

A Snapshot of High Potential Impact Research on Dementia in Australia

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INTRODUCTION

With the announcement of the Boosting Dementia Research Initiative (BDRI) in 2014, the Australian Government invested an additional \$200M in dementia research, and established the NHMRC National Institute for Dementia Research (NNIDR) from 2015-2020 to oversee the Initiative and drive coordination and collaboration across the dementia research sector. This investment has produced significant advances across the research spectrum, from increased understanding of disease mechanisms to diagnosis, drug discovery and delivery, clinical treatment, quality care, and risk reduction and prevention.

The sector has grown in capacity and capability to be a high achieving and highly respected body of researchers operating with new scale and focus, across disciplines. This is evidenced by high quality publications, ground-breaking research outputs, and the leveraging of new funding sources.

Dementia Research and Translation in Australia

In 2020, there are an estimated 459,000 Australians living with dementia and this number is increasing by around 250 people each day. Dementia Australia estimates around 1.6 million Australians are involved in the care of someone living with dementia.

The Australian dementia research and translation sector is large, complex and diverse. In addition to those people directly impacted by dementia, the sector includes researchers across the pipeline from basic science, clinical and population health to health services research, clinicians and a wide variety of allied health practitioners in primary care and other health service settings, aged care providers and workers, international collaborators and programs, industry partners, policy makers at local, state and national levels and the broader Australian community.

The BDRI funding has been leveraged through a variety of other funding sources. These include Commonwealth funding via the National Health and Medical Research Council (NHMRC), Australian Research Council (ARC), Medical Research Future Fund (MRFF), Cooperative Research Centre (CRC) Scheme and Dementia and Aged Care Services Fund, Dementia Australia Research Foundation, the Dementia Centre for Research Collaboration (DCRC), Cognitive Decline Partnership Centre (CDPC), a variety of philanthropic sources including (but not limited to) the JO & JR Wicking Trust, the Masonic Foundation, the Yulgilbar Foundation, Australian Alzheimer's Research Foundation (AARF) and the Brain Foundation. In addition, there is now a growing involvement of the biotechnology and aged care industry in research.

This funding has supported dementia research and translation across Australia including hubs of activity such as the Clem Jones Centre for Ageing Dementia Research, the Centre for Healthy Brain Ageing, the Melbourne Dementia Research Centre and the Wicking Centre. Research and translation activities have been further enabled by initiatives such as the DCRC, CDPC and Dementia Training Australia.

Most recently, the Australian Dementia Network (ADNeT) has been launched to provide a sustainable, translational research infrastructure that enables ongoing, high quality research and clinical care for Australians living with, or at risk of, cognitive impairment and dementia.

The *NNIDR Strategic Roadmap for Dementia Research and Translation 2019* outlines five priority areas of research to meet the urgent challenge that dementia presents to Australia's health, economy and society. This paper provides a snapshot of the progress made in each of these priority areas (focusing on research funded by the BDRI and other funders) towards achieving impact for people living with dementia and their carers. The paper also identifies gaps in research, future funding requirements and considerations, provides a timeline for impact and uses a high level publication analysis to map Australia's dementia research focus areas.

PRIORITY ONE

Improving dementia diagnosis and prevention

Impact summary

- BDRI-funded research studies to identify pre-symptomatic markers of disease are producing promising results. Future funding will be required to support the next phase of research to achieve clinical impact: validation studies and human trials to prove reliability, specificity and sensitivity of these markers for early detection of dementia.
- Studies assessing non-invasive pre-symptomatic markers of dementia (imaging, electroencephalogram [EEG] patterns, retinal imaging, blood-based biomarkers) are likely to have impact in 5 - 10 years.
- Interventions for dementia risk reduction and prevention have produced positive outcomes, which are already being integrated into larger, multi-domain prevention trials. Funding will be required to support broad implementation of these programs within healthcare and community.
- The most successful research outcomes are those generated from large-scale, collaborative projects where data, infrastructure and expertise are shared across institutes and organisations. Funding to support and broaden these collaborations will facilitate timely research outcomes through access to at-risk populations required for clinical trials and validation studies.

Overview

The focus of Priority One is twofold: (1) to understand the causes of dementia and identify reliable pre-symptomatic markers to develop a conclusive diagnostic test for dementia, and (2) to identify risk and protective factors for dementia to enable health system measures and population level behavioural change that can help to prevent dementia.

Progress towards impact

1. New and less invasive diagnostic approaches

An earlier diagnosis of dementia requires the identification of reliable, pre-symptomatic markers of disease. To date, the BDRI has supported 26 projects (\$12.8M) that seek early markers of dementia using a variety of techniques. These include:

- Genetic and epigenetic biomarkers¹
- Blood-based biomarkers²
- Nasal tissue biomarkers³
- Neuro-imaging studies⁴

¹ Lupton M, Halliday G, Lim Y, Sachdev P, Blair I, Buckberry S, Renteria Rodriguez M, Bodea G, Couttas T, Ryan J

² Gupta V, Blaine R, King A, Loy C,

³ Loy C,

⁴ Breakspear M, Tan R, Kumfor F

- Retinal imaging/ocular changes⁵.
- Brain wave (EEG) patterns derived from brain stimulation studies⁶
- Combined genetic, cognitive, neuroimaging and environmental markers⁷

Due to the large scale, prospective and longitudinal nature of these studies, there is a significant time frame to implementation. Studies that use non-invasive methods (e.g. imaging, EEG patterns, retinal imaging, blood-based biomarkers) are likely to have the earliest impact, however, still require a large number of participants (pre-and post-symptomatically) and validation in subsequent cohorts. Projected timeline for implementation and impact of BDRI-funded research is estimated to be no earlier than 5-10 years. Recently, the first clinical application of retinal hyperspectral imaging in humans with and without moderate–high brain amyloid beta load was published (not funded by the BDRI) highlighting the potential for funding in this area⁸.

The timeline for identification of sensitive and reliable genetic, epigenetic, blood and nasal biomarkers, alone or in combination with other biopsychosocial or environmental factors, is likely to be longer, given the need to recruit patients (or access and screen existing samples), develop methods and tools, analyse data, validate findings and confirm in clinical trials. Projected timeline for implementation and impact is estimated to be greater than 10 years.

Improving assessment tools

The BDRI has supported the development and validation of tools that more accurately assess cognitive functioning. This has included tools that assess performance in activities of daily living, for example spatial tracking processes and economic decision making⁹ (\$614,000). These tools have contributed to the cognitive training module of the Maintain Your Brain¹⁰ project.

2. Interventions for dementia risk reduction and prevention

The identification of risk factors for dementia offers opportunities for strategic interventions to reduce or prevent the onset of disease, particularly in at-risk populations. Evidence to date has pointed to several lifestyle risk and protective factors for dementia. Risk factors include physical inactivity, low education, obesity, hypertension, diabetes and depression. New emerging evidence indicates that sleep disturbance, hearing loss and social isolation are likely to be major risk factors worthy of investigation.

Strengthening the evidence base to support timely and effective interventions that target these factors has been the focus of studies supported by the BDRI. To date, 22 studies (\$24.5M) have been funded trialling interventions to reduce risk or prevent progression of dementia through increasing engagement in physical activity¹¹, cognitive training¹², improving sleep¹³ or supporting vascular health¹⁴.

A further six studies¹⁵ (\$4.6M) focus on developing an evidence base to support pharmaceutical best-practice and pre-surgical care to identify which medications and surgical processes should be avoided to prevent cognitive decline.

⁵ Golzan M, Frost S, Gupta V

⁶ Goldsworthy M, Robinson G.

⁷ Renoir T, Yassi N, Lewis S

⁸ <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6748929/>

⁹ Lampit A

¹⁰ Brodaty H

¹¹ Gardiner P, MacPherson H, Brown B, Smith A, Callisaya M, Brodtmann A, Smith A, Gardiner P, Pipingas A

¹² Mowszowski L, Bahar-Fuchs A, Brodaty H

¹³ Phillips C, Hoyos C, Duffy S, D’Rozario A, Naismith S, Naismith S

¹⁴ Keage H, Takechi R, Yassi N, Brodtmann A

¹⁵ Evered L, Nguyen T, Wong R, Kalisch-Ellett L, Samaras K, Moran C

Other studies seek to identify optimal levels of social interaction to prevent cognitive decline¹⁶ (\$735,000) and optimise the physical environment to support brain health¹⁷ (\$738,000).

- a) Activity interventions: In the first year of the BDRI, several studies were commenced that either tested the efficacy of physical activity (and diet) programs or trialled new interventions to prevent cognitive decline. Many of these have now been completed and have provided proof-of-principle data to inform larger scale testing. Some are already being validated in randomised controlled trials, while others are being used to inform the development of web-based tools and programs for clinical application. Other trials focus on activity interventions in high risk groups (type 2 diabetes, stroke survivors), with completion anticipated within the next five years. The projected timeline for impact of interventions is estimated to be 5-10 years. The projected timeline for the development of personalised approaches for optimising activity and dietary composition in the clinical care setting is estimated to be 10+ years.
- b) Cognitive training interventions: BDRI-funded cognitive training projects have largely focussed on optimising the delivery method of cognitive training programs to enable timely interactions and enhance outcomes, particularly in high-risk groups. Initial studies have already had impact, informing cognitive training interventions in current randomised controlled trials (CogMax trial, PROTECT trial, Maintain your Brain trial) funded through the BDRI. These studies have just commenced so the projected timeline for impact is around five years, but evidence in this field is mounting and this work would now benefit from larger scale implementation studies across the healthcare setting (e.g. memory clinics).
- c) Improving sleep: A body of work now shows that sleep disturbance and sleep disorders (e.g. sleep apnoea) are common in older people, are risk factors for dementia and contribute to more rapid cognitive decline. A number of deep phenotyping studies are underway to examine the mechanisms by which sleep disturbances or disorders may be harmful. In addition, large national multi-site feasibility trials that target at risk groups are currently underway. The projected timeline for impact of the large collaborative trials is estimated to be 5–10 years.
- d) Vascular health: Studies supported by the BDRI investigating the role of vascular health in dementia are broad in scope, comprising animal studies that seek to improve cerebrovascular integrity, prevention trials in high risk groups, and developing a combined vascular-cognitive risk score using magnetic resonance imaging (MRI). The projected timeline for impact of projects developing interventions from animal work is 10+ years, while the vascular cognitive risk score could be implemented in 0-5 years, depending on infrastructure support and system readiness.
- e) Pharmaceuticals: BDRI support has enabled investigations to optimise prescribing practice and medication use to minimise cognitive decline in at-risk populations. These have included the identification of drugs that contribute to cognitive impairment and improving understanding and appropriate use of medications and supplements that support brain health. Guidelines have already been developed for deprescribing practice, with immediate impact expected. The projected timeline for impact for the supplementation trial is estimated to be 5-10 years, while the trial testing efficacy of metformin is estimated to be 10+ years, given this commenced only recently.
- f) Social health reserve: A single epidemiological study commenced recently, which will assess socialisation factors that promote healthy ageing¹⁸. The outcomes of this study will guide interventions, public health campaigns and personalised approaches for healthy ageing. The projected timeline for impact is estimated to be 10+ years, given its recent commencement.

