, ECU

Depression has been proposed to be co-morbid in approximately 30% of Alzheimer's disease (AD) patients and to increase future risk of the disease. Diet is also an established risk factor for AD including hypertension, obesity, and diabetes, and has also been proposed to directly affect AD risk.

My PhD will utilise network analysis, a statistical approach that can explore complex relationships, to examine diet's contributions to the association between depression and AD. This method allows relationships to be visually represented, and provides information on which factors have the greatest impact in these relationships. The study will utilise data collected from the AIBL Study, and hospital data from Oman to explore the complex relationship between diet, depression and AD. In 2022 my PhD candidature was confirmed with ECU after submitting my research proposal and giving a presentation.

KELSEY SEWELL
STUDENT PROFILE

Supervisors:
A/Prof Belinda Brown, Murdoch University
A/Prof Stephanie Rainey-Smith, Murdoch University
Prof Jeremiah Peiffer, Murdoch University
Prof Hamid Sohrabi, Murdoch University
Prof Kirk Erickson, AdventHealth Research Institute

My work has used data from the Australian Imaging, Biomarkers and Lifestyle (AIBL) study, and Intense Physical activity and Cognition (IPAC) study, to examine the effects of exercise and sleep on memory and thinking skills in older adults.

The overarching aim of this research is to identify how we can best preserve memory in ageing, by considering how people with different sleeping patterns may experience varying memory benefits from exercise.

Our results have indicated that exercise may be able to compensate for some of the negative effects that poor sleep has on memory and thinking skills. Further research is required to corroborate these findings, but for now, it is clear that living an active lifestyle is beneficial for maintaining brain function in ageing.

ANJANA RAJENDRA
STUDENT PROFILE

Supervisors:
Dr Catherine Bondonno, Edith Cowan University
A/Prof Stephanie Rainey-Smith, Murdoch University
Prof Jonathan Hodgson, Edith Cowan University
Dr Nicky Bondonno, Edith Cowan University
Dr Samantha Gardener, Edith Cowan University

I am currently a PhD student at Edith Cowan University's School of Medical and Health Sciences. I am investigating the association between dietary nitrate and cognition, cognitive decline, dementia and markers of brain health. My most recent work has been focused on understanding the relationship of dietary nitrate and cognition.

Using data from the Australian Imaging, Biomarkers and Lifestyle (AIBL) Study conducted at AARF, I have demonstrated that habitual intake of dietary nitrate from sources where nitrate is naturally present impacts cognitive performance in an APOE genotype contingent manner.

These results suggest that a 60mg/day higher intake of plant-derived nitrate could protect cognition, thereby reducing the risk of Alzheimer's disease.

AIBL STUDY

Prof Ralph Martins, Macquarie University and Edith Cowan University
Mr Kevin Taddei, MSc, Edith Cowan University
Prof Hamid Sohrabi, Murdoch University
A/Professor Stephanie Rainey-Smith, Murdoch University
Dr Prashant Bhardawaj, Edith Cowan University
Dr Samantha Gardener, Edith Cowan University
Dr Binosha Fernando, Edith Cowan University
Dr Eugene Hone, Edith Cowan University
Dr Steve Pedrini, Edith Cowan University

Still going strong! Since 2006, the Australian Imaging, Biomarkers and Lifestyle Study (AIBL) has been uniting Alzheimer's researchers across Australia. That's 16 years of commitment!

AIBL is at the forefront of Alzheimer's disease research, having contributed to the development of new diagnostic criteria for Alzheimer's disease that permit earlier and more accurate diagnosis, and to the design of early intervention trials aimed at preventing the development of dementia.

The longstanding and highly respected study has led to increased Australian collaboration with international Alzheimer's groups, and continues to collect valuable data which adds to the body of knowledge in the search for earlier diagnosis and treatment of Alzheimer's disease.

AARF contributes to the AIBL study by providing the clinical and laboratory research facilities to the research team.

In 2022, data collection for the AIBL study continued, despite ongoing pandemic-related disruptions. Individuals who have participated in the study since it began underwent their 180-month (15 years) follow-up assessment, whilst those who joined the study later underwent assessments ranging from 54 (4.5 years) to 126 month (10 years) of follow-up.

> " The commitment of this group of Australians over this long period - 16 years - is an amazing contribution. People putting their valuable time into making research possible that we will all benefit from.
> - Liza Dunne, CEO

The study has collected up to eight "time-points" of data at 18-month intervals from over 2350 participants, yielding a current database of 8592 person-contact years. The amazing commitment of the study participants has enabled AIBL researchers to make world-class contributions to understanding the natural history of Alzheimer's disease progression.

After a long wait, and years of work behind the scenes (led by Kevin Taddei), Q4 of 2022 finally saw the addition of brain tau imaging (using a positron emission tomography, or PET, camera) to the array of assessments undertaken as part of the AIBL study.

Within the brain, tau protein is responsible for maintaining the structure of brain cells (neurons). However, in Alzheimer's disease, the structure of tau is altered which results in tangles of tau protein forming within brain cells. These tangles disrupt cell function and contribute to cell death. The location and quantity of these tangles within the brain is proposed to be closely related to changes in memory and thinking that occur as Alzheimer's disease progresses.

The implementation of this new technology in the AIBL study will improve our understanding of both the development of Alzheimer's disease over time, as well as factors that modify disease risk. This new technology will also aid in the development of blood biomarkers for disease diagnosis and assessment of future risk.

In 2022, AIBL maintained its position at the forefront of Alzheimer's research globally. Further refinement and validation of blood biomarkers for Alzheimer's disease occurred as did enhancement of our understanding of lifestyle influences on cognition and Alzheimer's disease.

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

NUTRITION

A/Prof Stephanie Rainey-Smith, Murdoch University
Dr Binosha Fernando, Edith Cowan University
Dr Samantha Gardener, Edith Cowan University
Dr Rodrigo Canovas, CSIRO

The role of diet and the development of Alzheimer's disease is a fascinating area of research, and the body of knowledge in this area is growing every year.

It has already been established that there are a variety of dietary factors that improve the health of the brain in older adults who may develop Alzheimer's disease. The team at AARF, led by A/Prof Stephanie Rainey-Smith, has achieved several milestones in their research endeavours.

This research has made significant advancements and has successfully published several papers. The collection of the clinical data and the laboratory work is all conducted at AARF's facilities.

During 2022 the Nutrition and Alzheimer's disease research area was successful in the publication of a manuscript titled 'Potential role of dietary nitrate in relation to cardiovascular and cerebrovascular health, cognition, cognitive decline and dementia: a review' which was the work of Ms Anjana Rajendra, a PhD student supervised by A/Prof Rainey-Smith and Dr Samantha Gardener. This review paper concentrated on the current evidence regarding dietary nitrate's potential role in cerebrovascular health, cognitive function, and brain health.

A second manuscript was submitted and is currently under peer review authored by Dr Samantha Gardener and A/Prof Stephanie Rainey-Smith. The objective of this study was to assess the validity of an Alzheimer's disease-specific dietary questionnaire using detailed records of how much participants eat, as well as blood levels of the micronutrients including vitamin E and beta carotene.

A/Prof Rainey-Smith said, "Validation of dietary questionnaires is vital as the accurate assessment of usual dietary intake is crucial to understanding the association between diet and chronic diseases." She said incorrect information may lead to false associations between dietary factors and disease risk and prevention.

Also in 2022, Mr Hilal Salim Said Al Shamsi achieved his PhD confirmation of candidature and was therefore able to commence his research project in the Nutrition and Alzheimer's disease field investigating the contribution of diet to the relationship between depression and Alzheimer's-related traits.

Mr Al Shamsi is an international student supported by a research scholarship funded by the Omani Consulate and his project will utilise data from the Australian Imaging, Biomarkers and Lifestyle (AIBL) study, as well as hospital data from Oman. Mr Al Shamsi is supervised by Dr Binosha Fernando, A/Prof Stephanie Rainey-Smith, Dr Samantha Gardener, and Dr Rodrigo Canovas of CSIRO.

PREVENTING ALZHEIMER'S

By focusing on prevention, we offer hope for future generations. We strive to create a future where Alzheimer's is preventable, ensuring better overall brain health and well-being for individuals and society.

OUR RESEARCH STARTS WITH YOU

Alice Gerrans' love for her late husband Ross shines as strong as ever. "We were so good together. He made me laugh so much," said Alice.

Alice knows firsthand the devastating impact of Alzheimer's disease, having lost Ross to the disease in October 2021, just after his 81st birthday.

Her passion for finding a cure and helping others affected by Alzheimer's has inspired her to leave a bequest to the Australian Alzheimer's Research Foundation in her Will.

"I believe strongly that one day there will be a cure. Look how far we have come with other diseases."

Many people include a gift in their Will to AARF, and every bequest goes towards research that improves our understanding of the disease.

When they met more than 20 years ago, Ross was an enthusiastic sportsman and tennis coach who ran the Pro Tennis Coaching School in Perth. Alice would help by taking the kindergarten classes, fixing tennis nets and restringing racquets. "I still can't play tennis though," she laughs.

When they moved to their Jolimont retirement village, Ross started a bowls group and encouraged people to join and have fun, even if they had no bowls experience.

Later, when he was affected by Alzheimer's disease but was still a good bowler, his friends would help him by reminding him which end they were playing and which bowls were his. He was still playing tennis in his 80th year. "He had his friends around him till the end," said Alice.

Over the years, Alice has raised nearly $5,000 for AARF by doing sewing jobs for her fellow residents in her retirement village. "A lot of little jobs add up to a lot," said Alice. "If it is kaput, I can fix it."

Alice's ongoing hard work and dedication to Alzheimer's research is leaving a lasting legacy of love and hope for future generations.

