The Academy of Medical Sciences

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Early detection of neurodegenerative conditions in primary care and the community

28 February 2024

Academy of Medical Sciences' FORUM workshop, held in partnership with Alzheimer's Research UK and Alzheimer's Society

Alzheimer's Society

ALZHEIMER'S RESEARCH UK FOR A CURE

Alzheimer's Research UK

Almost one million people are living with dementia today. Tragically, not one of them will survive. Alzheimer's Research UK exists to change that. As the UK's leading dementia research charity, Alzheimer's Research UK is working to revolutionise the way dementia is treated, diagnosed and prevented. They will then find a way to cure dementia. To do this, Alzheimer's Research UK are investing in the best research, powering the most forward-thinking scientists and joining forces with world-class organisations. They will not stop until dementia can no longer destroy lives. Alzheimer's Research UK exists for a cure.

Alzheimer's Society

Alzheimer's Society is the UK's leading dementia charity, working towards a world where dementia no longer devastates lives. They do this by giving help to those living with dementia today, and providing hope for the future. With one in three people born in the UK today set to be diagnosed with dementia in their lifetime, Alzheimer's Society provides direct dementia support services, funds dementia research, and campaigns for action on dementia in order to make dementia the priority it needs to be. Alzheimer's Society is made up of people living with dementia, carers, trusted experts, campaigners, researchers, clinicians and more, acting as a collective force with unparalleled knowledge and over 40 years' experience addressing the biggest challenges facing people living with dementia.

The Academy of Medical Sciences

The Academy of Medical Sciences is the independent, expert voice of biomedical and health research in the UK. Our Fellowship comprises the most influential scientists in the UK and worldwide, drawn from the NHS, academia, industry and the public service. Our mission is to improve the health of people everywhere.

The Academy of Medical Sciences' FORUM provides an independent platform for senior leaders from across academia, the commercial sector, government, and the charity, healthcare and regulatory sectors to come together with patients and take forward national discussions on scientific opportunities, technology trends and associated strategic choices for healthcare and other life sciences sectors.

Opinions expressed in this report do not necessarily represent the views of all participants at the event, the Academy of Medical Sciences, Alzheimer's Research UK, Alzheimer's Society or its Fellows.

All web references were accessed in July 2024.

Early detection of neurodegenerative conditions in primary care and the community

FORUM workshop on Wednesday 28 February 2024

Jointly hosted by the Academy of Medical Sciences, Alzheimer's Research UK and Alzheimer's Society

Contents

Executive Summary

This is a transformative time for detecting, diagnosing and treating neurodegenerative conditions. There is an opportunity to rethink current pathways and design a future-facing service to improve health and wellbeing outcomes and optimise the use of health resources.

Neurodegenerative conditions cause damage to the nervous system, particularly the brain. These conditions include Alzheimer's disease and other causes of dementia, and Parkinson's, amongst others. Detection and confirming diagnosis of most neurodegenerative conditions is challenging and often lengthy. Improving early detection of neurodegenerative conditions has many advantages that rely on timely access to support and treatment.

Improved early detection in primary care could help people get a timely diagnosis in secondary care. People could then access any emerging treatments and opportunities to participate in research studies earlier. There is some evidence that treating earlier may be more effective.[1,2,3] People could also address modifiable risk factors (such as high blood pressure, smoking and lack of physical activity) earlier, which may reduce symptom severity and delay progression.[4,5,6,7] Earlier detection could give people clarity about their symptoms, allowing them to plan ahead and take part in decision making.

Emerging tools for detecting neurodegenerative conditions include blood tests, digital tests of cognition, specialist eye scans, and artificial intelligence algorithms for interpreting data. Some tools could be used by primary care clinicians[8] in general practice, pharmacies, opticians and dentists, to explore the possibility that a person may have a neurodegenerative condition. They could then make faster, more accurate referrals to secondary care, leading to more focused use of secondary care resources and faster diagnosis.

To explore how to enable earlier detection of neurodegenerative conditions in primary care and community services, the Academy of Medical Sciences, Alzheimer's Research UK and Alzheimer's Society organised a FORUM meeting in February 2024. The meeting brought together people with lived experience of neurodegenerative conditions with primary and secondary care practitioners, funders and representatives from charities, academia and industry. Participants agreed the choice to participate (or not) in tests for neurodegenerative conditions should remain with the patient. Five priorities emerged from discussions:

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[1] Van Dyck C, *et al.* (2022). *Lecanemab in early Alzheimer's disease.* The New England Journal of Medicine **388(1)**, 9–12.
[2] Sims J, *et al.* (2023). *Donanemab in early symptomatic Alzheimer disease: the TRAILBLAZER-ALZ 2 randomized clinical trial.* JAMA **330(6)**, 512–527.
[3] JJ Cerqueira et al. (2018). *Time matters in multiple sclerosis: can early treatment and long-term follow-up ensure everyone benefits from the latest advances in multiple sclerosis?* Journal of Neurology, Neurosurgery and Psychiatry **89**, 844–850.
[4] Livingston G, Huntley J, *et al*. (2020). *Dementia prevention, intervention, and care: 2020 report of the Lancet Commission.* Lancet **396(10248)**, 413–446.
[5] Ascherio A, Schwarzschild M, (2016). *The epidemiology of Parkinson's disease: risk factors and prevention*. The Lancet Neurology **15(12)**, 1257–1272.
[6] Tsukita K, Samaki-Tsukita H, Takahashi R, (2022). *Long-term effect of regular physical activity and exercise habits in patients with early Parkinson disease*. Neurology **98(8)**, 859–871.
[7] Mukadam N, *et al.* (2024). *Changes in prevalence and incidence of dementia and risk factors for dementia: an analysis from cohort studies*. The Lancet Public Health **9(7)**, 443–460.
[8] Such as general practitioners, nurses, advanced clinical practitioners, pharmacists, physician associates and optometrists.

1. The case for early detection should be rigorously assessed, considering the whole pathway from detection to diagnosis and care

Early detection enables early diagnosis and treatment. Modelling and pilot studies are needed to predict and demonstrate that introducing tools in primary care can improve speed and accuracy of referral and diagnosis, and improve health outcomes. A health-economic case for early detection should be developed that considers impacts on and interactions between various parts of the health and social care system. Pre- and post-diagnostic support packages should be developed with input from people living with neurodegenerative conditions, to help people navigate detection, diagnosis and care. Pathway improvement should aim to reduce regional variability. Pathways should be co-designed with people who are living with, and affected by, neurodegenerative conditions.

2. Detection requires integration of multiple sources of data

Different tools may provide different information about the presence of disease, the risk of future disease, and changes in symptoms over time. A combination of tools may be required to provide complementary data. Primary care clinicians will need training to help them interpret and communicate this data. Methods (such as artificial intelligence) to integrate data from multiple sources and generate predictions could be useful as decision-aides to primary care clinicians. Standards developed in collaboration with primary care clinicians and people living with neurodegenerative conditions will be important, so that detection and referral is consistent across services. People should be supported to understand their results, their risks and the choices available.

3. Roles and responsibilities of health workers in early detection should be clarified across different primary care and community settings

In addition to the general practitioners, primary care clinicians from a variety of professions in general practice could be more involved in early detection. They could counsel people on test limitations, administer tests, interpret results, and manage referrals. Some tests could be used in other primary care and community settings including pharmacies, opticians, and pilot health services, such as the brain health services in Scotland.[9] Clarifying responsibilities, coordinating between services and providing relevant workforce training will be important.

4. A greater focus on early detection may require changes in mindset among clinicians, policymakers and the public

Neurodegenerative conditions are often considered to be untreatable or an unavoidable part of ageing, which may discourage people coming forward for early detection. There is growing awareness that symptoms may be a late-stage manifestation of declining brain health that could potentially be delayed or prevented. Lessons on prevention could be learned from disease areas like cardiovascular disease, including by building scalable, inexpensive brain health assessments into routine health checks. [10] Awareness should be raised amongst healthcare staff, policymakers, and the public of the evidenced benefits of maintaining brain health and early detection. A public brain health campaign based on recent progress could create hope and expectation that these conditions can be treated, delayed or prevented.

5. Equity, evidence and iterative improvement should underpin future developments

Access to detection and diagnostic services should be made equitable and inclusive – for example, removing financial barriers (e.g. for specialist eye scans). The rapid progress in this area should be reviewed regularly to highlight opportunities. Research should be embedded to iteratively improve detection, diagnosis and treatment of neurodegenerative conditions.

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[9] https://www.brainhealth.scot/brainhealthservices
[10] https://www.nhs.uk/conditions/nhs-health-check/

Proposed next steps

Workshop participants proposed next steps for earlier detection of neurodegenerative conditions in primary care and the community, and highlighted remaining evidence gaps. These are listed here in brief. For details of the full discussion, please see the full report below.

1. The case for early detection should be rigorously assessed, considering the whole pathway from detection to diagnosis and care

1.1. More evidence should be gathered about whether earlier treatment with pharmacological and non-pharmacological interventions is more effective for various neurodegenerative conditions, investigating whether effectiveness varies according to each stage of the disease. The potential causal relationship between lifestyle risk factors and different neurodegenerative conditions should be explored, and the impact of lifestyle modifications assessed.

1.2. How and when to embed opportunities to participate in clinical research alongside early detection should be investigated.

1.3. Current clinical pathways for people coming forward with symptoms of neurodegenerative conditions should be reviewed, including regional variations and health outcomes. The logistical and economic impact of introducing different detection tools on diagnostic and treatment pathways should be modelled.

1.4. Based on modelling data, the use of different tools should be piloted within various primary and community health settings and in different populations. Lessons can be learned from ongoing pilot schemes, such as the Blood Biomarker Challenge.[11] These pilot schemes could gather and consolidate real-world data on test usage, performance, impact on the detection and diagnostic pathway, and outcomes.

1.5. Pre- and post-diagnosis packages of information and support for people living with and affected by a neurodegenerative condition should be developed, to help people navigate the diagnostic journey. Medical charities and patient support groups may be well placed to do this.

1.6. The National Institute for Health and Care Excellence (NICE) should be encouraged to develop guidelines for the management, and eventually treatment, of mild cognitive impairment.

2. Detection requires integration of multiple sources of data

2.1. The feasibility and acceptability of integrating data from multiple sources/tests to assess a person's risk of a neurodegenerative condition (potentially using technologies such as machine learning/AI) should be investigated. Such technologies could be used to build a decision-support tool. The desired characteristics and communication preferences for a decision-support tool for use in primary care should be established, in collaboration with primary care clinicians and people living with neurodegenerative conditions.

2.2. It will be important to investigate what information people want from tests that detect neurodegenerative conditions and when, and how best to communicate about test results, health risks and the choices available to people who may have a

[11] https://www.alzheimers.org.uk/news/2024-04-04/uk-comes-step-closer-blood-tests-diagnosing-dementia

neurodegenerative condition. Existing guidance and approaches to communication in other disease areas, such as cardiovascular disease, should be learned from.[12,13]

2.3. Standardised criteria and data standards for the use of tools in detection, referral and diagnosis should be developed for different relevant neurodegenerative conditions at different stages, to improve consistency across services.

3. Roles and responsibilities of health workers in early detection should be clarified across different primary care and community settings

3.1. The circumstances in which it may be appropriate for practitioners in primary and community services beyond general practice to refer directly to relevant specialists should be considered, and the acceptability to various practitioners and the public explored.

