

## Alzheimer's Disease Health System Readiness – The Time to Act is Now

*Alzheimer's disease is one of Europe's largest public health crises, but #WeWontRest until new innovation and treatments can halt the disease in its tracks.*

Alzheimer's disease (AD) is a progressive neurodegenerative disease that damages healthy cells in the brain causing cognitive impairment and functional disability. AD is the most common form of dementia and may contribute to 60-70% of the cases.<sup>1</sup> Alzheimer's disease and other forms of dementia affect around 10 million people in Europe, and this number is expected to increase to 14 million by 2030.<sup>2</sup> The societal and economic cost of dementia in Europe is estimated to increase to over €250 billion by 2030 (with over 50% of this due to informal care costs), the equivalent of the whole GDP of Finland.<sup>3</sup> AD is thus not only a debilitating and progressive disease affecting the daily lives of people, their families, and carers, but also a huge burden for our economy and European nations' healthcare and social care systems.

Currently, therapies available can help to manage symptoms of the disease such as cognitive impairment, agitation, aggression, or insomnia, offering a limited extension to "normal" living. Fortunately, there is hope on the horizon. Disease Modifying Therapies (DMTs) targeting earlier stages of Alzheimer's disease that are currently in development have the potential to change the lives of both patients and carers and to substantially reduce the societal and economic burden of the disease. DMTs have the potential to delay the onset or progression of Alzheimer's, allowing patients to live an independent life, for longer. Delaying in the onset or progression of Alzheimer's is expected to have a large impact for the quality of life of patients, their carers and families.

**However, for people living with dementia, their carers, and society to benefit from these innovations, clinical practice will have to transform and align with the progress made in AD understanding and science. Healthcare systems in Europe currently lack the capacity to detect, diagnose and treat AD effectively, hindering the ability to rapidly move a DMT for AD from approval into widespread clinical use. This could leave a large number of patients without access to transformative care when a breakthrough occurs.**

We now know that Alzheimer's disease pathology begins 10-20 years before the onset of the first symptoms. Access to a DMT for AD will require early detection, timely diagnosis, and appropriate monitoring of patients with mild cognitive impairment (MCI) and/or in the early stages of the disease, before changes in cognition or behavior occur. Timely and accurate diagnosis will be essential for identifying patients that could benefit the most from DMTs.

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<sup>1</sup> WHO Dementia Key facts, <https://www.who.int/news-room/fact-sheets/detail/dementia>

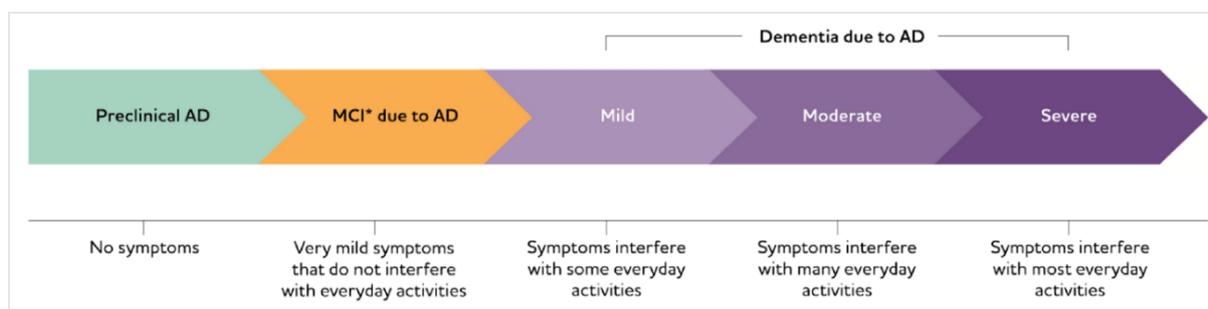
<sup>2</sup> Alzheimer Europe, Dementia in Europe, Yearbook 2019, <https://www.alzheimer-europe.org/Publications/Dementia-in-Europe-Yearbooks> ; <https://www.alzheimer-europe.org/Research/European-Collaboration-on-Dementia/Cost-of-dementia/Prognosis-to-2030>

