RETHINKING

ALZHEIMER'S DISEASE PATHWAY

From Diagnosis to Care

EBC European Brain Council

efpia

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For more information about "Rethinking Alzheimer's disease", please visit: www.braincouncil.eu/projects/rethinking-alzheimers-disease/

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EXECUTIVE SUMMARY

More than 55 million people worldwide currently live with dementia, of which Alzheimer's disease (AD) is the most common form, possibly contributing to 60–70% of cases (Wimo et al., 2023). While AD is often considered a devastating disease against which nothing is possible, society is now entering an era where we are starting to rethink AD as a treatable and manageable condition. This shift in our way of viewing AD has a solid scientific base to support it, and has been largely driven by research-led innovation. Our new understanding of the disease and the advent of biomarkers –biological indicators in our bodies that help doctors diagnose diseases, monitor conditions, and evaluate treatment effectiveness - have already revolutionised the way we diagnose AD. This has profound implications for treatment, as early diagnosis opens windows of opportunity for disease modification. With this transformation comes a call for adequate policy frameworks to ensure that benefits in the scientific field are translated into improved lives for people living with AD and their families.

Indeed, the next revolution of understanding AD, brought about by scientific advancements, is multidisciplinary, holistic and personalised treatment, care and management at the biological, psychological, social and societal level. In addition to pharmacological treatments, new neuromodulatory (e.g., deep brain stimulation, transcranial magnetic stimulation, gamma stimulation) and non-pharmacological treatment and care approaches (e.g., telemedicine, physical exercise, diet, socially assistive robots, occupational therapy) show promise. Thanks to this rich pipeline, in the next years we might witness a wave of new interventions and a further and more profound shift from AD care to active treatment and management of early-stage disease.

As the implications will be profound, this transformation requires society to rethink its collective approach and vision towards AD. Preventing AD, slowing its progression, and extending the independence of people living with AD will significantly impact brain health throughout someone's lifetime (Long et al., 2023). While in 2019, dementia cost global economies 1.2 trillion euros of which approximately 50% is attributable to informal care (e.g., family members and close friends; Wimo et al., 2023), treatments might delay direct and indirect costs associated with late-stage AD and alleviate this burden on families and caregivers, and eventually on society. On the other hand, proper treatment, care and optimal management will effectively help us in preserving the brain capital – which refers to the collective cognitive resources, mental health, and intellectual abilities of individuals within a society - of the mid-age and elderly population, with significant effects on productivity, regional competitiveness (Smith et al., 2021) and society at large towards the United Nations' 17 Sustainable Development Goals (SDGs; United Nations, 2024).

To make sure that new AD treatments will be accessible, safe and effective in the most appropriate patient population, several gaps, barriers and challenges at structural, societal and scientific level will need to be addressed. We need to ensure well-defined post-diagnostic pathways with allocated funds, timely access to innovative treatments and patient support, and maintain high-quality post-diagnostic care. This report highlights how a new understanding of AD has revolutionised the field, leading to innovative treatments, with profound implications for the European society.

FOREWORD

In the rapidly changing field of healthcare, few challenges are as significant and widespread as those presented by Alzheimer's disease. As our global population ages, the prevalence of dementia, including Alzheimer's, continues to rise, placing immense strain on healthcare and social systems, people living with Alzheimer's, and their families. It is within this context that the Perspective Paper, "Rethinking Alzheimer's Disease Pathway: From Diagnosis to Care," stands out as a critical and timely addition to the conversation about this growing public health issue.

The aim of this report is not merely to document the status quo, but to challenge it—to rethink how we approach Alzheimer's treatment, care and management. By offering a comprehensive review of current practices, identifying challenges, gaps and barriers, and proposing policy recommendations, this report seeks to reshape the Alzheimer's disease healthcare pathway in ways that enhance outcomes and quality of life for all involved, and reduce the impact on society.

At the heart of our approach is the patient-centered philosophy. We advocate for a paradigm shift that prioritises the needs, values and experiences of people living with Alzheimer's and their families. This entails early and accurate detection and diagnosis, using a personalised approach – the right treatment for the right person at the right time - and most innovative or advanced treatment plans, and holistic care strategies.

Furthermore, this report emphasises the importance of interdisciplinary collaboration. Effective management of Alzheimer's disease requires the united efforts of policy makers, payers, neurologists, geriatricians, psychiatrists, primary care physicians, mental health professionals, caregivers, and support networks. By creating a collaborative framework, we can ensure that people living with Alzheimer's disease receive the best care at every stage of their journey.

Equally significant is our emphasis on leveraging technological advancements. Innovations in diagnostic tools, digital health platforms, and assistive technologies hold great promise in transforming the Alzheimer's Disease care pathway. This report highlights the potential of these technologies to improve diagnostic accuracy, streamline care coordination, and enhance support for people living with Alzheimer's and their families.

Ultimately, "Rethinking Alzheimer's Disease Pathway: From Diagnosis to Care" is a call to action. It is an invitation to policymakers, regulators, researchers, healthcare professionals, and advocates to adopt comprehensive and forward-thinking policies and regulations, rethink existing patient pathways, and to ensure that innovation is made available to patients in the EU.

By embracing this challenge, we can significantly reduce the impact of Alzheimer's disease and improve the lives of millions worldwide.

As we move forward, let us remain committed to innovation, collaboration and patient-centered care. Together, we can rethink the way we deal with Alzheimer's and offer hope, dignity, and a better quality of life for all those living with the disease.

Prof. Suzanne Dickson
President, European Brain Council

CALL TO ACTION: POLICY RECOMMENDATIONS

We are at a historical crossroads in the management of Alzheimer's disease (AD), with new treatments becoming available in various countries. For the first time in history, science is delivering new, potentially disease-modifying treatments for devastating diseases such as AD. Yet, the current healthcare system and regulatory and policy frameworks do not easily allow the implementation of such innovations, even for the subset of people living with AD who would be eligible.

Now is the time to make sure that the post-diagnostic care pathway is optimised to the person needs and that the healthcare systems in each country are properly harnessed and informed to provide the most appropriate treatments to the right patient at the right time.

For this reason, we call on policymakers to drive regional, national, EU, and international policies that can help to improve the lives of people living with the disease, define a post diagnostic pathway through sufficient guidelines and funds allocated for optimal implementation, which will also improve alignment and harmonisation of the pathways across the countries. We need to ensure that health systems are better prepared to support the post-diagnostic pathway now, and when innovative tools and therapies become available.

There is a strong need to support the creation of a new healthcare environment across Europe that will:

1 **Recognise the benefits of improved patient outcomes through ensuring and maintaining high standard quality in post-diagnostic care**

2 **Improve timely local, regional and national access to innovative treatments and holistic care across the entire disease trajectory, including patient and psychosocial support and shared decision making, to improve the quality of life for people living with AD and their caregivers**

3 **Build trust to allow for the adoption and implementation of guidelines and standardised protocols for the post-diagnostic care**

RECOMMENDATIONS

Recommendation • 1

Make Alzheimer's Disease and Brain Health a National, European and Global Public Health Priority

Recommendation • 2

Promote Training, Education and Awareness Raising in Healthcare Professionals and Citizens

Recommendation • 3

Leverage Data, Information Sharing and Technology

Recommendation • 4

Provide Access to Optimisation and Implementation of Innovation

Recommendation • 5

Ensure Dedicated Funding to support Alzheimer's Research and Infrastructure Development

Recommendation • 6

Increase Patient and Public Involvement

Recommendation • 7

Integrate Multidisciplinary Care Teams

Recommendation • 8

Define post-diagnostic pathways through guidelines and funds allocated for optimal implementation

LIST OF ENDORSERS

To help improve the quality of life and care for people living with Alzheimer's disease in Europe, the following organisations endorse the Rethinking Alzheimer's Disease Perspective Paper, including the call to action and policy recommendations.