AU-ARROW

Prof Ralph Martins, Macquarie University and Edith Cowan University
Dr Samantha Gardener, Edith Cowan University
Mr Kevin Taddei, MSc, Edith Cowan University
A/Prof Stephanie Rainey-Smith, Murdoch University
Prof Hamid Sohrabi, Murdoch University
A/Prof Roger Clarnette, University of Western Australia

Eating well and staying fit are good for your body – but can they also help your brain? The AU-ARROW study looks at how lifestyle modifications might reduce the risk of developing Alzheimer's disease.

Changing the habits of a lifetime by choosing healthy eating options and doing regular exercise is part of what's covered in the study. It also looks at helping people stay socially active and engaging in brain training exercises.

"Research has shown that lifestyle modifications can have a significant impact on brain function and reduce the risk of dementia," said Dr Samantha Gardener.

Recruitment of participants into this study commenced in February 2022 and has been ongoing throughout the year with flyers distributed to over 50 Independent Living Villages and nearly 40 Rotary Clubs.

Many people were interested in joining the study — one Facebook advertisement provided 147 contacts! Inclusion criteria were relaxed to allow more people to join, including raising the body mass index inclusion from 35 to 39-or-under. Participants are asked to exercise regularly at a specified local gym, and the recruitment zones were expanded to include a gym in Carine, adding to the existing locations.

"We get to know our participants really well when they are in a study," Dr Gardener said. "We value our research volunteers and appreciate the time and effort they contribute towards advancing our understanding of Alzheimer's disease."

The next step in AU-ARROW is to randomise participants into one of the two study arms – the Multidomain Lifestyle Intervention, or the Health Education and Coaching group.

Carolina Castro, a recipient of a PhD scholarship from the Australian Alzheimer's Research Foundation, took over the role of AU-ARROW study dietician and will be guiding participants through the MIND (Mediterranean-DASH Intervention for Neurodegenerative Delay) diet and its benefits for cognitive performance throughout the two-year intervention.

The name of the study - AU ARROW - is a handpicked acronym taken from the full name: "AUstralian multidomain Approach to Reduce dementia Risk by prOtecting brain health With lifestyle intervention study".

The study has attracted international interest, with three presentations on the AU-ARROW study given at the Alzheimer's Association International Conference in San Diego in July 2022.

The AU-ARROW project is primarily funded by a Medical Research Future Fund (MRFF) grant, a US Alzheimer's Association grant, and with funding from Alzheimer's WA, the Lions Alzheimer's Foundation, AARF, Macquarie University and Edith Cowan University. The aim is to recruit 600 participants, with 300 at Macquarie University in NSW and 300 at AARF in WA. In addition to funding, AARF provides the research facilities for the WA arm of the study.

The AU-ARROW study is a member of the worldwide consortium, called World-Wide FINGERS (WW-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.

CAROLINA CASTRO
STUDENT PROFILE

Supervisors:
Prof Hamid Sohrabi, Murdoch University
Prof Ralph Martins, Macquarie University and ECU
Dr Juliana Chen, The University of Sydney
Dr Belinda Brown, Murdoch University
Dr Ruey Leeng Loo, Murdoch University
Dr Cintia Dias, Macquarie University

I have been always passionate about a healthy lifestyle and the prevention of diseases. I am a qualified accredited practicing Dietitian/Nutritionist with over 10 years of experience in clinical nutrition. Currently, I am doing my PhD at Murdoch University, undertaking the Nutritional Psychiatry course at Deakin University, and just completed my post-graduate studies in neurological diseases at Filadelfia University in Brazil. The key findings of my review and metanalysis is the concept that supplementation with medium-chain fatty acids (MCFAs) increases ketone bodies in the blood.

AUSTRALIA DEMENTIA NETWORK

Prof Ralph Martins, Macquarie University and Edith Cowan University
Prof Hamid Sohrabi, Murdoch University
Mr Kevin Taddei, MSc, Edith Cowan University
A/Prof Stephanie Rainey-Smith, Murdoch University
Dr Samantha Gardener, Edith Cowan University

In late 2022, Australian Dementia Network (ADNeT) unveiled its Neuropsychology Norming Tool (ANNT) for use in Australian Memory Clinics to assist with the diagnosis of Alzheimer's disease.

A national collaboration between experts from 17 institutions and led by the University of Melbourne, ANNT was designed to help clinical neuropsychologists, to accelerate a clinical diagnosis of Alzheimer's disease and other dementias. It is now being tested to assess its ease of use.

Prof Ralph Martins is an ADNeT Chief Investigator and part of the national ADNeT Management Team. AARF supports ADNeT in various ways and provides clinical neuropsychologists and facilities for the program in WA.

ADNeT was created in 2019 by the Australian Government to boost research into dementia and has brought together Australia's leading researchers, clinicians and consumers to create a powerful network for dementia prevention, treatment and care.

The three core aims of ADNeT are: to establish a Clinical Quality Registry of people diagnosed with dementia and mild cognitive impairment; to establish a collaborative network of clinicians conducting high-quality dementia assessments at Memory Clinics across Australia; and to providing dementia screening of patients suitable for participation in clinical trials.

The Memory Clinics had a productive year that saw regular well-attended webinars and peer support programs, as well as the expansion of its national network to include more than 150 specialised dementia assessment services. Ongoing support was provided to these clinics to integrate the Memory and Cognition Clinic Guidelines into their practice, with a view to streamlining service provision and improving patient outcomes.

To complement the Cognition Clinical Guidelines, seven clinics trialled a Quality Improvement program which involved a self-assessment to evaluate their service delivery and organisational processes. Additionally, a new research project exploring the application of cognitive intervention programs in Memory Clinics was started.

The Screening and Trials initiative aims to accelerate the development of effective therapies to prevent or treat dementia and provide more Australians access to the latest potential therapies through participation in trials.

The national network provides new technology such as novel brain scans and blood tests that identify people suitable for early treatment trials aimed at slowing down and, ultimately, preventing dementia.

Screened
1,034
1,034 FULLY SCREENED & TRIAL-READY

Registered
3,100
3,100 REGISTERED IN VOLUNTEER PORTAL

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

SLEEP

A/Prof Stephanie Rainey-Smith, Murdoch University
Prof Ralph Martins, Macquarie University and Edith Cowan University

Good sleep is often seen as being essential to wellbeing, but we are just beginning to understand how important sleep is to brain health.

The Sleep Improvement Study (SIS) team, led by Associate Professor Stephanie Rainey-Smith, is investigating possible links between poor sleep behaviour and cognitive decline. SIS is supported by AARF, with funding from the National Health and Medical Research Council (NHMRC), and the US-based Alzheimer's Association.

The study continues to recruit older Australians who say they are sleeping poorly, who undergo tests to measure their memory language and recognition skills. They also undertake behavioural training to improve their sleep. The effect of this behavioural intervention has on memory and markers of brain health has produced fascinating results.

The SIS team celebrated several successes in 2022. PhD candidate Louise Pivac (Murdoch University, co-sponsored by AARF) presented results from her studies at the Alzheimer's Association International Conference. The presentation was focussed on understanding the relationship of sleep to accumulation of the Alzheimer's hallmark, amyloid beta, in the brain.

A/Prof Rainey-Smith opened the CogSleep Centre for Research Excellence Annual Symposium in Sydney, giving a keynote address on her Sleep and Alzheimer's disease research program.

Louise Pivac was awarded a Travel Fellowship which enabled her to attend the Symposium and present findings from her PhD studies.

Her outstanding presentation was recognised by winning the Student Research Excellence Presentation Award.

Louise was also selected as a finalist for the prestigious 2022 Sleep Health Foundation Emerging Sleep Hero Award. This competition, open to students working in sleep research throughout Australia and New Zealand, requires the finalists to prepare a video presentation summarising their research. The final was in September, and Louise won the 'People's Choice Award'.

The presentation highlighted that the amount of sleep, and the efficiency of that sleep (time spent in bed, asleep), are particularly important for accumulation of Aβ-amyloid in the brain. This adds support to the idea that improving sleep could have an important role to play in slowing the rates at which Aβ-amyloid is accumulating in the brain, and thus delaying the onset of Alzheimer's disease symptoms.

Additional funding will be provided by the NHMRC thanks to a successful Synergy Grant application on which A/Prof Rainey-Smith and Prof Ralph Martins are Investigators. The Synergy Grant, appropriately named 'SIESTA' brings together leading researchers from across Australia and the world to improve understanding of how sleep disturbance contributes to cognitive decline, which can lead to dementia. A/Prof Rainey-Smith will use her share of the $5 million grant to fund additional assessments in SIS, whilst Prof Martins will use his share to fund biomarker investigations across multiple sleep studies.

Meet Louise Pivac

I'm Louise Pivac, a neuroscience PhD candidate at Murdoch University. Having reached the point in my PhD where I am ready to start analysing the interim results from the Sleep Improvement Study (SIS), I am coordinating the effort to conduct quality control assessments of the data.

I'm going through the data to make sure it's usable and reliable, and getting the statistical groundwork done. Next will come the exciting part where I can begin to assess the results of our intervention.

I am in regular contact with my supervisors, collaborators and fellow authors to determine the best models for data analysis. I'm in contact with people all over the world.

I am preparing a poster of findings from two of my research papers to present to the international research community at the Alzheimer's Association International Conference which is taking place in Amsterdam in 2023.

Meanwhile, I am writing a paper for publication which outlines what we currently know about the relationship between sleep, memory and thinking skills and brain-based biomarkers of Alzheimer's disease.

I attend meetings of our own local lab group, join webinars from national and internal organisations for students that I have joined, and sit on a national student committee. These help form important connections with the research community. It's crucial to keep up to date with what's happening in research, so I'm always reading what other researchers are doing and papers they have cited in the same area. You've got to keep on top of what's happening to keep ahead.

An afternoon with
Maggie and Ralph

In 2022, we had the pleasure of organizing an event featuring Maggie Beer AO, a renowned celebrity chef and passionate advocate for healthy aging, together with internationally acclaimed Alzheimer's disease researchers Professor Colin Masters AO and Professor Ralph Martins AO.