3.2. The potential for different staff (such as nurses) in general practice to be involved in detecting neurodegenerative conditions, along with relevant training needs, should be explored.

4. A greater focus on early detection may require changes in mindset among clinicians, policymakers and the public

4.1. The training and continuing professional development of general practitioners and other relevant primary care clinicians should reflect the latest advances in the detection, diagnosis and treatment of neurodegenerative conditions.

4.2. Integration of brain health assessments into both pre-existing routine health checks and care plans for people with a condition that puts them at risk of developing a neurodegenerative condition should be explored.

4.3. The potential for an evidence-based public health campaign to promote brain health and prevention should be explored. Some workshop participants suggested that the government, in collaboration with medical charities, would be well-placed to deliver this campaign.

Taking forward many of these next steps would require a multi-stakeholder approach, particularly including input from people with lived experience of neurodegenerative conditions, those affected (including their families), and clinicians.

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[12] Patient Information Forum (2023). *Communicating benefits, risks and uncertainties.* https://pifonline.org.uk/resources/how-to-guides/communicating-benefits-risks-and-uncertainties/.

[13] Schulberg SD, *et al.* (2022). *Cardiovascular risk communication strategies in primary prevention. A systematic review with narrative synthesis.* Journal of Advanced Nursing **78(10)**, 3116–3140.

Introduction

More than one million people are living with a neurodegenerative condition in the UK.[14] Neurodegeneration happens when nerve cells in the brain and wider nervous system lose function over time. Neurodegenerative conditions include Alzheimer's disease and other causes of dementia (including but not limited to frontotemporal dementia, Lewy body dementia and vascular dementia), Parkinson's, and amyotrophic lateral sclerosis (ALS, also called motor neurone disease), amongst others. In the UK, with an ageing population, the numbers of people living with dementia specifically are projected to rise from an estimated 982,000 to 1.4 million by 2040.[15] Tackling dementia-causing diseases has been a national priority, demonstrated by the UK Dementia Mission.[16] The Mission was launched to speed up the development of new treatments and diagnostic tools.

Neurodegenerative conditions can be difficult to detect and diagnose. They are detected in primary care settings such as general practice. Diagnosis often requires specialist secondary care expertise and technologies such as structural magnetic resonance imaging (MRI)[17] and positron emission tomography (PET)[18] scans. These scans can provide insights into the type of neurodegeneration present.

Early detection in primary care is essential for timely diagnosis. Currently, if a general practitioner suspects a person may have a neurodegenerative condition, they often conduct a series of cognitive tests. Blood tests are also used to rule out other possible causes. If neurodegeneration is suspected, the person is referred to a neurologist, geriatrician or psychiatrist in a secondary care service for diagnosis.[19] If Alzheimer's is suspected, the person is often referred to a memory clinic.[20] After referral by primary care, diagnosing the type of neurodegenerative condition is challenging. Waiting lists for diagnostic specialist services are also long, partially because many people referred do not have a neurodegenerative condition.[21]

In primary care, it is challenging to detect that a person may have a neurodegenerative condition, especially during the early stages. Symptoms are often not specific, and public awareness about symptoms is limited. Some people may have prodromal symptoms (such as REM sleep behaviour disorder or depression), which are non-specific indicators that a person is at risk of developing a neurodegenerative condition. Prodromal symptoms can be linked to a range of illnesses and can begin years before symptoms specific to a condition emerge.

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[14] https://www.mrcctu.ucl.ac.uk/our-research/neurodegenerative-diseases/
[15] https://www.alzheimers.org.uk/about-us/policy-and-influencing/dementia-scale-impact-numbers
[16] https://www.gov.uk/government/publications/life-sciences-vision-missions/dame-barbara-windsor-dementia-mission
[17] An MRI scan uses strong magnetic fields and radio waves to produce detailed cross-sectional images of the inside of the body. The scanner is operated by a radiographer, who interprets the images the scanner produces on a computer. The results of an MRI scan can be used to help diagnose conditions, plan treatments, and assess how effective previous treatment has been.
[18] PET scans produce detailed three-dimensional images of the inside of the body.
[19] Secondary care is when a patient receives care for their specific illness or condition beyond the primary care they have already received. Secondary care can be understood as more specialist care provided by a practitioner with specialist expertise or a specialised facility – for example, neurology, gastroenterology or cardiology departments of a hospital.
[20] Also called memory assessment services, memory clinics are where specialists in neurodegenerative conditions assess and diagnose memory disorders.
[21] Cook L, Souris H, Isaacs J, (2020). T*he 2019 national memory service audit*. https://www.england.nhs.uk/london/wp-content/uploads/sites/8/2020/04/The-2019-national-memory-service-audit.pdf. Also see https://www.alzheimers.org.uk/blog/functional-cognitive-disorder-fcd and https://www.alzheimers.org.uk/news/2022-09-23/people-dementia-face-two-year-wait-diagnosis.

Novel tools are emerging to help detect neurodegenerative conditions. Some tools could help support practitioners' awareness that a neurodegenerative condition may be the cause of symptoms. Biochemical tests are being developed to track levels of biomarkers (biological markers) of nerve damage (such as neurofilament light chain)[22] in blood or other biological samples.[23] AI-assisted analysis of routine eye scans of the retina scans could soon allow detection of a range of neurodegenerative conditions.[24] A range of computer-based neurocognitive tests can probe memory and other cognitive functions. These tools could potentially be implemented in primary care and community settings to improve the accuracy of referrals. [25] [26] More accurate referrals to specialist services would result in resources directed to people most in need. These tools could also help rule out neurodegenerative conditions, so other causes of symptoms are considered.

Earlier detection and diagnosis of neurodegenerative conditions could have many advantages.[27] People living with a neurodegenerative condition could access early interventions when available. The benefits of early intervention are exemplified by disease-modifying treatments for relapsing remitting multiple sclerosis. Although not a cure for MS, disease-modifying treatments reduce damage to the nerves and can decrease the number and severity of relapses and the worsening of disability. Similarly, based on current evidence, disease-modifying treatments for Alzheimer's lecanemab and donanemab have only shown effectiveness in the early stages of disease.[28,29] Another potentially beneficial intervention is the modification of known risk factors. [30,31,32,33] These modifications could include stopping smoking, increasing exercise, and managing blood pressure. Earlier detection could also enable people living with a neurodegenerative condition to participate in clinical trials, obtain support earlier and plan ahead.

To explore the opportunities for earlier detection of neurodegenerative conditions in primary care and community settings specifically, the Academy of Medical Sciences, Alzheimer's Research UK and Alzheimer's Society organised a FORUM meeting in February 2024. The meeting brought together people with lived experience of neurodegenerative conditions, practitioners from primary and secondary care, funders and representatives from various

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[22] Neurofilament light chain (NfL) is a biomarker for neurodegenerative conditions including Alzheimer's disease, multiple sclerosis and ALS. It can be measured in biofluids including through cerebrospinal fluid (CSF) and blood tests. Although NfL is not usually found in blood, it is released into cerebrospinal fluid and blood if there is an injury to the nerve cells.
[23] Mullard A (2023). *NfL makes regulatory debut as neurodegenerative disease biomarker.* https://www.nature.com/articles/d41573-023-00083-z.
[24] Song A, Johnson N, *et al.* (2021). *Optical coherence tomography in patients with Alzheimer's disease: what can it tell us?* Eye Brain **13**, 1–20.
[25] Primary care settings are usually the first point of contact a person has with the healthcare system. They include general practices, pharmacies, and dental and optometry services.
[26] Community health services are delivered in people's homes, community hospitals, intermediate care facilities, clinics and schools. Practitioners can include physiotherapists, speech and language therapists, and specialist nurses.
[27] Alzheimer's Research UK (2021). *The right to know: accurate and earlier diagnosis of dementia* https://www.alzheimersresearchuk.org/wp-content/uploads/2021/05/ARUK-The-Right-to-Know_Accurate-and- Earlier-Diagnosis-of-Dementia_25May21.pdf.
[28] Van Dyck C, *et al.* (2022). *Lecanemab in early Alzheimer's disease.* The New England Journal of Medicine **388(1)**, 9–12.
[29] Sims J, *et al.* (2023). *Donanemab in early symptomatic Alzheimer disease: the TRAILBLAZER-ALZ 2 randomized clinical trial.* JAMA **330(6)**, 512–527.
[30] Livingston G, Huntley J, *et al.* (2020). *Dementia prevention, intervention, and care: 2020 report of the Lancet Commission.* Lancet **396(10248)**, 413–446.
[31] Rasmussen J, Langerman H (2019). *Alzheimer's Disease – why we need early diagnosis.* Degenerative Neurological and Neuromuscular Disease **9**, 123–130.
[32] Ascherio A, Schwarzschild M (2016). *The epidemiology of Parkinson's disease: risk factors and prevention*. The Lancet Neurology **15(12)**, 1257–1272.
[33] Tsukita K, Samaki-Tsukita H, Takahashi R (2022). *Long-term effect of regular physical activity and exercise habits in patients with early Parkinson disease.* Neurology **98(8)**, 859–871.

charities, academia and industry. The workshop agenda, participant list and a glossary can be found in Annex 1, Annex 2 and Annex 3, respectively.

The meeting was co-chaired by:

- **Dr Ruth McKernan CBE FMedSci**, Venture Partner at SV Health Investors and Trustee of Alzheimer's Research UK.
- **Dr Sara Humphrey**, a general practitioner with an Extended Role in Older People and Associate Clinical Director Dementia at NHS Bradford Districts Health & Care Partnership; NHS England Clinical Lead for Older People's Mental Health and Dementia in Yorkshire Region Team; Honorary Professor at Bradford University.

Opportunities for early detection

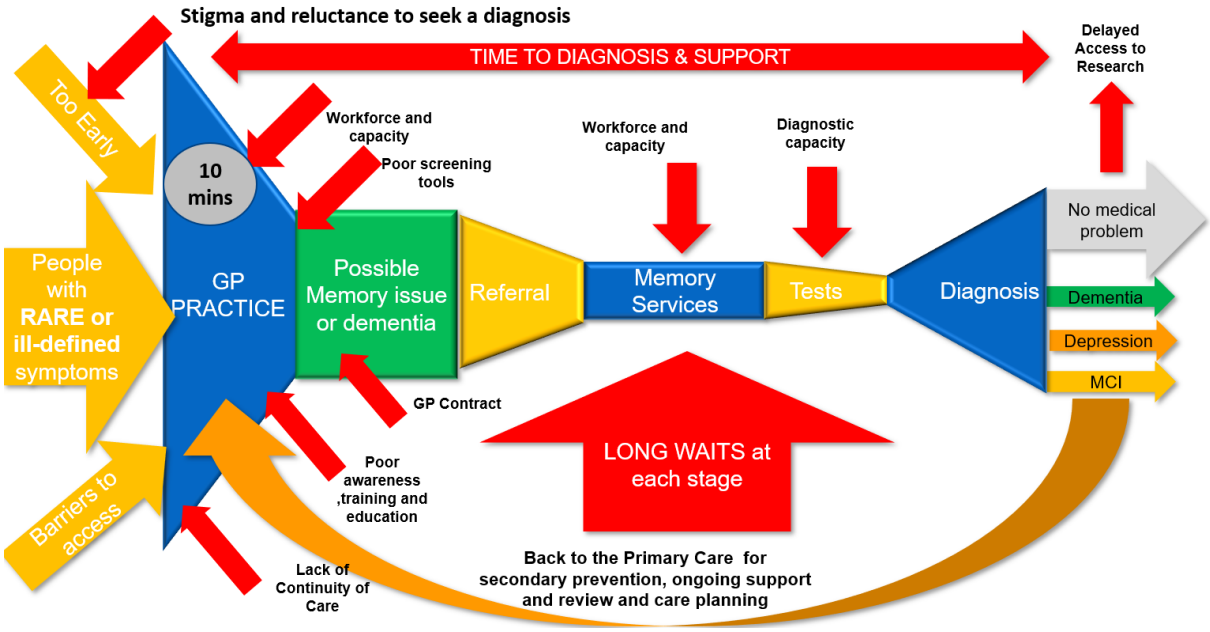
The effective and timely detection of neurodegenerative conditions with novel tools in primary care will require a high-quality diagnostic pathway. The co-chairs of the workshop, **Dr Sara Humphrey** and **Dr Ruth McKernan CBE FMedSci**, outlined some of the potential requirements for enabling earlier detection in primary care, as well as some emerging tools and current initiatives.