<sup>3</sup> Alzheimer Europe, Cost of illness and burden of dementia in Europe – Prognosis to 2030, [www.alzheimer-europe.org/Research/European-Collaboration-on-Dementia/Cost-of-dementia/Prognosis-to-2030](http://www.alzheimer-europe.org/Research/European-Collaboration-on-Dementia/Cost-of-dementia/Prognosis-to-2030); EurActiv, Rising dementia numbers in EU causes alarm, [www.euractiv.com/section/health-consumers/news/rising-dementia-in-the-eu-causes-alarm/](http://www.euractiv.com/section/health-consumers/news/rising-dementia-in-the-eu-causes-alarm/)

If people cannot be diagnosed and treated in time, their cognitive abilities will continue to decline, potentially leading to dementia and rendering innovative treatments ineffective. The COVID-19 pandemic showed us the need to take steps to prepare for future public health crises to avoid devastating effects for patients and healthcare systems alike. As AD poses to be one of Europe’s most significant public health crises, we need to act now as over 1 million patients living with early stages of Alzheimer’s will develop dementia between 2020 and 2050 while waiting for treatment.<sup>4</sup>

### The Alzheimer’s disease continuum<sup>5</sup>

AD progresses along a continuum from preclinical disease characterized by normal cognition and abnormal brain biomarkers to mild cognitive impairment and then clinically apparent dementia. The current research efforts are focused on the early stages of disease, where it is believed that there will be the best chance at slowing or preventing the progression of the disease. This requires that the health care system is able to detect and diagnose as early as possible.



### Detection

AD is characterized by the accumulation of toxic amyloid beta plaques in the brain and its downstream effects, including the aggregation of tau protein, potentially leading to neuronal loss. Research has shown that this abnormal accumulation of toxic amyloid beta is present in the brain decades before symptom onset and its detection indicates a higher risk of developing Alzheimer’s disease.<sup>6</sup>

MCI due to AD is one of the earliest stages of the disease when symptoms start to become more visible and can be detected. Currently, detection of MCI due to AD is a challenge. Research suggests some patients are not aware of their underlying status and feel the social stigma of an AD diagnosis; and many general practitioners lack the knowledge in identifying early symptoms of AD, which may be difficult to differentiate from other conditions (i.e. stroke).<sup>7</sup> Recent innovations in digital technology and artificial intelligence tools provide novel ways to assess cognitive functions and help healthcare professionals to objectively detect AD prior to the onset of symptoms.

<sup>4</sup> RAND, Assessing the preparedness of the health care system infrastructure in six European countries for an Alzheimer’s treatment, [https://www.rand.org/pubs/research\\_reports/RR2503.html](https://www.rand.org/pubs/research_reports/RR2503.html)

<sup>5</sup> Alzheimer’s Association, 2020 Alzheimer’s disease facts and figures. *Alzheimers Dement.* 2020;16(3):391-460.

<sup>6</sup> Livingston et al. (2017), Dementia, prevention, intervention, and care. *The Lancet*, Vol. 390, Issue 10113, pp. 2673-2734. Accessible at: [https://doi.org/10.1016/S0140-6736\(17\)31363-6](https://doi.org/10.1016/S0140-6736(17)31363-6)

<sup>7</sup> D Wilkinson et al (2004), The Role of General Practitioners in the Diagnosis and Treatment of Alzheimer’s Disease: A Multinational Survey. *Int Med Res.* Mar-Apr 2004;32(2):149-59. doi: 10.1177/147323000403200207.