¹⁶ Brodaty H (SHARED project)

¹⁷ Astell-Burt T

¹⁸ Brodaty H (SHARED project)

- g) Physical environment - Green spaces (e.g. parks and tree canopy) may help reduce the risk of dementia by improving mental health and cognition, promoting physical activity and social support, reducing social isolation, reducing depression, obesity, cardiometabolic disease risk and buffering harms from traffic-related air pollution. A 15-year longitudinal study will examine whether exposure to green space offers protection from dementia. The projected timeline for impact is estimated to be 15+ years.

3. Holistic risk prevention programs

BDRI has supported large scale programs (such as the Maintain Your Brain and BetterBrains programs; \$8.3M) that adopt a more holistic approach to prevention, comparing and/or combining interventions to increase activity and cognitive training, reduce depression/anxiety, address weight, and improve mood, sleep and dietary habits¹⁹. The intention of these studies is to identify personalised approaches that can be implemented and/or supported in the primary care setting targeting risk factors to prevent memory decline. If effective, these programs could be rolled out more broadly, with impact expected in the next 5-10 years.

The effectiveness of a new GP risk prevention program, the Holistic Approach in Primary care for Preventing Memory Impairment aNd Dementia (HAPPI MIND) program, is currently in its first year of funding²⁰. This programme comprises self-management training, practical behaviour change techniques and GP-coordinated interdisciplinary management of risk factors in 45-65 year old men and women at risk of cognitive impairment, and will be compared against usual care. Given this trial is being conducted through 40 GP clinics across NSW and Victoria, it is likely to have widespread uptake and immediate impact should the program prove effective on completion (in 2024).

Through a recent targeted call for dementia risk reduction and prevention research, the BDRI supported a program to translate current evidence on risk reduction into a series of outputs, including a risk assessment tool, and advice, training programs and resources for clinical and public health professionals, policy makers, people with dementia and the broader public (\$2 million; 2019-2024²¹). Given this project has adopted an integrated development and training approach with engagement of policy and health professionals, the projected time for impact is 5-10 years.

Other funded dementia projects to improve dementia diagnosis and prevention

Research to identify early biomarkers of dementia has received funding from multiple sources, including the NHMRC (six projects in 2018-2019), Dementia Australia Research Foundation (DARF) and the AARF (12 grants 2014-2018), the Brain Foundation²² and philanthropy (Masonic Foundation: Judith Jane Mason & Harold Stannett Williams)²³. Following biomarker validation, funding will be required to support development of new assessment and diagnostic tools integrating multiple factors (biomarkers, cognitive capacity, activity levels, social participation, pharmaceuticals, environment).

Research to develop new, earlier diagnostic tools and markers for dementia have been funded by the ARC (four projects during 2014-2020). This includes a Linkage grant to develop improved multi-modal retinal scans for early diagnosis (funded 2016-2020). Once complete, these tools will require further validation and, if proven effective, further funding to support clinical trials and implementation.

¹⁹ Maintain Your Brain program – Brodaty H; Better Brains - Lim Y

²⁰ George J

²¹ Anstey K

²² Kirkcaldie, Utas 2019-2019

²³ Kirkcaldie, Utas 2017-2020

Also focused on improving diagnosis are two large studies currently in progress supported by the Yulgilbar Alzheimer's Research Program (2018-2020). The first is investigating the use of nanotechnology for improving imaging techniques to accelerate diagnosis²⁴ (\$1M) while the second seeks to better understand dementia through the use of brain organoids and artificial intelligence²⁵ (\$500,000).

Biotechnology companies Cogstate and CSL are examples of translational impact of research in priority two. Cogstate²⁶ is a spin out of the University of Melbourne. It has developed a computerized cognitive assessment platform. CSL has developed a commercial software image analysis used for reading positron emission tomography (PET) scans for diagnosis of Alzheimer's disease. This work has now been outsourced to a small startup called Maxwell Plus²⁷ with support from the Queensland Government.

Studies to improve diagnosis in culturally and linguistically diverse (CALD) populations through e-interpreting and to improve the diagnosis experience of carers of people living with dementia have been supported by the Dementia Australia Research Foundation (DARF). Once completed, the outcomes of these studies can be implemented immediately to improve the diagnosis experience, with funding required for evaluation and further optimisation if necessary.

Research to reduce dementia risk has been recently supported by the MRFF under the International Clinical Trials and Registries Capacity initiative (\$3.1M)²⁸. This large multi-modal randomised clinical intervention trial to reduce dementia risk is a two-year, international study that will track cognitive changes, conduct brain imaging and clinical assessments and measure blood biomarkers. While this trial will be conducted in Australia, it aligns directly with the US-POINTER study, meaning that outcomes can be immediately compared between the two countries. If found comparable, this will accelerate the next steps of research implementation.

Also focused on reduction of dementia risk are 14 grants supported by the DARF and AARF (\$825,000; 2014-2018). These studies have included developing new digital technologies for dementia risk assessment and monitoring, understanding the impact of stress on dementia risk and improvement of local public health preventative campaigns.

A study supported by the Department of Health: Dementia and Aged Care Services (DACs) is developing a model to measure consumer dementia knowledge and literacy utilising a large Australian community sample (\$349,200; 2017 – 2020)²⁹.

Research to increase community awareness will begin in 2020 supported by the MRFF Keeping Australians Out of Hospital Initiative³⁰. This study will support a large program to increase community awareness about dementia risk factors (\$2.4M). The research will focus on the prevention of obesity through physical activity and improved eating behaviours, particularly during the 'critical' age periods of adolescence, preconception and pregnancy, infancy and childhood.

²⁴ Sachdev, UNSW

²⁵ Jagadish, ANU

²⁶ <https://www.cogstate.com/>

²⁷ <https://www.chiefentrepreneur.qld.gov.au/stories/maxwell-plus>

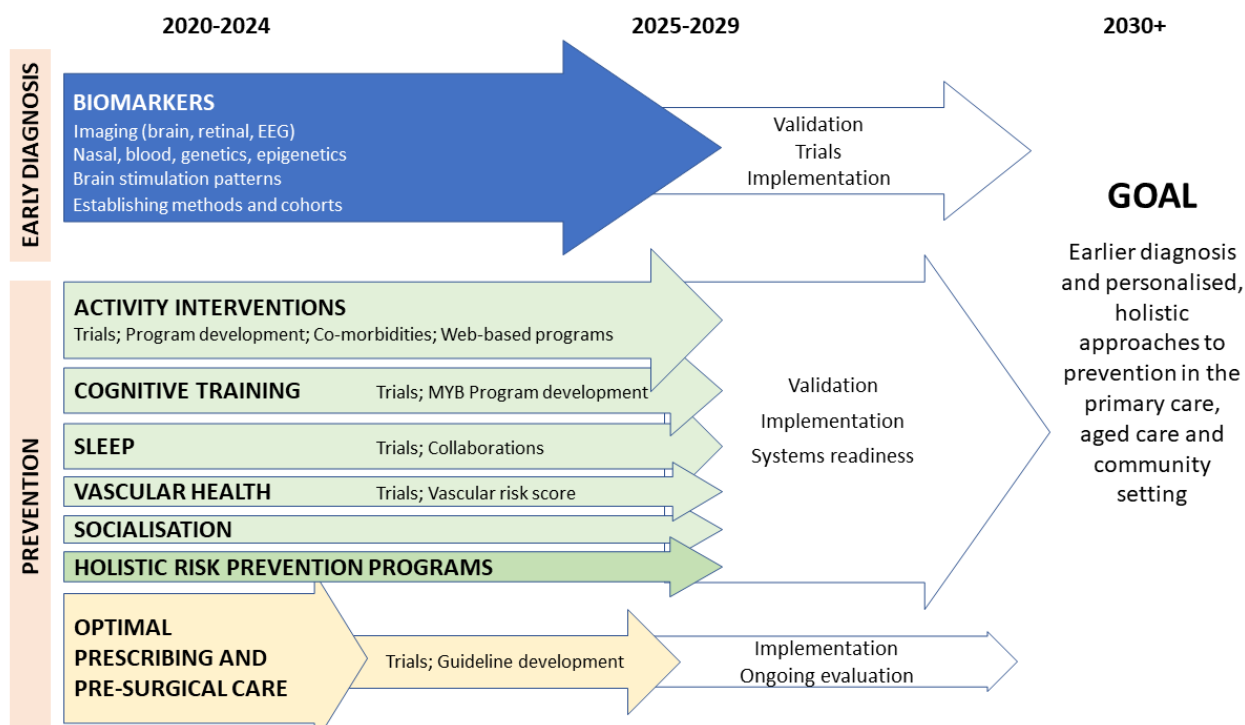
²⁸ Martins, Macquarie University, AU-ARROW study, 2019

²⁹ McInerney F; Wicking Centre UTAS

³⁰ Vickers J, Wicking Centre University of Tasmania 2019

Timeline for impact

Filled arrows indicate current funded projects. Clear arrows indicate projects required to reach goal.



Gaps in current research

Current studies to develop interventions for modifiable risk factors are largely focused on at-risk groups aged over 65 years. Only one study is addressing a risk factor that occurs earlier in life (i.e. obesity³¹) while other known risk factors are not being addressed (e.g. low levels of education before 11-12 years, hypertension, depression and hearing loss at 45-54 years). Successful interventions implemented at earlier time points may significantly reduce the incidence and burden of dementia.

There are very few studies aimed at increasing awareness for dementia in the community or public understanding of dementia and its risk factors. The few that are funded have been supported by the DARF and focussed on small populations.

The potential impact of this research includes reduced incidence of disease, increased engagement with health services, reduced stigma, and increased understanding and support for people with dementia to remain living in the community.

There are no studies specifically addressing improving healthcare services for risk reduction nor for optimal support services in those receiving post-diagnostic support. Many people are waiting over three years for a dementia diagnosis and when they receive one, they do not receive any post-diagnostic care. Investment will be required to drive rapid implementation of early intervention approaches, such as cognitive training programs, exercise, sleep and depression management. This would optimise risk reduction and provide optimal post-diagnostic care.