There are challenges in the current pathway for detection and diagnosis in primary care, as outlined by **Dr Sara Humphrey**, from her perspective as a general practitioner (Figure 1). Dr Humphrey noted that there is limited availability in primary care of effective detection tools for helping staff decide when to refer people for diagnosis. She also explained that general practitioners have limited capacity and are often only able to see each people in 10-minute time slots. Symptoms of neurodegenerative conditions can be non-specific, develop rapidly or gradually, and vary between people with the same condition. People may be reluctant to seek a diagnosis due to stigma,[34] or face barriers accessing general practice appointments. They may also not be aware of the symptoms of different neurodegenerative conditions to watch out for.

Increasingly, multidisciplinary teams deliver care in general practice, including general practitioners as well as advanced clinical practitioners, physician associates, pharmacists and nurses. These multidisciplinary teams can increase capacity, which could be an opportunity to enable earlier detection of neurodegenerative conditions. However, such team working poses a challenge for the continuity of care of people at risk or living with a neurodegenerative condition.[35] The reduction in continuity of care could make it more difficult to detect and track the development of symptoms over time. Dr Humphrey emphasised that continuity of care is important to realise the full benefits of early detection. It can increase the quality of care and potentially improve treatment and outcomes.[36] This is particularly important as people living with neurodegenerative conditions often have additional health conditions (comorbidity) that can complicate treatment. Training about neurodegenerative conditions will also be important for general practice staff to detect symptoms early.

[34] https://www.lse.ac.uk/News/Latest-news-from-LSE/2022/j-October-22/As-many-as-84-per-cent-of-people-living-with-dementia-report-experiencing-discrimination-new-toolkit-aims-to-reduce-stigma
[35] https://www.health.org.uk/publications/long-reads/measuring-continuity-of-care-in-general-practice
[36] Delgado J, Evans PH, *et al.* (2022). *Continuity of GP care for patients with dementia: impact on prescribing and the health of patients.* British Journal of General Practice **72(715)**, e91–98.

Figure 1: The challenges in the current pathway for detection and diagnosis – Dr Sara Humphrey



To improve early detection in primary care, Dr Humphrey described the importance of 'making every contact count'.[37,38] There is an opportunity to detect neurodegenerative conditions every time someone has an appointment with a general practitioner or other healthcare professional. Other opportunities to improve early detection include raising awareness of symptoms and reducing access barriers. Dr Humphrey outlined that a high-quality pathway for detection and diagnosis should be:

- Evidence-based
- Non-stigmatising
- Personalised and appropriate for each person
- Timely and resource efficient
- Easy to access, with continued access to treatment, prevention techniques and research opportunities after diagnosis
- Able to provide pre-diagnostic and post-diagnostic support

In her talk, **Dr Ruth McKernan** spoke of the exciting opportunities for improving the early detection of neurodegenerative conditions. One of the drivers of early detection will be new treatments: over 125 drugs are now in development for Alzheimer's disease alone.[39] The Dame Barbara Windsor Dementia Mission could give further impetus to identifying biomarkers and developing treatments.

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[37] Public Health England, NHS England, Health Education England (2016). *Making every contact count: consensus statement.* https://assets.publishing.service.gov.uk/media/5c338360e5274a65a5da03d5/Making_Every_Contact_Count_Consensus_Statement.pdf.
[38] Public Health England (2020). *Making every contact count: evaluation guide for MECC programmes.* https://www.gov.uk/government/publications/making-every-contact-count-mecc-practical-resources/mecc-evaluation-guide-2020.
[39] https://dementiastatistics.org/statistics/treatment-pipeline/

Dame Barbara Windsor Dementia Mission[40]

Announced in 2022, **the UK Dementia Mission** has been a government initiative. The Mission aims to accelerate the development of treatments and diagnostics for neurodegenerative conditions. Working across academia, industry and the NHS, and in partnership with other initiatives, the Mission focuses on biomarker development, data and digital sciences, and accelerating clinical trials. So far, up to £120 million of funding has been committed to the Mission.

Many tools are being developed for the detection and diagnosis of neurodegenerative conditions. For example, significant progress has been made in identifying blood biomarkers for blood tests.[41] The Digital Medicine Society has also catalogued 99 different technologies currently being developed for use in neurodegenerative conditions.[42] Many such tools are used in clinical trials or other research settings. However, there is little evidence on how to implement them at scale in clinical practice. Understanding how these tools can be used will be important. Different tools could be used for detecting initial symptoms, confirming a diagnosis, determining disease subtypes, monitoring disease progression, or demonstrating drug efficacy.

[40] https://www.gov.uk/government/publications/life-sciences-vision-missions/dame-barbara-windsor-dementia-mission
[41] Alcolea D, *et al.* (2023). *Blood biomarkers in neurodegenerative diseases: implications for the clinical neurologist.* Neurology **101(4)**, 172–180. Also see https://www.ucl.ac.uk/brain-sciences/dementia-ucl-priority/how-biomarkers-offer-new-hope-diagnosing-and-treating-alzheimers and https://www.ox.ac.uk/news/2023-12-05-researchers-develop-blood-test-identify-individuals-risk-developing-parkinson-s.
[42] https://datacc.dimesociety.org/digital-measures-adrd/

Reshaping the pathway

A range of different neurodegenerative conditions were explored during the workshop. Two case-studies (Alzheimer's disease and multiple sclerosis) were of particular focus. Participants considered the challenges detecting both conditions, and the lessons to be learned from the improved detection and diagnosis of multiple sclerosis.[43]

Alzheimer's disease and other causes of dementia

Alzheimer's disease is the most common cause of dementia in the UK. Generally, the patient journey begins with a visit to a primary care service after they or someone close to them notice symptoms. If a neurodegenerative condition is suspected, the practitioner then uses a range of different assessments, including cognitive tests. Blood tests are also often taken to rule out other possible causes of symptoms. Detecting cognitive impairment is often the first step to identifying Alzheimer's disease – although impairment can be caused by other conditions and Alzheimer's can present in different ways. Early detection of cognitive impairment could enable people to plan for the future, access any research studies, potentially benefit from early treatments, and participate in decisions about their care.[44]

If a person shows signs of Alzheimer's disease, they are often referred to a memory clinic. Multiple visits to a general practice may be required before referral. People often face an extended period of assessment with long waits at each stage before clinical diagnosis, which can take longer than a year.[45,46] During the workshop, **Michael Petley** spoke about his own route to diagnosis with an atypical type of dementia called primary progressive aphasia (PPA) (Box 1).

Box 1: Diagnosis of an atypical type of dementia: the patient perspective

Michael Petley described how it took four years for him to get a diagnosis. He spoke of the uncertainty this created for him and his family. His wife first noticed his symptoms and encouraged him to seek a diagnosis. After referral by a general practitioner, initial tests were inconclusive. His own research led him to suspect he had PPA. Michael suggested that earlier diagnosis could have prevented years of frustration and would have enabled him to access support from experts and PPA support groups sooner.

[43] Multiple sclerosis was considered in this workshop about neurodegenerative conditions because in the later phase of MS nerves are damaged and degenerate irreversibly, resulting in permanent loss of nerve function seen in progressive MS.
[44] https://www.alz.org/professionals/health-systems-medical-professionals/cognitive-assessment
[45] NHS England (2019). *The 2019 national memory service audit* https://www.england.nhs.uk/london/wp-content/uploads/sites/8/2020/04/The-2019-national-memory-service-audit.pdf.
[46] Alzheimer's Society (2023). *Improving access to a timely and accurate diagnosis of dementia in England, Wales and Northern Ireland.* https://www.alzheimers.org.uk/about-us/policy-and-influencing/improving-access-timely-accurate-diagnosis-dementia-england-wales-northern-ireland.

Professor Craig Ritchie, Professor of the Psychiatry of Ageing at the University of Edinburgh and CEO and Founder of Scottish Brain Sciences, felt that a shift in outlook could improve detection and diagnosis. He suggested that Alzheimer's should be seen less as a 'memory disorder' and more as a consequence of a longer-term gradual decline in 'brain health'. This decline eventually leads to dementia. Early interventions during the progression of Alzheimer's (pharmacological or non-pharmacological) could help to maintain brain health and independent living as long as possible.

Novel brain health service models are being piloted to explore how an approach that focuses on prevention and early detection could work. One such pilot is Brain Health Scotland.[47] People can attend 'brain health services' accessed by walking in with no need for an appointment. People can also be referred by their general practitioner. Anyone can attend the service, regardless of age. The services do not diagnose people but use a series of assessments to stratify them according to their risk of developing dementia. Low-risk people are provided with lifestyle advice. Intermediate-risk people receive a personalised prevention plan and are followed up after 2 years. High-risk people are reviewed sooner or referred to memory clinics.

There was a wide range of opinion about the value of early detection and diagnosis without effective treatments. Michael was keen to find out the cause of his symptoms and found a diagnosis useful in the absence of a specific treatment. Many participants similarly felt that they would seek an early detection and diagnosis. However, some participants felt they personally would obtain little value from early detection and diagnosis without an effective treatment available. Discussions during the workshop demonstrated how complex the situation can be. For example, sometimes the desire for assessment can come from families rather than the person living with the neurodegenerative condition themselves, such as when someone is in denial about their symptoms. Some people's symptoms, such as difficulties with memory, may also make it difficult for them to accept that they may have a neurodegenerative condition.

Most participants agreed that the decision whether to seek a detection and diagnosis should be the choice of the person who may have a neurodegenerative condition, in conversation with their loved ones and healthcare professionals. Alongside access to early detection and diagnosis, participants felt that people should be made aware of opportunities to take part in research studies. Participating in research would give people with neurodegenerative conditions earlier access to new treatments as they emerge. Most importantly, participants agreed that to give people the choice of whether to seek detection and a diagnosis or not, an accessible and timely pathway for detection and diagnosis should be put in place. Otherwise, the absence of a pathway will make that choice for them.

Multiple sclerosis

The detection and diagnosis of multiple sclerosis (MS) has its own opportunities and challenges, with lessons to learn from recent progress. Some of these challenges have features in common with other neurodegenerative conditions. **Professor Anna Williams**, Professor of Regenerative Neurology at the University of Edinburgh, discussed how MS can be difficult to diagnose as symptoms are non-specific and can vary between people.

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[47] Ritchie CW, Waymont JMJ, *et al.* (2022). *The Scottish brain health service model: rationale and scientific basis for a national care pathway of brain health services in Scotland*. The Journal of Prevention of Alzheimer's Disease **9(2)**, 348–358.

