efpia

POSITION PAPER

TAKING ACTION TOGETHER

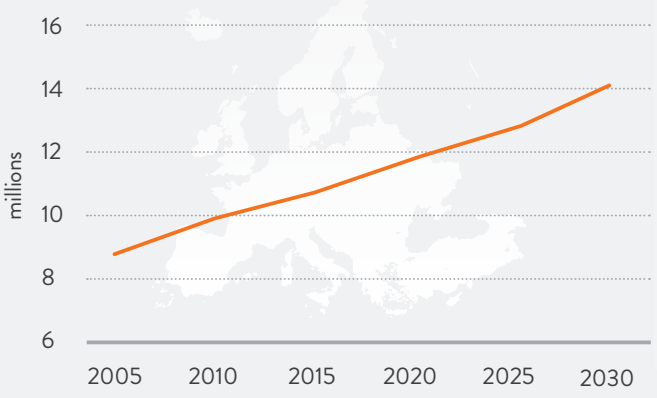
TO ENSURE A BRIGHTER TODAY AND TOMORROW FOR PEOPLE WITH ALZHEIMER'S DISEASE

ADDRESSING THE GROWING BURDEN OF ALZHEIMER'S DISEASE
NAVIGATING A CHALLENGING ENVIRONMENT

Today, over 11 million people in Europe are living with Alzheimer's Disease and other forms of dementia, with the number expected to increase to 14 million by 2030.[1,2] In Europe, the societal and economic cost of Alzheimer's Disease has been estimated to increase by 43% between 2008 and 2030 to over €250bn, the equivalent to the GDP of Finland.[3] This will not only have significant implications for those affected by Alzheimer's Disease and their families, but also for healthcare systems across Europe.

Even though substantial and continuous research has been, and still is, conducted on Alzheimer's Disease, these efforts have not yet delivered an effective disease modifying treatment that might slow down the progression of the disease (disease modifying treatment – DMT). Of the 413 clinical trials (covering phases I-III) that ran between 2002 and 2012, for instance, only one medicine was approved – a success rate of less than 1%.[4] This is a testament of our still developing understanding of the underlying causes of the condition. As we learn more about the pathology of the disease, different theories are emerging on what causes its development and progression to more severe stages. Current theories on the cause of Alzheimer's Disease and its progression range: from the excessive accumulation of a protein fragment in the brain, to chronic inflammation of the nervous tissue (for instance, due to brain injury or infection), to the potential impact of gut microbes on the brain as well as environmental factors. As clear indicators are lacking and research is not focused on one root cause, this further contributes to the lengthy treatment development process.

GRAPH 1: PROGNOSIS FOR THE NUMBER OF PEOPLE LIVING WITH DEMENTIA IN EUROPE UNTIL 2030[1]



THE SOCIETAL AND ECONOMIC COST OF ALZHEIMER'S DISEASE IN EUROPE IS ESTIMATED TO INCREASE TO €250BN BY 2030[3]

ADVANCING SCIENTIFIC RESEARCH FOR A BRIGHTER FUTURE FOR PEOPLE WITH ALZHEIMER'S DISEASE

Despite frequent setbacks in clinical trials, scientific progress is advancing rapidly and industry continues to invest significantly. In addition to DMTs, industry is investing in the development of innovative symptomatic treatments for Alzheimer's Disease, both for cognitive and non-cognitive symptoms.

THE DEVELOPMENT TIME FOR A DMT TO REACH A PATIENT IS ESTIMATED TO BE MORE THAN 9 YEARS[5]

THERE ARE CURRENTLY 135 INVESTIGATIONAL TRIALS ONGOING IN TREATMENTS FOR ALZHEIMER'S DISEASE[6]

Overall, there are 135 clinical trials for Alzheimer's Disease in development, with 110 of them in the late stages (phase II and phase III).[5] We hope that a DMT, which could delay the onset of the condition, could be available as early as 2021. Innovative treatments for behavioural symptoms are following closely. Together, these treatments have the potential to significantly reduce the burden on affected patients, their carers and healthcare systems across Europe.

PREPARING OUR HEALTHCARE SYSTEMS TO ENSURE PATIENT BENEFIT

Patients can only benefit from advances in treatment if healthcare systems are appropriately equipped to enable patient access to innovation along the whole of the disease pathway. In order to realise the scientific potential, we – health authorities, regulators, the scientific community, industry – need to work together in a number of areas:

1. PATIENT IDENTIFICATION AND SCREENING

CORRECTLY IDENTIFYING AND SCREENING THOSE AT RISK OF OR ALREADY LIVING WITH ALZHEIMER'S DISEASE IS A DIFFICULT TASK

The absence of a clear biomarker indicating the risk of progressing to Alzheimer's Disease makes screening and identification of at-risk populations challenging.

Testing those potentially at risk of developing Alzheimer's Disease often involves invasive and cost-intensive diagnostic mechanisms, such as lumbar puncture (taking fluid from the spine) or PET scans (an image test with radioactive tracers), in a population that has yet to develop symptoms.

This raises questions about the benefit of current diagnostics and their reimbursement, creating further barriers to identifying potential patients at an early stage.