EXERCISE

A/Prof Belinda Brown, Murdoch University

Evidence is increasing that the more physically active you are throughout your life, the lower your risk of developing dementia, according to A/Prof Belinda Brown.

"We know that physical activity and exercise are not routinely prescribed as a preventative approach for dementia. Our team aims to change this," said A/Prof Brown, Head of Graduate Research Education and Training at Murdoch University.

She said the team was focussed on identifying the best approaches for improving brain health in older adults. "We are also focussed on understanding why some people may benefit from certain activities over others," she said.

The AIBL study is conducted at AARF and has been running for 16 years. As well as being a source of valuable data, the structure of the study helps to teach and develop up-and-coming researchers and clinicians. A/Prof Brown said that AIBL had united Alzheimer's researchers across Australia.

In 2022, PhD candidate Kelsey Sewell (Murdoch University), used data from the Australian Imaging, Biomarkers and Lifestyle (AIBL) study to examine long-term relationships between brain health and physical activity. This work, published in Alzheimer's and Dementia journal, was one of the most comprehensive examinations of the link between physical activity and cognition to date.

"We found that higher levels of physical activity at baseline (measured by an activity monitor) were associated with less risk of cognitive decline up to 10 years later," Ms Sewell said. "These results also demonstrated that the intensity of physical activity may be important for cognitive function."

She said moderate intensity exercise was the minimum intensity required to predict preserved cognition, but greater benefits were observed for higher intensity physical activity.

During her PhD candidacy, Ms Sewell also used results of the Intense Physical Activity and Cognition (IPAC) study, which was a collaboration between Murdoch University and AARF. The study examined 99 older adults who undertook 6 months of high-intensity or moderate intensity exercise (or were part of the control group). All participants had comprehensive cognitive testing and an MRI scan to evaluate brain volume.

The team's analysis of the IPAC study found that people who experienced the biggest improvements in cardio-respiratory fitness gained the greatest benefits in terms of improvement on tasks assessing memory and executive function.

Building on the original findings, the team examined the IPAC data further to find out what other factors may contribute to cognitive response to exercise.

Ms Sewell was particularly focused on whether sleep may play a role in how exercise influences the brain. The findings revealed that moderate intensity exercise may be most beneficial for cognitive function in people with poorer sleep (specifically low sleep efficiency, which is the percentage of time spent in bed asleep).

"These results further support the notion that exercise may be able to compensate for some of the negative effects that poor sleep has on cognition," said A/Prof Brown.

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

I completed my PhD in October 2022, which focused on how traumatic brain injury (concussions) impact the ageing brain. I also examined if lifestyle-based strategies could promote recovery and long-term health outcomes for older adults who have experienced concussions. I'm thankful to AARF, which provided an annual top-up scholarship to support my PhD research.

I was able to use data from the Intense Physical Activity and Cognition (IPAC) study, and also worked in collaboration with a team of researchers from the Curtin Neuroscience Laboratory who conducted an Australia-wide survey of concussion-related experiences. From this study, we were able to evaluate peoples' post-concussion exercise habits as well as its role in self-reported recovery.

AARF was a great learning platform for me, as I was a research assistant for WAMS and IPAC (2014-2018) before transitioning to my PhD (2019-2022).

GUT MICROORGANISMS

Dr Binosha Fernando, Edith Cowan University
Prof Ralph Martins, Macquarie University and Edith Cowan University

A team of PhD students are exploring various dietary factors that may improve brain health, which may assist in reducing the risk of developing Alzheimer's disease, according to Dr Binosha Fernando, a Research Fellow at Edith Cowan University.

Working with Dr Fernando, the students are examining probiotics intervention, dietary patterns such as the Mediterranean diet, and microbial imbalance in the gut. Others are looking at the potential benefits of sorghum polyphenols in Alzheimer's disease.

Dr Fernando's work at AARF is aimed at understanding the gut-brain connection and if it influences Alzheimer's disease, considering three separate projects: dietary protein and fibre; the effect of polyphenols; and the effect of gut organisms.

POLYPHENOLS

One of the possibilities being investigated by Dr Fernando's team is the potential of nutrient-rich foods such as the cereal grain sorghum, goji berries and grape seed. These foods are high in natural polyphenols which naturally target multiple pathways related to Alzheimer's disease, such as tau protein build up.

"Sorghum has some unique features which are important to reduce Alzheimer's disease pathology," Dr Fernando said.

"My work so far has shown that polyphenols from sorghum, goji berries and sea buckothen could reduce the amyloid beta, tau levels and oxidative stress at a cellular level," Dr Fernando said.

GUT MICROBIOTA

The gut microbiome is made up of the trillions of microorganisms that live in the intestinal tract and are critical to health and wellbeing. Research has found correlations between gut microbiome differences and tau levels and plasma amyloid beta levels (related to Alzheimer's disease) but more work needs to be done to understand the relationship.

"There is very little research into the gut related to Alzheimer's disease progression. It is therefore necessary to gain a better understanding of the microbial community diversity and the function of these communities due to Alzheimer's disease pathology," Dr Fernando said.

Dr Fernando collects samples and uses data collected in the Australian Imaging, Biomarkers and Lifestyle Study (AIBL) to further knowledge in this area and to help determine the risk to population before symptoms appear.

DIETARY PROTEIN AND FIBRE

Dr Fernando's work suggests that a diet high in protein and fibre may confer some protection against Alzheimer's disease. She is also studying the relationships between diet and depression, diet and biomarkers of brain health derived from neuroimaging, and diet and biomarkers derived from blood.

"We hope to enhance our understanding and knowledge of the role of diet in preventing Alzheimer's disease, and also the diet's impact on depression," Dr Fernando said.

As a result of these projects, future studies will be able to identify strategies for delaying or preventing the onset of Alzheimer's disease.

Sorghum
5th
The unique grain ranks fifth in world cereal production

Students
6
A team of PhD students works out of Dr Fernando's lab

DIAGNOSING ALZHEIMER'S

Establishing accurate and efficient diagnostic approaches is challenging, yet vital. A simple and reliable diagnostic tool would revolutionize Alzheimer's diagnosis, improving outcomes and transforming the field of research and treatment.

OUR RESEARCH STARTS WITH YOU

"Five years ago, I wouldn't have said I was a bike rider, but here we are!" So says David Abud, who has cycled hundreds of kilometres to raise money for Alzheimer's research.

Riding his bike down the country roads of Victoria has been cathartic for David, who has organised a group ride from Ballarat to Horsham for several years, raising over $27,000 for AARF. The idea was suggested by a friend who knew David – a consummate sportsman — was searching for a cause.

"I was talking to one of my friends and he asked, 'Why don't you do it for your dad?'" David said.

David's father is Dr Rodney Abud, who had been an active member of his community and a well-respected doctor since the 1960s. He helped consolidate the clinical practice in Horsham and was Wimmera Base Hospital's management board president for many years. He established the Peter James Centre, which provides rehabilitation and aged-care services, and also set up a similar service at Donvale Rehabilitation Hospital.

"David, a Senior Theatre Technician, said his father had worked until he was 79 and was diagnosed with dementia at 82, and subsequently with Alzheimer's disease.

It was a bit of a shock," he said. Sadly, his father deteriorated rapidly and is now in full-time care at a facility in Heidelberg.

The seed of the idea to fund-raise by cycling has developed into an annual event, with David leading riders through the beautiful countryside from Ballarat, to Ararat or Hamilton, to a finish line in Horsham – a distance of more than 300 km.

Before taking up cycling, David played in the National volleyball team for 10 years and played high-level AFL football.

While his high-profile sporting days may be behind him, there are many miles of road ahead to ride. Thank you, David, for riding for research!

RETINAL IMAGING

Prof Ralph Martins, Macquarie University and Edith Cowan University
Dr Eugene Hone, Edith Cowan University
Dr Shaun Eslick, University of Western Australia
Dr Shaun Frost, CSIRO

The challenge of diagnosing Alzheimer's disease still presents an enormous hurdle for healthcare professionals and researchers.

Current diagnosis methods rely on extensive cognitive testing and evidence from family members, or costly brain imaging methods such as Positron Emission Tomography (PET) scans to measure brain amyloid levels.

Because the eye is a developmental extension of the brain, it shares many resources and has a direct neurological link via the retina.

Dr Eugene Hone, Senior Research Fellow on the Retinal Imaging study based at the Australian Alzheimer's Research Foundation (AARF), said, "With the latest diagnostic tools being limited by several factors including cost, time, and availability, it is imperative that faster and cheaper methods be developed."

The hyperspectral retinal imaging project is a novel technique that has potential to improve many aspects of early screening for Alzheimer's disease. The primary goal of this project is to develop a cost effective, widely available and non-invasive retina scan for the diagnosis and monitoring of Alzheimer's disease (AD).

Dr Hone said, "Retinal hyperspectral imaging is a non-invasive scan and does not require expensive facilities, reagents and equipment, compared to brain imaging."

He said the prototype has been considered as a breakthrough device by the National Institute of Health (NIH) in USA. This means that research must be conducted to determine whether the instrument can show reproducible data in clinical settings. If so, then the NIH will support acceleration of its development into a clinically available device for AD diagnosis.

The main instrument used is provided by industry partner Optina diagnostics, the manufacturer of the hyperspectral instrument, and allows imaging of the retina at a range of specific wavelengths without the need for any dyes or stains to be applied to the eye.

Images are collected at very high speed – 92 per second – while the patient sees a rapid rainbow of colours. Each scan collects millions of pixels of data. The images will be analysed using machine learning (also known as Artificial Intelligence) due to the large amount of spectral data they contain.

Development of the analysis methods for the retinal images has begun and is primarily undertaken by PhD student Mr Purna Poudel, who commenced in March 2022.

Dr Hone said, "While we are continuously collecting images from participants, designing and coding of the analysis software is ongoing. The initial focus is on mapping of the blood vessels in the eye to determine their tortuosity, a measure of how many curves and how acute these are."