Only one study aims to improve methods for diagnosis in CALD populations, using e-translation.

³¹ Vickers J, Wicking Centre University of Tasmania 2019

Future funding requirements and considerations

Studies seeking new diagnostic approaches are in the discovery stage of research and will require continued funding to progress to validation, trials and implementation. This type of research benefits strongly from concerted, collaborative (state, nation-wide or global) efforts to facilitate ongoing basic research and clinical trials and successful and ongoing validation, over the longer term. Sharing of resources (samples, methods, data) and leveraging from existing cohorts and registries (including ADNeT) will significantly expedite these studies. There is also considerable interest among prevention researchers in pooling cross-sectional and intervention data which could be facilitated by ADNeT.

Dementia is characterised by a lengthy prodromal period. This aetiology is an important consideration in future funding for dementia research. Investment in longer term studies which demonstrate high potential for impact should be considered along with a targeted approach to leveraging existing Australian longitudinal and cohort studies, including *45 and Up*³², the *Australian Imaging, Biomarkers and Lifestyle Flagship Study of Ageing (AIBL)*³³, the *Health in Men Study (HIMS)*³⁴, *Ten to Men*³⁵ and the *Australian Longitudinal Study on Women's Health*, and incorporating brain imaging or new biomarkers as they are developed. This was the approach used in the first clinical retinal hyperspectral imaging study in humans, where assistance with study participant recruitment and PET scan and clinical data were provided by the AIBL study. Broader adoption of this approach could accelerate research outcomes to uncover optimal time windows for primary and secondary prevention and lead to successful randomised controlled trials. These studies are long term which underscores the need for continuing support of BDRI Fellows.

There is a need to understand whether targeted strategies to reduce dementia in midlife are essential or whether a unified approach to reducing the burden of chronic disease would have broad impact. Investment in behaviour change research is required to address lifestyle-based risk factors (such as diet) for dementia. Collaboration with researchers with expertise in prevention of other chronic diseases such as cancer, cardiovascular disease and diabetes may accelerate progress in this area. This may open up additional avenues of funding through the MRFF, health charities and philanthropy.

The development of personalised approaches to prevent dementia onset or cognitive decline, while already commenced, will likely need further optimisation following the outcomes of current intervention trials. This will require continued investment. These approaches will also require funding to ensure system readiness for implementation to achieve maximum impact (e.g. infrastructure, staffing, awareness, training). The Prevention Special Interest Group is currently conducting a survey to map out prevention approaches and will be an important resource. Similarly, it will be critical to coordinate with other prevention initiatives such as the DCRC.

Implementation studies in healthcare and community settings are essential to ensure optimal translation of research findings into practice. These studies require specific resources and skills which will be different across disciplines. An overarching approach to facilitate and enable successful implementation of findings across the Australian dementia research sector could be considered.

³² <https://www.saxinstitute.org.au/our-work/45-up-study/>

³³ <https://aibl.csiro.au/>

³⁴ <https://www.perkins.org.au/wacha/our-research/mens/mens-health-1/>

³⁵ <http://www.tentomen.org.au/>

PRIORITY TWO

New targets, new technologies, new drug candidates

Impact summary

- The majority of BDRI-funded studies seeking new targets, new technologies and new drugs are in the early stages of the scientific process and will require significant ongoing investment to deliver impact.
- Studies that assess non-invasively collected biomarkers in concert with cognitive-behavioural outcomes are likely to have the earliest impact, but require access to large patient cohorts to test and validate new interventions. This will require ongoing investment to produce impact.

Overview

The focus of Priority Two is understanding the pathologies of various dementias and targeting these mechanisms for successful diagnosis and treatment. The majority of work funded by the BDRI in this priority falls under the umbrella of basic science, identifying molecular and cellular mechanisms underlying neurodegeneration and new potential targets for treatment.

Progress towards impact

1. New targets

Twenty two research studies have been funded in this area (\$12.6M) with a broad range of approaches including post-mortem brain tissue³⁶, animal models³⁷, genetics³⁸, membrane and receptor biology³⁹, autophagy⁴⁰, neurotrophic proteins⁴¹, axonal degeneration⁴², heavy metals⁴³, inflammatory responses⁴⁴, vascular changes⁴⁵ and Lewy body formation⁴⁶. Being at the earliest stages of the scientific pipeline, these studies are unlikely to have clinical impact within 10 years.

Human studies funded by the BDRI are investigating potential new biological markers/targets through assessing non-invasively collected biological samples or using imaging tools in combination with cognitive-behavioural data⁴⁷ (\$1.3M). One of these has developed into a larger collaboration (NHMRC funded Healthy Brain Project, 2016-2020) which is likely to expedite bench to bedside translation. The expected impact is 10+ years.

³⁶ Barton S, Purushothuman S

³⁷ James S; Burrows E

³⁸ Barton S, Dobson-Stone, Smith, N, Rea, S

³⁹ Scott D, Abdul-Ridha A, Ooi L, Burrows E

⁴⁰ Rea S, Bharadwaj P, Turner B

⁴¹ Du X

⁴² Coakley S

⁴³ Greenough M, McAllum E, James S, Heffernan A, Ayton S

⁴⁴ Grubman A, Bhatia S, Medeiros R

⁴⁵ Sutherland B

⁴⁶ Purushothuman S

⁴⁷ Buckley R, Leyton C

Publicly available human data from genetic studies are also being used to identify new mechanisms and potential new targets that cross over with other neurodegenerative disorders⁴⁸. This study (\$868,000) is part of a larger research program being conducted with European collaborators, funded through the NHMRC EU-JPND scheme. This study has multiple outcomes with varied timelines for impact: improved classification of dementia phenotypes will be available in the short term (0-5 years) with immediate and ongoing impact. Identification of new mechanisms contributing to neurodegeneration will require confirmation, likely to have impact in 10+ years.

Mechanistic studies funded by the BDRI have led to the development of models that closely mimic the neural environment (e.g. cells⁴⁹, membranes and scaffolding⁵⁰) which allow assessment of mechanisms and efficacy of potential new treatments (\$1.2M). These studies have results expected in the short term (0-5 years), which can then be applied to assist with the identification and testing of new targets and new drugs in the future. The clinical impact of this larger body of translational work is estimated to be longer term (10+ years).

2. New technologies

BDRI funded studies are exploring new technologies that can deliver therapeutics non-invasively across the blood brain barrier (BBB). These include nanoparticle delivery systems tailored for efficient and controlled delivery and release of drugs which cannot cross the BBB on their own in target brain tissue⁵¹ (\$2.5M). Funded research largely focuses on assessing the nanomaterials in in vitro and in vivo models using state-of-the-art imaging technologies. Key to the success of nanotechnology projects are national⁵² and international⁵³ collaborations to provide access to relevant experimental models to test efficacy of nano formulations. The expected impact of these projects is 10+ years given that nanotechnology and nanomedicine are relatively new fields in Australia.

3. Non-pharmaceutical approaches

The BDRI has supported five programs (\$2.1M) investigating new non-pharmaceutical therapeutic targets and approaches to treat dementia, including brain stimulation⁵⁴, behavioural changes, cognitive therapy⁵⁵ and speech therapy⁵⁶. These studies address potential processes and treatment in common with other neurodegenerative conditions, including Motor Neurone Disease and Huntington's disease. As these are currently being trialled in humans, they are likely to produce outcomes and have broader impact in 5-10 years.

4. New drugs

Research assessing the efficacy of pharmaceutical therapies is still in its infancy, predominantly involving cellular, animal or ex vivo brain tissue analysis. Studies include investigation of the effects of chronic BACE (β -site amyloid precursor protein-cleaving enzyme 1) inhibition on cognition, motor function and spine morphology in mice, using a BACE inhibitor provided by the pharmaceutical company Janssen⁵⁷. Clinical trials with this drug were recently discontinued due to safety concerns, highlighting the challenge of identifying drug candidates.

⁴⁸ Wray N

⁴⁹ Okolicsanyi R

⁵⁰ Martin A

⁵¹ Nisbet D, Shi B, Kempe K, Shimoni O

⁵² Kempe K

⁵³ Shi B

⁵⁴ Hoy K

⁵⁵ Steiner G, Hsieh S, Glikman-Johnston Y

⁵⁶ Vogel A

⁵⁷ Munro K

5. Enhanced system readiness

One study has addressed ethical implications of genetic screening for wide-spread assessment of biomarkers⁵⁸. This was not the initial focus of this project but was an issue encountered and investigated further by the research team. Further studies are required to enable smooth translation of research outcomes.

Other funded dementia projects seeking new targets, new technologies and new drug candidates

Analysis of NHMRC funding support for dementia projects commencing over 2018 and 2019 demonstrates strong success of applications focused on understanding mechanisms and identifying new targets for dementia treatment. In total, 45 of the 51 NHMRC supported dementia projects (89%) during 2018 - 2019 focused on the identification of new targets and new drugs. This included two large program grants, one investigating biomarkers to aid clinical trials⁵⁹ (\$13.5M; 2018-2022) and the other genetics and treatment for frontotemporal dementia and motor neurodegeneration syndromes⁶⁰ (\$17.5M, 2018-2022)⁶¹.

Research funding to support exploration of the biological mechanisms underlying dementia has also been provided by the DARF and AARF⁶², the Brain Foundation⁶³, the Yulgilbar Foundation⁶⁴ and the Rebecca L Cooper Medical Research Foundation⁶⁵. The ARC has supported a number of studies through the Discovery Projects Scheme that explore new targets and new technologies for dementia treatment. This includes research of cellular and mouse models to assess changes in neuronal morphology⁶⁶ and brain plasticity⁶⁷ with age, memory formation and pathology, exploring neuronal repair mechanisms⁶⁸ and developing advanced MRI techniques to significantly reduce scan time⁶⁹.

Funding from biotech companies have also supported mechanistic studies to understand disease progression. This has included funding from the biotech company, uBiome, to investigate the association between the gut microbiota and cognitive decline⁷⁰. Actinogen has commercialised a drug Xanamen, for treatment of Alzheimer's Disease and mild cognitive impairment. The drug, developed at the University of Edinburgh, is a cortisol inhibitor and the XanaHES trial has shown promising results in phase 1 studies⁷¹. The MRFF has recently supported Professor Terence O'Brien (Monash University) and collaborators to evaluate the effectiveness and safety of sodium selenate as a disease modifying treatment for patients with behavioural variant Frontotemporal Dementia (2019-2024).

