Alzheimer’s Research UK’s
Five-Year Research Strategy
2022
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Foreword

It really does feel like change is on the horizon. In recent years, the dementia research community has made profound advances in knowledge and understanding of the diseases that cause dementia. There are now, finally, treatments and tests within reach that are set to transform the options available to people affected by dementia.

This new dawn is, in large part, because of the research investment that’s been made to tackle the most challenging health issue of our time.

But generating knowledge on its own isn’t enough to bring these research breakthroughs to the clinic, and to the people who so urgently need them. So the challenge is to build on this knowledge to transform the lives of people living with dementia now and in the future. We have uncovered so many vital pieces of the complex puzzle of dementia – now we need to slot them together, while uncovering the remaining pieces.

Doing so will be no easy task. It will need a concerted effort on all fronts, driven by a research community that is well supported, collaborative and open to new ideas and ways of working.

As one of the world’s leading dementia research charities, at Alzheimer’s Research UK we have a proud track record of funding world-class work that catalyses progress, whether that be through supporting basic biological inquiry, drug discovery work, or early detection programmes. The charity’s recent growth means we are well placed to support the research community to deliver on the challenges that have been identified in this new five-year strategy.

I want to acknowledge the hard work and sharp insight from our Scientific Advisory Board, led by Professor James Rowe, that went in to developing this strategy. I’m excited that, for the first time, the charity will be stepping deeper into the clinical research space, as well as continuing its existing activity in fundamental and translational research. This is a testament to the profound advances that have brought us to this point and our supporters who have the vision and foresight to enable us to fund our ground-breaking research.

The strategy focuses on three areas – treatment, diagnosis and prevention – and in doing so, its primary goal is to deliver impact that is meaningful to people affected by, or at risk of, dementia. This is something we’ve kept at the forefront while developing it – most importantly by involving those affected by dementia in the process. Everything Alzheimer’s Research UK does needs to have a pathway to impact.

Now, more than ever, the research community will need to work together with funders, industry and people affected by dementia to tackle the challenges we face in the field. Our new strategy will act as a catalyst, making that happen.

With this strategy, I sincerely believe that the charity is primed to support the research community to solve the dementia puzzle – and deliver real, tangible, progress for the millions of people around the world who are affected by the devastating diseases that cause dementia.

Dr Susan Kohlhaas
Director of Research, Alzheimer’s Research UK
Dementia research – the story so far

Dementia is a global crisis. Here in the UK, nearly one million people are living with dementia, and it is consistently one of the leading causes of death.

Beyond this devastating impact, it affects so many others too. According to the second wave of Alzheimer’s Research UK’s Dementia Attitudes Monitor (2021), over half the UK population report that they know someone who was diagnosed with the condition.

And yet despite the terrible impact of dementia, and in stark contrast with other leading causes of death like heart disease or cancer, there are still no treatments available on the NHS that can slow or stop it.

- **1906** – Alzheimer’s disease first described by Alois Alzheimer. Researchers begin to study post-mortem brain samples of people who had died from dementia, and identify plaques and tangles.
- **1960s** – Researchers develop the first validated measurement scale for assessing cognitive and functional decline.
- **1970s** – Discovery of low levels of the neurotransmitter acetylcholine in those with Alzheimer’s disease. This lead to development of cholinesterase drugs to relieve symptoms.
- **1980s** – Discovery of amyloid-β and tau proteins as major components of plaques and tangles.
- **1990s** – Development of techniques to identify amyloid-β and tau in cerebrospinal fluid and blood, paving the way for improvements in dementia diagnosis.
- **2000s** – New imaging techniques, such as amyloid-β positron emission tomography (PET) are developed and begin to impact dementia diagnosis.
- **2010s** – Large genetic studies reveal new risk genes, yielding further clues as to the mechanisms driving Alzheimer’s disease.
- **2020** – Lancet Commission on Dementia sets out evidence for 12 modifiable risk factors that account for up to 40% of dementia cases worldwide.
- **2022** – Early trial data suggest anti-amyloid drug, lecanemab, can slow cognitive decline in people with early Alzheimer’s disease.

In terms of dementia research spending, the UK landscape has seen significant developments over the last decade, both in terms of direct investment in research, and with the establishment of world-leading initiatives, such as the UK Dementia Research Institute and Dementias Platform UK.

In the summer of 2022, the UK Government restated its commitment to double dementia research funding, and set out to launch a £95m Dementia Mission to accelerate the development of new treatments.

