Department of Health & Social Care
Major conditions strategy: call for evidence

Submission from UK Dementia Research Institute (UK DRI)
27th June, 2023

About you

In what capacity are you responding to this survey?

> An individual sharing my professional views such as a healthcare professional or on behalf of my organisation

Your organisation

Which of the following best describes how are you responding to this survey?

> As an academic, researcher or on behalf of a university

What is the name of your organisation (or organisations if submitting a joint response)?

> UK Dementia Research Institute (UK DRI)

Contacting you

Are you happy to share your email address with the Department of Health and Social Care?

> yes

What is your email
address?

> o.marshall@ukdri.ucl.ac.uk

**Priorities for the next 5
years**

Would you like to answer questions about cardiovascular diseases?

> No

Would you like to answer questions about chronic respiratory diseases?

> No

Would you like to answer questions about dementia?

> Yes

Would you like to answer questions about musculoskeletal conditions?

> No

Would you like to answer questions about cancer?

> No

Would you like to answer questions about mental health?

> No

Dementia

In your opinion, which of these areas would you like to see prioritised for dementia? (Select up to 3)

Preventing the onset of dementia through population-wide action on risk factors and wider influences on health (sometimes referred to as primary prevention)	
Delaying the progression	X

of dementia through clinical interventions for individuals at high risk (sometimes referred to as secondary prevention)

Getting more people diagnosed quicker	X
Improving treatment provided by urgent and emergency care	
Improving non-urgent and long-term treatment and care to support the management of dementia	X

Tackling the risk factors for ill health

Do you have any suggestions on how we can support people to tackle these risk factors?

Yes

Suggestions for tackling the risk factors for ill health

Modifiable risk factors account for about 40% of worldwide dementias (The Lancet). The contributing environmental and lifestyle factors are highly complex and not fully understood. Further investment into research will improve our understanding and facilitate the effective targeting of preventative interventions, promoting health equity. Relevant UK DRI programmes include:

• Professor Paul Elliott (UK DRI Group Leader, Imperial) studies how environmental, lifestyle, genetic and metabolic risk factors interact to determine our dementia risk. Using powerful technologies and sophisticated data analyses, Elliott hopes to uncover subtle shifts, which will reveal new insights about neurodegenerative diseases and how to prevent them.

• Professor Joanna Wardlaw (UK DRI Group Leader, Edinburgh) and her team study the heart-brain connection, and the determining factors – including socioeconomic status – that influence cognitive decline. They are also researching preventative interventions, running one of the few randomised clinical trials in the world that uses drugs to prevent vascular dementia, known as the LACI trials. These show considerable promise for preventing vascular causes of cognitive decline.

• Professor David Sharp (UK DRI Centre Director, CR&T) is analysing lifestyle data, taken from a range of digital devices, of people in the early stages of disease. This enables researchers to look upstream and identify patterns that may have contributed to their disease and investigate factors that influence variation in disease progression, including co-morbidities like infection. The team has developed new digital approaches to monitoring people in their homes that promise to provide new approaches to slowing disease progression and improving the quality of life of people affected by dementia.

Research into genetic risk will enable the stratification of the population into high- and low-risk groups for disease, based on inherited factors. This research is very promising and needs further support. This stratification will facilitate effective targeting of prevention interventions, and the concentration of resources where they are most needed, helping to tackle health inequality.

• An expert in 'big data', Prof Valentina Escott-Price (UK DRI Group Leader) uses large datasets to identify total genetic risk (genetic liability) to neurogenerative disorders. Using computational approaches to make sense of increasingly large sets of genetic data and electronic health records, she is aiming to redefine how dementia risk is detected and understood.

• Professor Julie Williams (UK DRI Centre Director, Cardiff) conducts pioneering research into how our genes influence our risk of Alzheimer's disease, including working on the 92 risk genes now identified, and developing a genetic test which can predict the risk of Alzheimer's with 80% accuracy.

NB: Most dementia cases are unlikely to be preventable through primary prevention. (In Alzheimer's, genes contribute around 70% of the risk.) However, there is a wide window for secondary prevention, since neurodegenerative diseases are present years/decades before symptoms emerge. It is critically important that the Government supports research into biomarkers (including genetics), to enable disease detection well before symptoms appear. The UK DRI has several active work programmes on biomarkers and tools for early detection, including fluid, digital and functional markers. Please see the following question.

Supporting those with conditions - supporting local areas to diagnose more people at an earlier stage

Do you have any suggestions on how we can better support local areas to diagnose more people at an earlier stage?