A further \$1M in MRFF funding has recently been allocated to the Clem Jones Foundation to lead a network of partners around Australia and New Zealand to build a business case for developing a prototype ultrasound device for the treatment of Alzheimer's disease⁷². This funding follows successful demonstration

⁵⁸ Medeiros R.

⁵⁹ Bush A

⁶⁰ Halliday G

⁶¹ NHMRC funding 2018-2019 for 46 projects and \$72,071,240, compared to 52 projects and \$45,243,535 commencing in 2013-2014

⁶² 27 focussed studies, each 1-2 years in duration and \$50,000- \$75,000; Total \$1.645 million over 2014-2019.

⁶³ Taberlay P et al, epigenetic neuronal signatures of Alzheimer's disease; \$33,000 2017-2018

⁶⁴ King A, Axonal degeneration and protection; \$30,000, 2015-2018.

⁶⁵ Taberlay P, New geNOMeC maps of neuronal epigenetic changes in Alzheimer's disease. \$24,971; 2017-18.

⁶⁶ Yazike; Breadmore M; Goetz J; Wilson M

⁶⁷ Semmler J;

⁶⁸ Ekberg J; Chung; Separovic F

⁶⁹ Kennedy R

⁷⁰ Ziebell J; \$12,000; 2018-2020

⁷¹ <https://smallcaps.com.au/actinogen-medical-breakthrough-study-results-alzheimers-drug-xanamem/>

⁷² QBI; MRFF Frontiers Phase 1 2025

of the therapeutic application of this technology from a mouse model of Alzheimer's disease in 2015. A further \$10M Australian Government commitment and a \$5M Queensland Government pledge have been received for the ultrasound project⁷³. The research team has now partnered with medical-device engineers and clinicians and will begin humansafety trials soon.

Researchers at the Clem Jones Centre for Ageing Dementia Research are developing novel research tools to advance dementia research⁷⁴. One of these, funded by an ANZ Trustee Mason Foundation Grant, is an antibody against the protein tau, that can help detect late-stage pathology in tissue with Alzheimer's disease or frontotemporal dementia. This antibody was licensed to Merck-Millipore in 2018, with the Queensland Brain Institute (QBI) to share in the proceeds of commercialisation.

Funding to support the development and trials of digital technologies has received funding from the ARC. An ARC Linkage grant supported by the EU Joint Programme – Neurodegenerative Research, has supported researchers to explore the use of “smart glasses” for people with cognitive decline. The glasses have embedded sensors that automatically detect the activity being performed and provide feedback. These will increase autonomy by improving safety awareness around the home⁷⁵.

A clinical trial is currently underway, supported by private company funding, to test the efficacy, feasibility and usability of the company's facial recognition technology (mobile app⁷⁶) for identifying the presence and severity of pain in institutionalised patients with dementia. The founders of the digital healthcare company (EPAT PTY LTD⁷⁷) were researchers from Curtin University⁷⁸.

⁷³ https://qbi.uq.edu.au/files/47156/QBI_Annual_Report_2018.pdf

⁷⁴ https://qbi.uq.edu.au/files/47156/QBI_Annual_Report_2018.pdf

⁷⁵ Ramos F

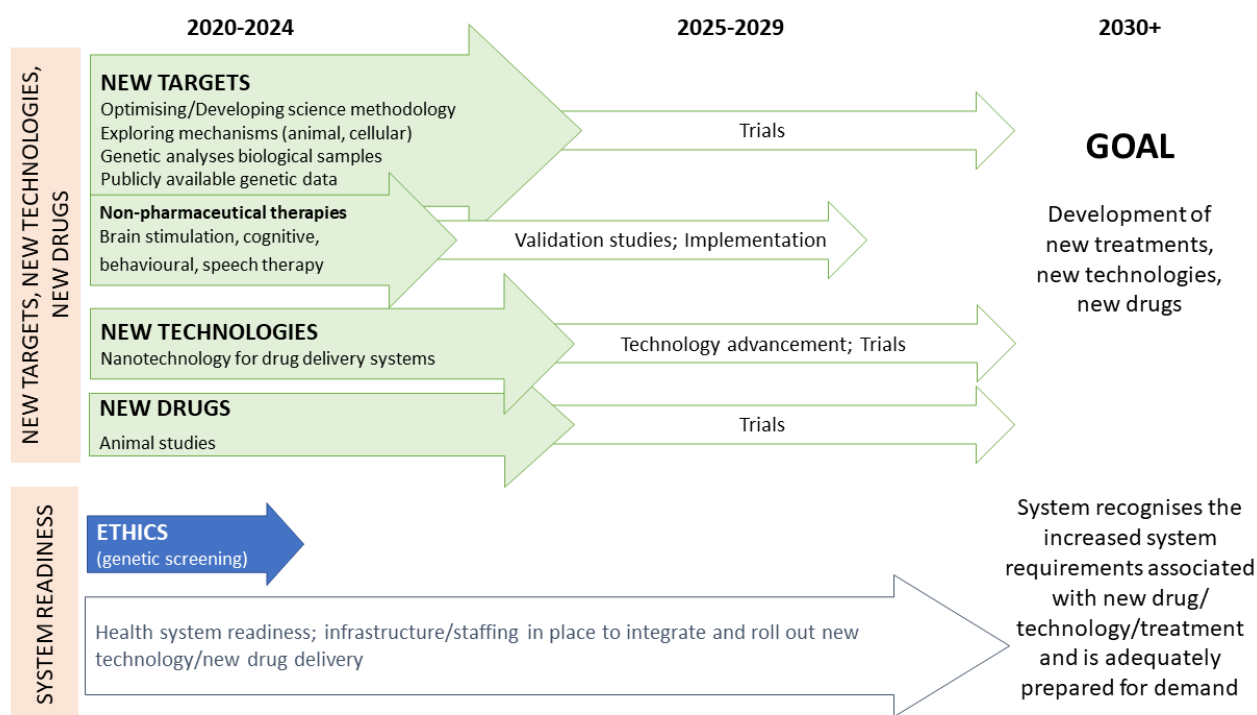
⁷⁶ <https://painchek.com/wp-content/uploads/2018/01/1684087.pdf>

⁷⁷ EPAT: Electronic Pain Assessment Technology

⁷⁸ Professor Jeff Hughes and Mustafa Atee

Timeline for impact

Filled arrows indicate current funded projects. Clear arrows indicate projects required to reach goal.



In some areas, the timeline for impact could be accelerated with adequate funding. Transcranial magnetic stimulation (TMS) was recently approved by the Medicare Services Advisory Committee. The process of implementation will occur over the next 12 – 18 months. There are already a number of TMS services throughout Australia with imminent plans for expansion to rural centres. If TMS is shown to be effective for Alzheimer’s Disease in a large-scale clinical trial, translation would be supported by this nation-wide infrastructure. While the cost of running large-scale randomised controlled trials of technology interventions is relatively low in comparison to pharmaceutical trials, the success rate for funding these trials is low.

Gaps in current research

There are very few studies focused on drug development for dementia and those studies that are funded are at very early stages of research. This appears to be consistent with the international drug development effort, with no significant new progress in this area. The only recent development in this area has been the announcement by Biogen to bring its anti-amyloid drug aducanumab to the FDA for approval, despite previous failure in a phase 3 trial⁷⁹.

In anticipation of a new therapy proving efficacious, an understanding of the health system requirements is needed to support the wide-spread implementation of this therapy. A report has been recommended by NNIDR to highlight the capacity and infrastructure changes to support a new therapy, funding models to deliver new schemes, health professional awareness and education, collaborative approaches between government and charitable organisations to ensure and support equitable access to therapy, ongoing assessment of progress, needs and gaps. Researching best approaches to implement these changes will be required to ensure health system readiness, and rapid and timely implementation of new therapies. Best

⁷⁹ <https://www.neurologylive.com/clinical-focus/aducanumab-heads-to-the-fda-after-biogen-analysis-proves-positive-in-early-alzheimer-disease>

methods for increasing public awareness of any new therapeutic will also need to be considered in this system evaluation.

Future funding considerations and requirements

A consideration for future funding under this priority is a focus on an experimental therapeutic approach to developing new treatments in dementia. The US National Institute of Mental Health has adopted an approach to supporting clinical trials that focus on an intervention's target or mechanism of action by which the intervention might modify the symptoms of interest⁸⁰. A similar targeted framework combining mechanisms and targets could accelerate impact and progress. ADNeT will play a critical national role in driving clinical trials and getting biotechnology companies integrated with the Australian research effort.

Studies currently funded through the BDRI and joint international initiatives e.g. EU-JPND and NHMRC are predominantly in the discovery phase and will require ongoing support to progress to pre-clinical and clinical studies. While some funded studies have not yet generated any tangible outcomes, a number show considerable promise. Research of this nature could potentially attract industry or venture capital funding and/or be conducted with international partners. This will require coordination as effective technology transfer requires dedicated support and expertise and is not viable or accessible for the vast majority of health and medical researchers in Australia.

Effective translational research is facilitated through a collaborative, cross disciplinary approach, supporting engagement of experts across basic science, clinical trials, social science, public health, implementation and/or policy and active involvement of consumers. This has been identified as a major strength of the BDRI investment to date with the most impactful BDRI-funded projects having been delivered through multi-centre collaborations. These collaborations have been strengthened through NNIDR forums and events, resulting in sharing of advice, knowledge, and/or access to samples, data and/or patients. In contrast, BDRI-funded researchers working in isolation and not embedded in the dementia research community report slow progress, unforeseen hurdles and limited access to patients/data/samples. Strategies that actively support collaboration and exchange (e.g. events, cross discipline/cross institution funding schemes) and shared access to research infrastructure, data, expertise, support and advice will lead to more effective research and more expedient outcomes, increasing potential and progress towards research translation. Continued funding support for ADNeT and other large data-sharing platforms will enable internationally competitive dementia research, and quantifiable progress towards this priority goal. Dedicated effort will be required to ensure that ADNeT is an accessible platform that supports both evidence-based and blue sky approaches.

Ensuring health system readiness will require a cross-sectoral approach, potentially performed in collaboration with relevant government agencies. Assessing consumer readiness and raising awareness will require active consumer involvement, which may be achieved through collaboration with Dementia Australia.