In the European Union, it is estimated that approximately 20 million individuals over age 55 have MCI,<sup>8</sup> although most people have not been tested for disease pathology, as there is currently no treatment option. Thus, when a therapy first becomes available, there would be a substantial number of MCI cases that would require detection. Timely detection can also help to delay the need for the high levels of care associated with severe Alzheimer's disease, which is estimated to cost healthcare systems approximately €20 billion annually across the EU.<sup>9</sup>

#### Recommendations to EU Member States:

- Raise awareness of early symptoms of Alzheimer's disease among the general public.
- Support better access to expertise through new care pathways that would support general practitioners (or primary care providers) to identify MCI symptoms early on, use cognitive assessments and refer most at-risk patients to dementia specialists for further clinical evaluation.
- Increase the number of physicians and other healthcare professionals who are trained and able to perform cognitive assessments and increase general dementia training time for all healthcare professionals.
- Leverage digital tools that can provide quantifiable indicators and biomarkers of patients' cognitive functions.
- In line with the recommendations of the Models of Patient Engagement for Alzheimer's Disease (MOPEAD), implement targeted screening of populations at risk to ensure Alzheimer's early detection and access to treatment.<sup>10</sup>
- Ensure access to post-diagnostic support for people with dementia and their carers

#### Diagnosis

The current AD diagnostic pathway requires a comprehensive medical assessment using a variety of examinations and tests that aim to rule out all possible causes of dementia-like symptoms, including: thorough medical history, physical and neurological exams, mental status and mood testing (including cognitive testing). If the evaluation confirms MCI and does not find an alternative explanation for it, individuals would then be referred to testing for biomarkers.

Confirmatory biomarker testing is necessary for an accurate AD diagnosis. At the moment, this can be done either via a lumbar puncture (Cerebrospinal Fluid - CSF) or through neuroimaging (amyloid PET scan). However, such tests are not currently widely used in clinical practice. Lumbar Punctures are well accepted for diagnostic purposes by neurologists in Europe but not fully available outside specialist centres or among other dementia-specialists.<sup>11</sup> There are also some barriers related to the reimbursement of lumbar punctures and CSF/amyloid beta testing across Europe. PET scans are generally considered expensive, there is limited PET capacity and they are not easy to scale-up. Blood

<sup>8</sup> RAND, Assessing the preparedness of the healthcare system infrastructure in six European countries for an Alzheimer's treatment, [https://www.rand.org/pubs/research\\_reports/RR2503.html](https://www.rand.org/pubs/research_reports/RR2503.html)

<sup>9</sup> EFPIA Alzheimer's Disease Platform: <https://www.efpia.eu/we-wont-rest/innovation/alzheimer-s-disease/>

<sup>10</sup> For instance, screening mammography is the most common and widely practiced breast cancer screening tool worldwide. Early detection of breast cancer has helped decrease morbidity, as the cancer is treated by less toxic therapy, increased 5 year survival rates for all type of breast cancer and reduced mortality rates overall (3% among women aged 40–49 years, 8% in women aged 50–59 years, 21% among women aged 60–69 years, and 13% in women aged 70–74 years). *Breast cancer screening programs: Review of merits, demerits, and recent recommendations practiced across the world*, Tajammal Abbas Shah and Shaista Salman Guray, *Journal of Microscopy and Ultrastructure*, Volume 5, Issue 2, June 2017, Pages 59-69.

<sup>11</sup> Current Approaches and Clinician Attitudes to the Use of Cerebrospinal Fluid Biomarkers in Diagnostic Evaluation of Dementia in Europe, available at <https://pubmed.ncbi.nlm.nih.gov/28826189/>

based biomarkers that could also be used for confirmatory diagnosis are currently in development and may be available in the near future, thus helping to make AD confirmatory diagnosis easier.

Other existing barriers to timely diagnosis include a lack of confidence regarding diagnostic procedures, lack of time by the healthcare provider, and for some countries, there is insufficient reimbursement, as well as the attitude of healthcare professionals towards the usefulness of available pharmacological and non-pharmacological treatment options.<sup>12</sup> Another major constraint is represented by the lack of specialists to assess and diagnose AD patients with MCI or in the early stage of dementia.