He said the measurements were necessary to separate them from the retinal surface to allow quantification of both these individual image parts as they contained different proteins and therefore, had different spectral properties.

"We have also commenced developing the software to examine the spectral properties of specific regions of interest in the retinal images and correlating this spectral data with brain amyloid scores," Dr Hone said.

PURNA CHANDRA POUDEL
STUDENT PROFILE

Supervisors:
Dr Eugene Hone, Edith Cowan University
Dr Shaun Frost, CSIRO
Dr Shaun Eslick, Macquarie University
Prof Ralph Martins, Macquarie University and ECU

The main objective of my study is to detect and identify the features in the retina which are associated with brain amyloid status in a larger well-characterised cohort.

This information will be used to formulate an effective non-invasive, predictive model that can address the existing limitations.

The experimental analysis will be carried out using the Python programming language and obtained inferences will be presented using statistical and machine learning techniques.

thank you

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 appreciate your support and simply could not do what we do without it.

BLOOD BIOMARKERS

Prof Ralph Martins, Macquarie University and Edith Cowan University
Dr Pratishtha Chatterjee, Macquarie University
Dr Steve Pedrini, Edith Cowan University

New research has shown the potential to diagnose the risk of developing Alzheimer's disease ten years before symptoms appear — and it could be as easy as a simple blood test.

Prof Ralph Martins, Director of Research at AARF, said, "This new blood biomarker research shows a very high degree of accuracy in identifying people who are at risk of developing Alzheimer's, but show no symptoms."

This opens a critical window of opportunity. "It may be possible to change the disease trajectory using drug or lifestyle interventions before the brain is damaged," Prof Martins said.

The results of the latest findings were published in late December 2022 and involved nearly 40 scientists in Australia, the US and Europe. The study determined that Alzheimer's-related proteins are elevated in patients up to a decade before degeneration of the brain leads to the onset of symptoms.

Prof Martins was a senior author of the new study, which used data from several groups of patients, including those at AARF's facility.

"We think the reason so many clinical trials have failed, is that people's brains have been severely compromised by the time treatments were attempted," said Prof Martins.

This research was made possible thanks in part to the support of the Pinnacle Charitable Foundation, Spheria Asset Management and Resolution Capital who are providing philanthropic support for this project. The project also received support from a substantial gift in Will donation which enabled consumables for the SIMOA machine utilised in this research.

The team will characterize the NFL variants in different types of dementias and determine if specific variants are associated with Alzheimer's disease pathology. AARF supports the salaries of the researchers working on a blood test to diagnose Alzheimer's disease as well as providing world-class facilities.

Current practice for diagnosing Alzheimer's disease is costly brain imaging and a battery of cognitive tests that can only be relied on once symptoms have started to appear.

"Hopefully, with a much earlier diagnosis, drugs and lifestyle interventions such as the AU-ARROW study supported by the Foundation will be far more effective," said Prof Martins.

Dr Prashant Bharadwaj, a researcher at Edith Cowan University, is one of the researchers focused on developing a blood test for Alzheimer's disease. His research has been recognised by being awarded a grant of $250,000 over the next two years by The National Foundation for Medical Research and Innovation.

Working in collaboration with scientists from Macquarie University, Australian Genomic Research Facility, and Proteomics International, the research will focus on identifying specific proteins in the blood, particularly the neurofilament light (NFL) protein, which has been shown to be a good indicator of brain degeneration.

DR STEVE PEDRINI
RESEARCHER SPOTLIGHT

Dr Steve Pedrini is a highly qualified researcher with a strong background in biology and patho-physiology. He obtained his BSc/MSc in Biology from the University of Bologna in Italy in 1997. In 2017, he embarked on his PhD journey and successfully completed it in 2022.

Dr Pedrini's PhD explored the role of High-Density Lipoprotein (HDL) in Alzheimer's disease and his work provides insights into how HDL may contribute to the development and progression of Alzheimer's disease.

He has also examined plasma biomarkers associated with Alzheimer's disease which are associated with increased brain amyloid beta protein deposition and cognitive decline.

Dr Pedrini's research is of great significance because it provides a deeper understanding of the blood-based biomarkers of Alzheimer's disease and highlights the importance of identifying and characterizing additional plasma biomarkers that could potentially improve diagnosis.

CHILDHOOD DEMENTIA

Dr Prashant Bharadwaj, Edith Cowan University

Childhood dementia is a group of rare genetic diseases that is estimated to affect one in every 2,800 babies.

Dr Prashant Bharadwaj is leading the way to discover biomarkers for childhood dementia, in collaboration with researchers all over Australia.

AARF is very proud to be supporting Dr Prashant Bharadwaj in this critical research, which is conducted at our world-class facilities in Perth.

Symptoms of childhood dementia vary and start from age of 3 onwards. The symptoms are usually obvious in most cases as the children develop facial abnormalities. In some cases, parents may have noticed developmental delays. All children with dementia will progressively lose skills they have already developed, such as the ability to walk, talk and recognise their loved ones. Life expectancy is between 10 to 20 years.

Children with dementia may experience confusion and memory loss, personality and behavioural changes, trouble with concentration and communication, anxiety and fear. It is clinically characterized by severe degeneration of the central nervous system with a learning disorder and associated behavioural abnormalities.

Dr Bharadwaj, an expert in autophagy and Alzheimer's disease, has initiated a lab-based and clinical biomarker study in childhood dementia. For the lab-based study Dr Bharadwaj has established a stem cell lab for human-derived neuron cell models in collaboration with Dr Isaac Canals (Lund University, Sweden) to model Sanfilippo syndrome, a common cause of childhood dementia in Australia.

Dr Bharadwaj said, "The stem cell lab will allow us to investigate disease mechanisms and develop new treatment strategies for Sanfilippo syndrome and related childhood dementias."

As well as being funded by AARF, Dr Bharadwaj's work is supported by a grant of $250,000 awarded by the WACRF (WA Child Research Fund) in 2021. 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, which is especially important when administering or researching any intervention.

He said the project would add to the knowledge base about this group of diseases and may uncover new treatment approaches. "These relatively non-invasive markers could be very useful tools to measure response to new treatments in clinical trials," Dr Bharadwaj said.

Dr Bharadwaj is working closely with clinicians across Perth, including Dr Maina Kava (Consultant Paediatrician, PCH) and neurologists to recruit families affected by childhood dementia. He also works in collaboration with the Childhood Dementia Initiative (CDI) and doctors at the Queensland Children's Hospital and Royal Melbourne Hospital.

Disorders
70

Childhood dementia results from progressive brain damage and is caused by over 70 rare genetic disorders.

Children
2,300

An estimated 2,300 Australians are living with childhood dementia.

TREATING ALZHEIMER'S

If we can find effective treatments for Alzheimer's disease, we have the potential to halt or delay cognitive decline. We are incredibly proud of the work we are doing to bring hope and progress to those affected by Alzheimer's disease.

OUR RESEARCH STARTS WITH YOU

The Stadium Masters Swimming Club has been supporting AARF for the past five years and have raised an incredible $27,000 towards research into Alzheimer's disease.

In 2022, the club's highly successful Swim for Memory event had 14 teams of four swimmers who came together to swim and raise money for Alzheimer's research.

Club stalwart Barry Green said that in the hour-long relay challenge, swimmers did hundreds of sponsored laps at the HBF Stadium indoor pool in Perth.

"As a club, we wanted to give back to the community. The Australian Alzheimer's Research Foundation is doing great work in the research field," he said.

Barry, who swims at least four times a week, said club members benefited from structured training programs which were supervised by qualified coaches. It was too easy to be lenient on yourself if you swam alone, he admitted.

"Some of our members like to compete in the pool and open water Master's Swimming events, while many just want to improve their swimming ability and fitness and enjoy the social aspects. It is easier and more fun to swim in structured group sessions."

Club members range in age from their 30s to over 80 and from novices to old hands. They enjoy getting together for fitness, friendship and fun. Thank you for raising vital funds for Alzheimer's research!

SMALL MOLECULE DRUG DEVELOPMENT

Dr Prashant Bharadwaj, Edith Cowan University

Good things come in small packages! Dr Prashant Bharadwaj has been investigating the possibility of a Small Molecule Drug in the fight against Alzheimer's disease.

For nearly a century, small molecule drugs have been the backbone of the pharmaceutical industry. They offer advantages over other therapeutics in that most can pass through the blood brain barrier, cell membranes, to reach intracellular targets, and their distribution can be specifically tailored e.g. to allow for systemic exposure with, or without, brain penetration.

Dr Bharadwaj's team reported a new method to alleviate cell dysfunction/death and promote the clearance of the Alzheimer's disease-related protein beta-amyloid. The experiments were undertaken at the Australian Alzheimer's Research Foundation facilities.

> **"**
> Utilizing this new model, we have identified a small molecule inhibitor, that reduces autophagy and apoptotic mediated cell death in Alzheimer's disease.   - Dr Bharadwaj

Within the fields of molecular biology and pharmacology, a "small molecule" is a low molecular weight organic compound that may regulate a biological process, with a size on the order of 1 nanometer, 10 times bigger than the size of an atom.

Dr Bharadwaj's proposed project builds on robust preliminary evidence. The study will involve screening of several million molecules using AtomNet, an Artificial Intelligence (AI) neural network.

In 2020, the project was awarded the Atomwise / Artificial Intelligence Molecular Screen award (AIMS), which provides in-kind support to aid scientists pursuing drug discovery.

Dr Bharadwaj said Atomwise had completed in silico screening for USP14 binding small molecules using the proprietery AI software. The AI technology can virtually screen billions of chemical compounds to select those that are most likely to bind a target protein with high affinity.

"Next, we will conduct lead development and identify functional candidates for their ability to modulate beta-amyloid and Tau protein aggregation and cell death. This involves mammalian cell models to identify the most effective drug candidates," he said.