The word ‘dementia’ is an umbrella term for symptoms like memory loss, confusion and personality changes. It is caused by a number of diseases including:

- Vascular dementia
- Dementia with Lewy bodies
- Alzheimer’s disease
- Frontotemporal dementia
- Other rarer diseases

![Diagram](image.png)
Alzheimer’s Research UK – history and achievements

Founded in 1992 as the Alzheimer’s Research Trust, today the charity has grown to become the largest dementia research charity in the UK. Our early work was dedicated to supporting collaborative projects through a nationwide Research Network, as well supporting early career researchers to work in dementia. Our major focus until recently has been research seeking to understand the fundamental biology of the diseases that cause dementia.

Since its founding, Alzheimer’s Research UK has grown substantially, particularly in the last 10 years.

Our focus on funding the highest quality, collaborative and international-facing research has helped to increase our impact, and we have taken on a vital role as a catalyst for dementia research, using our investments to fill gaps and speed progress for people with dementia. More recently we have broadened our focus to include translational research, and we are now looking to bolster our clinical research activity in the coming years.

Since we were founded, we have invested more than £150 million in research which has contributed to major discoveries in the fields of drug discovery, diagnostics, genetics, and development of new experimental models.

Our research into genetics has contributed to the identification of more than 70 risk genes for Alzheimer’s disease, providing vital clues to new treatment approaches and opening new drug development programmes. For example, in 2012, our researchers identified mutations in an immune system gene called TREM2 that are linked to Alzheimer’s. Drugs that target TREM2 are now in development. We have also continued to make in-roads in rarer dementias – for example, work in frontotemporal dementia leading to an international consortium, contributing to the discovery of five new risk genes and a potential new diagnostic tool.

Our partnerships have had a major impact. The Insight 46 study, which we co-fund with the Medical Research Council, the Alzheimer’s Association of America and others, has advanced the understanding of dementia’s risk factors and the role of brain changes in its development. Since 2007, Brains for Dementia Research, a network of six brain banks funded in partnership with the Alzheimer’s Society, has distributed over 37,000 tissue samples to researchers, making more than 300 discoveries possible.
The UK Dementia Research Institute, established in 2017 with funding from the Medical Research Council, Alzheimer’s Research UK and the Alzheimer’s Society, has increased dementia research capacity in the UK. The Institute now has over 750 scientists working in dementia research and has contributed to key discoveries in neurodegeneration research, including studying potential links between COVID-19 and dementia.

As well as fundamental research, our strategic investments have led to a shift towards translational research in the UK, as exemplified by our Drug Discovery Alliance. With over 80 scientists working across three institutes, the DDA is working on more than 20 different targets in dementia research, has formed over 135 collaborations in 11 different countries and has leveraged an additional £20 million from external investors, on top of our total investment of £55 million to date. The Alliance has been responsible for broadening out the targets being investigated in dementia research into fields such as neuroimmunology, lysosomal biology and synaptic health. It is now poised to expand its work in future through partnerships.

More than half of the discoveries funded by Alzheimer’s Research UK have involved international collaborations. Our scientists have worked with researchers in over 72 countries across the world to advance dementia discoveries.

The proportion of ‘Open Access’ research we fund, (i.e published research that is accessible to all) has doubled in the past 10 years – as of 2019 over 90% of the discoveries we’ve funded are open to all.

Recognising that a major barrier to improving outcomes for people affected by dementia is a lack of timely and accurate diagnosis, we recently established our Early Detection of Neurodegenerative diseases programme (EDoN). This pioneering programme aims to develop and test new digital technologies that can detect subtle signs of the diseases that cause dementia 10-15 years earlier than current methods. This, in turn, can give people opportunities to participate in research earlier, increasing the chances of finding effective treatments.

Thanks to 30 years of investment, hard work and progress, we are now at a tipping point.
The challenges ahead

Although funding levels have increased in recent years, dementia research has still been under-funded compared with other disease areas that pose similar health challenges.

Beyond limitations in investment, we believe there are three key challenges that, if overcome, will transform the lives of millions who are set to develop dementia in the years to come. All of these challenges will need to be met with advances in fundamental science, as well as a multidisciplinary approach.

1. The urgent search for treatments

The most pressing challenge is the search for treatments that either delay, or even halt, the progression of dementia. While there have been major setbacks in the field over the years, the announcement in October 2022 from the CLARITY-AD clinical trial points to a hopeful future. The trial’s key finding - a small but statistically significant slowing of cognitive decline with the anti-amyloid drug lecanemab - is an historic milestone. Nevertheless, the drug still faces significant regulatory hurdles. Right now, there are currently no disease modifying treatments approved for use in the UK.