There are different categories and subtypes of MS, which present different challenges.

- **Relapsing remitting MS** is a type of MS where there are periods of recovery ('remission') between episodes of worsening symptoms (relapses). Relapsing remitting MS is hard to detect because of the diversity of possible symptoms and their absence during remission. If a primary care clinician suspects an individual has MS, they are referred to a neurologist for assessment. Sometimes, MS can be detected following routine eye scans. Timely detection and diagnosis of relapsing remitting MS is important as effective disease-modifying treatments are now available. These target the immune responses responsible for nerve damage. Detection and diagnosis of relapsing-remitting MS is much quicker than it was fifty years ago. This is partially because of increased awareness about the benefits of early treatment and changes in diagnostic criteria.
- **Progressive MS** is characterised by ongoing deterioration of symptoms. Progressive MS is occasionally an initial diagnosis (primary progressive MS). However, it usually develops following relapsing remitting MS (secondary progressive MS). The transition from relapsing remitting MS to secondary progressive MS is difficult to detect and there is no specific diagnostic test. Researchers are exploring the possible use of blood, cerebrospinal fluid, neurophysiological and MRI biomarkers.[48] If new tools become available, there may be an opportunity to improve the detection of primary progressive MS and the onset of secondary progressive MS. These tools could be used in primary care and community health settings. Early detection of progressive MS will become especially important when treatments are developed; clinical trials for neuroprotective drugs[49] are currently underway.[50] During a panel discussion, **Jacqueline Krarup** described her personal journey with secondary progressive MS (Box 2).

Box 2: Living with multiple sclerosis: the patient perspective

Jacqueline Krarup described how her MS was detected by the healthcare system years after her symptoms first occurred. At first her physical symptoms, including numbness, resolved without a diagnosis being made. Jacqueline likely had undiagnosed relapsing remitting MS at this stage. A later visit to the opticians then found signs of optic neuritis, which led to a diagnosis of secondary progressive MS. Jacqueline highlighted how a key barrier to people seeking early diagnosis of MS is worry about discrimination or stigmatisation. To help overcome this barrier, employers should be more willing to accommodate people living with disabilities.

[48] Krajnc N, Bsteh G, *et al.* (2021). *Clinical and paraclinical biomarkers and the hitches to assess conversion to secondary progressive multiple sclerosis: a systematic review.* Frontiers in Neurology **12(666868)**.
[49] Neuroprotective drugs aim to promote the survival of nerve cells and delay neurodegeneration.
[50] https://www.mssociety.org.uk/research/explore-our-research/search-our-research-projects/octopus

New initiatives and research

Advances in the detection and diagnosis of neurodegenerative conditions are partially driven by developments in policy and research. During the meeting, a panel discussed the opportunities and challenges of new policy initiatives and detection tools. The panel included representatives from stakeholder groups including industry, government and healthcare:

- **Dr Ashton Harper**, Head of Medical Affairs, Roche Diagnostics UK & Ireland
- **Jacqueline Krarup**, Patient expert living with secondary progressive MS
- **Mr Praveen J. Patel**, Consultant Ophthalmologist, Moorfields Eye Hospital NHS Foundation Trust, and Honorary Clinical Lecturer UCL Institute of Ophthalmology
- **Professor Nadeem Sarwar**, Co-chair of the UK Dementia Mission, and Corporate Vice President, Novo Nordisk.

Mr Praveen Patel explained Optical Coherence Tomography (OCT) eye scans could become a powerful new tool for detecting a wide range of neurodegenerative conditions early. OCT scans can detect early signs of degeneration of retinal nerve cells, providing a 'window into the brain' through eye health. OCT scans are quick, relatively cheap, and are becoming a routine service offered in many high-street opticians.

There are challenges implementing new tools to detect neurodegenerative conditions. Dr Ashton Harper described how the identification and use of biomarkers is essential for clinical trials. Biomarkers are important for recruitment of trial participants and for assessing response to treatment. However, Dr Harper suggested that there is a disconnect between the use of tools in trials and their application in clinical practice. There is an opportunity to accelerate the translation of these tools from research settings to clinical practice, potentially including primary care. These tools could then be used to complement clinical assessments.

The development and use of new diagnostic tools and treatments has been supported by policy initiatives such as the Dame Barbara Windsor UK Dementia Mission. Professor Nadeem Sarwar described how dementia is a uniquely challenging disease, but two disease-modifying therapies are showing promise. The use of blood and digital biomarkers to detect neurodegenerative conditions would enable the UK to do novel trials for new tools and treatments at scale. Professor Sarwar emphasised that the biggest asset the UK has for driving innovation is health data. He highlighted how a system that brings together different health data could accelerate the discovery of new tools and treatments.

Mapping the way forward

There is much research into tools to detect neurodegenerative conditions. To ensure that this research reaches people living with a neurodegenerative condition, it is important to consider what may be required to integrate these tools into health systems. Participants discussed next steps for enabling earlier detection and the use of detection tools in primary care and the community, and highlighted remaining evidence gaps. Participants identified the following themes:

1. The case for early detection should be rigorously assessed, considering the whole pathway from detection to diagnosis and care.
2. Detection requires integration of multiple sources of data.
3. Roles and responsibilities of health workers in early detection should be clarified across different primary care and community settings.
4. A greater focus on early detection may require changes in mindset among clinicians, policymakers and the public.
5. Equity, evidence and iterative improvement should underpin future developments.

1. The case for early detection should be rigorously assessed, considering the whole pathway from detection to diagnosis and care

As previously outlined, there are potential benefits to earlier detection of neurodegenerative conditions.[51] Participants suggested that more research is needed to build a robust case for early detection for a range of conditions, while considering the pathway as a whole.

Gathering and sharing more evidence on the potential benefits of timely detection and diagnosis could increase public interest in early detection. Some people may prefer not to know that they have, or are at risk of developing, a neurodegenerative condition. They may fear being diagnosed with a condition that they consider to be untreatable, losing their job or driving licence, and possible implications for insurance. If the benefits of early detection are evidenced and communicated, people potentially living with a neurodegenerative condition and those affected may raise concerns about symptoms earlier. Doctors may also be more likely to investigate possible symptoms at an early stage if there are demonstrable benefits to doing so.

Early detection enables earlier diagnosis

Currently, the journey of the person living with a neurodegenerative condition through the healthcare system is lengthy, disjointed and variable, often depending on local availability of services. Some participants also reflected that a substantial proportion of people currently referred to specialist brain health services do not have the condition they are referred for. Early detection tools present the opportunity to improve this journey by speeding up and increasing accuracy of referral. Improving triaging in primary care could allow neurologists to focus time and resources on people who most need their expertise, potentially speeding up diagnosis depending on demand. Participants noted that it will be important to model and monitor how many people who may have a neurodegenerative condition move through each

[51] https://www.alzheimers.org.uk/about-dementia/symptoms-and-diagnosis/dementia-diagnosis/benefits-of-getting-dementia-diagnosis and https://www.alzheimers.org.uk/blog/why-spotting-early-signs-dementia-important.

stage of the detection and diagnostic pathway and how fast, before and after a new tool is implemented.

The performance characteristics of a tool will affect how people move through the detection and diagnostic pathway. In particular, the sensitivity (certainty whether a person has the condition)[52] and specificity (certainty whether a person does not have the condition)[53] of the tool. The sensitivity and specificity of tests will also vary in different populations. Tests with high specificity in a memory clinic population may be less specific in the general population. Modelling could be used to assess how tests with different performance characteristics can be best used in different settings, including the impact on system efficiencies. This modelling data could be used to fast-track pilot trials of novel biomarkers and other detective tools to gather data on health outcomes and economic value in different populations and parts of the healthcare system. These studies could build on clinical studies already underway, such as the Blood Biomarker Challenge project.[54]

Pharmacological treatments

Enabling earlier access to drugs and other pharmacological therapies that slow disease progression would be a clear benefit of earlier detection (that leads to earlier diagnosis). Available treatments for conditions like MS significantly improve quality of life. Access to these treatments currently require a confirmed diagnosis. In many cases, early treatment of neurodegenerative conditions is thought to be more effective. The AttackMS trial is a study gathering evidence about the potential benefit of earlier detection and treatment of MS, by treating people within 14 days of presenting with possible MS symptoms with a disease-modifying drug.[55] Participants suggested that the potential benefit of treating early in progression of a condition should be examined for emerging treatments. However, many neurodegenerative conditions do not yet have disease-modifying drugs available.

Non-pharmacological interventions

Early detection could give people the opportunity to address relevant comorbidities and modifiable risk factors of their condition. In addition to improving the general health and wellbeing of people with neurodegenerative conditions, modifying risk factors could potentially help delay the progression of neurodegenerative conditions or symptoms.[56] Non-pharmacological modifications of risk factors may include increased physical activity and exercise, cognitive training, stopping smoking, countering hearing loss, and controlling high blood pressure.[57] For example, there is some evidence that nutrition and lifestyle changes may reduce the symptoms and delay the progression of Parkinson's.[58,59] More robust research into the impact of lifestyle changes and other non-pharmacological interventions on the progression of a wide range of neurodegenerative conditions would be useful to continue to

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[52] High sensitivity tools are likely to detect all individuals who might have a neurodegenerative condition. However, if low in specificity, a high sensitivity tool may also result in the incorrect detection of a neurodegenerative condition in people who do not have the condition (false positives). These people would need further assessment to confirm a diagnosis.
[53] High specificity tools are more likely to detect the individuals who definitely have the neurodegenerative condition. However, if low in sensitivity, a high specificity tool may also lead to some cases being missed (false negatives).
[54] https://www.alzheimers.org.uk/news/2024-04-04/uk-comes-step-closer-blood-tests-diagnosing-dementia
[55] https://www.clinicaltrials.gov/study/NCT05418010 and https://mstrust.org.uk/information-support/podcasts/what-happens-when-you-treat-ms-really-early-we-learn-about-attackms.
[56] Rasmussen J, Langerman H (2019). *Alzheimer's disease – why we need early diagnosis.* Degenerative Neurological and Neuromuscular Disease **9**, 123–130.
[57] Livingston G, Huntley J, *et al.* (2020). *Dementia prevention, intervention, and care: 2020 report of the Lancet Commission.* Lancet. **396(10248)**, 413–446.
[58] Ascherio A, Schwarzschild M (2016). *The epidemiology of Parkinson's disease: risk factors and prevention.* The Lancet Neurology **15(12),** 1257–1272.
[59] Tsukita K, Samaki-Tsukita H, Takahashi R (2022). *Long-term effect of regular physical activity and exercise habits in patients with early Parkinson disease.* Neurology **98(8),** 859–871.

build the case for early detection. This would build on the learning from long-term randomised controlled trials that have shown potential benefit of simultaneous lifestyle interventions in a variety of areas, such as diet, exercise, cognitive training and monitoring vascular risk.[60]

Earlier access to clinical trials

Early detection could increase the recruitment of people in the early stages of a neurodegenerative condition to research studies and clinical trials. Opportunities to participate in clinical trials benefit the people living with a neurodegenerative condition as well as the trial, giving earlier access to novel tools and treatments and additional monitoring of the progression of their condition.[61] To ensure early detection leads to access to clinical trials, opportunities to access research should be embedded in primary care.