Finally, the lead candidate drugs will be assessed for their neuroprotective ability.

Working with the project is PhD student Ajish Ariyath, who was awarded the Edith Cowan University Deputy Vice Chancellor strategic PhD scholarship for Alzheimer's disease drug development. Mr Ariyath has more than 5 years of industry experience in India and is an expert in stem cell biology.

The team has currently screened 72 Atomwise compounds and identified areas which will need to be investigated further.

In the future, it is hoped this research will lead to business partnerships and engagement with investors, invention disclosures and patent applications, and lead drug development pipeline.

AI

Artificial Intelligence is being used to transform drug discovery. Using AI to aid analysis helps to accelerate the research strategy.

TESTOSTERONE STUDY

Prof Ralph Martins, Macquarie University and Edith Cowan University
Prof Hamid Sohrabi, Murdoch University
Mr Kevin Taddei, MSc, Edith Cowan University
A/Prof Roger Clarnette, University of Western Australia

Committed volunteers are furthering the cause of medical research into Alzheimer's disease by participating in the Testosterone Study being conducted by AARF.

The study aims to determine the effect testosterone can have on brain amyloid levels and cognition. It is recognised that sex hormones positively affect brain function, but their impact on cognition is less well understood.

With the generous support of AARF, the study has reached 75% of its recruitment target. However, more men aged 60-80 with lower-than-average testosterone levels are still required to complete the clinical study, which is conducted in Perth and in Sydney.

Previous research has demonstrated that Alzheimer's disease is caused by the abnormal build-up of amyloid protein in brain cells. The build-up is linked to abnormal brain function, leading to the cognitive symptoms that accompany Alzheimer's disease.

Led by Prof Ralph Martins, the team followed up with pioneering lab-based studies which revealed that treatment with the naturally-occurring hormone, testosterone, reduced amyloid build-up in their model.

The discovery ignited 20 years of research, with early work focusing on the safety of testosterone administration to men.

The current clinical trial aims to determine if testosterone can help prevent the development of Alzheimer's disease by decreasing the levels of amyloid protein in the brain.

The study involves an initial brain scan to look at amyloid levels in the brain. Participants then receive 13 months of treatment and some memory testing, before a final brain scan to see if testosterone treatment has prevented the build-up of the amyloid protein in the brain.

Prof Martins paid tribute to the late Dr Malcolm Carruthers, a highly respected men's health specialist who was the pioneer of Testosterone treatment for depression and cognition in men. Dr Carruthers' influence was instrumental in introducing Professor Ralph Martins to this line of research more than 20 years ago, which ultimately led to our Testosterone Clinical Trial. Dr Carruthers followed the research closely and generously donated to AARF for the trial. Prof Martins said, "Malcolm was a dear friend, colleague and world authority on Testosterone Deficiency, and I will cherish the times we spent discussing this research."

"AN IMMENSELY REWARDING EXPERIENCE"

Peter Plavina was a study participant in the Testosterone Study and said the experience had been entirely positive.

I found the entire experience immensely rewarding. I learned lots about how rigorous clinical trials are conducted and about Alzheimer's disease.

As time went by, I became increasingly aware of the immense investment in me by the team, not to mention the high costs of the scans and tests. I also benefitted by having several developing medical issues identified, by chance, during the scans and blood tests. I appreciated that I was under intense medical surveillance for those 18 months!

I joined the study because I wanted to make a small contribution to the body of knowledge on preventative treatments on Alzheimer's disease.

I hope that my efforts and involvement may help lead to successful treatments and prevention strategies.

> You are all doing great work and for a very worthwhile cause. It was a great experience for me.

One of the things I really appreciated during my time on the trial was the interaction with the researchers and staff. It was first class!

I enjoyed the conversations, and I appreciated the interest shown in me as an individual, by each of the researchers. I also appreciated the medical discussions on matters unrelated to the clinical trial which I had from time to time.

I look forward to one day being able to read the outcomes of the study.

Peter

CLINICAL TRIAL DIVISION

The Clinical Trials Division (CTD) of AARF is dedicated to investigating new treatments for Alzheimer's disease.

The team of nine clinicians and clinical trial staff works out of the Hollywood Specialist Centre, based at Hollywood Private Hospital in Perth.

Every day, the team works with participant volunteers and runs clinical trials from major pharmaceutical companies to examine new potential treatments to delay and prevent the progression of Alzheimer's disease.

The team is supervised by A/Prof Roger Clarnette, a senior specialist physician at Fremantle Hospital and Hollywood Private Hospital, who has a particular interest in memory loss and Alzheimer's disease.

The trials are conducted globally, with the CTD team being one of hundreds of locations involved in recruiting participants to test new potential treatments. These trials are run under strict national and international standards.

> Those who participate in clinical trials benefit from regular and thorough review of their condition. In addition, the focus of all trials is participant safety. The aim of these studies is to potentially facilitate future use of effective treatments.   - A/Prof Roger Clarnette.

Clinical trials are one of the final stages of a long and careful research and development process. There are multiple reasons participants volunteer to participate in clinical trials including helping others, advancing science, having a chance to receive innovative treatments or having additional health care, free of charge.

Every participant is a valuable member of the AARF team, working together to find effective ways to prevent, treat and manage Alzheimer's disease.

BREAKTHROUGH APPROVALS GRANTED

In a significant breakthrough for the Alzheimer's community, the US Food and Drug Administration (FDA) recently granted accelerated approval for two new treatments for Alzheimer's disease in June 2021 and January 2023. It has been almost two decades since a new treatment for the disease was approved, highlighting the critical need for a treatment.

The two FDA approved treatments, Aducanumab (aka Aduhelm) and Lecanemab (aka Leqembi), use a similar mechanism to target and break down amyloid-beta plaques, a hallmark in the Alzheimer's brain.

As part of the FDA approval process, Biogen is required to run a new clinical trial to verify the clinical benefit of the Aduhelm drug. It is hoped the data will support the full approval of Aduhelm to the general population worldwide. AARF is proud and excited to be taking part in this study and to have the opportunity to provide access to Aduhelm to participants in the early stages of Alzheimer's disease in WA.

AARF is also taking part in studies using Leqembi. The AHEAD3-45 study is currently recruiting and targeting a preclinical Alzheimer's disease population, that is those without symptoms but with risk factors. The ClarityAD study for mild Alzheimer's disease is ongoing at AARF and was the study that provided the data for the Leqembi FDA submission.

Janssen

Novo Nordisk

Roche

EISAI

Biogen

We partner with pharmaceutical companies worldwide

CURRENT ALZHEIMER'S DISEASE STUDIES

These studies are ongoing at the Foundation and do not need new participants.

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

A phase two B / three open-label extension to confirm the safety and efficacy of Sigma-1 in subjects with early Alzheimer's disease.

In addition to evaluating the effects on cognition and functioning, ANAVEX also explores sleep outcomes, behavioural and psychological symptoms, changes in the daily functioning of participants and changes in caregiver burden.

The medication aims to restore cellular balance by targeting sigma-1 and muscarinic receptors. It is administered by oral tablet once a day.

EISAI CLARITYAD BAN2401-G000-301 (Phase 3)

A phase three open-label extension to confirm the safety and efficacy of lecanemab in subjects with early Alzheimer's disease.

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.

It is administered via intravenous infusion once a fortnight.

BIOGEN EMBARK 221AD304 (Phase 3)

A phase three safety study to evaluate the efficacy and safety BIIB037 (aducanumab) in subjects with Alzheimer's disease who had previously participated in the aducanumab studies 221AD103, 221AD301, 221AD302 and 221AD205

It is a two-year study involving monthly infusions of aducanumab.

JANSSEN Autonomy 63733657ALZ2002 (Phase 2)

A phase two safety study to evaluate the efficacy and safety of JNJ-63733657, an Anti-tau Monoclonal Antibody, in participants with with mild cognitive impairment early Alzheimer's disease.

The drug is administered by monthly infusion and is proposed to prevent tau collection in the brain, a known hallmark of AD.

UPCOMING ALZHEIMER'S DISEASE STUDIES

These studies will commence in 2023 at AARF.

Eli Lilly TRAILRUNNER-ALZ2 LAKD & Eli Lilly TRAILRUNNER-ALZ3 LAKF (Phase 3)

A phase three safety study to evaluate the efficacy and safety of subcutaneous remternetug in early symptomatic Alzheimer's disease.

This study is testing the hypothesis that study medication, remternetug, is superior to placebo on slowing clinical progression in participants with early symptomatic Alzheimer's disease in either a subcutaneous or intravenous administration method in participants aged 60 - 85 over 30 months.

AbbVie ABROAD M23-515 (Phase 2)

A phase two safety study to evaluate the efficacy of Synaptic vesicle glycoprotein 2A (ABBV-552) in participants aged 50 to 90 years with mild Alzheimer's disease

This study will assess how safe and effective ABBV-552 is in treating symptoms of early AD. Adverse events, change in disease activity, how ABBV-552 moves through body of participants and the body response to ABBV-552 will be assessed. It is administered by tablet once a day for 12 weeks.

UPCOMING ALZHEIMER'S DISEASE STUDIES

These studies will commence in 2023 at AARF.

BIOGEN ENVISION 221AD305 (Phase 3b/4)

A phase four safety study to verify the clinical benefit of Aducanumab (BIIB037) in participants with Alzheimer's disease.

Aducanumab, trade name Aduhelm, was approved by the US FDA as a treatment for AD under the accelerated approval pathway. Consistent with the accelerated approval regulations, this study is being conducted to fulfil a post-marketing requirement from the FDA to verify the clinical benefit of aducanumab.

It is administered by infusion once a month for 24 months.

CASSAVA PTI-125-07 (Phase 3)

A phase three safety study to evaluate the efficacy of simufilam 100 mg tablets in subjects with mild-to-moderate AD. Simufilam is a novel drug that targets Filamin A (FLNA), a protein highly expressed in the brain and plays an important role in maintaining healthy cell functions.