The lecanemab results are cause for cautious optimism, and other anti-amyloid trials are due to report in the near future. However, given the complexity of dementia, truly life-changing treatment will likely involve a multi-pronged approach, potentially using several treatments in combination to tackle different aspects of a disease. This will require a much more detailed understanding of the underlying processes driving the development of dementias, including rarer, non-Alzheimer’s dementias. This necessitates research that focuses on a broad range of mechanisms, rather than a narrowing of focus. And beyond the development and testing of treatments that target different mechanisms of action, a future challenge is to develop tools and approaches that make late-stage clinical trials less risky.
2. The need for next-generation diagnostics

Many people with dementia are diagnosed late on in their disease course, when clinical symptoms are all too apparent and often already impacting their lives. However, the brain changes associated with the different diseases that cause dementia can begin decades before clinical symptoms appear. Treatments that alter the course of dementia may be more effective if given earlier, so this will require earlier and more accurate diagnosis.

Blood-based biomarkers to support earlier and accurate diagnosis have been developed – the challenge will be translating their use into clinical practice. Similarly, improvements in understanding the molecular nature of the diseases that cause dementia will need to be accompanied by ways to diagnose people with these different types and subtypes. A further challenge is to diagnose mixed dementias, and different aspects of dementia pathology, to allow a more personalised, targeted approach to treatment.

Digital technology offers the possibility of measuring the very earliest changes in symptoms for people with diseases that cause dementia, far more sensitively than current diagnostic techniques.

3. Reducing the risk of dementia

In 2020, the Lancet Commission on Dementia identified 12 modifiable risk factors linked to the development of up to 40% of dementia cases. Interventions against these factors could reduce dementia rates. The Commission report also highlighted that those living in the most deprived areas have the highest risk of dementia, and so have the most to gain from such interventions.

It’s become clear that these risk factors are complex and interrelated, and associated with other disease areas – a picture that will need work to clarify. Studies of genetic risk factors have yielded clues into potential treatment avenues, but there is more to do to determine how genes and environment interact to influence dementia risk. Dementia organisations will need to collaborate with others to work out how to change individual and societal risk of dementia, and there are major challenges in getting underserved groups into research, to develop preventative approaches that work for all sectors of society.

Alzheimer’s Research UK has a track record of working collaboratively to build on progress that’s already been made to tackle the bottlenecks faced by dementia researchers. We will continue to use our funding to catalyse research into the areas that have remained under-addressed.
Our Research strategy

This research strategy has been developed in collaboration with our Scientific Advisory Board, with input from people affected by dementia. It identifies and addresses the major opportunities to advance dementia research over the coming years.

Reflecting the three main challenges we've identified in dementia research, we have distilled our research strategy into three priority areas that must be tackled to make a difference to people's lives: treatment, diagnosis and prevention. While our new strategy focuses on these, it’s important to acknowledge that progress in all of them will be driven by continued progress in fundamental understanding of the biology of the diseases that cause dementia.
Treatment

We will accelerate the search for treatments that slow the course of dementia, and tackle its symptoms.

The last five to ten years have seen an explosion of new strategies and targets that could lead to promising treatments. As of early 2022 there were 230 dementia trials ongoing, and for Alzheimer’s disease there are now 143 treatments in 172 trials covering a broad range of treatment mechanisms. Continued investment in translational research is required to move discoveries from the laboratory into clinical trials as quickly as possible.

It will be vital to identify, develop and test a range of treatments to serve the wide spectrum of people affected by dementia, building on the work of initiatives like our Drug Discovery Alliance. These alternative approaches must go beyond the amyloid hypothesis. Research that broadens our understanding of disease mechanisms will broaden our treatment options.

We will:

• Launch Clinical Trials Groups for dementia across the UK, to develop and promote innovations in dementia clinical trial design, outcome measures and delivery mechanisms, providing a pathway for novel and repurposed medicines to be studied at pace.

• Invest in research to understand mechanisms of the diseases that cause dementia through our response mode grant rounds, our strategic partnership with the UK Dementia Research Institute and international partnerships.

• Continue to foster and invest in interactions between academic research and industry, such as our Drug Discovery Alliance and the Dementia Discovery Fund, to increase the range and breadth of treatments that go into clinical studies.

• Work in partnership to promote engagement and recruitment in underserved communities.

“As a clinician seeing patients in the NHS I am all too aware of the devastating effects that dementia has on individuals and their families. While there is much that we can do to help and to support people now, we are desperately in need of better diagnostics and new treatments that are proven to help. As a researcher, I can see that major advances are just around the corner.