- 5 Ironmans Beat Alzheimer's Association, Switzerland
- Ace Alzheimer Center Barcelona*, *Spain*
- Alzheimer Center Amsterdam, *Netherlands*
- Alzheimer's Disease International, *United Kingdom*
- BrainFit4Life *Switzerland*
- European Academy of Neurology, *Austria*
- European Federation of Neurological Associations, *Belgium*
- European Psychiatric Association, *France/Belgium*

* **Members:** Universitat Internacional de Catalunya (UIC), Centro de Investigación Biomédica en Red Enfermedades Neurodegenerativas (CIBERNED)

Lewy Body Ireland
Ireland

Memory Center of the University Hospitals of Geneva,
Switzerland

Mental Power Foundation for Brain Health,
Poland

Tallaght University Hospital,
Ireland

World Dementia Council,
United Kingdom

INTRODUCTION

"What we are experiencing is a big cultural thinking change of Alzheimer's, beyond care. Alzheimer's is going to be a treatable disease."

Maria Teresa Ferretti, Neuroscientist and Science Advocate

Millions of Europeans will develop Alzheimer's disease (AD) in the next decades (Eurostat.). Already more than 55 million people (of which two thirds are women) currently live with dementia worldwide, whereof AD is the most common form (60–70% of cases) (Wimo et al., 2023). While AD is often considered a devastating disease against which nothing can be done, society is now entering an era where we start to rethink AD as a treatable and manageable condition.

AD is characterised by slow and progressive loss of nerve cells in the brain resulting in the impaired formation of new memories, difficulties with language and processing of images, and decline in executive function –the capacity of going through a series of steps, like following a recipe to cook a meal or booking a flight online. AD symptoms also include behavioural alterations such as apathy, irritability or even aggressive behaviour.

"What shocked me, beyond the cultural stigma surrounding dementia, was that many doctors and nurses working with people living with dementia were unaware that dementia is an umbrella term. They lacked a basic understanding of the different diagnoses within dementia."

Helena Quaid, Lewy Body Ireland

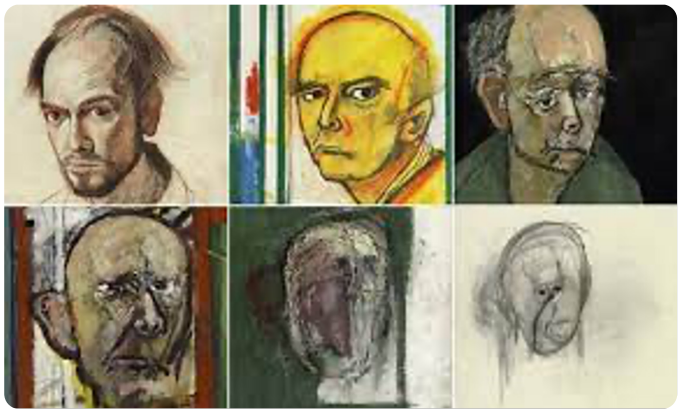


Figure 1
The progression of Alzheimer's disease captured by a series of self-portraits by artist, and person living with dementia, Image © William Untermohlen

Box 1 Alzheimer's disease in brief

1. Is Alzheimer's disease (AD) a normal part of ageing?

No, even though the risk of AD increases with age (2024 AD facts and figures), AD is not and should not be considered as a natural part of ageing.

2. Is AD the same as dementia?

No, AD is the most common cause of dementia and may contribute to 60-70% of the cases (Wimo et al., 2023). In total, there are over 200 causes of dementia.

3. What is dementia?

Dementia is not a specific disease but an umbrella term referring to an impairment of cognition profound enough to affect daily life functions. It eventually results in loss of independence, autobiographic memories, and self-identity (Figure 1). Dementia is often accompanied by changes in emotions as well as to altered behaviours and personality.

4. What causes AD?

While the precise etiology of AD remains to be elucidated, research has revealed that the cognitive decline of people living with AD is linked to two major lesions observed in their brains (Figure 2: amyloid plaques and neurofibrillary tangles). Those amyloid plaques and neurofibrillary tangles are thought to be toxic to neurons and reduce the number of brain cells (neurons) and the connections between neurons (synapses).

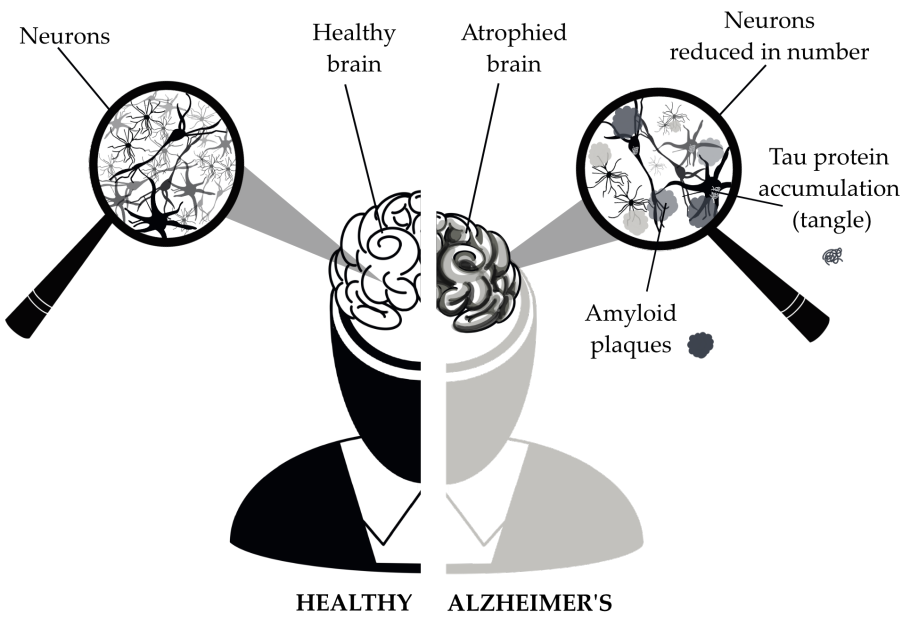


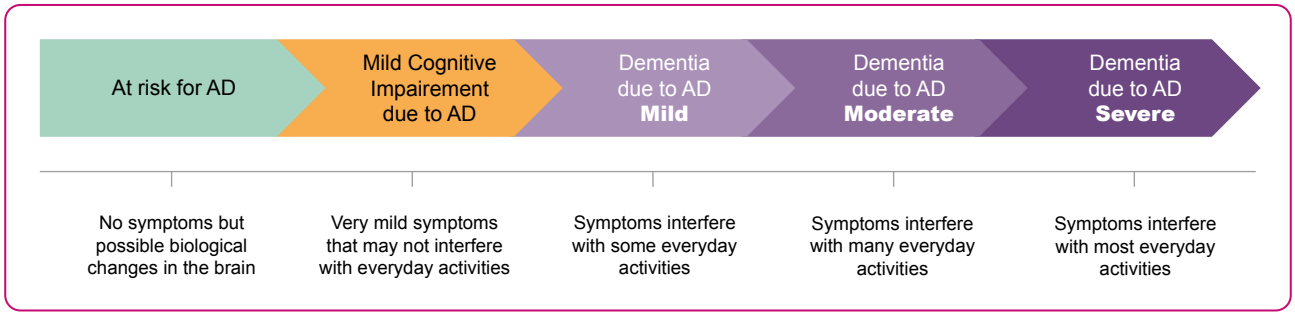
Figure 2
A healthy brain compared to a brain with Alzheimer's disease pathology, Image © Maya Uccheddu