The study medication binds to this altered FLNA and restores its normal function to disable the amyloid beta pathway and consequently reduce neurodegeneration.

It is administered by oral tablet twice a day over 12 months.

IMUNEBIO MINDFUL XPRO-AD-02 (Phase 2)

A phase two safety study to evaluate the efficacy of XPro™ in patients with mild AD with biomarkers of inflammation.

The elevated level of Tumor Necrosis Factor (TNF) is one of the common characteristics associated with AD aetiology. XPro™ inhibits the bioactivity of TNF to reduce neuroinflammation and AD progression.

It is administrated by subcutaneous injection once a week for 6 months.

NOVO NORDISK EVOKE/+ (Phase 3a)

A phase three safety study to evaluate the efficacy of oral semaglutide in subjects with early AD.

Semaglutide is a GLP-1 receptor agonist used for the treatment of type 2 diabetes. Recent clinical data has shown that this medication reduces the risk of dementia, lowering brain inflammation.

It is administered by oral tablet once a day over 36 months.

PRECLINICAL STUDY

This study recruits participants who have no symptoms of Alzheimer's disease but are interested in learning if they are at risk based on blood sampling and brain scans.

EISAI AHEAD3-45 (Phase 3)

A phase three safety study to evaluate the efficacy of lecanemab in subjects with preclinical AD and elevated amyloid (A45 Trial) and in subjects with early preclinical AD and intermediate amyloid (A3 Trial).

The 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.

CONCLUDED IN 2022

These clinical trials into Alzheimer's disease were concluded 2022.

Roche Graduate/Postgraduate WN29922/WN42171 (Phase 3/3b). This study aimed to evaluate the safety and efficacy of the drug Gantenerumab.

Greenvalleypharma Green Memory GV971-007 (Phase 3). The study medication targeted gut bacteria in the hope of reducing inflammation in the body, which is believed to be related to brain deterioration.

Roche Skyline WN42444 (Phase 3). This Phase 3 study aimed to evaluate the efficacy of Gantenerumab on participants with risk factors for AD, but no current symptoms.

YOUR SUPPORT

Your contribution enables us to push the boundaries of knowledge and develop innovative approaches to combat this disease. We extend our heartfelt gratitude for standing alongside us in our quest to deliver better outcomes for those at risk of Alzheimer's disease.

OUR RESEARCH STARTS WITH YOU

How many push-ups can you do? Inspiration came to Herbert Selva Kanagasabai, of Melbourne, when he was reading an article by a Professor of kinesiology.

As a healthy 80-year-old, he wondered if he could do 80 push-ups, far more than the article suggested would be likely. He decided to give it a go and used his challenge to raise an incredible $6101 for Alzheimer's research, after seeing the impact of the disease on families of friends and colleagues.

"I generally keep myself fit, doing about 25 push-ups a day, but I had to step it up a little bit to do this," Herbert said. He allowed a timeframe of six months in which to try and build up to 50… but surpassed that by far on the day.

He emailed his friends, family, former rugby teammates and colleagues and asked for $1 per push-up. "I think most of them thought I might make it to 30 push-ups!"

He encouraged people to keep up their fitness as they age, pointing out that as you get older, it is easier to stay fit than to get fit. "Plus, it's good for the joints and flexibility."

"I try to maintain my level of fitness and my weight, and I find it difficult to sleep if I don't walk for at least an hour, or exercise," he said.

Herbert came to Australia from Sri Lanka nearly 50 years ago and worked at the Middendorp Electric Company (now called Middy's) in Melbourne until he retired at 76-years-old.

He said the co-owner of the company, the (late) Hugh Middendorp, was an inspirational and active man who encouraged his workers to exercise, and who himself went for long walks every day until his mid-80s.

"He really encouraged everyone to keep as active as possible. He set an example by taking a walk every day at lunchtime. If you saw him coming you knew your lunch was over – it was time to walk in the park with the boss!"

RESEARCH STARTS WITH YOU

Our fundraising community is made up of incredibly generous people, who are all working together to achieve one vision... A world without Alzheimer's disease.

The Australian Alzheimer's Research Foundation is the nation's largest non-government funder of Alzheimer's disease research. As such, we rely greatly on donations from our many generous supporters.

THANK YOU

YOUR SUPPORT MAKES ALL THE DIFFERENCE

We are incredibly grateful that so many people share our vision.

Fundraisers joined an amazing total of 35 external events such as fun runs, marathons and organised swimming races, raising funds through online platforms such as Grassrootz and Just Giving. As you have been supporting us, we have been behind you every step of the way, with advice, encouragement and those amazing stand-out purple tee-shirts so everyone knows why you are racing. Thank you!

The concept of workplace giving is on the rise, with a 49% percent rise in the amount raised through this pre-tax system. It's something that every company should think about, as it is an extremely simple way for people to raise funds for Alzheimer's research.

Workplace giving, also known as payroll giving or pre-tax giving, involves employees making regular donations to the Australian Alzheimer's Research Foundation from their pre-tax income. Workplace giving can be even more effective if your company agrees to match employee donations dollar for dollar, thus maximising donations and building workplace giving into the workplace culture.

A small regular gift to support Alzheimer's research will make all the difference. We are extremely grateful to work with several loyal, committed corporate partners and their staff through the workplace giving program.

The tangible support of our donors allows AARF to be a pioneering force in the understanding of Alzheimer's disease.

These include National Australia Bank, Google, Microsoft, Citi Australia, Dell Technologies, Juniper, Visa, Findex, Westpac Group, IQVIA, PwC Services Trust, Rio Tinto Services Ltd, Ernst & Young, Toyota Finance Australia, Stockland, Suncorp Group, Pinnacle and affiliated Fund Managers, Vita Group Limited, Australia Post, Thermo Fisher Scientific, and Equifax.

A significant portion of our income in 2022 was from bequests. It is a great honour to receive these funds and we ensure careful stewardship of the bequests to enable the long-term support of Alzheimer's research.

We are extremely grateful for the help of our supporters, donors, fundraisers, research volunteers, corporate and government partners who share our vision and enable us to continue our critical research work.

Donors
2,480
Every supporter shares in our success and achievements

Raised
$2.2m
Our pioneering research is only possible due to our generous supporters

> *We really feel that we can help and contribute in a meaningful way. Our support benefits multiple areas, and the collaboration has a ripple effect across the globe. Collaborating is echoed and reflected in what we do, so for a small Foundation like ours to see such the far-reaching impact is fantastic.*

Mary Jung, Pinnacle Charitable Foundation

Pinnacle Charitable Foundation

Thank you to the **Pinnacle Charitable Foundation** and affiliated fund managers **Spheria Asset Management** and **Resolution Capital** for their generous and continuing support.

Their substantial contributions have provided significant support and allowed for the advancement of specific Alzheimer's research programs, including those aimed at understanding cell biology and gene mutation, as well as research into developing an early stage blood biomarker test.
The relationship with AARF has developed organically over several years, and is a truly valued partnership.

MAKING IT EASY

Technology makes it simple to raise funds in the community, with dedicated online platforms to securely receiving collected money.

Grassrootz is the main online platform used by AARF donors when they are raising funds in organised events across Australia. This fundraising solution is capable of facilitating any size of event, from small community gatherings to mass participation events with tens of thousands of entries.

Anyone can register for an event and raise money for the Australian Alzheimer's Research Foundation. In 2022, runners entered marathons, fun runs, swimming races and bike rides to raise vitals funds for research.

Online platforms such as Just Giving and My Cause are also handy for people who have had a great idea to raise money for research and would like an easy way to collect the money.

Hosting a morning tea or having a momentous hair cut – there are so many inspiring ways to get the community involved. Our fundraisers often tell us how generous people are, especially when they know that their money will be spent on research into Alzheimer's disease.

Celebrating a special occasion, such as a wedding, anniversary or birthday is always a memorable occasion, and many people choose to support research into Alzheimer's disease by asking for donations in lieu of gifts. What a wonderful gift to give and receive!

Whether it's $2 or $200,000, any funding the Australian Alzheimer's Research Foundation receives takes us a step closer to our vision — a world in which Alzheimer's disease no longer exists.

Events
35
Fundraisers who run, swim, walk and ride for Alzheimer's research have joined 35 different events.

Bequests
$1.5m
We work carefully with families to ensure that the donor's wishes are respected and the gift has a lasting impact.

Regular Gifts Make Our Day!

Thank you to **Alt Surfaces**, whose generous regular donation is always gratefully received. The high-end specialist flooring company, based in Melbourne, has been a loyal corporate sponsor of AARF for several years.

"As a family run business, we're very proud to support a Foundation that's close to our hearts," said Richard Di Bartolo, from Alt Surfaces in Victoria.

Regular corporate donations from companies like Alt Surfaces make an immense difference. Thank you!

We're proud to support and partner with the Australian Alzheimer's Research Foundation to join their fight to save memories and lives. We have sadly witnessed family members live with this disease. We know first-hand the devastating effects this disease has on loved ones.

Richard Di Bartolo, Director of Alt Surfaces

Alt.

SCIENTIFIC PUBLICATIONS

Scientific publications act as conduits, allowing researchers to share their work with the global scientific community. Dissemination of knowledge opens doors to a world of opportunities.

OUR RESEARCH STARTS WITH YOU

I volunteered to take part in the clinical trials because Alzheimer's is one of the conditions that many aged people think might afflict them.

One of the most interesting aspects of being in a clinical trial is being conscious of the possibility that the program I am participating in will contribute to a better understanding of the dreadful condition and perhaps even to its effective treatment.

I hope that Alzheimer's will soon be 'conquered' (if that is the right term), but I hope that a better understanding of the condition will make it possible to treat those who develop it, and to advise their friends and relations to help them cope with it.