As a result, there are currently significant delays in diagnosing AD. Research shows that 50% of patients with any form of dementia are not formally diagnosed.<sup>13</sup> Almost 62% of healthcare providers worldwide think that dementia is part of normal ageing.<sup>14</sup>

#### **Recommendations to EU Member States:**

- Integrate diagnostic tests used to confirm amyloid positivity, including PET scans and CSF, within the clinical pathway, and support their reimbursement.
- Support the development of alternative, lower-cost options for routine tests in primary care settings such as amyloid testing by blood-based biomarker and other clinical diagnosis tools that could facilitate differential diagnosis and triaging in primary care settings.<sup>15</sup>

### **AD Interventions and Treatment**

Access to an early AD diagnosis provides patients and their carers with the possibility to access available interventions earlier (i.e. non-pharmacological interventions, pharmacological clinical trials, counselling, and life-planning). In the near future when DMTs are available, an early clinical diagnosis will facilitate early treatment, which can maximise the cost-effectiveness of the intervention and increase the benefit to someone living with AD and their carers.

The co-location of memory clinics with general hospitals or inpatient psychiatric facilities can provide access to the necessary procedural skills and infrastructure needed. Memory clinics will also need to be established to handle routine cases in the same community, with specialist centres handling complex cases and research.

Some future DMTs are expected to be administered intravenously. Thus, the capacity of the healthcare system to deliver infusions will be a key factor to allow access to treatment. Currently, infusion capacity seems to be insufficient to address AD future demands in a number of European countries.<sup>16</sup> Similar challenges were addressed for immunomodulating antibodies for inflammatory diseases in the late 1990s, and, more recently, the introduction of biologic therapies for multiple cancers, rheumatoid arthritis, and other conditions, such as multiple sclerosis, have required expansion of infusion

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<sup>12</sup> The MOPEAD project: Advancing patient engagement for the detection of “hidden” undiagnosed cases of Alzheimer’s disease in the community [https://17215c60-696c-4eb6-9adb-50cde843a50f.filesusr.com/ugd/e8882a\\_acac8530e4e445fdbdc7e85dc70712d7.pdf](https://17215c60-696c-4eb6-9adb-50cde843a50f.filesusr.com/ugd/e8882a_acac8530e4e445fdbdc7e85dc70712d7.pdf)

<sup>13</sup> Rates of formal diagnosis of dementia in primary care: The effect of screening. Relkin N. Screening and early diagnosis of dementia. *Am J Manag Care.* 2000;6(22 Suppl):S1111–S1118. Eichler T., Thyrian J., Hertel J., Köhler L., Wucherer D., Dreier A. Rates of formal diagnosis in people screened positive for dementia in primary care: Results of the DelpHi-trial. *J Alzheimers Dis.* 2014;42:451–458.

<sup>14</sup> World Alzheimer Report 2019: Attitudes to dementia, available at <https://www.alz.co.uk/research/WorldAlzheimerReport2019.pdf>

<sup>15</sup> Palmqvist et al., 2019

<sup>16</sup> RAND, Assessing the preparedness of the healthcare system infrastructure in six European countries for an Alzheimer’s treatment, [https://www.rand.org/pubs/research\\_reports/RR2503.html](https://www.rand.org/pubs/research_reports/RR2503.html)

capacity.<sup>17</sup> Infusion capacity was expanded through the increased use of private infusion networks, home infusion and increased delivery within multidisciplinary primary care settings.

#### **Recommendations to EU Member States:**

- Strengthen infusion capacity in both primary care setting and via home infusion services.
- Increase the use of memory clinics. Follow the examples of Canada, Norway or the UK that demonstrate how to approach multidisciplinary care in AD.<sup>18</sup>
- Support a shift from care to active treatment, increasing the use of large multi-specialty practices.<sup>19</sup>
- Create new care pathways to recruit and train AD specialists, including neurologists, to meet the increased need for AD diagnosis.