The window of opportunities: Mild Cognitive Impairment

In the first symptomatic stage of the disease (called 'mild cognitive impairment – MCI; See Figure 3), people living with AD have changes in cognition but still preserve their ability to function independently. The disease then progresses to mild, moderate, and severe dementia, with progressive loss of function and independence. MCI offers therefore a unique window of time to tackle AD and potentially halt or slow down its progression.

Interestingly, it is now known that the disease already starts and is visible in the brain up to 20 years before symptoms may appear (Jia et al., 2024). This long, silent phase of AD might, in the future, offer an opportunity to prevent disease progression, even before symptoms appear; more research is needed in this field.

Alzheimer's Disease Continuum*



**Although these arrows are of equal size, the components of the AD continuum are not equal in duration.*

Figure 3
Adapted from Alzheimer's Disease Facts and Figures 2024 (Alzheimer's Association, 2024). Dubois et al. (in press). Schematic depicting the progressive clinical stages of AD, from at risk for AD to severe dementia due to AD. The identification of early clinical stages (MCI) and at risk stages opens various opportunities for secondary and tertiary prevention as well as early treatment.

RETHINKING ALZHEIMER'S DISEASE PHASE I: MAPPING THE DETECTION AND DIAGNOSTIC JOURNEY

"My story is a story of voice and rights. Having received an early diagnosis has enabled me to become an advocate for those living with Alzheimer's, to ensure their voice is heard and that they are involved. We have the experience. It is important that law makers understand and act upon our needs."

Helen Rochford-Brennan, Irish Dementia Working Group

In the first part of the Rethinking AD project (Dumas et al., 2023), we focus on the mapping of the detection and diagnostic journey. The diagnosis of Alzheimer's disease (AD), either in its early or advanced phase, is often shocking for people and their families to receive, but it may also provide relief and a starting point for which to receive the proper treatment and care. It often arrives after years of uncertainties, struggles and sacrifices from the families –because of the difficulties experienced in receiving a proper diagnosis, or other related obstacles.

As our understanding of AD at a biological level improves, so does our ability to detect and diagnose AD based on the presence of biological signs of the disease in the individual patient (called ´biomarkers´), reducing our reliance on clinical manifestations on AD alone. This transformation from a purely clinical diagnosis approach to a diagnosis where biology and clinical features are interpreted together represents a profound transformation in the field of AD, and is key for implementation of correct and impactful treatments.

"Education should start with those who provide the diagnosis."

Kevin Quaid, Lewy Body Ireland

Alzheimer's Disease Biomarkers

In a variety of diseases, from cancer to diabetes, diagnosis is based and supported by some measure of physical function, for instance, blood analysis and imaging results. Such readouts of a physical or pathological process that can help in a diagnosis are called 'biomarkers' in medicine.

Until 15 years ago we did not have biomarkers specific to AD. To support the diagnostic process, the scientific community has now developed new tools that allow the specialists to 'see' inside the brains of the people living with AD without the need to wait for an autopsy. Several biomarkers have been developed and validated in the clinical and/or research context (Hampel et al., 2022), including:

- Imaging PET (Positron Emission Tomography)-tracers (a type of brain scan) for detecting aggregates of toxic proteins characteristic of AD - amyloid and tau (see Box 2).
- Fluid biomarkers in cerebrospinal fluid (which is the liquid surrounding the brain and spinal cord) that can reveal the presence of amyloid and tau in the brain, as well as neuro-inflammation and neurodegeneration.
- Blood biomarkers, which are currently in development might allow quick identification and diagnosis of AD pathology in people living with cognitive impairment, and could be implemented already in primary care.

Box 2 The Revolution of Biomarkers

The impact of biomarkers has been manifolding (Hampel et al., 2022):

- Introduced molecular, precision medicine diagnosis of people living with AD, confirming or refuting clinical diagnosis in a person suspected of AD.
- Revealed the existence of a 'silent'/'invisible' (i.e., prodromal) phase of a disease that occurs decades before the appearance of symptoms (Jia et al., 2024).
- Opened the possibility of early diagnosis and even secondary prevention in individuals that have biomarker evidence of AD pathology but no clinical symptoms yet.

Biomarker Detection and Diagnosis open the way to early prevention and treatment

Currently several clinical centers have started to use biomarkers to confirm the suspect of a clinical diagnosis of AD dementia, according to research criteria (Jack et al., 2024). To be implemented, this biomarker-based approach requires a new patient pathway, which could include a first-line diagnostic workup in primary care followed by a second-line diagnostic and decision-making done by a specialist (Hampel et al., 2023; Dumas et al., 2023; See Figure 4). For this to happen it will be crucial to potentiate the early detection capability of primary care and general practitioners (GPs).

This new approach, which combines careful clinical evaluation with molecular profiling, is paving the way to the development of early and tailored treatments as well as secondary prevention strategies, transforming the post diagnostic pathway for patients.