Earlier access to support

As previously mentioned, early detection and subsequent diagnosis could enable people to access emotional and practical support sooner. Support could include mental health support; access to support networks and patient communities; and access to social care. Whether access to support is an incentive to seek early detection will depend on an individual's presentation of symptoms, needs and preferences. Participants noted that availability of support varies between regions. Equitable access, including for underserved groups (including those from minority backgrounds and rural areas or areas of high deprivation), should be a priority.

Participants noted that people would benefit from pre-diagnostic as well as post-diagnostic support, helping them to manage their symptoms and navigate the pathway for detection and diagnosis. Some people coming forward for assessment will go on to be diagnosed with a neurodegenerative condition, whereas others will either be told they do not have a neurodegenerative condition or leave the pathway with a less certain outcome. Less certain outcomes could include a probability score or risk assessment for a particular neurodegenerative condition or a diagnosis of mild cognitive impairment (MCI; Box 3). This can still be informative; results could reveal any cognitive decline compared with what would be expected, or prompt clinicians to investigate other possible causes of symptoms. Careful communication and support will be required to help people navigate any uncertainty. NICE guidelines for the diagnosis, management and treatment of people with MCI would be useful.

Box 3: Mild cognitive impairment (MCI)

People with problems with memory, language or judgement may receive a less certain diagnosis of MCI. MCI can have different causes, but people with MCI are at a greater risk of developing Alzheimer's disease and dementia. People with MCI currently receive little support, but their numbers are likely to increase with an ageing population. Support could include advice about living with MCI and information about the likelihood of developing a neurodegenerative condition. Detecting the signs of MCI early

[60] https://fbhi.se/the-finger-study/
[61] Juganavar A, *et al.* (2023) *Navigating early Alzheimer's diagnosis: a comprehensive review of diagnostic innovations*. Cureus **15(9)**, e44937.

could enable people to make modifications to their lifestyles to address known risk factors, which may prevent or slow the development of a neurodegenerative condition.

Evidence should be gathered from people living with neurodegenerative conditions on what type of support may be required or preferred both pre- and post-diagnosis. Support packages should be developed based on this evidence to bring together information and connect people living with a neurodegenerative condition to networks and communities. Charities and patient groups can provide valuable information, signposting and support throughout the patient journey. It may also be appropriate to begin certain kinds of treatment for people living with a neurodegenerative condition before a firm diagnosis can be made, such as non-pharmacological interventions to help improve overall brain health.

Improvements in health and care system efficiency and economic benefits

In addition to the health benefits, the potential economic benefits of early detection should be considered and assessed. This has to be demonstrated for individual tools during health technology assessment. Long-term, system-wide benefits should also be assessed as part of this process. For example, if prevention and effective treatment is possible, the long-term economic benefits of investment in early detection include reduced pressure on healthcare services and carers, and greater societal productivity as people can stay in the workforce for longer.

Participants noted that a common challenge for monitoring the economic benefits of early detection is that different parts of the healthcare system have different budgets, which are managed separately. Costs associated with early detection could increase for one part of the healthcare system (for example, primary care) while saving money or capacity in another (for example, memory clinics). Reducing peoples' progression to advanced dementia will also impact social care budgets. Currently, the cost of providing social care to people with dementia is £17.2 billion, a figure predicted to rise to £40.7 billion by 2040.[62] Participants felt that a more joined-up approach between primary, secondary and social services could help address these issues. Modelling and health-economic analyses should be used to explore the economic implications of early detection for different parts of the health and social care system, as has been done for kidney disease and other conditions.[63] Recently established NIHR-funded policy research units in dementia and neurodegeneration hosted by Queen Mary University of London and the University of Exeter could be well placed to address such evidence gaps.[64]

A whole pathway approach is needed and people living with neurodegenerative conditions should be involved

As demonstrated above, realising the benefits of early detection is reliant on later parts of the diagnostic pathway (for example, provision of post-diagnostic care and access to treatments). A whole-pathway approach to implementing tools for early detection would help identify

[62] Alzheimer's Society (2024). *The economic impact of dementia.* https://www.alzheimers.org.uk/sites/default/files/2024-05/the-annual-costs-of-dementia.pdf.
[63] Kidney Research UK (2023). *Kidney disease: a UK public health emergency. The health economics of kidney disease to 2033.* https://www.kidneyresearchuk.org/wp-content/uploads/2023/06/Economics-of-Kidney-Disease-full-report_accessible.pdf.
[64] https://www.nihr.ac.uk/documents/nihr-policy-research-units-2024-2028/34065

potential national, regional and local bottlenecks in the system, to realise the benefits and avoid any unintended consequences.

Involving people living with a neurodegenerative condition, as well as those affected such as their families, in the design and evaluation of pathways will be important. Participants noted that assumptions are often made about what people who may have a neurodegenerative condition and their families need or prefer from a diagnostic test or pathway. This may be partly due to a wide range of personal opinions about whether receiving an early diagnosis for a neurodegenerative condition is desirable. The needs of people seeking clarity about their symptoms and their preferences should be considered at each step.

Next steps proposed by participants:

1.1 More evidence should be gathered about whether earlier treatment with pharmacological and non-pharmacological interventions is more effective for various neurodegenerative conditions, investigating whether effectiveness varies according to each stage of the disease. The potential causal relationship between lifestyle risk factors and different neurodegenerative conditions should be explored, and the impact of lifestyle modifications assessed.

1.2 How and when to embed opportunities to participate in clinical research alongside early detection should be investigated.

1.3 Current clinical pathways for people coming forward with symptoms of neurodegenerative conditions should be reviewed, including regional variations and health outcomes. The logistical and economic impact of introducing different detection tools on diagnostic and treatment pathways should be modelled.

1.4 Based on modelling data, the use of different tools should be piloted within various primary and community health settings and in different populations. Lessons can be learned from ongoing pilot schemes, such as the Blood Biomarker Challenge.[65] These pilot schemes could gather and consolidate real-world data on test usage, performance, impact on the detection and diagnostic pathway, and outcomes.

1.5 Pre- and post-diagnosis packages of information and support for people living with and affected by a neurodegenerative condition should be developed, to help people navigate the diagnostic journey. Medical charities and patient support groups may be well placed to do this.

1.6 The National Institute for Health and Care Excellence (NICE) should be encouraged to develop guidelines for the management, and eventually treatment, of mild cognitive impairment.

2. Detection requires integration of multiple sources of data

Clinical decision-making, including the detection of disease, is based on the integration of health data about an individual from various sources. Novel tools could give primary care clinicians access to additional information to help make decisions on referrals and interventions. Some participants pointed out that combining data from physiological tests (such as blood tests) with functional tests (such as wearable devices) could be particularly powerful for early detection (and later for measuring changes in disease over time). Participants noted that many tests could help stratify people according to their risk of developing a neurodegenerative condition. Primary care clinicians will need training in how to interpret data from any tools they use, taking into account the limitations of the tool (for

[65] https://www.alzheimers.org.uk/news/2024-04-04/uk-comes-step-closer-blood-tests-diagnosing-dementia

example, its sensitivity and specificity). They should also receive training in how to communicate with people who may have a neurodegenerative condition, about any inherent uncertainty in the results.

Standardised criteria for the use of tools for the detection, referral and diagnosis of different neurodegenerative conditions could ensure that the pathway for detection and diagnosis is consistent across services. Standardisation of measurements and data from tests, particularly biomarker tests, may also be required.

Tools and technologies that participants highlighted could be used to support early detection:

- Blood biomarker tests may be used in primary care to help detect neurodegenerative conditions earlier. For example, the p-tau217 immunoassay is a blood test that detects a protein[66] associated with Alzheimer's-type pathology, which recently became commercially available.[67] It stratifies people into three groups, rather than giving a definitive diagnosis:
    - Those very likely to have Alzheimer's disease
    - Those very unlikely to have the condition
    - An intermediate group that may require further monitoring and/or assessment.

  Blood prick tests for people to take at home could also potentially be prescribed in the future. The acceptability of at-home blood tests should be explored with the public and clinicians.
- Genetic tests could also provide data to help detect those at higher risk of neurodegenerative conditions (for example, having the APOE-e4 form of the APOE gene[68] is a known genetic risk factor for Alzheimer's disease, though risk is different for men and women).
- Optical Coherence Tomography (OCT) scans take a 3D image of the retina, which can be used to look for non-specific indicators of neurodegeneration. New developments in scanning technologies mean that OCT scans are becoming readily available at any opticians, and may soon be able to give more specific diagnostic information. The use of machine learning/AI to interpret images from OCT scans could also help detect early signs of neurodegeneration. Eventually, AI may also be able to detect specific conditions, including Parkinson's.[69]
- Cognitive and neuropsychological exams (on paper or digitally) are used to evaluate memory, attention, and language and communication skills. Some existing tests are relatively straightforward and are already used in some general practice services for early detection.
- Publicly available digital apps and games to detect and monitor changes in cognitive function, gait, posture and behaviour are being developed. These could help primary care

[66] The symptoms of Alzheimer's disease are thought to be partly caused by abnormal amyloid and tau proteins. Abnormal beta-amyloid can clump together, forming clusters and then plaques that damage neurons. Amyloid clusters can then cause a surge in abnormal tau. Abnormal tau can clump together to form neurofibrillary tangles, causing neurons to die. The p-tau217 immunoassay can identify Alzheimer's disease by measuring levels of the biomarker p-tau (phosphorylated tau) in the blood.

[67] Ashton NJ, *et al.* (2024). *Diagnostic accuracy of a plasma phosphorylated Tau-217 immunoassay for Alzheimer Disease pathology*. JAMA Neurology **81(3)**, 255–263.

[68] APOE is the name of the gene, which everyone has in some form. The three most common forms of the APOE gene are epsilon (e) 2, 3 and 4: these variants have slight differences in their DNA patterns. Like most genes, we inherit one form of APOE from each of our parents. Inheriting the e4 variant increases the risk of developing Alzheimer's disease, with the greatest risk occurring for those who inherit two copies.

[69] See Wagner SK, Romero-Bascones D, *et al.* (2023). *Retinal Optical Coherence Tomography features associated with incident and prevalent Parkinson disease.* Neurology **101(16)**, e1581–1593. Also see https://www.ucl.ac.uk/brain-sciences/dementia-ucl-priority/professor-pearse-keane-using-eye-health-detect-dementia.

clinicians detect symptoms of various neurodegenerative conditions.[70,71,72] Some are designed as risk profiling tools such as apps that specifically assess an individual's risk of developing a neurodegenerative condition.[73] Participants noted how, depending on their accuracy,[74] personal risk profiling apps could help people decide whether to come forward for a brain health assessment. They suggested that these tools could also then provide brain health advice. However, it will be important to review the validity, reliability and accuracy of risk models and their applicability to different populations.[75]

- Wearable technologies for measuring gait, motion tracking or sleep could help detect neurodegenerative conditions, similar to the smartphone apps mentioned above. For example, accelerometer data can identify movement changes specific to Parkinson's several years before diagnosis.[76] Wearable devices could include consumer products such as smart watches, or bespoke medical devices designed for monitoring physiological traits, such as a portable electroencephalogram (EEG) to monitor brain activity.
- Data from health products and services marketed direct to the consumer (rather than via the health service) could be another source of data to help primary care clinicians and people with symptoms detect neurodegenerative conditions. Direct-to-consumer products or services are those marketed, advertised and sold directly to the customer or patient rather than the healthcare system. Relevant services include genetic data from commercial genome sequencing companies, health data generated by companies offering health screening services, or health apps collecting relevant data. Suggesting to developers of health apps that they could include a feature advising people when to seek the opinion of a healthcare professional may be useful. Participants noted that people sometimes bring the data they have gathered elsewhere to the attention of a healthcare practitioner during consultations. They also noted that there is not currently a mechanism by which data from direct-to-consumer products and services can be routinely shared with primary care. The ethical considerations of such data sharing would need to be considered.
- Decision-support tools could be used to aid primary care clinicians in detecting individuals who may have, or be at risk of developing, a neurodegenerative condition. Some decision-support tools could help make an assessment using primarily a person's electronic health record data, such as the 'red flag' tool for detection of MS currently being piloted in the NHS. This tool advises a general practitioner when an individual's health record includes information that suggests they might have MS, and advises on initial investigations and referral. It also provides information on managing symptoms and support networks. Other decision-support tools could use AI-based algorithms to aggregate and interpret data from different tests, family history and patient health records. These algorithms could be used in primary care to produce a risk score for different neurodegenerative conditions.