“I am delighted therefore that Alzheimer’s Research UK’s new research strategy includes further expansion into the clinical research space, and I am excited that this will accelerate the translation of research findings through to tangible changes which will make real differences to patients.”

Prof Jon Schott
Chief Medical Officer, Alzheimer’s Research UK
Diagnosis

**We will develop early, fast, and accurate ways to diagnose dementia.**

Recent advances in blood biomarkers have enabled the detection of Alzheimer’s disease pathology with similar accuracy as PET and cerebrospinal fluid tests. Implementation of blood-based biomarkers within the NHS provides the opportunity to scale-up diagnostics to people with early symptoms of dementia and people at high risk. This will, in turn, provide opportunities for people in earlier stages of dementia to take part in research.

New digital technology may be able to increase the early detection of the consequences of brain changes, before symptoms are noticeable or disabling, and may enable people to participate in trials at an earlier stage, where treatments are more likely to be effective.

We need new tools and expanded clinical training to differentiate between different forms of dementia. As well as providing better care for people with dementia, better diagnosis will improve drug development and clinical trials.

**We will:**

- Develop and validate new tools that **harness advances in technologies**, including digital technologies, to detect early changes in brain function with a high degree of sensitivity through the Early Detection of Neurodegenerative diseases programme.

- Fund research to **develop novel diagnostic tools**, including digital tools, genetic, fluidic and imaging tests, to detect the earliest signs of dementia and quantify dementia risk.

- Fund research to develop diagnostic tools and biomarkers to **differentiate between forms of dementia**, prioritising tools that have potential to increase impact of future treatments.

- Fund research to validate novel detection tools across **different populations** and invest in activities that **implement new technologies** into diagnostic pathways.

“When I found out that I have inherited the gene that caused my mum’s dementia, it was an incredibly tough thing to hear. But there was also a massive sense of relief. Not knowing was a burden I couldn’t live with.

“The progress being made in dementia research gives me hope that we’re heading towards a revolution in the way dementia is diagnosed and treated, so I won’t have the same experience as my mum. And I believe that, with its new strategy, Alzheimer’s Research UK will be leading the charge.”

Jordan Adams

**Jordan’s mother’s dementia was caused by a rare faulty gene that he has inherited, meaning he will also develop dementia in around 20 years’ time.**
Prevention

We will improve understanding of the modifiable risk factors associated with dementia and make progress in risk reduction.

To reduce the number of people who develop dementia, research must identify and test interventions that are relevant to people of all backgrounds. Dementia prevention strategies are likely applicable across the whole lifespan. Therefore, supporting good brain health may require working with age-groups, communities, funders and policy-makers who have not traditionally been engaged with the challenge of dementia.

We will:

• Fund research that improves our understanding of the risk factors associated with dementia and how they inter-relate through our response mode grant round and in partnership with others.

• Collaborate to develop and test interventions to prevent dementia, bringing in perspectives and opportunities from other disease areas.

• Work across academic, health and public health sectors to ensure that underserved populations are included in research related to prevention and risk reduction.

“My career so far has been focusing on understanding the underlying genetic causes for Alzheimer’s disease. Now is the time for us to build this knowledge into ways of helping people susceptible to developing dementia. Dementia research organisations, policy makers and the public health sector must work together to develop preventative approaches that work for people from all backgrounds and sectors of society.”

Prof Julie Williams
Director of UK Dementia Research Institute, Cardiff
Research Culture

**We will ensure the research environment in the UK is conducive to rapid progress.**

As the UK’s leading dementia research charity, Alzheimer’s Research UK has a duty to foster a research culture that will accelerate progress in research. We will continue to encourage and promote open science, data sharing, public engagement in research, and we will measure impacts that matter most to people affected by dementia.

In addition to this, we’ve identified three priority areas that need a step change if we are to achieve our ambitious strategy.

**Equity, Diversity, and Inclusion in research**

Treatments and interventions are needed for everyone affected by, or at risk of, dementia regardless of background. Lack of diversity in research exacerbates inequalities in healthcare, education, and outcomes. It is vital that treatments meet the needs of everyone who may face dementia. We will work with others to increase the number and proportion of people from underserved communities in research. As a funder we will ensure our grant holders are developing equity, diversity and inclusion plans in their work.

We believe that diversity in the research workforce will lead to better and more relevant research with greater long-term impact. Researchers from different backgrounds are more likely to consider and overcome different barriers and improve opportunities for research participation from underserved communities. Our early careers programme will specifically promote diversity and inclusion in science.