I was born in Malta in 1940 as Axis bombers pounded the island. I remember my mother cooking on a makeshift stove in the garden. She used to rush out from the rock shelter during lulls in the bombardment to put more sticks into the fire below the cooking pot!

I met my wife Judith when I was studying at Manchester University, after which I became a lecturer in history at the Royal University of Malta. Judith and I married in 1967.

Our daughter was born in 1969. We chose to migrate to Australia, which was the best thing I ever did (apart from marrying a wonderful wife). I retired aged 55 and returned to historical research. In 2011, I took my doctorate for a thesis on the building of Valletta, the capital of Malta.

I was widowed eight years ago. That was a dreadful blow: my wife Judith was wonderful. I have kept busy publishing historical articles, singing in choirs, and coaching elderly people how to use computers.

I am always made welcome when I arrive at the Clinical Trials Division, and I feel well looked after when I am there.

Though my memory is not as good as it used to be I am, in Aussie speak, as happy as Larry.

Roger

SCIENTIFIC PUBLICATIONS

BIOMARKERS

Li Y, Schindler SE, Bollinger JG, Ovod V, Mawuenyega KG, Weiner MW, Shaw LM, Masters CL, Fowler CJ, Trojanowski JQ, Korecka M, Martins RN, Janelidze S, Hansson O, Bateman RJ. Validation of Plasma Amyloid-β 42/40 for Detecting Alzheimer Disease Amyloid Plaques. *Neurology*. 2022 Feb 15;98(7):e688-e699.

Huang X, Li Y, Fowler C, Doecke JD, Lim YY, Drysdale C, Zhang V, Park K, Trounson B, Pertile K, Rumble R, Pickering JW, Rissman RA, Sarsoza F, Abdel-Latif S, Lin Y, Doré V, Villemagne V, Rowe CC, Fripp J, Martins R, Wiley JS, Maruff P, Mintzer JE, Masters CL, Gu BJ. Leukocyte surface biomarkers implicate deficits of innate immunity in sporadic Alzheimer's disease. *Alzheimers Dement*. 2022 Nov 9.

Guévremont D, Tsui H, Knight R, Fowler CJ, Masters CL, Martins RN, Abraham WC, Tate WP, Cutfield NJ, Williams JM. Plasma microRNA vary in association with the progression of Alzheimer's disease. *Alzheimers Dement (Amst)*. 2022 Feb 5;14(1):e12251.

Doré V, Doecke JD, Saad ZS, Triana-Baltzer G, Slemmon R, Krishnadas N, Bourgeat P, Huang K, Burnham S, Fowler C, Rainey-Smith SR, Bush AI, Ward L, Robertson J, Martins RN, Masters CL, Villemagne VL, Fripp J, Kolb HC, Rowe CC. Plasma p217+tau versus NAV4694 amyloid and MK6240 tau PET across the Alzheimer's continuum. *Alzheimers Dement (Amst)*. 2022 Apr 5;14(1):e12307.

Fowler CJ, Stoops E, Rainey-Smith SR, Vanmechelen E, Vanbrabant J, Dewit N, Mauroo K, Maruff P, Rowe CC, Fripp J, Li QX, Bourgeat P, Collins SJ, Martins RN, Masters CL, Doecke JD. Plasma p-tau181/Aβ1-42 ratio predicts Aβ-PET status and correlates with CSF-p-tau181/Aβ1-42 and future cognitive decline. *Alzheimers Dement (Amst)*. 2022 Nov 25;14(1):e12375.

Laffoon SB, Doecke JD, Roberts AM, Vance JA, Reeves BD, Pertile KK, Rumble RL, Fowler CJ, Trounson B, Ames D, Martins R, Bush AI, Masters CL, Grieco PA, Dratz EA, Roberts BR. Analysis of plasma proteins using 2D gels and novel fluorescent probes: in search of blood based biomarkers for Alzheimer's disease. *Proteome Sci*. 2022 Jan 26;20(1):2

Thota RN, Chatterjee P, Pedrini S, Hone E, Ferguson JJA, Garg ML, Martins RN. Association of Plasma Neurofilament Light Chain With Glycaemic Control and Insulin Resistance in Middle-Aged Adults. *Front Endocrinol (Lausanne)*. 2022 Jun 20;13:915449.

Chatterjee P, Pedrini S, Ashton NJ, Tegg M, Goozee K, Singh AK, Karikari TK, Simrén J, Vanmechelen E, Armstrong NJ, Hone E, Asih PR, Taddei K, Doré V, Villemagne VL, Sohrabi HR, Zetterberg H, Masters CL, Blennow K, Martins RN. Diagnostic and prognostic plasma biomarkers for preclinical Alzheimer's disease. *Alzheimers Dement*. 2022 Jun;18(6):1141-1154.

Dhiman K, Villemagne VL, Fowler C, Bourgeat P, Li QX, Collins S, Rowe CC, Masters CL, Ames D, Blennow K, Zetterberg H, Martins RN, Gupta V. Cerebrospinal fluid levels of fatty acid-binding protein 3 are associated with likelihood of amyloidopathy in cognitively healthy individuals. *Alzheimers Dement (Amst)*. 2022 Dec 4;14(1):e12377.

BIOMARKERS

Dhiman K, Villemagne VL, Fowler C, Bourgeat P, Li QX, Collins S, Bush AI, Rowe CC, Masters CL, Ames D, Blennow K, Zetterberg H, Martins RN, Gupta V. Cerebrospinal Fluid Neurofilament Light Predicts Risk of Dementia Onset in Cognitively Healthy Individuals and Rate of Cognitive Decline in Mild Cognitive Impairment: A Prospective Longitudinal Study. *Biomedicines*. 2022 Apr 30;10(5):1045.

EXERCISE

Pedrini S, Chatterjee P, Nakamura A, Tegg M, Hone E, Rainey-Smith SR, Rowe CC, Dore V, Villemagne VL, Ames D, Kaneko N, Gardener SL, Taddei K, Fernando B, Martins I, Bharadwaj P, Sohrabi HR, Masters CL, Brown B, Martins RN. The Association Between Alzheimer's Disease-Related Markers and Physical Activity in Cognitively Normal Older Adults. *Front Aging Neurosci*. 2022 Mar 28;14:771214.

Frost NJ, Weinborn M, Gignac GE, Xia Y, Doré V, Rainey-Smith SR, Markovic S, Gordon N, Sohrabi HR, Laws SM, Martins RN, Peiffer JJ, Brown BM. The Effect of Self-Paced Exercise Intensity and Cardiorespiratory Fitness on Frontal Grey Matter Volume in Cognitively Normal Older Adults: A Randomised Controlled Trial. *J Int Neuropsychol Soc*. 2022 Oct;28(9):902-915.

Sewell KR, Rainey-Smith SR, Villemagne VL, Peiffer J, Sohrabi HR, Taddei K, Ames D, Doré V, Maruff P, Laws SM, Masters CL, Rowe CC, Martins RN, Erickson KI, Brown BM. The interaction between physical activity and sleep on cognitive function and brain beta-amyloid in older adults. *Behav Brain Res*. 2023 Feb 2;437:114108.

WAMS

Tarawneh HY, Jayakody DMP, Sohrabi HR, Martins RN, Mulders WHAM. Understanding the Relationship Between Age-Related Hearing Loss and Alzheimer's Disease: A Narrative Review. *J Alzheimers Dis Rep*. 2022 Sep 12;6(1):539-556.

Tarawneh HY, Sohrabi HR, Mulders WHAM, Martins RN, Jayakody DMP. Comparison of Auditory Steady-State Responses With Conventional Audiometry in Older Adults. *Front Neurol*. 2022 Jul 4;13:924096.

Seneviratne R, Weinborn M, Badcock DR, Gavett BE, Laws M, Taddei K, Martins RN, Sohrabi HR. The Western Australia Olfactory Memory Test: Reliability and Validity in a Sample of Older Adults. *Arch Clin Neuropsychol*. 2022 Nov 21;37(8):1720-1734.

Finch PM, Sohrabi HR, Drummond PD. Olfaction in complex regional pain syndrome. *Pain Med*. 2022 Nov 21:pnac180.

SCIENTIFIC PUBLICATIONS

DIAN

Chhatwal JP, Schultz SA, McDade E, Schultz AP, Liu L, Hanseeuw BJ, Joseph-Mathurin N, Feldman R, Fitzpatrick CD, Sparks KP, Levin J, Berman SB, Renton AE, Esposito BT, Fernandez MV, Sung YJ, Lee JH, Klunk WE, Hofmann A, Noble JM, Graff-Radford N, Mori H, Salloway SM, Masters CL, Martins R, Karch CM, Xiong C, Cruchaga C, Perrin RJ, Gordon BA, Benzinger TLS, Fox NC, Schofield PR, Fagan AM, Goate AM, Morris JC, Bateman RJ, Johnson KA, Sperling RA; Dominantly Inherited Alzheimer's Network Investigators. Variant-dependent heterogeneity in amyloid β burden in autosomal dominant Alzheimer's disease: cross-sectional and longitudinal analyses of an observational study. *Lancet Neurol.* 2022 Feb;21(2):140-152.

Shirzadi Z, Yau WW, Schultz SA, Schultz AP, Scott MR, Goubran M, Mojiri-Forooshani P, Joseph-Mathurin N, Kantarci K, Preboske G, Wermer MJH, Jack C, Benzinger T, Taddei K, Sohrabi HR, Sperling RA, Johnson KA, Bateman RJ, Martins RN, Greenberg SM, Chhatwal JP; DIAN Investigators. Progressive White Matter Injury in Preclinical Dutch Cerebral Amyloid Angiopathy. *Ann Neurol.* 2022 Sep;92(3):358-363

Buckles VD, Xiong C, Bateman RJ, Hassenstab J, Allegri R, Berman SB, Chhatwal JP, Danek A, Fagan AM, Ghetti B, Goate A, Graff-Radford N, Jucker M, Levin J, Marcus DS, Masters CL, McCue L, McDade E, Mori H, Moulder KL, Noble JM, Paumier K, Preische O, Ringman JM, Fox NC, Salloway S, Schofield PR, Martins R, Vöglein J, Morris JC; Dominantly Inherited Alzheimer's Network. Different rates of cognitive decline in autosomal dominant and late-onset Alzheimer disease. *Alzheimers Dement.* 2022 Oct;18(10):1754-1764.