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[70] Colivicchi A (2023). *NHS to pilot puzzles app to speed up dementia diagnosis* https://www.pulsetoday.co.uk/news/clinical-areas/neurology/nhs-to-pilot-puzzles-app-to-speed-up-dementia-diagnosis/

[71] See https://www.esneft.nhs.uk/new-smartphone-app-helps-patients-with-parkinsons/

[72] Staffaroni AM, Clark AL, *et al.* (2024). *Reliability and validity of smartphone cognitive testing for Frontotemporal Lobar Degeneration.* JAMA Network Open. **7(4)**, e244266.

[73] Sindi S, *et al.* (2015). *The CAIDE Dementia Risk Score App: the development of an evidence-based mobile application to predict the risk of dementia* Diagnostic Assessment and Prognosis **1(3)**, 328–333.

[74] Mohanannair Geethadevi G, *et al.* (2023). *What tools exist to assess the presence of multiple risk factors for dementia in middle-aged people, and can they correctly predict future dementia?* Cochrane Database of Systematic Reviews **6**.

[75] Ibid.

[76] Schalkamp AK, Peall KJ, *et al.* (2023). *Wearable movement-tracking data identify Parkinson's disease years before clinical diagnosis.* Nature Medicine **29(8)**, 2048–2056.

Next steps proposed by participants:

2.1 The feasibility and acceptability of integrating data from multiple sources/tests to assess a person's risk of a neurodegenerative condition (potentially using technologies such as machine learning/AI) should be investigated. Such technologies could be used to build a decision-support tool. The desired characteristics and communication preferences for a decision-support tool for use in primary care should be established, in collaboration with primary care clinicians and people living with neurodegenerative conditions.

2.2 It will be important to investigate what information people want from tests that detect neurodegenerative conditions and when, and how best to communicate about test results, health risks and the choices available to people who may have a neurodegenerative condition. Existing guidance and approaches to communication in other disease areas, such as cardiovascular disease, should be learned from.[77,78]

2.3 Standardised criteria and data standards for the use of tools in detection, referral and diagnosis should be developed for different relevant neurodegenerative conditions at different stages, to improve consistency across services.

3. Roles and responsibilities of health workers in early detection should be clarified across different primary care and community settings

A critical question to consider is who should be responsible for discussing detection and diagnostic information, referring people for further tests, advising people on possible interventions and support, and monitoring these activities. In addition to general practitioners, some participants suggested that other health workers in primary care and the community could contribute, including practice nurses, practice-based or community pharmacists, optometrists and physician associates. Any changes in responsibilities should be accompanied by appropriate training of the relevant staff group.

Participants particularly discussed where the responsibility for onward referral of people to specialist diagnostic services should lie. Although currently onward referral is predominantly handled by general practitioners, some suggested that other services (such as pharmacists, optometrists and dentists) could potentially refer directly in certain situations, based on criteria that would need to be agreed. For example, direct referral may be appropriate if a test taken in their service has highly specific and sensitive results. Direct referral to services such as memory clinics could save time and reduce pressures on general practice. Other participants felt that direct referral may not always be appropriate. They felt that general practitioners have a more holistic view of a person's medical history and should therefore retain responsibility for onward referral.

Opticians, pharmacies and general practice services have different data systems and so participants noted that linking patient health data to facilitate early detection may be a

[77] Patient Information Forum (2023). *Communicating benefits, risks and uncertainties.* https://pifonline.org.uk/resources/how-to-guides/communicating-benefits-risks-and-uncertainties/.
[78] Schulberg SD, *et al.* (2022). *Cardiovascular risk communication strategies in primary prevention. A systematic review with narrative synthesis.* Journal of Advanced Nursing **78(10)**, 3116–3140.

challenge. Recent efforts of NHS England to integrate community pharmacy data systems with general practice records may begin to address this in England.[79]

Next steps proposed by participants:

3.1 The circumstances in which it may be appropriate for practitioners in primary and community services beyond general practice to refer directly to relevant specialists should be considered, and the acceptability to various practitioners and the public explored.

3.2 The potential for different staff (such as nurses) in general practice to be involved in detecting neurodegenerative conditions, along with relevant training needs, should be explored.

4. A greater focus on early detection may require changes in mindset among healthcare staff, policymakers and the public

Current approaches to neurodegenerative conditions may be changing. Conditions such as Alzheimer's disease are currently often considered to be untreatable and terminal conditions that are an inevitable result of old age. An alternative perspective is emerging, that dementia is a late-stage symptom of deterioration in 'brain health'. If neurodegenerative conditions begin decades before symptoms appear, it may be possible to slow or even prevent their progression at these early stages. This shift in thinking about brain health could have radical implications for how neurodegenerative conditions and dementia are perceived and treated.

There may be lessons to be learned from other disease areas. In cardiovascular disease, huge advances in reducing mortality were achieved due to improved prevention and better treatments.

- Biomarkers such as cholesterol levels and blood pressure have become standard ways for assessing cardiovascular health that are regularly and routinely monitored in the population. Simple tests of relevant indicators could also be used to monitor brain health.
- An increased focus on brain health and general health promotion could deliver similar gains as the promotion of heart health.
- The use of different tools and multiple sources of data to detect neurodegenerative conditions may mean that the information communicated to people who may have the condition is complex and nuanced. Those who treat cardiovascular disease are familiar with using risk scores and algorithms to guide interventions and communicate with people at risk.[80] There are opportunities to learn from how probabilistic information can be communicated effectively when detecting neurodegenerative conditions.

Participants discussed how to build early detection of neurodegenerative conditions into existing care initiatives, as has been done for cardiovascular disease. One practical suggestion was to add brain health assessments to existing regular health checks, such as the health 'MOTs', or NHS Health Checks for 40–74-year-olds.[81] Such assessments could use scalable, inexpensive tools, such as simple blood tests and digital cognitive tests. The Brain Health

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[79] Lipanovic D (2023) *NHS England says community pharmacists will be able to access GP records from January 2024.* https://pharmaceutical-journal.com/article/news/nhs-england-says-community-pharmacists-will-be-able-to-access-gp-records-from-january-2024.
[80] Schulberg SD, *et al.* (2022). *Cardiovascular risk communication strategies in primary prevention. A systematic review with narrative synthesis.* Journal of Advanced Nursing **78(10)**, 3116–3140.
[81] https://www.nhs.uk/conditions/nhs-health-check/

Services in Scotland provide an alternative health check model where assessments are focused on the brain.[82] Relevant assessments could be added to personal care plans for people with conditions that then put them at risk of developing a neurodegenerative condition. For example, people with high blood pressure, high blood cholesterol levels, type 2 diabetes, hearing loss or depression may have higher risk of developing neurodegenerative conditions that cause dementia.[83] Neurodegenerative conditions such as Parkinson's can also put people at higher risk of developing dementia.[84]

It will be important to communicate the long-term benefits of both early detection and prevention to healthcare practitioners and policymakers. Healthcare services should be made aware of new developments as they arise, so that they can prepare for the latest advances in research, and communicate opportunities to people living with a neurodegenerative condition. The training and continuing professional development of primary care clinicians should reflect the latest advances in diagnosing and treating neurodegenerative conditions. It will be beneficial to also ensure policymakers are aware of latest developments, to prepare services and consider opportunities for prevention. Policymakers should also consider the longer-term implications of earlier detection and diagnosis. This could be aided by researchers collaborating with policymakers to identify key evidence gaps and inform long-term strategic planning for early detection.

Public awareness of the progress around the detection and treatment of neurodegenerative conditions should be raised. Understanding that there are steps people can take to reduce their risk of, detect and treat neurodegenerative conditions, could encourage a greater focus on maintaining 'brain health'. Some participants suggested that a public campaign would be useful to address and reduce the fatalism surrounding neurodegenerative conditions. If perceptions remain negative about the consequences of a diagnosis, people are likely to also be deterred from seeking out an early detection. A public health campaign about brain health could promote a 'culture of hope', but many participants felt that a stronger evidence base would be required about the benefits of early detection to make a compelling, evidence-based case as mentioned earlier in this report. This could build on Alzheimer's Research UK's Think Brain Health.[85] The potential impact of demand on healthcare services would need to be considered.

[82] See https://www.brainhealth.scot/brainhealthservices
[83] Alzheimer's Society (2021). *Risk factors for dementia.* https://www.alzheimers.org.uk/sites/default/files/pdf/factsheet_risk_factors_for_dementia.pdf
[84] https://www.alzheimers.org.uk/about-dementia/types-dementia/parkinsons-disease
[85] https://www.alzheimersresearchuk.org/brain-health/check-in/

Next steps proposed by participants:

4.1 The training and continuing professional development of general practitioners and other relevant primary care clinicians should reflect the latest advances in the detection, diagnosis and treatment of neurodegenerative conditions.

4.2 Integration of brain health assessments into both pre-existing routine health checks and care plans for people with a condition that puts them at risk of developing a neurodegenerative condition should be explored.

4.3 The potential for an evidence-based public health campaign to promote brain health and prevention should be explored. Some workshop participants suggested that the government in collaboration with medical charities would be well-placed to deliver this campaign.

5. Equity, evidence and iterative improvement should underpin future developments

Throughout discussions, participants highlighted that equity will be important. Health inequalities in the UK are associated with geography, gender, ethnic background and socioeconomic status. The incidence of dementia is over 20% higher among Black adults than in the general population.[86] Black and South Asian people with dementia are also likely to die at a younger age than White people.[87] These inequalities may reflect exposure to risk factors, but also suggest less timely detection and diagnosis in minority groups. This could be due in part to barriers in healthcare access or cultural factors including stigma of neurodegenerative conditions. Patient pathways should not be designed in a way that disadvantages certain groups. For example, detecting neurodegenerative conditions through OCT scans could create a financial barrier because scans are often 'optional extras' in vision assessments and require additional payment.

Participants also noted that developments to pathways should be iterative and underpinned by evidence. Existing pathways should be examined to see what is currently working, so that research is not duplicated. Developments to pathways could be used as opportunities to reduce silo-working and gather more research on neurodegenerative conditions. Some participants felt that the use of new tools and changes to care pathways should not be hindered by a desire to design perfect solutions. Waiting for a perfect solution would delay people who may have a neurodegenerative condition benefitting from existing early detection tools, technologies and approaches. Instead, much could be gained from trying things out and learning from experience.

[86] https://dementiastatistics.org/perceptions-and-inequalities/inequalities/
[87] Mukadam N, Marston L, *et al.* (2022). *Incidence, age at diagnosis and survival with dementia across ethnic groups in England: a longitudinal study using electronic health records.* Alzheimer's & Dementia **19(4)**, 1300–1307.