⁸⁰ <https://www.nimh.nih.gov/funding/grant-writing-and-application-process/concept-clearances/2013/nimhs-new-focus-in-clinical-trials.shtml>
<https://www.nimh.nih.gov/about/strategic-planning-reports/introduction.shtml>

PRIORITY THREE

Improving quality of life and provision of care

Impact summary

- The majority of current BDRI-funded studies will provide proof of principle for effective well-being and quality of life programs. These will require further funding to support necessary infrastructure and capabilities for broader uptake and implementation.
- BDRI-funded research investigating the needs of the dementia workforce are ongoing. Current studies are generally focused on a single point of care. The cross sectoral needs of people with dementia and their carers requires research attention.
- There is very little research currently focused on end of life care.

Overview

The focus of Priority Three is informing health system change that will improve quality of life and enable provision of quality care, recognising the needs, strengths, preferences and values of people with dementia, their carers and families and those who are supporting them in the home, community and formal care setting.

Progress towards impact

1. Supporting well-being and quality of life in the home and community care setting

Improving well-being and quality of life in the home requires recognition of the unmet needs of people living with dementia and their carers, and the limitations of current care and home support packages. Research supported by the BDRI has started to identify and test home care delivery models, test interventions that promote independence and is working towards policy change to enable broader and increased utilisation of home-based services to improve post-diagnostic well-being, quality of life and care supports in the home (\$7.06M)⁸¹. Initial impact from these studies is expected in the next 5-10 years but will be dependent upon access to resources and funding that support implementation of these findings.

Several randomised controlled trials have recently commenced with BDRI support that test self-management interventions and promote independence in the home and community care setting⁸² (\$4.2M). Included in these studies are development of resources and training/educational programmes for carers. These studies are likely to have impact in 5-10 years.

Other BDRI supported studies are developing tailored and meaningful activity programs, communication strategies, falls prevention programs⁸³ and physical environmental supports⁸⁴ for people with dementia and their families to support continued living and optimise wellbeing in a safe and supported home environment⁸⁵. These studies (\$2.5M) will be complete within five years, with impact expected within 10 years.

⁸¹ Phillipson L, Sanson-Fisher R, Brodaty H, Sanson-Fisher R, Carey M

⁸² Anstey K, Dow B, Jeon Y

⁸³ Taylor M

⁸⁴ Loetscher T

⁸⁵ Bennett S

Current research also seeks to improve safety of people with dementia and their carers and families through raising awareness about, and supporting, driving cessation⁸⁶. These studies are currently underway, with impact expected within the next 10 years.

The impact of group music therapy and group singing on levels of depression, cognitive function, quality of life, and other symptoms of dementia, as well as the cost effectiveness of these therapy sessions, has been the focus of five studies (\$3.4M) funded by the BDRI⁸⁷. These studies have already resulted in the identification of barriers and facilitators to this therapy being used in the aged care setting and the trial of best practice guidelines for music use in aged care facilities and by home carers. Ongoing randomised controlled trials assessing the ability of carer delivered and group music therapy to improve symptoms in people with dementia will be completed within five years, and greater impact likely in 5-10 years with broader implementation of these programs.

2. Improving provision of care and health services

The development of national, evidenced-based, guidelines and best practice recommendations are essential to implementing smooth, consistent, and evidence-based approaches that improve the quality of life and the quality of care. Research supported by the BDRI has enabled the development of the following key guidelines:

- Dementia in people with Intellectual Disability: Guidelines for Australian GPs⁸⁸
- Deprescribing Cholinesterase Inhibitors and Memantine⁸⁹
- Recommendations for the Nomenclature of Cognitive Change Associated with Anaesthesia and Surgery—2018⁹⁰.

Impact from these studies is expected within the next five years.

Further guidelines and best care recommendations are expected in the future: two current studies, one of which involves establishing a national quality collaborative, are implementing care approaches that promote independence, support rehabilitation and post-diagnostic care for people with dementia⁹¹, and another is piloting a dementia clinical quality registry that identifies variation in clinical care provision (for guideline recommendations)⁹². Impact from these studies is expected within the next 5-10 years.

The BDRI has supported research to optimise medication use and prescribing practice to improve outcomes and quality of life. Seven studies (\$3.9M) have resulted in the development of evidence-based deprescribing practice safety guidelines to ensure personalised care in the acute and at-home settings⁹³, and optimisation of pharmaceutical management of comorbidities in dementia, including depression and anxiety⁹⁴. Importantly, this research has also extended to developing methods to improve staff training in safe medication use⁹⁵.

The BDRI has supported research investigating best methods to support the dementia care workforce. Outcomes already generated include the evaluation of computerised neuropsychological assessments to

⁸⁶ Scott T, Scott T

⁸⁷ Baker F, Garrido S, Baird A, Tamplin J, Baker F

⁸⁸ <https://3dn.unsw.edu.au/sites/default/files/Guidelines%20for%20Australian%20GPs%20Dementia%20in%20Intellectual%20Disability.pdf>

⁸⁹ <https://cdpc.sydnev.edu.au/wp-content/uploads/2019/06/deprescribing-guideline.pdf>

⁹⁰ <https://anesthesiology.pubs.asahq.org/article.aspx?articleid=2707390>

⁹¹ Laver K, Low L

⁹² McNeil J

⁹³ Gnjdic D, Etherton-Beer C, Bell S, Reeve E

⁹⁴ Tan E, Dissanayaka N, Bell S

⁹⁵ Gilmartin-Thomas J

support screening and monitoring⁹⁶, development of training materials, structured modules⁹⁷ and virtual and telehealth training programs⁹⁸ to upskill staff in optimal medication use and the prevention of cognitive and functional decline in aged care facility residents and community-dwelling residents. Health literacy resources and clinical guidelines for patients with dementia and intellectual disabilities have already been developed for GPs to support provision of quality care⁹⁹, while electronic systems are being developed to improve nurse assessments in acute care in the hospital system¹⁰⁰. These studies (\$5.2M) are expected to have impact within the next five years, with greater impact achieved with broader implementation. Other studies that aim to improve capacity, build resilience and monitor social connectedness in the dementia care workforce are ongoing¹⁰¹.

3. Advanced care planning

A single BDRI-supported research study (\$598,000) aims to explore current understanding of advance care planning and treatment decision-making by people with dementia and their carers, including the preferred timing for these discussions and willingness to use an online resource to engage in this process¹⁰². This information is being used to optimise and trial different methodologies that will increase engagement with advanced care planning processes.

4. Understanding the cost of health service delivery

Ensuring long-term financial sustainability of dementia services requires robust health economics analyses of service cost and service utility. A single study funded by the BDRI (\$734,000)¹⁰³ is exploring these measures, with outcomes expected within five years.

Other funded dementia projects to improve quality of life and care provision

In 2020, NHMRC will commence support for the Centre of Research Excellence in Neuroimaging¹⁰⁴, through \$2.5M funding to develop a platform that transforms Australian neuroimaging into an interconnected, collaborative research and clinical network, which standardises and synchronises imaging methods across the country. This platform will be used to conduct cutting edge research on novel techniques that improve the patient journey, and accelerate their translation into widespread clinical practice, bringing world-class neuroimaging to all Australians.

NHMRC will also support the Centre of Research Excellence in Interactive Digital Technology to Transform Australia's Chronic Disease Outcomes (2020-2024)¹⁰⁵. While not focused on dementia, this \$2.5M investment will support research to co-design interactive digital technologies that can be used to optimise the user experience and be integrated into routine healthcare to address chronic diseases that often co-occur with or increase risk for dementia.

⁹⁶ Kochan N

⁹⁷ Mortby M, Evans E

⁹⁸ Laver K, Gilmartin-Thomas J

⁹⁹ Evans E

¹⁰⁰ Martin-Khan M

¹⁰¹ Evans E, Elliot K

¹⁰² Bryant J

¹⁰³ Comans T

¹⁰⁴ Bammer, University of Melbourne; 2020-2024

¹⁰⁵ Oldenburg, University of Melbourne; 2020-2024

A NHMRC project grant¹⁰⁶ researching improvements in health service delivery received funding from the NHMRC in the 2018-2019 funding period. This study seeks to support appropriate delivery of care to Australians living in residential aged care. Sources of similar research support include the Masonic Centenary Medical Research Foundation in collaboration with Masonic Care Tasmania¹⁰⁷ and the Tasmanian Community Fund^{108, 109}.

A number of research studies to improve care and quality of life were supported by the Cognitive Decline Partnership Centre (CDPC). The CDPC was one of three Partnership Centres for Better Health funded from 2013-2019. The CDPC received \$25M from six partner organisations, including the NHMRC, Department of Health and Ageing, industry partners (Brightwater Care Group, HammondCare and Helping Hand Aged Care) and Dementia Australia. In the Evidence for Change report¹¹⁰, the CDPC reports significant impact from supported research activities, ranging from the development of clinical practice guidelines, new care and respite models across Australia, adoption of uniform policies and practices by financial, legal and health organisations, the development of evidence-based tools and strategies to build and develop the care workforce and improved medication management practices.

Three ARC Linkage Grants are currently supporting research collaborations to improve quality of life and care for people living with dementia. These span programs that explore financial decision making with age related cognitive decline¹¹¹, develop tools to assess driving performance¹¹² and develop a quality of life assessment for economic evaluation of services¹¹³. The development of new instruments and tools will need to be validated in different populations and can then be implemented more broadly.

The DARF and AARF have made significant investment into improving care and support for people living with dementia and their carers. During 2014-2019, 29 studies to improve care (total \$1.8M) have been supported through these schemes. The scope of this research includes: improving evidence on nutritional needs; optimising dosage regimens; preventing co-morbidities; supporting creation of dementia friendly environments; increasing understanding of carer needs; trialling carer support interventions; developing educational programs for emergency departments, and, developing national policy to improve dementia care and safety.

Two ARC Discovery Projects also aim to improve quality of life and care. The first is testing a creative arts intervention to increase social participation¹¹⁴, while the second aims to improve health services through understanding the ethical considerations for treatment and policy creation, by exploring the capacity for those living with dementia to retain social agency, values and relationships¹¹⁵.

Timeline for impact

Filled arrows indicate current funded projects. Clear arrows indicate projects required to reach goal.

¹⁰⁶ Braithwaite - CareTrackAged: appropriate care delivered to Australians living in residential aged care

¹⁰⁷ Lea E; \$250,000; 2017-2019.

¹⁰⁸ Scott J, \$58,626 2016-2019.