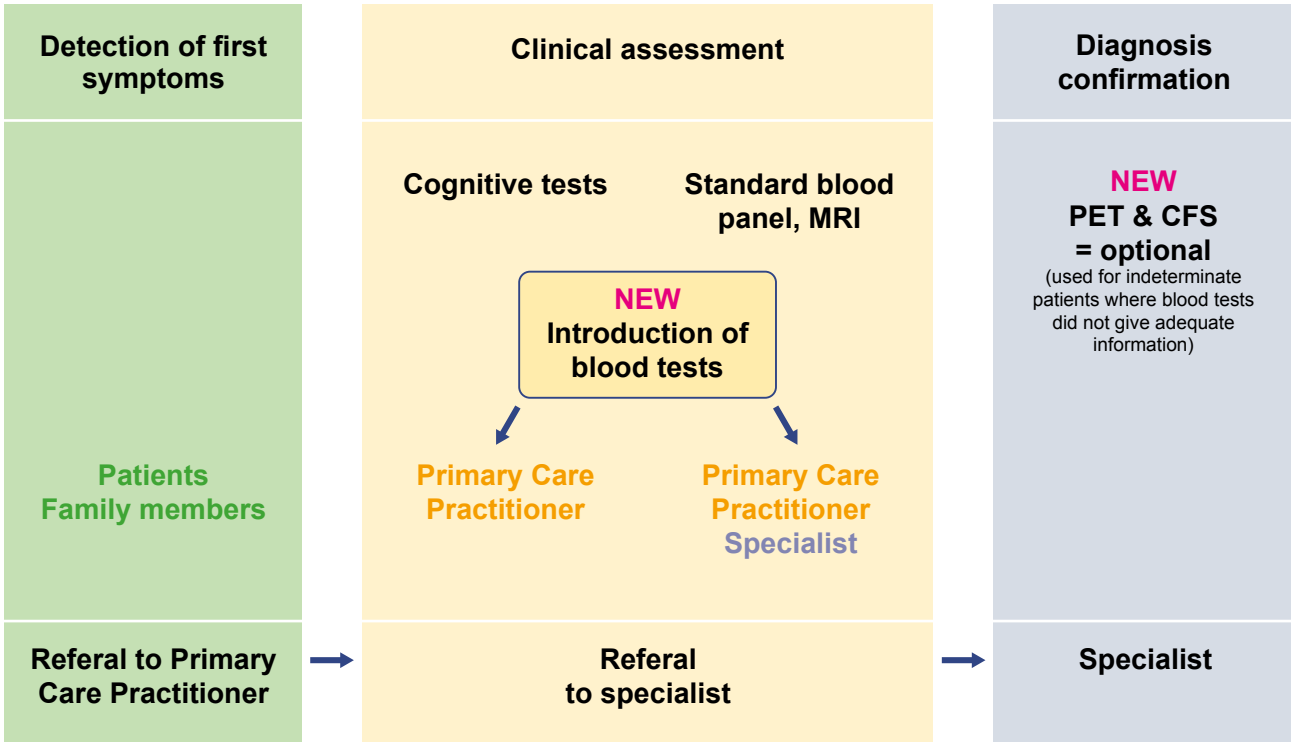


Figure 4
New Detection and Diagnosis Pathway

COMPREHENSIVE OVERVIEW OF CURRENT PATIENT POST-DIAGNOSTIC PATHWAY IN EUROPE

"We need more emphasis on shared decision making and that also implies a lot of emphasis on information provision."

Wiesje van der Flier, Alzheimer Center Amsterdam

The current post-diagnostic journey includes pharmacological symptomatic treatment and social care and support (Frederiksen et al., 2021). Ideally, both require careful examination of the person by specialised centers who follow the individual and their family throughout their journey. As discussed in section 6 on Unveiling Current Gaps and Challenges, this is far from common practice in the current European landscape.

Current Pharmacological Treatment Options

Medical management of symptoms and comorbidities is the main goal of current treatment of people living with Alzheimer's disease (AD). Current treatment options available in Europe for AD are all symptomatic, meaning that they target symptoms and not the underlying biology of the disease. This type of treatment cannot slow down the progression of the disease. Some of the most commonly utilised agents approved and used in Europe for the treatment of dementia symptoms are listed in Table 1.

At the European level, it is noteworthy that cholinesterase inhibitors, the most commonly prescribed class of drugs for AD symptoms, are generally reimbursed and supported by national healthcare systems, though there are exceptions. For example, in France, these drugs were removed from the list of reimbursable medications on August 1, 2018, due to concerns about their limited effectiveness (Walsh et al., 2019; Herr et al., 2021). This decision led to an increased reliance on other healthcare resources in the French context.

Table 1: Commonly used pharmacological treatment of Alzheimer's disease symptoms

Current Pharmacological Treatment	Symptoms Relieved
Drugs that boost the activity of selected population of neurons (rivastigmine, donepezil, galantamine, so called `cholinesterase inhibitors´; Marucci et al., 2020).	Temporarily alleviate symptoms and improve motivation, memory and concentration.
Memantine, which serves to buffer excessive levels of a neurotransmitter (glutamate) that in high levels is toxic to neurons (Liu et al., 2020).	Memantine can help people living with AD in mid and later stages of dementia, slowing down the progression of symptoms such as disorientation and difficulties carrying out daily activities.
Herbal extracts to support brain function and quality of life (extracts of Gingko biloba for dementia; European Medicine Agency).	Gingko biloba slightly improve memory and cognition in people living with dementia, but the evidence is mixed.
Atypical antipsychotic drugs: Only risperidone is approved in Europe for behavioural disorders in dementia; other antipsychotics are prescribed "off label."	Management of neuropsychiatric symptoms such as agitation and psychosis. Higher risk of mortality in this fragile population and treatment should be kept to a minimum in duration and dosing.
Antidepressants	Treatment of depressive symptoms
Anticonvulsant	In case management of seizures is required.

Other Non-Pharmacological Approaches

Last but not least, the field is actively exploring additional approaches that can support people living with AD and improve their and their caregivers' quality of life, often alongside pharmacological treatment.

The care of AD often involves occupational therapy, which includes cognitive and behavioural activities aimed at enhancing the quality of life for these people and, in turn, their caregivers (Pardo-Moreno et al., 2022). In early stages of AD (mild to moderate dementia stage), cognitive stimulation therapy has the best and most promising evidence for effect. It is the most widely applied psychosocial treatment used to improve cognitive function and alleviate depression (Saragih et al., 2022).

Our growing understanding of risk factors for AD is opening new opportunities in the field of lifestyle-based prevention. At the moment, 14 modifiable risk factors have been identified, which taken together might help prevent approximately 40% of cases of AD (Livingstone et al., 2024). While the current focus is on primary prevention (i.e., reducing the risk of developing the disease altogether), secondary and tertiary prevention (aiming at slowing down the disease before severe symptoms appear) are also possible and represent an important approach in the post-diagnostic pathway (Lee et al., 2022).

Evidence supports the concept that measures aimed at modifiable risk factors (such as increased physical exercise) can be beneficial also in MCI patients, delaying the progression of the disease (Lee et al., 2022). In this line, advice on brain-healthy living (e.g., physical and mental activity, social interaction, smoking cessation, healthy eating, low intake of alcohol, sleep hygiene, and correction of visual and hearing problems) has been recommended, even in previously diagnosed patients (de la Rosa et al., 2020).

Regarding cost-effectiveness of non-pharmacological approaches, the AD intervention with the strongest evidence of cost-effectiveness has been documented as maintenance cognitive stimulation therapy (Eaglestone et al., 2023). Case management, occupational therapy and dementia care management also showed good evidence of cost-effectiveness (Eaglestone et al., 2023).

Social Care Services

In parallel to pharmacological treatment, formal dementia-specific support and care structures in different European countries exist with wide variability across countries and even within regions of the same country (Schmachtenberg et al., 2022). In particular, 18 significant social care services were identified in the 2020 European Dementia Monitor (e.g.,assistive technologies/ICT solutions; Support groups for people living with dementia and carers; day, residential/nursing home, and palliative care; Alzheimer Europe, 2020).

While there is an increase in the number of countries where most services are considered as being sufficiently available, a majority of European countries continue to report that services are insufficiently available or absent (Alzheimer Europe, 2020). In general, social care services across Europe face challenges, and most of the burden of care falls on the primary care partners and family.

Several experts are therefore calling for restructuring measures in their countries, such as a consistent national strategy for dementia care (Romania), a different structuring of the care system (Germany), or an expansion of existing structures (Austria) (Schmachtenberg et al., 2022). This could be used as a starting point for transnational networking of dementia care and the development of European strategies to establish minimum standards in the care of people living with dementia and their relatives (Alzheimer's Disease International, 2024).