Conclusion

We may be at a turning point in detecting, diagnosing and treating neurodegenerative conditions. The need has never been greater, with the number of people in the UK living with dementia projected to hit one million by 2030. Effective pharmacological treatments for slowing or preventing the progression of neurodegenerative conditions such as Alzheimer's may soon be available in the UK. Timely detection and diagnosis will be critical to allow people living with a neurodegenerative condition to access these treatments. Timely detection could also enable non-pharmacological interventions to potentially prevent or delay the progression of disease – for example, lifestyle modifications to address risk factors that are correlated with poorer outcomes. It will be important to build an evidence base on the efficacy of non-pharmacological interventions, as well as pharmacological interventions. Other potential benefits of early detection include access to clinical research and pre-diagnostic support, and the opportunity to plan ahead.

Novel tools such as blood biomarker and digital tests present an opportunity to improve early detection and diagnosis. Novel detection tools could be implemented in primary care services such as general practices, alongside existing cognitive and neurofunction tests. The use of relevant data from wearables and health apps could also be valuable. Using these tools in primary care services could then triage referrals for diagnosis and improve specialist service capacity. Other primary care contractors and community services (including pharmacies and opticians) could also become involved in early detection. This would require a review of roles and responsibilities.

Improving the early detection, diagnosis and treatment of neurodegenerative conditions is a national priority. Services offering detection and diagnosis of neurodegenerative conditions should be accessible and timely for people concerned about their risk. General practitioners and other primary care clinicians could be given a greater role in the detection of neurodegenerative conditions. This could be done through the implementation of novel detection tools in primary care. It will be important to assess how these tools could be used to deliver maximum benefit to people living with a neurodegenerative condition, as well as system efficiency. To be effective, general practitioners and other relevant healthcare staff should be consulted on changes to the pathway for detection and diagnosis and their capacity considered. People at risk of or living with a neurodegenerative condition, as well as those affected, will also need to be involved in changes to pathways so that their needs and preferences are central.

Annex 1: Agenda

Time	Session 1: Opportunities for detecting neurodegenerative diseases in primary care and the community
10.00 – 10.20	**Opening remarks from Co-chairs** • **Dr Ruth McKernan CBE FMedSci** Venture Partner, SV Health Investors and Trustee, Alzheimer's Research UK • **Dr Sara Humphrey GP,** Associate Clinical Director Dementia, NHS Bradford Districts Health & Care Partnership; NHSE Clinical Lead for Older People's Mental Health and Dementia in Yorkshire Region Team; Honorary Professor, Bradford University
10.20 – 10.30	**Talk: A lived experience perspective: living with atypical dementia** **Michael Petley**
10.30 – 10.45	**Talk: Multiple sclerosis** **Professor Anna Williams**, Professor of Regenerative Neurology, University of Edinburgh
10.45 – 11.00	**Talk: Alzheimer's disease (and other causes of dementia)** **Professor Craig Ritchie** Professor of the Psychiatry of Ageing, University of Edinburgh; CEO and Founder of Scottish Brain Sciences
11.00 – 11.05	**Break**
11.05 – 11.50	**Panel discussion: Enabling the early detection of neurodegenerative diseases in primary care and the community** • **Ashton Harper** Head of Medical Affairs (UK & Ireland), Roche Diagnostics • **Jacqueline Krarup** Patient expert living with secondary progressive MS • **Mr Praveen J. Patel,** Consultant Ophthalmologist, Moorfields Eye Hospital NHS Foundation Trust and Honorary Clinical Lecturer UCL Institute of Ophthalmology • **Professor Nadeem Sarwar,** Corporate Vice President, Novo Nordisk; Co-chair of the UK Dementia Mission
11.50 – 12.05	**Break**
	Session 2: Breakout groups
12.05 – 12.35	**Breakout Session 1: Needs, opportunities and feasibility** *Attendees were split into breakout groups and given an example diagnostic pathway (either Alzheimer's disease and other dementias, or multiple sclerosis) as a starting point for discussions (although participants were welcome to discuss other neurodegenerative diseases throughout).* **Discussion questions:** • What are the key challenges faced by healthcare professionals and patients in primary care and community settings concerning the detection of neurodegenerative disease? • What is the potential for detecting neurodegenerative disease early in primary and community care settings? What factors are limiting or enabling the realisation of that potential?
12.35 – 13.30	**Lunch**
13.30 – 14.15	**Breakout Session 2: Possibilities and next steps** *In the same groups and with the same worked example, participants discussed and proposed **4–5 next steps** for enabling early detection of neurodegenerative diseases (including the use of novel tools) in primary and community care settings.* **Discussion questions:** • What key features are needed to enable the use of tools in primary and community care settings? How might this differ from tools designed for use in secondary care settings?

	• What research and evidence is needed for these tools to be used in primary and community care settings? • What features and innovations to current systems, including diagnostic pathways, might be required to support and facilitate beneficial and efficient* early detection? Which key individuals and groups might be involved in this? **Detection that is beneficial to the patient and healthcare professional, while also improving the efficiency and integration across primary and secondary care systems.*
14.15 – 14.20	**Break**
14.20 – 15.00	**Breakout Session 3: Lessons to be learned and non-disease specific opportunities for detection** *In the same groups, participants discussed how some of these next steps, and broader themes, could potentially also be applied to the early detection of other neurodegenerative diseases in primary and community care settings.* **Discussion questions:** • Which of the identified challenges and opportunities could also be relevant to other neurodegenerative diseases? • Which of the identified next steps are applicable to the detection of other neurodegenerative diseases? Which are not? If not, why not? • Are there any opportunities to develop patient-centric* techniques and tools that would facilitate the detection of (and potential distinction between) a breadth of neurodegenerative diseases? How might this relate to the detection of other, non-neurodegenerative diseases? **Tools and techniques that consider the patient experience, such as ensuring that the person experiencing symptoms does not to go through a lengthy process involving several different tests to rule out various neurodegenerative diseases.*
15.00 – 15.15	**Break**
	Whole-group discussion
15.15 – 16:25	**Feedback & whole-group discussion**: **Next steps for enabling early detection of neurodegenerative diseases in primary care and the community**
16.25 – 16.30	**Closing remarks by the Co-Chairs**
16.30	Event close

Annex 2: Participant list

Co-chairs

- **Dr Ruth McKernan CBE FMedSci**, Venture Partner, SV Health Investors and Trustee, Alzheimer's Research UK
- **Dr Sara Humphrey**, a general practitioner with an Extended Role in Older People and Associate Clinical Director Dementia at NHS Bradford Districts Health & Care Partnership; NHS England Clinical Lead for Older People's Mental Health and Dementia in Yorkshire Region Team; Honorary Professor at Bradford University.

Participants

- **Hiba Adan**, PhD Student, King's College London
- **Dr Alison Buick,** Head of Global Business Development, Cumulus Neuroscience
- **Fiona Carragher,** Executive Director of Research and Influencing, Alzheimer's Society
- **Professor Camille Carroll,** Professor of Clinical Neuroscience and Honorary Consultant Neurologist, Newcastle University
- **Dr Sam Creavin,** NIHR Clinical Lecturer in General Practice, Bristol Medical School
- **Professor Charles ffrench-Constant FMedSci,** Pro-Vice Chancellor for Medicine and Health Sciences, University of East Anglia
- **Dr Amy Davies,** Senior Consultant, IQVIA
- **Eric Deeson,** Public Involvement Volunteer
- **Dr Karen Harrison Dening,** Head of Research & Publications & Director of Admiral Nursing, Dementia UK
- **Professor Ruth Dobson,** Consultant Neurologist, Queen Mary University of London
- **Dr Megan Eldred,** Senior Policy Advisor and Dementia Mission Lead, Office for Life Sciences
- **Jodie Forbes,** Public Contributor
- **Dr Eve Forrest,** Senior Portfolio Manager (Health and Human Behaviour Research), Economic and Social Research Council (ESRC)
- **Sarah Foster**, Policy Manager, Alzheimer's Research UK
- **Professor John Gallacher,** Professor of Cognitive Health, University of Oxford
- **Professor Gavin Giovannoni,** Professor of Neurology, Barts and the London School of Medicine and Dentistry
- **Professor Sir John Hardy FRS FMedSci,** Chair of the Molecular Biology of Neurological Disease, University College London
- **Dr Ashton Harper,** Head of Medical Affairs (UK & Ireland), Roche Diagnostics
- **Sadid Hoque,** Public Contributor
- **Dr Sara Imarisio,** Strategy Leader for Neuroscience, Medicines Discovery Catapult
- **Ian Jones,** Owner, Jinja Publishing Ltd
- **Dr Susan Kohlhaas,** Director of Research, Alzheimer's Research UK
- **Jacqueline Krarup,** Patient expert living with secondary progressive MS
- **Lucy Lehane,** Innovation Programme Lead, British In Vitro Diagnostics Association (BIVDA)
- **Shelle Luscombe,** Lived experience expert
- **Dr Charles Marshall,** Professor and Honorary Consultant Neurologist, Queen Mary University of London

- **Professor Christopher McDermott,** Professor of Translational Neurology and Honorary Consultant Neurologist, University of Sheffield
- **Laurel Miller,** Expert by experience (Parkinson's)
- **Dr Gita Khalili Moghaddam,** Principal Investigator, University of Cambridge
- **Dr Padraig Mulholland,** Senior Lecturer in Optometry, Ulster University
- **Dr Victor Neduva,** Senior Director, Discovery Research, MSD
- **Professor Alastair Noyce,** Professor in Neurology and Neuroepidemiology and Consultant Neurologist, Queen Mary University of London
- **Praveen J. Patel,** Consultant Ophthalmologist, Moorfields Eye Hospital NHS Foundation Trust and Honorary Clinical Lecturer UCL Institute of Ophthalmology
- **Michael Petley,** Lived experience of living with an atypical dementia
- **Alison Railton,** Head of Policy & External Affairs, Kidney Research UK
- **Professor Greta Rait,** Clinical Professor of Primary Care and Health Services Research, University College London
- **Dr Vanessa Raymont,** Associate Director, Dementias Platform UK
- **Dr Alastair Reith,** Senior Scientific Director (Novel Human Genetics Research Unit) and R&D Senior Fellow, GSK
- **Professor Craig Ritchie,** Chair of the Psychiatry of Ageing and Director of the Centre for Dementia Prevention, University of Edinburgh
- **Professor Jonathan Rohrer,** MRC Clinician Scientist and Honorary Consultant Neurologist, University College London
- **Professor Nadeem Sarwar,** Corporate Vice President, Novo Nordisk; Co-chair of the UK Dementia Mission
- **Professor Klaus Schmierer,** Professor of Neurology, Blizard Institute and Consultant Neurologist, Royal London Hospital, Barts Health NHS Trust
- **Professor Jonathan Schott,** Professor of Neurology, University College London
- **Dr Jina Swartz FMedSci,** Chief Medical Officer, Exciva
- **Dr Eugene Tang,** NIHR Clinical Lecturer in General Practice, Newcastle University
- **Professor Jessica Teeling,** Professor of Experimental Neuroimmunology, University of Southampton
- **Dr Emma Vardy,** Consultant Geriatrician, Salford Royal Hospital, Greater Manchester
- **Professor Angus Walls,** Director of the Edinburgh Dental Institute and Professor of Restorative Dentistry, University of Edinburgh
- **Professor Jason Warren,** Professor of Neurology and Consultant Neurologist, University College London
- **Professor Anna Williams,** Professor of Regenerative Neurology, University of Edinburgh
- **Nikki Zimmerman,** Direct Support Services Lead, Rare Dementia Support

Staff and secretariat

- **Rachel Bonnington,** Public Engagement Officer, Academy of Medical Sciences
- **Dr Hannah Chance,** Policy Officer, Academy of Medical Sciences
- **Dr Claire Cope,** Head of Policy, Academy of Medical Sciences
- **Dorian Crudgington,** Policy Intern, Academy of Medical Sciences
- **Dr Anna Hands,** FORUM Policy Manager, Academy of Medical Sciences
- **Kate Little,** FORUM Policy Officer, Academy of Medical Sciences
- **Shaheim Ogbomo-Harmitt,** Policy Intern, Academy of Medical Sciences

Annex 3: Glossary of useful terms

This section provides definitions for some of the terms relevant to the report.