### **Monitoring**

Office visits and imaging will likely be required to monitor treatment effectiveness and safety as part of a DMT's label and guidelines. While some countries in Europe will have sufficient Magnetic Resonance Imaging (MRI) capacity, there may be challenges in accessing an MRI in others. The need for follow-up visits will also compound any capacity constraints within specialist care, particularly due to the numbers of patients who would remain in a prolonged MCI state and the lack of experience and tools to monitor treatment effectiveness and detecting adverse effects by primary care providers.

#### **Recommendations to EU Member States:**

- Increase the use of primary care-led memory clinics and multidisciplinary care centres to monitor AD treatment and provide follow-up care.
- Support increases in MRI capacity in countries where it is needed.
- Increase training and education for primary care providers to support them in taking a greater role in monitoring treatment effect and detecting and addressing adverse events, like Amyloid-related imaging abnormalities (ARIA).

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<sup>17</sup> Tralongo et al., 2011

<sup>18</sup> Canada (Lee et al., 2014), Norway (Engedal, Guasdal, Gjora, and Haugen, 2012) and the UK (Greaves et al., 2015).

<sup>19</sup> Russell-Babin and Wurmser, 2016.

## Alzheimer's Disease Health System Readiness – A European call to action

Dementia was recently referred to in the European Commission Roadmap to the Pharmaceutical Strategy<sup>20</sup> as a major unmet medical need that requires innovation to align to public health and health systems' needs. We believe that we could be at a turning point in the fight against Alzheimer's disease and other forms of dementia. The COVID-19 crisis demonstrated the challenges faced by healthcare systems to respond to increased public health needs. Therefore, ensuring that healthcare systems are prepared to enable patients to benefit from future advances in AD detection, diagnosis and treatment requires public authorities to act now.

A combination of political leadership and ambitious policies, as well as continued innovation in diagnosis and treatment delivery, is urgently needed to respond to this challenge. This will entail ensuring that healthcare systems are ready to support the timely access to new diagnostic and pharmaceutical innovations to deliver high-quality healthcare for people living with Alzheimer's disease and other forms of dementia.

To do so, we need to ensure that political agendas in Europe make the fight against Alzheimer's disease and other forms of dementia part of their next healthcare policy priority. This should start at the European level and cascaded down to national healthcare systems.

We call on the EU Institutions to:

1. Demonstrate political leadership by making the fight against Alzheimer's disease and other forms of dementia a priority in European policies and dedicating funding to research and innovation, health, and social affairs.
2. Commit to develop and implement an ambitious European plan to beat Alzheimer's disease, using the model of what is currently being pursued in the cancer field with Europe's *Beating Cancer Plan*.<sup>21</sup>
3. Ensure that the EU4health programme fosters Member States collaboration in AD and exchange of best practices related to healthcare system readiness and social care systems for improved prevention, diagnosis, treatment and care.
4. Harmonise and disseminate independent and evidence-based detection and care guidelines for the benefit of healthcare providers, patients and their carers across Europe, including those currently in place by the European Academy of Neurology.
5. Support the adoption and implementation of national plans specifically dedicated to AD and other forms of dementia in line with the WHO's Global action plan 2017-2025. According to Alzheimer's Disease International, national plans are still the best tools available to effect change.<sup>22</sup> These plans should assess and set clear objectives towards national healthcare systems' readiness for the wave of disease-modifying therapies that is likely to enter the market in the near future.

**The time to ACT is NOW.**

<sup>20</sup> <https://ec.europa.eu/info/law/better-regulation/have-your-say/initiatives/12421-Pharmaceutical-Strategy-Timely-patient-access-to-affordable-medicines>

<sup>21</sup> <https://ec.europa.eu/info/law/better-regulation/have-your-say/initiatives/12154-Europe-s-Beating-Cancer-Plan>

<sup>22</sup> From Plan to Impact III Maintaining dementia as a priority in unprecedented times, Alzheimer's Disease International, 2020.