PIONEERING HORIZONS: INNOVATIVE TREATMENTS FOR ALZHEIMER'S DISEASE

"We need to embrace the role of technology and innovation to rethink the way we deal with Alzheimer's disease, which has been overlooked too many times."

Stelios Kympouropoulos,
Psychiatrist and Former MEP (EPP, Greece)

Novel therapies have emerged in the past few years and considerable progress has been made in both the development and approval of new treatments. For the first time in history, we are facing the possibility of treating Alzheimer's disease (AD), not just for its symptoms, but also for the underlying pathology per se, at least in its earliest stages.

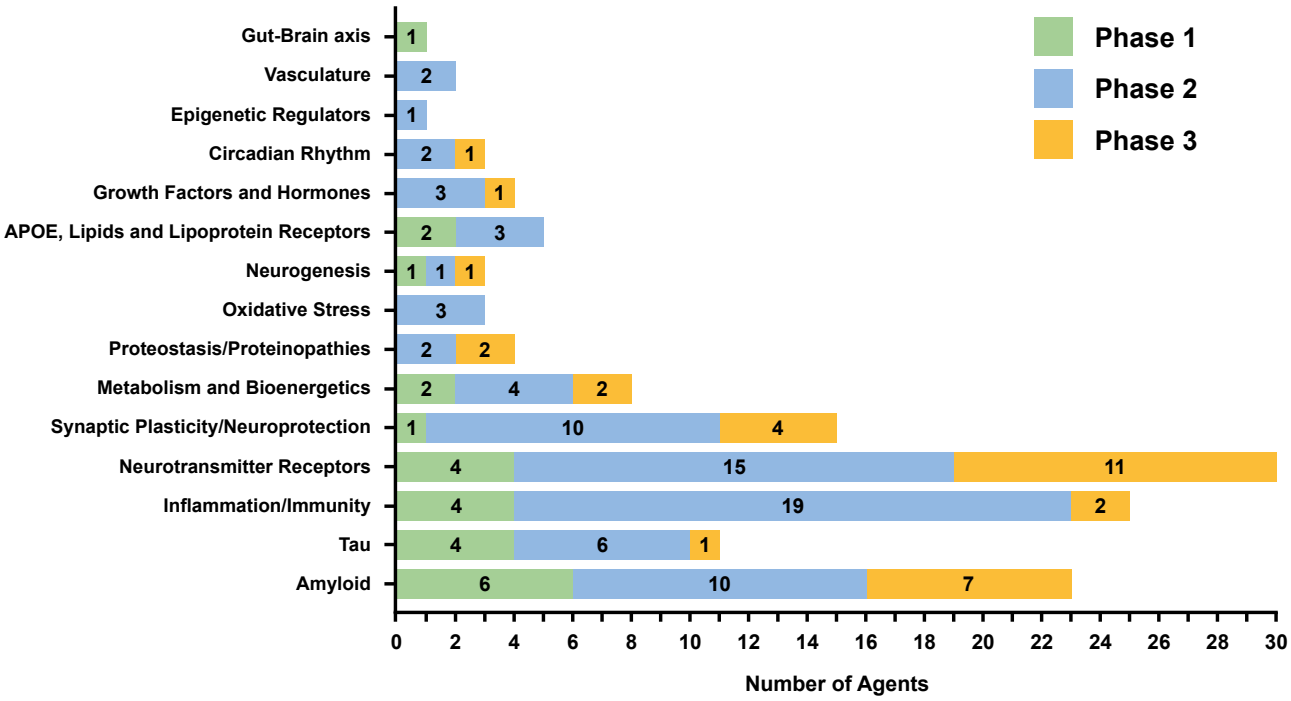


Figure 5
Alzheimer-related processes as categorised by the Common Alzheimer's Disease Research Ontology (CADRO) for agents in each phase of the Alzheimer's drug development pipeline (Cummings et al., 2024)

Pharmacological Therapies

"There is also a significant human rights aspect to consider. People living with dementia should be empowered to make informed choices about their own care and treatment."

Paola Barbarino, Alzheimer's Disease International

The pipeline of AD treatments is rich. As of January 1st, 2024, there were 164 clinical trials for AD assessing 127 drugs (Cummings et al., 2024). Of these, 48 trials were in Phase 3, 90 trials in Phase 2, and 26 trials in Phase 1. An astounding 76% of all the drugs currently tested are DMTs (Disease Modifying Treatments). These drugs target a variety of pathways, including amyloid beta peptide (18% of total drugs), tau (9%), neurotransmitters receptors (22%), and neuroinflammation (20%) (see Figure 5).

Anti-amyloid agent, such as monoclonal antibodies and small molecules, are among the most advanced new therapeutics for AD. Second generation monoclonal antibodies have been effective in significantly reducing brain amyloid levels and providing modest yet sustained clinical improvements over an 18-month period. Some DMT's (e.g., Aducanumab - Budd Haeberlein et al., 2022; Lecanemab - van Dyck et al., 2022; Donanemab - Sims et al., 2023) have already received approval from national regulatory agencies; Lecanemab and Donanemab are available in countries like the USA, Japan, and the United Kingdom.

It's important to note that, as of today, all amyloid-targeting monoclonal antibodies have been associated with side effects known as ARIA (amyloid-related imaging abnormalities; Hampel et al., 2023; See Box 3). This presents a safety issue for the entire class. However, through thorough analysis of clinical trial results, we now better understand the risk factors for these adverse events. With careful patient selection and monitoring, ARIA can be managed, allowing patients to be treated safely.

Box 3 Side effects of anti-amyloid agents called ARIA (amyloid related imaging abnormalities; Hampel et al., 2023)

ARIA can manifest as bleeding in the brain or a swelling of the brain, which is in most cases asymptomatic and harmless, resolving by itself in a few months or upon interruption of treatment. In 6-39% of people living with AD (depending on the particular antibody used) brain swelling can lead to symptoms, which are mostly minor such as headache, confusion, vomiting, visual or gait disturbance. Serious or severe neurological symptoms are rare but may require hospitalisation and specific monitoring and management (e.g., intensive care unit admission, EEG (electroencephalogram), corticosteroids, antiepileptics). The exact safety profile of this class of drugs is therefore under scrutiny and regular MRI (Magnetic Resonance Imaging) scans are required during treatment to monitor the emergence of ARIA.

To ensure that Europe remains at the forefront of these medical advancements and innovations, it is crucial to adapt regulations and policies to facilitate the swift evaluation of these new treatments. European health systems must be prepared to provide timely access to diagnosis, care, and treatment to benefit from these breakthroughs in AD management.

Gene-Therapy

For genetic cases of AD (the rare 3% of cases caused by genetic mutations), or for carriers of the genetic risk factor APOE4, scientists are currently exploring the use of gene editing (Thompson, 2024). While only tested in animal models for now, this could become the next frontier for human treatment in the future.

Neuromodulation

Neuromodulatory approaches are rising and could be used together with drugs for effective treatment of AD. Various forms of neurostimulation are currently under clinical testing for AD, including transcranial magnetic stimulation (TMS) (Chou et al., 2019), transcranial direct current stimulation (tDCS) (Majdi et al., 2022), and combined visual/auditory gamma stimulation (currently in phase 3 clinical trial – see National Library of Medicine - to assess its ability to slowing disease progression for subjects with mild to moderate AD) (Hajós et al., 2024).