In addition, a lack of robust measures to identify emerging symptoms and track disease progression poses challenges for health systems to develop effectively and implement clear care and treatment guidance.

Whilst early detection and diagnosis can help those affected access relevant information and support services, ethical challenges also remain around diagnosing patients in the current absence of an effective treatment.

2. OUTCOME CERTAINTY

THE SLOW PROGRESS OF THE CONDITION MEANS THAT TREATMENTS ARE BEING BROUGHT TO THE MARKET WHILST DATA IS STILL MATURING

Alzheimer's Disease develops over long periods of time and, therefore, treatment impact has to be measured over many years – often extending beyond the duration of a clinical trial. This poses challenges to existing models of assessing treatment outcomes and requires the translation of clinical endpoints into outcomes.

Current clinical endpoints were developed for treatments focused on later stages of the disease, when the decline of the person's cognitive function and therefore the potential treatment impact is more explicit. With current science focused on treating earlier stages of the condition before the onset of explicit symptoms, existing endpoints are not sufficiently sensitive to detect measurable treatment efficacy. Instead of focusing merely on symptoms, clinical endpoints need to target the pathology of the disease.

Moreover, a patient-focused assessment of benefit considering patients' quality of life would help better assess the benefit of treatments to those living with the disease and their carers. In the field of Alzheimer's Disease in particular, small improvements in the person's quality of life, such as the ability to independently walk to the supermarket, improved memory or sleep function, can make a significant difference in the lives of those affected and their families. Clinical endpoints need to better reflect this reality.

The recent publication of revised clinical trial guidelines for Alzheimer's Disease by the EMA and the FDA presents a welcome recognition of the need to develop new approaches which target the pathology of Alzheimer's Disease, not merely its symptoms, including tools to measure health-related quality of life.[6,7] Similar approaches should inform HTA processes across European healthcare systems to enable adequate assessment of advances in treatment and ensure timely patient access. To monitor and evaluate the development of outcomes data over time, post-clinical trial evidence infrastructure such as real-world evidence (RWE) registries are crucial since they enable patient access whilst confirming expected patient benefit over time.

IN EARLY 2018, BOTH THE EMA AND FDA PUBLISHED NEW GUIDELINES FOR ALZHEIMER'S DISEASE TRIALS TO BETTER MEASURE OUTCOMES FOR THE PRE-SYMPTOMATIC STAGES OF THE CONDITION

3. VALUE RECOGNITION

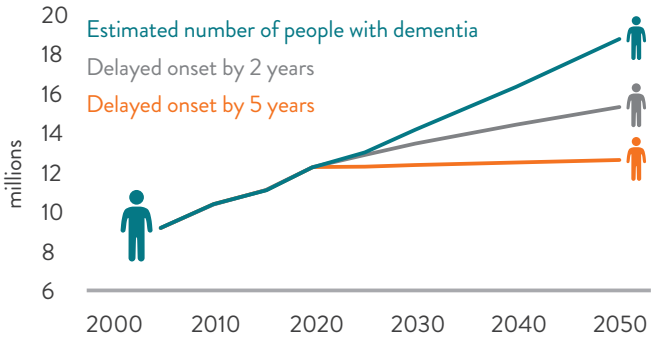
ADEQUATELY ASSESSING AND RECOGNISING THE VALUE OF INNOVATION IN TREATMENT POSES CHALLENGES TO CURRENT HEALTH TECHNOLOGY ASSESSMENT (HTA) MODELS

Current HTA models do not sufficiently account for the benefit and cost-effectiveness of early-intervention. In particular, they often do not appropriately take into consideration expected savings in indirect healthcare costs, for instance, savings incurred through the delay of the need for institutionalisation such as care provided in a nursing home setting.

It is estimated that 50% to 75% of the total cost of Alzheimer's Disease occurs during severe stages and is predominantly generated from cost associated with care provided in nursing homes.[8] DMTs have the potential to delay the onset of dementia, which would allow patients to retain cognitive function and lead an independent life for longer. This will not only positively impact on those affected but also reduce the burden of carers and families. Calculating the impact that prevention of disease progression has both on people with Alzheimer's Disease and their carers does not lend itself easily to existing models value assessment.

Common HTA models mainly focus on cost-effectiveness in relation to short-term direct healthcare cost and do not appropriately account for savings incurred in other parts of the healthcare system. Neither do they predict well the potential savings that preventing further deterioration in patients would bring. HTA models therefore need to evolve further to, at a minimum, appropriately recognise and account for expected savings in indirect costs across the entire health and social care system as well as develop tools and methods to better model future savings brought by early treatments at the onset of the disease. This is very likely to require the breakdown of traditional budget silos to enable the transfer across health and social care funding flows as well as a mind shift recognising that upfront investment in advances in treatment has the potential to lead to additional savings further along the care pathway.