Alzheimer's disease (AD)
A progressive neurodegenerative condition, with early signs including mild cognitive impairment and gradual memory loss. As the disease develops, other symptoms can include confusion, disorientation, difficulties making decisions and performing familiar tasks, problems with speech and mobility, personality changes, hallucinations, and anxiety or depression. AD is a common cause of dementia.

Biomarkers (and biomarker tests)
Biomarkers (biological markers) are a measurable indicator of biological states or conditions (including disease), and are often measured through blood, urine or soft tissue samples. Tests for biomarkers can be used to detect or confirm the presence of a disease or condition.

Clinical pathways
Also known as care pathways, clinical pathways are agreed-upon comprehensive and integrated plans for patient care during a given period. Clinical pathways aim to promote organised and efficient patient care based on evidence-based medicine, and to achieve the best possible patient outcomes. They are one of the main tools used to manage the quality and standardisation of care processes.

Cell
The basic building blocks of all living things, including plants and animals. Whether living on their own (e.g. bacteria, which are made up of a single cell) or as part of a multicellular organism, cells are usually too small to be seen without a light microscope.

Cerebrospinal fluid (CSF)
Fluid that flows in and around the hollow spaces of the brain and spinal cord. CSF acts as a shock absorber to the nervous system, cushioning the brain from damage, and providing basic immunological protection as well as clearing waste products from the brain.

Community care
Community health services include health promotion services and services delivered in people's homes, community hospitals, intermediate care facilities, clinics and schools. Community care practitioners can include physiotherapists, speech and language therapists, and specialist nurses.

Dementia
A general term to describe a group of symptoms associated with an ongoing decline of brain function. Dementia symptoms include the loss of memory, language, problem-solving and other thinking abilities. Dementia symptoms can be caused by diseases such as Alzheimer's disease.[88,89]

- **Frontotemporal dementia (FTD):** Sometimes called Pick's disease or frontal lobe dementia, FTD is an uncommon type of dementia that affects the frontal and temporal

[88] https://www.nhs.uk/conditions/dementia/symptoms-and-diagnosis/symptoms/
[89] https://www.alzheimers.org.uk/about-dementia/types-dementia

lobes of the brain and causes problems with behaviour and language. FTD is the most common form of dementia for people under 60 (young onset).

- **Lewy body dementia (LBD):** A form of dementia associated with abnormal deposits, called Lewy bodies, that affect chemicals in the brain. These changes, in turn, can lead to problems with thinking, movement, behaviour and mood.
- **Vascular dementia:** A common type of dementia caused by reduced blood flow to the brain. It is estimated to affect around 180,000 people in the UK. Many people with vascular dementia also have Alzheimer's disease.

Diagnosis
The identification and confirmation of an illness or other problem through an examination of a person's signs and symptoms. Attaining a diagnosis can then enable an individual to access the right treatments to help manage, slow or cure their condition; access support and strategies for living well with their condition; and access opportunities to take part in clinical trials for new tests and treatments.

Direct-to-consumer
The process of marketing, advertising and selling products directly to the customer or patient, rather than to the healthcare system.

Disease-modifying treatment/therapy or drugs
Treatments, therapies or drugs that could change (for the better) how a person's neurodegenerative condition develops over time. For example, this could be a drug that a patient takes, or a treatment that uses stem cells. A DMT isn't a cure, but it could make a real difference to a patient's quality of life. In MS, the primary goal of a DMT is preventing MS relapses (attacks) and reducing the accumulation of neurological impairment.

Drug
Any natural or artificially made chemical that is used as a medicine to treat illness or injury. Drugs are widely used for the prevention, diagnosis and treatment of disease and for the relief of symptoms. When ingested or otherwise introduced into the body, drugs can affect how the brain and the rest of the body work and cause changes in mood, awareness, thoughts, feelings or behaviour.

Magnetic Resonance Imaging (MRI) scan
An MRI uses strong magnetic fields and radio waves to produce detailed cross-sectional images of the inside of the body. The MRI scanner is operated by a radiographer, who interprets the images the scanner produces on a computer. The results of an MRI scan can be used to help diagnose conditions, plan treatments and assess how effective previous treatment has been.

Memory Clinic
Also called a Memory Assessment Service, a memory clinic is a medical clinic specialising in the assessment and diagnosis of memory disorders. GPs will often refer patients to memory clinics where specialists will then conduct a series of tests to diagnose a neurodegenerative condition.

Mild cognitive impairment (MCI)
Mild cognitive impairment is when a person starts to have problems with their memory, language or judgement. It can be caused by a range of factors, but it can also be the sign of a disease that will eventually cause dementia.

Motor Neurone Disease (MND)
Also called amyotrophic lateral sclerosis (ALS), MND is a rare condition that affects the brain and the nerves and causes rapidly progressing weakness. There is currently no cure for MND, and the condition can shorten life expectancy significantly.

Multiple Sclerosis
A lifelong neurological condition affecting the brain, spinal cord and optic nerves, caused by damage to the myelin sheath, the coating that protects nerves. Symptoms of MS are wide-ranging and can include fatigue, abnormal sensations, pain, muscle spasms and stiffness, and problems with mobility, the bladder and the bowel, vision, balance, co-ordination, thinking and learning.

- Relapsing remitting MS (RRMS) – the most common type of MS, characterised by individual episodes where symptoms emerge (attacks or relapses) followed by periods of recovery (remissions). In relapsing MS, people have distinct attacks of symptoms that then fade away either partially or completely. Symptoms they've had before might come back, or they might experience new symptoms.
- Secondary progressive MS (SPMS) – a stage of MS that comes after RRMS for many people, in which symptoms get progressively worse over time, without remission. Some people may still get relapses, but they do not tend to make a full recovery afterwards.
- Primary progressive MS (PPMS) – symptoms get progressively worse over time from disease onset, with few or no remissions, resulting in permanent neurological impairment. There can also be long periods where symptoms seem to be staying level. PPMS affects about 10–15% of people diagnosed with MS.

Myelin sheath
An insulating and protective layer made up of protein and fatty substances that wraps around nerves. The myelin sheath allows electrical impulses to transmit quickly along nerve cells and also assists in the regeneration of damaged nerve fibres.

Neurodegenerative disease or condition
Diseases that are primarily characterised by the loss of structure or function of neurons, in a process known as neurodegeneration. Alzheimer's and Parkinson's are among the most common neurodegenerative conditions.

Neurofilament
A microscopic filament (thread-like object or fibre) of protein found in neurons. Research has shown that neurofilament proteins are promising biomarkers of neurodegenerative condition and can be detected through cerebrospinal fluid and blood.

Nervous system
The nervous system includes the brain, spinal cord and a complex network of nerves. The nervous system has two parts: the central nervous system, which includes the brain and the spinal cord; and the peripheral nervous system, which is made up of nerves that branch off from the spinal cord and extend to all parts of the body.

Neurology
The branch of medicine dealing with the diagnosis and treatment of all categories of conditions and diseases involving the nervous system. **Neurologists** are practicing physicians who diagnose and treat neurological conditions, and often specialise in specific disease fields.

Neurons
Also known as nerve cells: electrically-excitable cells within the nervous system, which are responsible for carrying information throughout the human body using electrical and chemical

signals. Neurons connect together to make a neural network or circuit. There are three main types of neuron:

- Sensory neurons – carry sensory information (such as pain, touch, temperature, itch and stretch) from tissues and organs into the brain and spinal cord
- Motor neurons – transmit signals from the brain and spinal cord to muscles; required for motor control

Interneurons connect regions of the brain and nervous system, enabling communication between sensory or motor neurons. Interneurons play a vital role in reflexes and allow the brain to perform complex functions such as learning and decision-making.

Optic nerve
A nerve that transmits electrical impulses from the retina, in the back of the eye, to the visual cortex of the brain. Your brain processes this sensory information so that you can see; therefore, the optic nerve is critical for vision.

Parkinson's
A progressive neurodegenerative condition that affects the nervous system and the parts of the body controlled by the nerves. It is not yet known what causes Parkinson's, but people with Parkinson's do not have enough of the chemical dopamine in their brain because some of their dopamine-producing nerve cells stop working. The main symptoms are tremors, slowness of movement and rigidity. There is currently no cure for Parkinson's, but there are treatments to manage the condition. Around 153,000 people live with Parkinson's in the UK.

Positron Emission Tomography (PET) scan
Scans used to produce detailed three-dimensional images of the inside of the body.

Presentation (medical)
The appearance in a patient of illness or disease (such as the signs or symptoms of disease) to a medical professional.

Primary care
The first point of contact a patient has with the healthcare system, described as the 'front door' of the NHS. Primary care services include general practices, pharmacies, dental and optometry services.

Primary care clinicians
Primary care clinicians include clinicians based in general practices, pharmacies, dentists and optometry services. In a general practice, these might include the general practitioner as well as advanced clinical practitioners, physician associates, nurses and pharmacists.

Prodromal symptoms
The early signs or symptoms of an illness or health problem that appear before more diagnostically specific signs or symptoms start. These symptoms are often found in many other illnesses, so it isn't always clear at the time if this is a **prodrome** of a specific condition or something else. However, such symptoms may indicate a higher-than-average risk of developing symptoms and a diagnosis of that condition in future. For example, early impairments in behaviour, personality and language may be detected in Alzheimer's disease years before memory problems arise. Prodromal symptoms of Parkinson's include loss of smell (including identification, detection and discrimination of odours), constipation, mood disorders, and REM sleep behaviour disorder (RBD).

REM sleep behaviour disorder (RBD)
Rapid eye movement (REM) sleep is the stage of sleep where most dreams happen. Normally during REM sleep, the body experiences temporary paralysis of most of the body's muscles while the brain is active and dreaming. This allows us to dream quietly and safely throughout the night. For individuals with REM sleep behaviour disorder, paralysis does not occur during the REM stage and, instead, their body and voice perform their dreams while they remain asleep.

Risk factor
Something that may increase the chance of developing a disease or condition. Some risk factors such as lifestyle or diet can be controlled, while others such as age cannot.

Secondary care
The care a patient receives for their specific illness or condition beyond the primary care they have already received. Secondary care can be understood as more specialist care provided by a practitioner with specialist expertise or a specialised facility (e.g. neurology, gastroenterology or cardiology departments of a hospital).

Tissue
A group of cells that have similar structure and that function together as a unit (e.g. brain/lung/muscle/fat tissue).

Triage
A preliminary assessment of patients to determine which patients need to be prioritised for urgent care or treatment.

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