¹⁰⁹ Lea E \$90,000 2018-2020

¹¹⁰ https://cdpc.sydney.edu.au/wp-content/uploads/2019/11/CDPC_Final_Report_2019.pdf

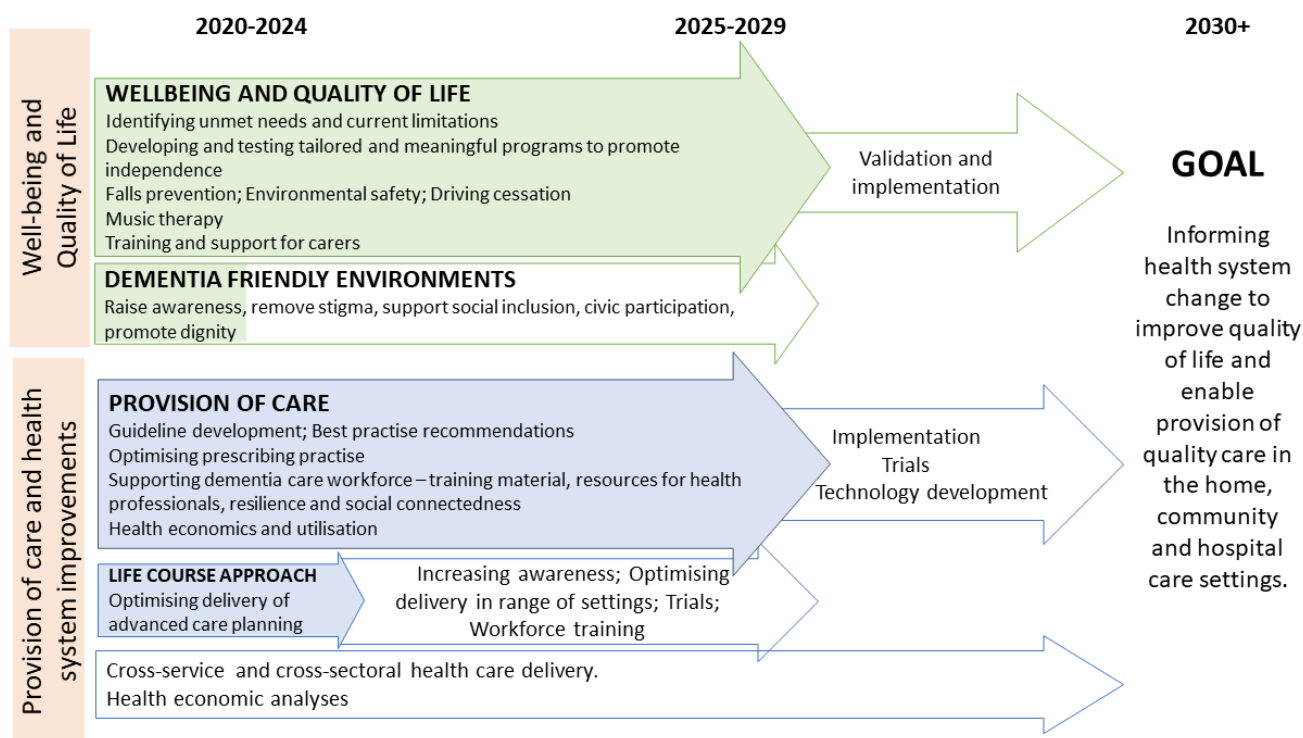
¹¹¹ Basu A, UQ; 2015-2019

¹¹² Meuleners L, Curtin University; 2017-2021

¹¹³ Ratcliffe J, UniSA, 2018-2022

¹¹⁴ Baker F; 2015-2017

¹¹⁵ Matthews S; 2018-2020.



Gaps in current research

Providing consistent, equitable and high-quality care at the right time across the disease course requires co-ordination and creating efficiencies between the health and social care systems. Currently funded research is focussed on single points of contact with health services (e.g. GPs, residential care staff, nurses in acute care setting). There are no funded studies exploring innovative ways to integrate, improve or combine health services or investigating cross-sectoral service delivery.

A single study is testing methods to facilitate advanced care planning, however research in all other areas relevant to providing and supporting quality experience and care at the end of life are lacking.

Currently funded research does focus on improving home care-supports and ensuring a safe home environment, however there is limited research on dementia-friendly communities and improvements in formal care environments. This area has been identified as a consumer priority and is critical to help remove the stigma currently felt by people with dementia and their carers, and support social inclusion, civic participation, and promote dignity and quality of life. Given that this area has a broader societal focus, alternative funding opportunities could be explored.

Future funding considerations and requirements

The interim report of the Royal Commission into Aged Care Quality and Safety¹¹⁶ has highlighted the inadequate integration of aged care with the broader health care system and called for more research into the care of older people and better integration of services at all levels to achieve person-centred care. This is an important consideration for funding an integrated approach to optimising the care journey for people living with dementia and their carers. Development of cross-health service and cross-sectoral service platforms will require buy-in and funding from local, state and federal health systems and collaboration

¹¹⁶ <https://agedcare.royalcommission.gov.au/publications/Documents/interim-report/interim-report-volume-1.pdf>

with other government agencies. Active engagement with key organisational executives, health service personnel and consumer advocacy groups will also be needed.

Many research progress reports in priority three indicate slow progress due to difficulties with recruitment or unanticipated changes to planned methodology. Overcoming these issues may be achieved through a targeted and sustained boost to research capacity in the aged care and general practice sector. A framework to facilitate cross-disciplinary collaboration as well as active engagement with people with dementia and their carers, alongside support for their involvement in all stages of research, could also be considered.

Research on quality of life and provision of care has the potential for broad uptake and implementation in 5 – 10 years but will require access to resources and funding to support the implementation of findings. Implementation requires diverse capabilities including consumers, aged care personnel and general practitioners. Dedicated funding schemes should acknowledge that many of those people required to achieve successful implementation have not pursued a traditional academic career path and funding should be contingent upon their demonstrated involvement and recognition.

An identified need is a clear path for engagement of researchers with Dementia Training Australia (DTA). DTA is a consortium funded by the Australian Government to provide nationwide education on the support and care of people living with dementia. This avenue has the potential to be transformational in driving implementation of dementia research and translation.

Ongoing funding for dementia care research will facilitate the development of trials, guidelines and broad/er implementation of research outcomes. Given these studies optimise service delivery in Australia, they are unlikely to receive funding from industry or international partners. Potential funding sources include the NHMRC, Department of Health, MRFF, philanthropy, consumer support organisations and local funding bodies.

Current research also focuses on improving quality of life in the home and community settings through development of e-health, virtual reality and other digital technologies. Further development, optimisation and implementation of these innovative technologies across Australia will require significant funding, potentially gained through traditional health funding schemes (e.g. NHMRC, MRFF) as well as from industry development schemes and industry partners, e.g. ARC, MTP Connect, Department of Industry, Innovation and Science, private companies.

There will be an ongoing need for cost-benefit and cost-utility analyses as new trials are commenced and initiatives implemented. Incorporating these analyses into current trials will allow decisions and services to be informed by cost of new initiatives, clinical effectiveness and value for money. This evidence will expedite implementation of cost-effective delivery models.

PRIORITY FOUR

Aboriginal and Torres Strait Islander Australians and Dementia

Impact summary

- Research involving Aboriginal and Torres Strait Islander communities is inherently expensive as it requires time and support for community navigation and consultation, research development and local workforce training. It must also be tailored for each community context.
- This research, if adequately supported, has high potential for impact.
- Ongoing funding will be required to ensure transferability of successful programs across Aboriginal and Torres Strait Islander communities, and to provide training to build the local workforce.

Overview

The focus of Priority Four is to develop new culturally safe and appropriate care models, assessments and tools that consider Aboriginal and Torres Strait Islander knowledge systems and the importance of country to promote healthy brain ageing and provide the highest standards of diagnosis, treatment and care to Aboriginal and Torres Strait Islander Australians.

Progress towards impact

1. Risk reduction and diagnosis

The BDRI is supporting four dementia prevention programs (\$10M), including community interventions and chronic health, and risk management programs specifically for Aboriginal and Torres Strait Islander people at risk of dementia¹¹⁷.

A five year BDRI supported study (\$3.06M¹¹⁸) in its second year is assessing risk factor profiles for mild cognitive impairment in older Aboriginal and Torres Strait Islander people, evaluation of a technology-based healthy brain ageing program¹¹⁹ and developing dementia prevention, education and health promotion resources. This study will build on previous clinical research and will address different types of dementia in Aboriginal and Torres Strait Islander Australians, using neuroimaging and other biomedical techniques.

Impact from the above studies is expected upon study completion, due to the active engagement and involvement of Aboriginal and Torres Strait Islander communities in the creation and implementation of these programs.

2. Culturally informed services and workforce

While dementia is highly prevalent in Aboriginal and Torres Strait Islander Australians, no tools were previously available to assess quality of life of people living with dementia in this group. Research funded by the BDRI (\$623,000) has supported the development of the first quality of life tool and framework for

¹¹⁷ Smith K, Eades S, Strivens E, Sanson-Fisher R

¹¹⁸ Radford K

¹¹⁹ Building on a major outcome of the Dementia Development Fellowship awarded to A/Prof Kylie Radford – Standing Tall with Our Mob Program (STOMP)

service providers to identify and implement strategies to optimise the quality of life of Aboriginal and Torres Strait Islander Australians living with dementia or cognitive impairment. This work is currently being validated¹²⁰.

Research supported by the BDRI has also allowed the development of best practice guidelines by consensus, and a comprehensive assessment tool aimed to improve detection and management of dementia in the primary care setting in Aboriginal communities¹²¹ (\$4.3M). Improving timely diagnosis and best care delivery is the focus of an ongoing randomised controlled trial¹²² (\$598,000).

These programs are continuing to be co-developed with Aboriginal communities, Aboriginal community-controlled health services and local community services. Cultural knowledge and experiences that inform the development of these programs have been gathered using individual interviews, Aboriginal Elder yarning groups (men's and women's groups), and inclusion of members of local Aboriginal communities in research development. Aboriginal research officers and health workers have been employed on a number of these studies¹²³.

Other funded dementia projects to improve dementia outcomes in Aboriginal and Torres Strait Islander Australians

A NHMRC Centre of Research Excellence (CRE) scheme (\$2.5M) will be commenced in 2020 to improve healthcare equity. The project, STRENGTHENING systems for INdigenous healthcare Equity (CRE-STRIDE)¹²⁴, focuses on Indigenous leadership and community participation to translate quality improvement research into policy and practice. While not specifically focussed on dementia, this project may produce broader outcomes that impact on dementia care services for Aboriginal Australians.