GRAPH 2: ESTIMATED IMPACT OF DMT ON NUMBER OF PEOPLE AFFECTED BY DEMENTIA[11]



IT HAS BEEN ESTIMATED THAT THE INTRODUCTION OF A DMT BY 2020 THAT DELAYS THE ONSET OF THE DISEASE BY TWO YEARS WOULD REDUCE THE NUMBER OF PEOPLE AFFECTED BY DEMENTIA BY 19% IN 2050. THIS REDUCTION WOULD INCREASE TO 33% BY 2050 FOR A TREATMENT THAT DELAYS THE ONSET BY 5 YEARS

4. CAPACITY AND PREPAREDNESS OF HEALTHCARE SYSTEMS

HEALTHCARE SYSTEMS ARE STRUGGLING TO ADEQUATELY SUPPORT PEOPLE WITH ALZHEIMER'S DISEASE ACROSS THE DISEASE PATHWAY

Projections by Alzheimer's Europe indicate that the 11 million people affected by dementia in Europe today could increase to 14 million by 2030, with 70% of those affected by dementia-related Alzheimer's Disease.[9]

Enabling timely screening, diagnosis and treatment of such a large patient population at risk of developing or already living with Alzheimer's Disease will have an impact on existing services and medical resources across Europe.

As capacity for diagnostics, specialist visits and infrastructure for treatment already varies across systems in Europe, this is likely to result in even greater variation in patient access to the latest standard of Alzheimer's care.[10]

To address this, healthcare systems are likely to require upfront investment to develop the necessary service infrastructure, provide training and upskill the medical workforce.

LOOKING AHEAD TO A BRIGHTER TOMORROW FOR PEOPLE WITH ALZHEIMER'S DISEASE

Together with the medical community, EFPIA members are taking an active role by partnering with other stakeholders to overcome the challenges that persist. EFPIA members develop innovative screening solutions and diagnostics to facilitate early detection and diagnosis, ranging from digital tools to blood-based biomarker tests.

EFPIA members are also working with a wide range of stakeholders to develop more appropriate and sustainable value assessment and funding approaches. This includes support for initiatives to better capture the perspectives of caregivers and to accurately assess the patient, caregiver and societal value of Alzheimer's diagnosis and treatment.

CALL FOR ACTION

Ensuring that today's healthcare systems are ready to enable patients to benefit from future advances in treatment is a complex but necessary task. EFPIA members are calling on all stakeholders to jointly overcome the challenges that persist. We are calling on policymakers, governments, healthcare providers, payers, patient and carer organisations as well as the scientific community to continue the conversation and to drive the necessary change for a better today and tomorrow for people with Alzheimer's Disease.

REFERENCES: 1 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 2 EurActiv, Rising dementia numbers in EU causes alarm, www.euractiv.com/section/health-consumers/news/rising-dementia-in-the-eu-causes-alarm/ 3 EuroCoDe, European Collaboration on Dementia project, www.alzheimer-europe.org/Research/European-Collaboration-on-Dementia/Cost-of-dementia/Prognosis-to-2030 4 Cummings J, 2014, Alzheimer's disease drug-development pipeline: few candidates, frequent failures. Alzheimer's Research & Therapy, 2014 6:37, www.alzres.biomedcentral.com/articles/10.1186/alzrt269 5 Cummings J et al, 2018, Alzheimer's disease drug development pipeline: 2018. Alzheimer's and Dementia: Translational Research and Clinical Interventions, www.ncbi.nlm.nih.gov/pmc/articles/PMC6021548/ 6 European Medicines Agency, 2018. Revised guideline on clinical studies for Alzheimer's disease medicines, www.ema.europa.eu/en/news/revised-guideline-clinical-studies-alzheimers-disease-medicines 7 US Department of Health and Human Services Food and Drug Administration, 2018, Early Alzheimer's Disease: Developing Drugs for Treatment Guidance for Industry, www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM596728.pdf 8 Castro D et al, 2010, The economic cost of Alzheimer's disease: Family or public health burden? Dementia & Neuropsychologia, 2010 Oct-Dec, 4(4): 262–267, www.ncbi.nlm.nih.gov/pmc/articles/PMC5619058/ 9 Alzheimer's Disease International. World Alzheimer Report 2015. The Global Impact of Dementia: An Analysis of Prevalence, Incidence, Cost and Trends, www.worldalzreport2015.org/downloads/world-alzheimer-report-2015.pdf and EurActiv, Rising dementia numbers in EU causes alarm, www.euractiv.com/section/health-consumers/news/rising-dementia-in-the-eu-causes-alarm/ 10 Hlåvka J et al, 2018, Assessing the Preparedness of the Health Care System Infrastructure in Six European Countries for an Alzheimer's Treatment. RAND Corporation, 2018, www.rand.org/pubs/research_reports/RR2503.html 11 Projections included in Graph II have been calculated based on the model developed by the Office of Health Economics (OHE) (www.alzheimersresearchuk.org/wp-content/uploads/2015/01/OHE-report-Full.pdf) which estimates that the introduction of a DMT in 2020 that delays the onset of the condition by two years would lead to a reduction of people affected by dementia by 19% in 2050. According to OHE, this reduction would increase even further to 33% if the treatment delays the onset by five years. The baseline estimation for people affected by dementia was modelled based on the projection developed by Alzheimer's Europe[9] and Alzheimer's Disease International.[9]