Yes

Suggestions for dementia

Accurate diagnosis of dementia (including sub-typing) is challenging. Current methods are resource-intensive (PET scanning) and invasive (CSF testing). With new treatments for Alzheimer's disease now emerging, there is an urgent need for scalable, accessible and affordable diagnostic tools, to identify suitable candidates for treatment at an early enough stage of disease. The Government should urgently invest in promising research programmes to develop these tools, which will improve access to, and equity of, diagnosis. Programmes include:

• Fluid biomarkers: The UK DRI Biomarker Factory is a high-performance analytical platform for fluid biomarker development, validation and measurement. This includes biological signals found in the blood, paving the way for diagnostic blood tests for neurodegeneration. Led by Prof Henrik Zetterberg (UK DRI Group Leader, UCL), the platform accepts samples from researchers and companies internationally, accelerating progress across the whole research community. A diagnostic blood test would be deliverable in a range of healthcare settings, dramatically improving access to timely diagnosis.

• Digital biomarkers: Biological changes can be detected by digital technology, paving the way for new methods of detecting and measuring disease. The UK DRI's Minder platform, led by Professor David Sharp, facilitates personalised care by collecting health monitoring data in the home, in unprecedented detail and in real time. These data may also accurately measure disease presence and progression. Sharp is currently researching whether data generated by an inexpensive and commercially available sleep mat is an accurate indicator of neurodegenerative disease status and progression – opening the possibility remote detection in the future.

• Functional biomarkers: Dr Marc Aurel Busche (UK DRI Group Leader, UCL) is working to identify a neurophysiological marker that, if successful, will reveal subtle changes to the brain's circuitry at an early stage of Alzheimer's, before the tipping point into irreversible cognitive decline. Busche and his collaborators will harness a technique called whole-brain magnetoencephalography (MEG) and machine learning, to explore how different forms of neural replay – a well understood phenomenon involved in learning and spatial memory – are affected during the progression of Alzheimer's disease.

• Genetic risk: Professor Julie Williams (UK DRI Centre Director, Cardiff) conducts pioneering research into how our genes influence our risk of Alzheimer's disease, including working on the 92 risk genes now identified. Prof Valentina Escott-Price (UK DRI Group Leader) uses large datasets to identify total genetic risk, aggregating risk across all genes and integrating interactions between them. With more support, it will soon be feasible to stratify the population into high-risk and low-risk groups for neurodegenerative disease, based on inherited factors, as well as predict the disease age at onset and progression patterns. This will enable the targeting of diagnostic resources towards higher risk groups.

• Routinely collected electronic health records provide a rich source of data across the whole population. The Care Research & Technology Centre are developing new approaches to screening individuals affected by dementia for poor clinical outcomes, such as hospital and care home admission. The goal is to provide AI-guided algorithms designed to identify individuals at risk of developing dementia, or of rapid clinical decline.

Supporting those with conditions - supporting and providing treatment for people after a diagnosis

Do you have any suggestions on how we can better support and provide treatment for people after a diagnosis?

Yes

Suggestions for dementia

There are currently no disease modifying therapies for dementia. Due to historic underinvestment in discovery science, the dementia research pipeline is underpowered, and there is a large gap in our basic understanding. This is starting to change due to recent Government investment, but much more support is needed. With an ageing population, this additional resource is urgent.

Compared with similarly complex disease areas like cancer, our understanding of neurodegeneration lags behind, and we have fewer researchers, publications, clinical trials and available treatments:

• In the UK, for every one dementia researcher there are four researchers working on cancer.
• Globally, since the year 2000, 2,500,000 papers have been published on cancer, compared with under 180,000 on Alzheimer's disease.
• Since 2000, nearly 90,000 clinical trials have been run in cancer, compared with under 3,000 in Alzheimer's disease.
• The FDA has approved over 200 drugs for cancer since 2000, compared with just seven for Alzheimer's disease.

In cancer, strategic investment into research has yielded vital breakthroughs for patients, attracted £billions in investment from industry and created jobs: a recent analysis by CRUK estimated that every £1 invested in cancer research generated £2.80 of economic benefit. Even now, with a more mature research pipeline, Cancer Research UK still invests a large proportion (41%) of its research funds into discovery science, recognising that this is the engine that drives progress.

The same principle must now be applied to all neurodegenerative diseases. To make new treatments possible, create jobs and attract investment, the Government should strategically direct funding towards discovery science.

Government should also invest in innovative platforms and methodologies that could transform how clinical trials are conducted. This will incentivise external investment and accelerate progress for patients. Examples at the UK DRI include:

• MND-SMART: Researchers at the UK DRI at Edinburgh, led by Prof Siddharthan Chandran, are developing MND-SMART: a pioneering trial platform that will accelerate the delivery of urgently needed treatments. Unlike typical clinical trials which test a single treatment, MND-SMART is testing more than one at the same time. This means people in the trial are more likely to receive an active treatment compared to standard clinical trials where half of the participants receive a placebo.

• Digitally enabled clinical trials in the home: The UK DRI Care Research & Technology Centre (CR&T) is developing the Minder platform, which facilitates the continuous monitoring of health data, passively, from the home. This enables personalised care and joined-up service provision (please see other answers). In the future it may also enable clinical trials in the home, collecting continuous health data in real time for accurate measurement of progress/drug impact, and dramatically broadening access to trial participation.