ANTICIPATED PATHWAY TRANSFORMATIONS WITH INNOVATIVE TREATMENTS

"We need to acknowledge that a one size fits all approach is not going to work when dealing with Alzheimer's disease today. The complexities and variations in healthcare systems across different countries mean that policies and solutions must be adapted to fit local contexts."

Angela Bradshaw, Alzheimer Europe

The advent of innovative disease-modifying treatments means that a fraction of the people living with symptomatic Alzheimer's disease (AD) (those who are eligible for such treatments) in the future may decline less, later, or even stabilise for some time. While care will remain a fundamental aspect of the post-diagnostic pathway, the focus will increasingly move from care of advanced stages of the disease to treatment of people living with AD in their earliest stages (van der Flier et al, 2023), similar to what happens in oncology. This will have profound implications for public health and society at large.

Treatment Means Time

Slowing cognitive decline during the MCI phase will mean for people living with AD more 'functional' time (Wessels et al., 2023) in which the disease interferes to a lesser degree with daily activities, making it possible to enjoy life and be more independent, including spending time with family and friends, driving, engaging in hobbies, working, reading books, watching movies, and travelling. Every year of independence gained is a year of intense home-based or nursing home-based care avoided, with obvious cost savings for both healthcare services and families (Aye et al., 2023).

No Disease for Old Men

The earliest AD changes have been shown to occur in the brain upwards of 20 years before cognitive symptoms appear (Jia et al., 2024), indicating that the disease actually starts during middle age. The earlier we intervene in the disease continuum, the higher the chances are to interfere with the pathological process. AD will therefore progressively change its 'status' from a disease generally perceived as only affecting older citizens to a disease that can be prevented and treated throughout the lifespan (Frederiksen et al., 2021).

A Holistic and Personalised Approach

As a multitude of different complementary AD treatments and interventions will become available, future management and care of AD will need to focus on effectively integrating these different approaches with the aim to increase the quality of life of the person living with AD and its environment. Putting the person at the center and prioritising shared decision making, the specialists will need to tailor therapeutic strategies that target the individual characteristic of that person and uses complimentary approaches.

"We believe that the biggest advantage in the coming years will be the attention and resources directed toward dementia, allowing us to provide accurate information, address myths about dementia and significantly increase public awareness and health literacy."

Hana Marie Broulíková, Advisor, Ministry of Health on Implementation of the National Action Plan for Alzheimer´s Disease and Related Illnesses, Czech Republic

Brain Capital Gain

'Brain capital' indicates the brain health and skills of a population, is key to the growth of a society (Eyre et al., 2023). Delaying cognitive decline in at least a fraction of AD patients has profound implications on the trajectory of our ageing society and its collective brain capital. In this context, delaying progression in people living with AD will allow them to still contribute to the society for a longer period, to reduce societal costs for public health and to increase regional competitiveness (Letta, 2024; European Central Bank, 2024).

UNVEILING CURRENT GAPS AND CHALLENGES IN THE POST-DIAGNOSTIC CARE PATHWAY FOR ALZHEIMER'S DISEASE

As innovative treatments will become available and a rethinking of AD will set into motion, new challenges will arise. These new challenges will add to the currently existing gaps in the post-diagnostic pathway that need to be urgently addressed.

"We are advocating for a 10-year extension of the Global Dementia Action Plan to allow low-income countries time to develop plans of their own."

Paola Barbarino, Alzheimer's Disease International

Current Gaps

Gap 1 – European services for post-diagnostic pathway are currently insufficient to support people living with Alzheimer's disease (AD) and their caregivers, leading to fragmented care pathways

- Insufficient number of AD centers (Leroi et al., 2024).
- Long waiting lists for delivery of the therapy (Hlavka et al., 2019).
- Limited availability of specialists in neurology and geriatrics, especially in rural areas (Ng et al., 2021).
- Lack of holistic approach involving a truly collaborative, cross-disciplinary healthcare approach.
- Poor coordination among healthcare providers leading to gaps and delays in AD diagnosis, treatment and care management.
- Insufficiently available/absent psychosocial AD care services (Alzheimer Europe, 2020).
- Underutilisation of the development and implementation of innovative solutions such as text alerts and mobile apps for treatment follow-up (Alzheimer Europe, 2020).

Gap 2 – Lack of harmonisation in decision making that considers the needs of the individual patient and their caregiver(s)

- Insufficient shared decision making with people living with AD (e.g., treatment options, legal recommendations, end-of-life care and support; van der Flier et al., 2017).
- Lack of caregivers ad hoc logistical and necessary psychological support (Alzheimer Europe, 2020).
- Insufficient communication of diagnosis and discussion of next steps (Gauthier et al., 2021, 2022).

Gap 3 – Lack of Alzheimer's disease-specific focus

- Lack of awareness and knowledge of AD (how it is different from other forms of dementia, as well as the misconception that it is a part of natural ageing) and the existing treatment options among the general public and within the community of healthcare professionals.
- Insufficient funding and support for AD research for the development of new treatments and care strategies.
- Low number of AD-specific clinical trials in EU.

Challenges with New Treatments

The current healthcare systems are not properly equipped to provide new treatments to eligible patients once they become available (Hlvaka et al., 2019). The main gaps and challenges identified for amyloid DMTs (Disease Modifying Treatments) include:

Challenge 1 – Structural capacity

- Insufficient number of AD centres and specialists in Europe to roll out new treatments (Hlvaka et al., 2019).
- Not sufficient biomarker analysis tools (i.e., PET - Positron Emission Tomography - and CSF - CerebroSpinal Fluid - blood biomarkers; Eurostat.).
- Limited infusion capacity (e.g., in Italy, Sweden, and Germany waiting times have been estimated to extend between year 2030 and 2040 (Hlvaka et al., 2019).
- Insufficient number of MRI (Magnetic Resonance Imaging) (e.g., in Finland, that has 2.9 units per 100K inhabitants) would not allow for ARIA monitoring on a regular basis for all eligible people living with AD (Eurostat).
- Lack of ad hoc training and standardised protocols on the use of biomarkers as well as treatment protocols.

Challenge 2 – Implementation

- Shared decision making with people living with AD and co-design of care pathways (Leroi et al., 2024).
- Multidisciplinary care considering the patient needs and existing comorbidities, including mental health and nutrition.
- Equitable access: All eligible patients in Europe should have equitable access to innovative treatments such as DMTs. EU patients have the fundamental right to choose their treatment options, and it is crucial to uphold this right by providing early access to advanced medical therapies. To prevent Europe from lagging in the next wave of medical breakthroughs, concerted efforts are needed to reverse current trends and prioritise healthcare innovation. Maintaining Europe's strong position in healthcare innovation is essential for the well-being of its citizens and the global advancement of medical science (Jessen et al., 2024).
- Knowledge and stigma: Due to lack of knowledge, AD is still surrounded by stigma and fear. Society at large has little perception of the advancements of science in this field. To make sure that treatments can be delivered, people living with AD and their family members must be aware of them and approach the healthcare system in the first place.