Morris JC, Weiner M, Xiong C, Beckett L, Coble D, Saito N, Aisen PS, Allegri R, Benzinger TLS, Berman SB, Cairns NJ, Carrillo MC, Chui HC, Chhatwal JP, Cruchaga C, Fagan AM, Farlow M, Fox NC, Ghetti B, Goate AM, Gordon BA, Graff-Radford N, Day GS, Hassenstab J, Ikeuchi T, Jack CR, Jagust WJ, Jucker M, Levin J, Massoumzadeh P, Masters CL, Martins R, McDade E, Mori H, Noble JM, Petersen RC, Ringman JM, Salloway S, Saykin AJ, Schofield PR, Shaw LM, Toga AW, Trojanowski JQ, Vöglein J, Weninger S, Bateman RJ, Buckles VD. Autosomal dominant and sporadic late onset Alzheimer's disease share a common in vivo pathophysiology. *Brain.* 2022 Oct 21;145(10):3594-3607.

Vöglein J, Franzmeier N, Morris JC, Dieterich M, McDade E, Simons M, Preische O, Hofmann A, Hassenstab J, Benzinger TL, Fagan A, Noble JM, Berman SB, Graff-Radford NR, Ghetti B, Farlow MR, Chhatwal JP, Salloway S, Xiong C, Karch CM, Cairns N, Perrin RJ, Day G, Martins R, Sanchez-Valle R, Mori H, Shimada H, Ikeuchi T, Suzuki K, Schofield PR, Masters CL, Goate A, Buckles V, Fox NC, Chrem P, Allegri R, Ringman JM, Yakushev I, Laske C, Jucker M, Höglinger G, Bateman RJ, Danek A, Levin J; Dominantly Inherited Alzheimer Network. Pattern and implications of neurological examination findings in autosomal dominant Alzheimer disease. *Alzheimers Dement*. 2023 Feb;19(2):632-645.

Chatterjee P, Vermunt L, Gordon BA, Pedrini S, Boonkamp L, Armstrong NJ, Xiong C, Singh AK, Li Y, Sohrabi HR, Taddei K, Molloy M, Benzinger TLS, Morris JC, Karch C, Berman S,

DIAN

Chhatwal J, Cruchaga C, Graff-Radford NR, Day GS, Farlow M, Fox N, Goate A, Hassenstab J, Lee JH, Levin J, McDade E, Mori H, Perrin R, Sanchez-Valle R, Schofield PR, Levey A, Jucker M, Masters CL, Fagan AM, Bateman RJ, Martins RN, Teunissen C; and the Dominantly Inherited Alzheimer Network. Plasma glial fibrillary acidic protein in autosomal dominant Alzheimer's disease: Associations with Aβ-PET, neurodegeneration, and cognition. *Alzheimers Dement.* 2022 Dec 28.

O'Connor A, Rice H, Barnes J, Ryan NS, Liu KY, Allegri RF, Berman S, Ringman JM, Cruchaga C, Farlow MR, Hassenstab J, Lee JH, Perrin RJ, Xiong C, Gordon B, Levey AI, Goate A, Graff-Radford N, Levin J, Jucker M, Benzinger T, McDade E, Mori H, Noble JM, Schofield PR, Martins RN, Salloway S, Chhatwal J, Morris JC, Bateman R, Howard R, Reeves S, Fox NC; Dominantly Inherited Alzheimer Network. First presentation with neuropsychiatric symptoms in autosomal dominant Alzheimer's disease: the Dominantly Inherited Alzheimer's Network Study. *J Neurol Neurosurg Psychiatry*. 2023 May;94(5):403-405.

AIBL

Rosenich E, Bransby L, Yassi N, Fripp J, Laws SM, Martins RN, Fowler C, Rainey-Smith SR, Rowe CC, Masters CL, Maruff P, Lim YY. Differential Effects of APOE and Modifiable Risk Factors on Hippocampal Volume Loss and Memory Decline in Aβ- and Aβ+ Older Adults. *Neurolog*y. 2022 Apr 26;98(17):e1704-e1715.

Cespedes M, Jacobs KR, Maruff P, Rembach A, Fowler CJ, Trounson B, Pertile KK, Rumble RL, Rainey-Smith SR, Rowe CC, Villemagne VL, Bourgeat P, Lim CK, Chatterjee P, Martins RN, Ittner A, Masters CL, Doecke JD, Guillemin GJ, Lovejoy DB. Systemic perturbations of the kynurenine pathway precede progression to dementia independently of amyloid-β. *Neurobiol Dis.* 2022 Sep;171:105783.

Woodfield A, Porter T, Gilani I, Noordin S, Li QX, Collins S, Martins RN, Maruff P, Masters CL, Rowe CC, Villemagne VL, Dore V, Newsholme P, Laws SM, Verdile G; AIBL Research Group. Insulin resistance, cognition and Alzheimer's disease biomarkers: Evidence that CSF Aβ42 moderates the association between insulin resistance and increased CSF tau levels. *Neurobiol Aging.* 2022 Jun;114:38-48.

Pedrini S, Doecke JD, Hone E, Wang P, Thota R, Bush AI, Rowe CC, Dore V, Villemagne VL, Ames D, Rainey-Smith S, Verdile G, Sohrabi HR, Raida MR, Taddei K, Gandy S, Masters CL, Chatterjee P, Martins RN; AIBL Research Group. Plasma high-density lipoprotein cargo is altered in Alzheimer's disease and is associated with regional brain volume. *J Neurochem*. 2022 Oct;163(1):53-67.

Chatterjee P, Pedrini S, Doecke JD, Thota R, Villemagne VL, Doré V, Singh AK, Wang P, Rainey-Smith S, Fowler C, Taddei K, Sohrabi HR, Molloy MP, Ames D, Maruff P, Rowe CC, Masters CL, Martins RN; AIBL Research Group. Plasma Aβ42/40 ratio, p-tau181, GFAP, and NfL across the Alzheimer's disease continuum: A cross-sectional and longitudinal study in the AIBL cohort. *Alzheimers Dement*. 2023 Apr;19(4):1117-1134.

SCIENTIFIC PUBLICATIONS

GENETICS

Mehramiz M, Porter T, Laws SM, Rainey-Smith SR. Sleep, Sirtuin 1 and Alzheimer's disease: A review. *Aging Brain*. 2022 Sep 9;2:100050.

Wang T, Huynh K, Giles C, Mellett NA, Duong T, Nguyen A, Lim WLF, Smith AA, Olshansky G, Cadby G, Hung J, Hui J, Beilby J, Watts GF, Chatterjee P, Martins I, Laws SM, Bush AI, Rowe CC, Villemagne VL, Ames D, Masters CL, Taddei K, Doré V, Fripp J, Arnold M, Kastenmüller G, Nho K, Saykin AJ, Baillie R, Han X, Martins RN, Moses EK, Kaddurah-Daouk R, Meikle PJ. APOE ε2 resilience for Alzheimer's disease is mediated by plasma lipid species: Analysis of three independent cohort studies. *Alzheimers Dement.* 2022 Nov;18(11):2151-2166.

Cadby G, Giles C, Melton PE, Huynh K, Mellett NA, Duong T, Nguyen A, Cinel M, Smith A, Olshansky G, Wang T, Brozynska M, Inouye M, McCarthy NS, Ariff A, Hung J, Hui J, Beilby J, Dubé MP, Watts GF, Shah S, Wray NR, Lim WLF, Chatterjee P, Martins I, Laws SM, Porter T, Vacher M, Bush AI, Rowe CC, Villemagne VL, Ames D, Masters CL, Taddei K, Arnold M, Kastenmüller G, Nho K, Saykin AJ, Han X, Kaddurah-Daouk R, Martins RN, Blangero J, Meikle PJ, Moses EK. Comprehensive genetic analysis of the human lipidome identifies loci associated with lipid homeostasis with links to coronary artery disease. *Nat Commun.* 2022 Jun 6;13(1):3124.

NUTRITION

Jayatunga DPW, Hone E, Fernando WMADB, Garg ML, Verdile G, Martins RN. Mitoprotective Effects of a Synergistic Nutraceutical Combination: Basis for a Prevention Strategy Against Alzheimer's Disease. *Front Aging Neurosc*i. 2022 Feb 21;13:781468.

Jayatunga DPW, Hone E, Fernando WMADB, Garg ML, Verdile G, Martins RN. A Synergistic Combination of DHA, Luteolin, and Urolithin A Against Alzheimer's Disease. *Front Aging Neurosci.* 2022 Feb 16;14:780602.

Rajendra A, Bondonno NP, Rainey-Smith SR, Gardener SL, Hodgson JM, Bondonno CP. Potential role of dietary nitrate in relation to cardiovascular and cerebrovascular health, cognition, cognitive decline and dementia: a review. *Food Funct.* 2022 Dec 13;13(24):12572-12589.

Oluwole, O., Fernando, B., Lumanlan, J., Ademuyiwa, O., Jayasena, V. (2022). Role of phenolic acid, tannins, stilbenes, lignans and flavonoids in human health – a review. International Journal of Food Science and Technology, 57(10), 6326-6335

thank you

Our unwavering passion for fighting Alzheimer's disease is matched only by the generosity of our community.

We are committed to upholding the values of integrity and transparency in all our endeavours, and to being responsible stewards of the resources given to us.

Without your support, it would be impossible to pursue our goal . . .
a world where Alzheimer's doesn't exist.

Australian
ALZHEIMER'S
RESEARCH
Foundation