• LACunar Intervention Trial-3: Researchers at UK DRI Edinburgh are developing a platform trial in small vessel diseases, the commonest cause of vascular dementia. This will test readily available drugs that showed strong promise in LACI-2 (see earlier) as well as other repurposable drugs with relevant modes of action, and enabling efficient testing of novel agents emerging from discovery science.

Supporting those with conditions - enabling health and social care teams to deliver person-centred and joined- up services

Do you have any suggestions on how we can better enable health and social care teams to deliver person-centred and

joined-up services?

Yes

Suggestions for dementia

The UK DRI is conducting research that could radically transform the provision of care services, harnessing advances in AI and digital technology to facilitate personalised care in the home, link services, and shift the emphasis from treatment to prevention. Innovative modes of care delivery are now possible and could bring major benefits for people living with dementia, their carers, and social care and NHS services.

The use of data and digital technology in care provision facilitates highly personalised care provision. The UK DRI Care Research & Technology Centre (CR&T) is developing and translating technologies to enable people with dementia to live well, in their own homes. A diverse team of doctors, engineers and scientists, led by Prof David Sharp (UK DRI Centre Director at CR&T), is harnessing advances in artificial intelligence, engineering, robotics and sleep science to build a new platform that delivers the highest quality personalised care to people with dementia in their own homes. The team is guided by people with dementia and their caregivers, and investigates ways to keep people independent, improve their general health and sleep, and reduce confusion and agitation. The Minder platform synthesises data from sensors and devices around the home, such as sleep sensors or Alexa devices, to detect signs of problems early and minimise the risk of hospitalisations. The goal is to empower people with dementia and their caregivers, by creating dementia-friendly 'Healthy Homes' – intelligent environments that transform and personalise care.

The Minder platform also creates an exciting opportunity for data integration, to link services together and enhance clinical decision making. Minder generates real-time data from the home, which may be combined with existing health and social care information to facilitate personalized and joined-up care provision across a range of public services: this is being explored in West London. Further research is also underway to develop computational methods to integrate Minder with electronic healthcare records, including complex data types such as neuroimaging. The combination of data from Minder with health and social care information would give a much more complete picture of a person's wellbeing on a variety of measures, and across a span of days and weeks, instead of a snapshot of information taken during a short appointment or visit. This will help clinicians and carers to make the best possible decision about those in their care.

Supporting those with conditions - use of research, data, and digital technologies to improve outcomes for people with, or at risk of developing, the major conditions

Do you have any suggestions on how we can make better use of research, data, and digital technologies to improve outcomes for people with, or at risk of developing, the major conditions?

Yes

Suggestions for dementia

Research: The Government should strategically direct investment towards dementia discovery science, to pave the way for new treatments and fill the knowledge gap in dementia. There are no shortcuts to new treatments in neurodegeneration, but with the right investment the UK is well positioned to lead the way towards breakthroughs – which will create jobs, attract additional investment, and make new treatments possible.

Digital technology and data: Government should explore new approaches to digitally enabled personalised care provision in the home, which is now possible for the first time due to recent advances in AI and digital technology. The UK DRI's Minder platform, currently in its pilot phase, has the following potential benefits:
- Improvement of personalised care for people with dementia
- Support for carers and families
- Prevention of hospitalisations through the early detection of health conditions such as UTIs, relieving pressure on NHS services
- Use of data to coordinate and join up personalised care provision across services, enhancing and augmenting clinical/care decision-making
- Development of digital biomarkers that can aid detection, diagnosis and measurement of disease progression
- Discovery / validation of lifestyle risk factors through analysis of data generated by people in early stages of disease
- In the future, digitally enabled clinical trials in the home, which would transform

clinical research in neurodegeneration and dramatically broaden access to participation in trials

Using routinely collected data: There is a lot of relevant information on brain health and dementia risk captured in routine, inexpensive brain scans, which are increasingly performed for a wide range of reasons. However, the data are not used to their maximum advantage. Professor Joanna Wardlaw (UK DRI Group Leader, Edinburgh) and colleagues are working alongside Health Data Research UK, BHF Turing and other initiatives, to develop digital methods to extract relevant features from routine reports and NHS brain scans, and to make this information more standardised and readily available. Data scientists, imaging experts and computer scientists are working together to extract relevant features from routine NHS imaging, and make the most of what is already easily available.

Supporting those with conditions - improving access to palliative and end of life care

Do you have any suggestions of how we can improve access to palliative and end of life care?

Yes

Suggestions for dementia

In the future, personalised palliative care may be delivered in the home, with clinical and care decision making augmented by data from passive digital devices. The UK DRI's Minder platform is making this possible, by harnessing advances in digital technology and AI to create a radically new approach to personalised care provision, in an environment where people are most comfortable.