CALL TO ACTION: POLICY RECOMMENDATIONS

Recommendation 1

Make Alzheimer's disease (AD) and brain health a national, European, and global public health priority

- National level: Implement and support the development of national AD/dementia strategies based on clearly defined KPIs following WHO's guidelines, Sustainable Development Goals (SDGs) and recommendations from people living with AD, clinicians, health professionals, researchers, carers and civil society.
- European Commission (EC) level: Coordinate the AD/Dementia national strategies under an overarching EU policy framework with dedicated funding.
- EC level: Create a subgroup on Dementia within the EU's Expert Group on Public Health to define clear guidelines, establish a roadmap and identify best practices.
- EC & European Parliament (EP) level: Ensure that AD and dementia are considered in all aspects of policymaking, by involving all relevant parties in the design and monitoring of policies and expanding the cooperation between units of the EC.
- EP level: Support transversal approaches aiming to tackle (or better address) AD/dementia in the broader context of neurological and mental disorders through holistic and coordinated policy efforts.
- EP level: Increase political leadership on AD/dementia by designating Brain Health Ambassadors within the EP.
- International level: Continue the work made in the context of the WHO (World Health Organization) Global Action Plan on Dementia to seek its full implementation at the national level (Alzheimer's Disease International, 2024) and prioritise the extension of this global instrument, due to expiration in 2025, and enshrine diagnostics, treatment and care at the heart of all National Dementia Plans (Alzheimer's Disease International, 2024).

Recommendation 2

Promote training, education and awareness raising in healthcare professionals (HCPs) and citizens

Raise awareness about AD at national and EU level to reduce stigma.

- Foster and support educational and awareness campaigns in society and among HCPs at national and EU level about early detection of AD, access to diagnostic centres, and the benefits of the post-diagnostic care across the EU through existing funding and educational mechanisms.
- Provide ongoing training for healthcare professionals on the latest AD findings including early detection and treatment options.

- Increase available training and educational programming 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).
- Increase awareness and education in the society and among HCPs alike (on topics such as the difference between AD and normal ageing, AD and dementia, etc.) to tackle barriers in access to both diagnostic, treatment, and care.
- Expand possible training offered to other members of Public Administration (i.e., 1st responders, volunteers, police & fire services, etc.).
- Ensure that a module on dementia care is included in clinical and research curricula.

Recommendation 3

Leverage data, information sharing and technology

- Support a precision medicine approach based on biomarkers and predictive algorithms for treatment response (that consider both efficacy and safety).
- Facilitate exchange of best practices among member states in order to develop initiatives such as: EU Joint Actions on AD, EU AD registry, and monitoring based on a standardised set of statistics to regularly report for each country as an epidemiological surveillance of AD.
- Implement electronic health records (EHR) to streamline person living with AD data sharing and improve coordination of care.
- Initiate registries of family members and people diagnosed with AD.
- Develop and implement standardised protocols for the administration of DMTs (Disease Modifying Treatments) and monitoring of ARIA across excellence centres.
- Utilise big data and artificial intelligence (AI) to predict patient needs and optimise resource allocation for MRI units and infusion centres.
- Implement EHR to streamline patient data sharing and improve coordination of care (e.g., Involve clinicians, researchers, patients and carers in the implementation of the EHDS).

Recommendation 4

Provide access to optimisation and implementation of innovation

- Ensure the pathway model is flexible enough to give people living with AD equitable access to innovation and dedicated funding to reimburse the treatment and care pathway (e.g., through the implementation of policies that ensure all people living with AD, regardless of socioeconomic status, have access to innovative AD treatments).
- Provide reimbursement for people who cannot afford expensive treatments and MRI scans.
- Support the implementation of a structured and sustainable care pathways supported by clear guidelines and taking stock of innovative tools and therapeutic innovation.

- Optimisation of the innovative treatment delivery (i.e., increase the number and/or potentiate existing AD centres for the optimal care pathway in the post-diagnostic journey of AD patients).
- Increase infusion capacity for treatment delivery.
- Increase capacity for treatments monitoring.

Recommendation 5

Ensure dedicated funding to support Alzheimer's research and infrastructure development

- Ensure that Member States, the EC and private sector allocate sufficient funding to make the most of a coordinated efforts and approach to accelerate the development and distribution of innovative treatments (e.g., Innovative Health Initiative, European Partnership on Brain Health, Healthier Together initiative).
- Ensure that funding adequately matches the health, economic, social, and research challenges posed by AD and dementia (e.g., increase the funding for AD clinical trials, which are currently mostly run in the USA, not European context).
- Collaborative AD health system and implementation-focused research effort (e.g., Davos Alzheimer's Collaborative (DAC) looking inter alia at health systems preparedness and building on the findings of the DAC Learning Laboratory, World Dementia Council (WDC), World Health Organization (WHO) Global Action Plan on the public health response to dementia 2017-2025, Global Dementia Observatory, Intersectoral global action plan on epilepsy and other neurological disorders 2022-2031Renew the EU4H-2023-PJ-04 call with increased funding to further ensure that recommendations trickle down at national level and are implemented).
- Advocate for the increase in funding from governmental and non-governmental organizations to support AD research and infrastructure development.

Recommendation 6

Increase patient and public involvement

- Involve people living with AD, their carers, and their healthcare professionals to work alongside ministries of health, social affairs, education, research, industry to develop and allocate relevant funding to the plan.
- Involving people living with AD and their carers in the design and development of new clinical pathways, to ensure they are accessible, inclusive and patient-centered.
- Educate and raise awareness of patients and caregivers about the importance of regular monitoring and adherence to treatment plans.
- Integrate the voice of patients in the design of trial and especially endpoints.

Recommendation 7

Integrate multidisciplinary care teams

- Form multidisciplinary teams including neurologists, radiologists, nurses, psychiatrists, geriatricians, nutritionists and primary care physicians to provide comprehensive care (Gauthier et al., 2022).
- Call for the introduction of a skilled navigator designed to keep the person living with dementia at the heart of decision making by this multidisciplinary teams (Gauthier et al., 2022).
- Potentiate psychosocial care for AD patients.
- Use telemedicine to facilitate regular consultations and follow-ups, especially for people living with AD in remote locations.
- Support a shift from care to active treatment, increasing the use of large multi-specialty practices.

Recommendation 8

Define post-diagnostic pathways through guidelines and funds allocated for optimal implementation

- Fund and support the implementation of information-sharing mechanisms at all levels of the care pathways, from the caring team to the decision-making level. This will improve alignment and harmonisation of the pathways across countries.

CONCLUSION

Improving the health and wellbeing of citizens has become the top priority for many governments, and brain health should not be left behind. Brain diseases, neurological and psychiatric alike, are not just highly prevalent and costly to society, but are still amongst the most complex conditions to understand and treat. Their impact poses serious challenges for health systems, economies, patients, caregivers, and their families. Yet, brain conditions still lack the awareness and recognition they are due for a European Union that strives to build and maintain healthy and prosperous lives for all.

After decades of research and countless setbacks, we stand at a pivotal time; recent breakthroughs in diagnostics and the arrival of disease-modifying treatments are ushering in a new era of the care for Alzheimer's disease (AD). These advancements offer potential new options to slow the disease course and delay progression. Such innovations are urgently needed and could fundamentally alter the trajectory of AD management. We have a unique opportunity to reshape the future of Alzheimer's care in Europe, and the time is NOW. By adopting new innovative tools today with equitable access, we can accelerate our understanding of disease and advance the next generation of diagnostics and treatments. We must ensure that European patients are not left behind as new diagnostic tools and medicines become globally available. It is time to prepare European health systems for timely access to diagnosis, care, and treatment.