**We will**

- Change our **impact framework** to ensure we collect information in inclusive ways that capture impacts that are often unacknowledged in academic research but important to building an inclusive community. These could include, but are not limited to, public engagement and outreach, supporting and mentoring of researchers new to the field, and collaborations across disciplines.

- Ensure that our **events programme** is inclusive, offering flexible programmes that enable individuals with caring responsibilities to participate.

- Ensure that the research we fund includes **plans for equity, diversity and inclusion**.
Patient and public involvement

Patient and public involvement in research seeks to ensure that research is relevant and delivers outcomes that are important to people affected by dementia. We have involvement activities that complement our research programmes but we can, and will, do more to improve patient and public involvement in research.

**We will**

• Grow and improve patient and public involvement, seeking and building on feedback from people affected by or at risk of dementia. We will **train and support** people affected by dementia so they can contribute to our decision-making processes in a meaningful way.

• Support the research community, through our Research Network, to **develop public engagement and involvement activities** and to expand their breadth and reach to include underserved communities.
Networking and collaboration

An important aspect of a research programme is the depth and diversity of the collaborations it forges. Collaborations can foster new ideas and be greater than the sum of their parts. Having the time, space, and resources to build meaningful collaborations is essential.

Alzheimer’s Research UK funds a multi-centre Research Network around the UK which brings together researchers from different institutions. The future objectives of the Network will include fostering interdisciplinarity and collaboration in research, supporting early career researchers to establish themselves in dementia research, engaging and involving patients and the public in research, and sharing examples of best practice across the UK.

We will

• Continue to hold an annual conference to provide researchers from around the world the opportunity to present their work, hear from others and make connections.

• Promote and incentivise multidisciplinary collaboration through our funding schemes, networks and events including enhancing clinical involvement in our Network.
Beyond open grant rounds

The scale of the challenge we face in dementia requires a bold approach. As well as continuing to fund research through our regular open grant rounds, we will develop specific research calls, partnerships and initiatives that help answer our greatest challenges. The exact shape, timing, and scale of focussed calls will be tailored to the specific topic to be addressed.

**We will scope and fund one or two focused areas per year.**

Outlined below are key areas we will continue to develop to progress our strategy.

### Accelerating translation

Alzheimer’s Research UK has already framed many of our strategic initiatives around addressing the barriers to translation, and we will continue to actively address gaps in research translation.

We will ensure that all our funded research has a clear pathway to impact, and we will define and develop a programme to address issues with reproducibility in research. We will work actively with grant holders to understand and support the next steps to their research, whether through further Alzheimer’s Research UK programmes or via alternative funding mechanisms.

We will support cross-sector translational programmes and initiatives such as the Dementia Discovery Fund that support translation and foster commercialisation of research for patient benefit. We will review the way we identify Intellectual Property from the research we fund so that we increase the likelihood of generating impact for people affected by dementia, and we will explore different commercialisation models to help realise impact sooner.

### Strategic partnerships

Partnerships are the lifeblood of Alzheimer’s Research UK’s research programme. Our partnerships:

- Leverage knowledge and experience from other fields, industries or capabilities into research.
- Foster innovation.
- Bring cost savings that make our investments go further.

Strong partnerships between government, industry, academia and the third sector are essential to making more rapid progress in dementia research. Alzheimer’s Research UK has substantive experience in bringing the right stakeholders together for the benefit of dementia research.

We will continue to develop new partnerships that help us achieve our strategic objectives and will encourage, guide and support researchers to do so as well.
Our Research Strategy – ongoing governance

This Research Strategy has been approved by our Board of Trustees with input and advice from our Scientific Advisory Board. Following its publication, we will develop milestones and an implementation plan to be reviewed on an annual basis by our Scientific Advisory Board and Board of Trustees, and amended as necessary.

Our Scientific Advisory Board will recommend funding initiatives, partnerships and new activities throughout the life of our Research Strategy. Our strategic initiatives and response-mode funding will be overseen by individual panels and boards comprising experts in the field.

The research we fund will be peer-reviewed, assuring it is of the highest quality, with planning and monitoring of the pathways to impact. Each project is reviewed by a panel comprising of experts in the field. Where appropriate, we will also have people affected by dementia review the research we fund to advise on its relevance.

We will continue active membership of the Association of Medical Research Charities and ensure we meet best practice in research governance.

“I hope that research will help to improve the lives of people living with dementia in the future.

“I want to see improved diagnosis so other people won’t have to go through the lengthy and difficult process I have gone through, and for breakthroughs in research to lead to new treatments and preventative methods that will protect future generations.”

Imran Sherwani
Former GB men’s hockey player and Olympic Gold medallist

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