Two ARC Indigenous Discovery awards were awarded in 2019. The first focuses on developing evidence-based retention strategies for the Indigenous health and disability workforce (\$471,000)¹²⁵, and the second supports research investigating approaches used by Aboriginal community-controlled organisations to enable community ownership of holistic health and social programs (\$498,000)¹²⁶. The outcomes from both these grants will potentially have broad and important impact, supporting education, training and employment in the health sector to ensure benefits from projects are retained and shared to support improvements in Aboriginal and Torres Strait Islander health.

Funding from the Federal government has also been directed towards programs to improve Aboriginal health and care services in Tasmania. This has included funding from the Department of Health: Dementia and Aged Care Services (DACs) (\$834,757)¹²⁷ to provide individualised support, specialised training and build leadership in dementia care in a Tasmanian community. This project was funded 2017-2019.

The Department of Prime Minister and Cabinet – Indigenous Affairs office also funded the establishment of an Aboriginal Primary Health Care Worker program in Tasmania from 2018-2019 (\$78,000)¹²⁸. This was also supported by funding from Equity Trustees Limited (\$77,000)¹²⁹.

¹²⁰ Good Spirit, Good Life tool; Smith K

¹²¹ LoGiudice D, LoGiudice D

¹²² Bryant J

¹²³ Smith K: Good Spirit, Good Life tool; Smith K: DAMPAA program; Radford, K: Our MOB, Koori Active & Healthy Ageing Project, LoGiudiceD: Let's CHAT Dementia, IDEA-PC.

¹²⁴ Matthews V, University of Sydney

¹²⁵ Gilroy J, U Sydney

¹²⁶ Clapham K, U Woollongong

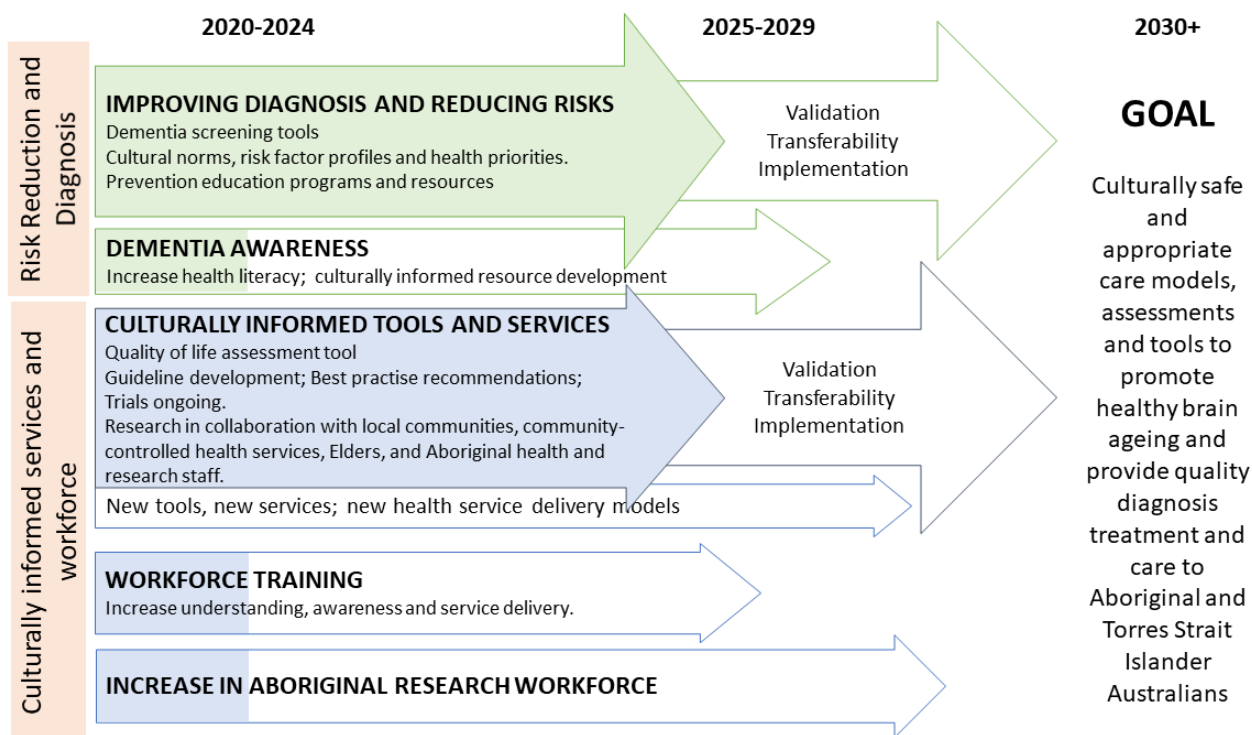
¹²⁷ Cox T, Wicking Centre UTAS

¹²⁸ Goldberg L

¹²⁹ Goldberg L, 2018-2019

Timeline for impact

Filled arrows indicate current funded projects. Clear arrows indicate projects required to reach goal.



Gaps in current research

No studies to date focus on the end of life period. Increased understanding of end of life decisions and care preferences will enable implementation of culturally sensitive care and supports during this period of life. Training programs for health care workers will be required.

Improving access to and delivery of care and engagement with health care services requires co-ordination and efficiencies between the health and social care systems and building collaborative relationships with Aboriginal and Torres Strait Islander communities. A limited amount of activity in this area is occurring in Tasmania. There are no funded studies exploring methods to integrate health care and social support services or investigating cross-sectoral service delivery.

Future funding considerations and requirements

Increased community awareness of dementia and engagement with services will be facilitated by further collaborative research that values Aboriginal and Torres Strait Islander knowledge systems to increase dementia health literacy among Aboriginal and Torres Strait Islander Australians. Further research will be required to identify service gaps and develop new tools and services to optimise dementia health care for Aboriginal and Torres Strait Islander Australians living in urban, regional and remote locations, broadening the focus from the acute and primary care setting to services in the home and community.

Dementia research in Aboriginal and Torres Strait Islander communities over the 2014-2019 period has been driven predominantly through targeted research calls. This includes five studies funded through the

targeted call for Dementia in Indigenous Australians¹³⁰, one study through the targeted call for Implementing Dementia Risk Reduction and Prevention Research¹³¹ and two studies through the targeted call for Implementation of Dementia Research into Clinical Practice and Care¹³². Two researchers were supported through BDRI NHMRC-ARC Dementia Research Development Fellowships¹³³.

Analysis of NHMRC funding in the three-year period prior to the BDRI's existence (2011-2013) found only one funded project focused on dementia in Aboriginal and Torres Strait Islander Australians¹³⁴. This illustrates the increased scope of projects that can receive funding when the specific needs of high-risk groups in the Australian population are recognised and targeted. This boost in research funding is likely to have significant impact for the communities where research is focused but will require further funding to ensure transferability of successful programs across Aboriginal and Torres Strait Islander communities, and to provide training to build the local workforce.

¹³⁰ LoGiudice D, Smith K, Eades S, Radford K, Sanson-Fisher R

¹³¹ Strivens E,

¹³² Bryant J, LoGiudice D

¹³³ Smith K, Radford K

¹³⁴ LoGiudice D, Health Outcomes of Older Indigenous Australians- a 5 year follow up study of a population at risk (2010-2012)

PRIORITY FIVE

Retaining and building Australian dementia research capacity

Impact Summary

- Over 100 researchers have been supported by the BDRI since it was implemented. The majority of BDRI Fellows are working in Priority Two (New targets, new technologies, new treatments), with three funded researchers working in Priority Four (Aboriginal and Torres Strait Islander Australians and dementia).
- The launch of ADNeT has significantly improved Australian dementia research capacity, with a growing number of collaborators and projects. Continued funding will be required to support this initiative beyond its current funding term and increase its scope.
- Continued strategic oversight of Australia's dementia research sector will be required to allow coordinated approaches to research, sharing of research infrastructure, data and expertise, and growth and development of the dementia research community.

Overview

The focus of Priority Five is to retain and build Australia's research capacity through growth and support of the dementia research workforce, provision of research infrastructure, delivery of forums and meetings, and facilitating robust, cross-sectoral programs that engage government, industry, philanthropy and consumers responding to a unified research strategy.

Progress towards impact

1. Researcher support

Under the BDRI, more than 100 researchers received four-year Fellowships at early to mid-career level, representing over one million hours of research activity. This investment has strengthened research teams and led to new collaborations across Australian universities and medical research institutes. The BDRI supported 75 NHMRC-ARC Dementia Research Development Fellowships (2016-2019) and 32 Boosting Dementia Research Leadership Fellowships (2017-2020) (Table 1).

Additional fellowships supporting dementia researchers have been granted through the NHMRC (Table 1). The majority of the fellowships granted since 2018 (34 of 44 Fellowships) focus on seeking new targets, new technologies and new drugs, with five fellowships each supporting research to improve early diagnosis and improving quality of life and quality of care.

Of the 12 fellowships supporting dementia research provided through the ARC, the majority are focused on Priority Two activities (Table 1). **Table 1:** Number of fellowships supported by the BDRI, NHMRC and ARC according to fellowship level.

			2016	2017	2018	2019	2020	2021	2022	2023	2024
Earlier Diagnosis and Prevention	BDRI	Early career	14	14	14	14					
		Mid career		6	6	6	6				
		Leadership									
	NHMRC	Early career			1	1	4	4	3	3	
		Mid career					-	-	-	-	
		Leadership					2	2	2	2	
ARC	Early career			1	1						
New targets, new technologies, new drugs	BDRI	Early career	41	41	41	41					
		Mid career		17	17	17	17				
		Leadership									
	NHMRC	Early career			2	12	13	13	11	1	
		Mid career			1	3	5	5	4	2	
		Leadership			3	6	16	16	13	10	
ARC	Early career	1	2	2	4	3	3				
	Mid-career	5	5	3	1	1	1	1	1		
	Senior					1	1	1	1	1	
Quality of life and quality of care	BDRI	Early career	18	18	18	18					
		Mid career		9	9	9	9				
		Leadership									
	NHMRC	Early career			1	2	2	2	2	1	
		Mid career				1	1	1	1		
		Leadership			2	2	2	2			
ARC	Early career	1	1								
Aboriginal and Torres Strait Islander Australians and Dementia	BDRI	Early career	2	2	2	2					
		Mid career									
		Leadership		-	-	-	-				
	NHMRC	Early career					-	-	-	-	
		Mid career					-	-	-	-	
		Leadership					-	-	-	-	
ARC	Early career	-	-	-	-						

2. Research capabilities

The launch of ADNeT, has significantly increased Australia’s dementia research capabilities. ADNeT received just over \$18M funding for the period 2018-2023. Bringing together Australia’s dementia stakeholders and through strong linkages with consumers, community groups, service providers, charities and industry bodies, ADNeT aims to improve care, expand access to specialist services and advanced diagnostic methods, and speed the development of effective therapies and disease prevention strategies for all Australians.

Through ADNeT, people living with dementia, and volunteers with, and at high risk of, cognitive decline will be registered and prepared for participation in clinical trials and other research programs. The registry will include high level, detailed information on treatments, imaging, biomarker analysis, environmental and psychological information. This will enable the sharing of genetic/genomic and phenotypic data across Australian research and clinical practice communities. In addition, ADNeT will focus on improved services in

Australia's network of memory clinics, including improved access to diagnostic services as well as post-diagnostic care, a national network and national harmonisation.

The Clem Jones Centre for Ageing Dementia Research received \$10M through the MRFF. This will be used to support research in the use of ultrasound technology to delay the effects of Alzheimer's disease. Researchers at the University of Sydney were awarded a \$2.5M NHMRC Centre of Research Excellence to Optimise Sleep in Brain Ageing and Dementia¹³⁵, which will focus on knowledge gain, trials, technology and building national capacity. Researchers at Macquarie University¹³⁶ received \$3M of MRFF funding to conduct an Australian version of the worldwide FINGERS trial (called AU-ARROW), which will focus on multifaceted risk reduction techniques.

The Wicking Dementia Centre was established in 2008 at the University of Tasmania through the support of the JO & JR Wicking Trust. The Trust has provided ongoing support for research and educational activities through almost \$8M in research funding to 2018¹³⁷. The goal of Stage Three of the Wicking Dementia Centre was to improve dementia literacy across Australia. Across 2018-2019, this saw the establishment of new partnerships with industry groups and organisations across Australia to deliver the Understanding Dementia Massive Open Online Training Course. This program has enabled further funding support from the MRFF to develop programs to reduce dementia risk¹³⁸.

3. Improved monitoring

The BDRI has invested \$2.6M in improving data methods and statistics to inform and support research through projects that seek to provide nation-wide monitoring, high quality data sets and analytic methods that provide reliable estimates of dementia incidence, prevalence and risk factors by different types of dementia¹³⁹. These will be essential instruments to allow evaluation of new diagnostic and preventative tools, monitor future health for allocation of funds/resources and to identify future research priorities. This work is being completed with involvement of the Australian Bureau of Statistics, Australian Institute of Health and Welfare and other health system agencies who currently collect and control dementia data.

These projects are likely to have immediate impact given the involvement of end users who will in parallel take up the improvements in methods and assessments of data quality in establishing a national dementia data asset for Australia. Projected timeline for impact is therefore at completion of project in 5 years.

Future funding considerations

The BDRI investment resulted in a significant boost to the capacity of Australia's dementia research sector. It is critical to ensure that this foundation for Australian dementia research is sustained and built upon, and the capabilities of the sector continue to grow and respond to community needs. This could include:

- Targeted support to boost capacity in underrepresented areas including aged care, general practice and Aboriginal and Torres Strait Islander communities. Researchers in all of these areas are much less likely to have followed a traditional academic career path. Avenues to foster their sustained engagement and recognition should be explored,
- Providing mechanisms to ensure sector-wide access to ADNeT,
- Provision of support to those joining the dementia research community who do not have established networks or collaborations. This could include state or national networking

¹³⁵ Naismith

¹³⁶ Martins

¹³⁷ https://www.utas.edu.au/_data/assets/pdf_file/0014/1212305/UOTWI190214-Annual-Report_vWeb_R2.pdf

¹³⁸ Vickers J, Wicking Centre University of Tasmania 2019

¹³⁹ Dobson A, Srikanth

opportunities for current or former BDRI-funded Fellows, peer support groups, focused roundtable sessions and active mentoring partnerships to facilitate introductions.

- Incentives to encourage cross-disciplinary collaborations to foster integrated approaches to improving outcomes for people living with dementia and their carers.
- Formal training and leadership programs to ensure early and mid-career researchers are armed with the skills they need to lead the national dementia research effort into the future. Dedicated sector leadership roles (e.g. chairs of working parties) could be considered to provide opportunities for emerging research leaders and build succession
- Sustained support for outstanding senior research leaders who are having research impact across all stages of the translation pipeline including biomarker discovery, early intervention and post-diagnostic care
- Building on the Australia Dementia Forum to further support coordination, collaboration and linkages across the entire dementia sector,

NNIDR established a Community and Consumer Involvement in Research program. Continuing support for this initiative will be critical to ensure the relevance and impact of the BDRI. It will be important to ensure active consumer involvement across all dementia research areas, recognising that there needs to be a diversity of consumer involvement across the life course and for different types of dementia. A concerted approach should be taken to recruit new consumers into this program to reflect this diversity and ensure that involvement is not onerous for contributors.

Core national capabilities and infrastructure are critical to advance dementia research in prevention, diagnosis, intervention, and care as noted by Pickett et al¹⁴⁰, This could include building on the successful establishment of ADNeT and other important sector resources (such as the CDPC, the DCRC, the Clem Jones Centre for Ageing Dementia Research, DTA), increasing alignment and involvement of practitioners, service providers and all relevant agencies across the dementia research sector and development of a national brain bank (building on current state-based initiatives) to facilitate coordinated access to brain tissue post mortem.

A recognised challenge in Australia is sourcing investment to enable promising research to be developed further. Some groups within the dementia research sector have found success through the MRFF scheme, while others will require other opportunities to implement, commercialise and upscale their research. Initiatives such as MTP Connect and the Biomedical Translation Fund could be explored for this purpose. One of ADNeT's roles is to attract biotech and pharma investment in dementia research in Australia, through provision of clinical trial design and access to patients and records. Partnerships will be required between researchers, ADNeT, international companies and other sources of funding to support translation, national and international impact of Australian dementia research. Continued sector-wide support of Australian dementia research will be required to allow coordinated approaches to research, sharing of research infrastructure, data and expertise, and growth and development of the dementia research community.

¹⁴⁰ <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6033035/>

Australia's Dementia Research Focus

1. Publications

A high-level analysis of dementia related publications was conducted in order to identify the emergence of dementia research areas in Australia since the launch of the BDRI in 2014.

Scopus searches were conducted to identify any publication originating from Australia in both 2014 and 2018 that included the keywords “dementia” or “Alzheimer”¹⁴¹. A detailed analysis of the author and indexed keywords for all publications was subsequently conducted using Vosviewer (Table 1).

Table 1: Vosviewer analysis of Australian dementia research hotspots by year of publication.

Year	Total publications	Keywords meeting initial threshold ¹⁴²	Keywords at end analysis ¹⁴³
2014	771	126	84
2018	1020	173	121

Vosviewer heatmaps present clusters of keywords in different intensities of colour and size, depending on the number of times keywords are mentioned in publications. The proximity of the words reflects co-use of keywords in publications.

Vosviewer heatmaps of Australian dementia research publication keywords at end analysis for 2014 (Figure 1A) and 2018 (Figure 1B) are shown below. It should be noted that the heatmap analysis reflects all dementia research-related publications arising from Australia and not specifically those arising from BDRI funded research.

There were several notable differences between the time periods.

- There was a clear increase (30%) in volume of publications from 2014 to 2018. In addition, the 40% increase in keywords that were included in the heatmap indicates the emergence of a broader portfolio of dementia research in Australia during that time period.
- “Systematic reviews”, “clinical trials” and “practice guidelines” did not make the threshold in 2014 but did in 2018. Other areas which emerged in research outputs by 2018 were nursing, quality of life and physical activity / exercise.

The emergence of systematic reviews and clinical trials/practice guidelines in publication heatmaps by 2018 is consistent with these areas being made possible by the longer term and larger scale funding provided by the BDRI. All of these approaches are an important foundation for dementia research and translation. Overall, the heatmap analysis is consistent with the BDRI enabling greater focus and productivity in the Australian dementia sector.

¹⁴¹ Scopus datasets used:

- TITLE-ABS-KEY (dementia) OR TITLE-ABS-KEY (alzheimers) AND AFFILCOUNTRY (australia) AND (LIMIT-TO (PUBYEAR , 2018))
- TITLE-ABS-KEY (dementia) OR TITLE-ABS-KEY (alzheimers) AND AFFILCOUNTRY (australia) AND (LIMIT-TO (PUBYEAR , 2014))

¹⁴² Threshold is keywords that occur greater than 25 times in the dataset

¹⁴³ Keywords were subsequently combined, for example human/humans, magnetic resonance imaging/nuclear magnetic resonance imaging etc, and journal specific keywords were removed, for example review, priority journal etc.

2. Clinical Trials Activity

Another indication of dementia research moving closer towards translation and impact is the growing number of clinical trials registered with the ANZ Clinical Trials Registry. During the period 2014-2016, 13 clinical trials were registered, which increased to 46 in the following three-year period (10 in 2017, 20 in 2018 and 16 in 2019). This is an excellent indication of the strengthening of the dementia research sector, with robust and high-level evidence expected in the coming years.

Conclusion

The analysis presented in this report is intended to provide a snapshot of research on dementia and cognitive decline that has high potential to provide a beneficial impact for the growing number of people living with dementia in Australia and their carers. This information is for leading agencies and initiatives, including the NHMRC, Dementia Australia and Dementia, Aging and Aged Care Mission¹⁴⁴, to inform future investment and funding strategies.

The study highlighted several key points:

- The impact of research on dementia and cognitive decline in Australia is growing but the future needs in each of the five research priority areas varies considerably. It is not a one-size-fits-all.
- The dementia research sector is a “tangled web” with many existing collaborations, partnerships, and synergies across the sector. Fostering, enabling and building connections across the sector that will be critical to enhancing further impact.
- The evidence of leverage of BDRI funding is widespread. This critical injection of funding has built capacity and capabilities across the sector but has also opened the door to a plethora of funding sources – many of which are co-funding major initiatives.

There are many lessons not only to be learned from the BDRI funding but from the experiences of other groups across the dementia sector in all disciplines. These lessons range from the challenges of facilitating genuine consumer involvement to ensuring access for under-represented groups or those new to the sector. Reinventing the wheel would be counterproductive. NNIDR had a vital role as the “honest broker” for Australian dementia research. It will be critical to build on this work to ensure that the effectiveness and inclusivity of the dementia research sector continues to grow for the benefit of the Australian community.

We thank all those who contributed to or commented on this report.

¹⁴⁴ <https://www.health.gov.au/initiatives-and-programs/dementia-ageing-and-aged-care-mission#:~:text=The%20Dementia%2C%20Ageing%20and%20Aged,care%20when%20they%20need%20it.>