The Perspective Paper "Rethinking Alzheimer’s Disease Pathway: From Diagnosis to Care," emphasises the critical need for a comprehensive and innovative approach to AD. As our understanding of the disease's complex pathology evolves, it becomes evident that early and accurate diagnosis is paramount. Advanced diagnostic tools and biomarkers to identify the disease at its earliest stages, potentially before significant cognitive decline occurs, are key for implementing early treatments, which are starting to emerge.

Society will witness a profound change in the next 10 years, and the healthcare system will need to prepare to accommodate such scientific and cultural change with ad hoc resources for faster diagnosis, treatment delivery and precision medicine.

As we strive for health equity, innovative solutions for AD treatments will need to be accessible, safe and effective for all members of the society.

Moreover, this paper highlights the importance of a multidisciplinary approach to care that not only focuses on medical treatment but also on the psychological and social well-being of people living with AD and their caregivers. By fostering a more holistic care model, we can work to improve the quality of life for those affected by AD, providing them with the support and resources needed throughout the progression of the disease.

Treating AD and slowing its symptoms is part of a larger priority in the context of European public health, namely preserving brain health. There is no health without brain health, and we cannot allow AD to mine the happiness and fulfillment of the lives of so many EU citizens. Individuals need to be informed about their risks of AD, be given the tools for a quick diagnosis and, if diagnosed, provided with the full spectrum of treatments, including pharmacological and non-pharmacological ones. We need to empower individuals in their care of their brains in the same way that it's done for other health focuses such as heart and lung health, and send a message of hope to the population that this terrifying disease can and must be tamed.

Ultimately, this Perspective Paper calls for continued research and collaboration across scientific, medical, and social domains to better understand AD and to develop more effective diagnostic and therapeutic strategies. As we rethink the AD pathway, we are encouraged to adopt a patient-centered approach that emphasises early intervention, personalised care, and more comprehensive support systems. This reimagined pathway offers hope for more effective management of the disease and a better quality of life for people living with AD (and their families). May this report serve as a catalyst for dialogue, understanding and progress.

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About RETHINKING ALZHEIMER'S DISEASE

Rethinking Alzheimer's disease (AD) is a research-driven project offering policy recommendations to make tangible changes with the aim to improve the lives of people living with Alzheimer's disease across Europe.

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About the European Brain Council

The European Brain Council (EBC) is a network of key players in the "brain space", with a membership encompassing scientific and professional societies, patient organisations and industry partners. A non-profit organisation based in Brussels, its main mission is to promote brain research with the ultimate goal of improving the lives of those living with brain conditions, neurological and mental alike.

About the European Federation of Pharmaceutical Industries and Associations

The European Federation of Pharmaceutical Industries and Associations (EFPIA) represents the biopharmaceutical industry operating in Europe. Through its direct membership of 37 national associations, 38 leading pharmaceutical companies and a growing number of small and medium-sized enterprises, EFPIA's mission is to create a collaborative environment that enables our members to innovate, discover, develop and deliver new therapies and vaccines for people across Europe, as well as contribute to the European economy.

For more information about "Rethinking Alzheimer's disease", please visit: www.braincouncil.eu/projects/rethinking-alzheimers-disease/

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She is the founder and president of the patient association for Parkinson's disease called "Awakening" in Osijek since 2013. In 2016, she became head of the Department for Neurodegenerative and Neuromuscular Disease at the University Hospital Centre Osijek and where they still hold that position today. In 2019, Svetlana became a subspecialist of neurodegenerative diseases. From 2021 onwards, she has been a member of the management group in the scientific panel for dementia and cognitive disorders of the European Academy of Neurology, and from 2022 she has been the co-chair in the same panel.

Svetlana has great experience as principal investigator and sub-investigator in many clinical trials in the field of the neurology. She is author of 33 publications, 2 manuals for Parkinson's disease and 3 book chapters, has been mentor of 30 student's graduation theses and 3 Ph.D. theses.

REFERENCES

2024 Alzheimer's disease facts and figures. Alzheimers Dement. 2024 May;20(5):3708-3821. doi: 10.1002/alz.13809. Epub 2024 Apr 30. PMID: 38689398; PMCID: PMC11095490.

Alzheimer's Association. 2024 Alzheimer's Disease Facts and Figures. Alzheimers Dement 2024;20(5).

Alzheimer Europe (2020). European Dementia Monitor 2020 - Comparing and benchmarking national dementia strategies and policies. ISBN 978-2-9199578-6-6, Luxembourg, Alzheimer Europe.

Alzheimer's Disease International (2024) From plan to impact VII: Dementia at a crossroads. London: Alzheimer's Disease International

Aye S, Jönsson L, Gustavsson A, Tate A, Ptacek SG, Eriksdotter M. Effect of mortality in cost-effectiveness modeling of disease-modifying treatment for Alzheimer's disease. Alzheimers Dement (Amst). 2023 Mar 29;15(1):e12422. doi: 10.1002/dad2.12422. PMID: 37009338; PMCID: PMC10053186.

Budd Haeberlein S, Aisen PS, Barkhof F, Chalkias S, Chen T, Cohen S, Dent G, Hansson O, Harrison K, von Hehn C, Iwatsubo T, Mallinckrodt C, Mummery CJ, Muralidharan KK, Nestorov I, Nisenbaum L, Rajagovindan R, Skordos L, Tian Y, van Dyck CH, Vellas B, Wu S, Zhu Y, Sandrock A. Two Randomized Phase 3 Studies of Aducanumab in Early Alzheimer's Disease. J Prev Alzheimers Dis. 2022;9(2):197-210. doi: 10.14283/jpad.2022.30. PMID: 35542991.

Chou YH, Ton That V, Sundman M. A systematic review and meta-analysis of rTMS effects on cognitive enhancement in mild cognitive impairment and Alzheimer's disease. Neurobiol Aging. 2020 Feb;86:1-10. doi: 10.1016/j.neurobiolaging.2019.08.020. Epub 2019 Aug 27. PMID: 31783330; PMCID: PMC6995441.

Cummings J, Zhou Y, Lee G, Zhong K, Fonseca J, Cheng F. Alzheimer's disease drug development pipeline: 2024. Alzheimers Dement (N Y). 2024 Apr 24;10(2):e12465. Dutch. doi: 10.1002/trc2.12465. PMID: 38659717; PMCID: PMC11040692.

Dubois B, Villain N, Schneider L, Fox NC, Campbell N, Galasko D, Kivipelto M, Jessen F, Hanseeuw B, Boada M, Barkhof F, Nordberg A, Frolich L, Waldemar G, Frederiksen KS, Padovani A, Planche V, Rowe C, Bejanin A, Ibanez A, Cappa S, Caramelli P, Nitrini R, Allegri R, Slachevsky A, de Souza L, Bozoki A, Widera E, Blennow K, Ritchie C, Agronin M, Lopera F, Delano-Wood L, Bombois S, Levy R, Thambisetty M, Georges J, Jones DT, Zabretski H, Schott J, Gatchel J, Swantek S, Newhouse P, Feldman HH, Frisoni GB. Alzheimer disease is a clinical-biological construct: An IWG recommendation. JAMA Neurol. 2014, in press.

De la Rosa A, Olaso-Gonzalez G, Arc-Chagnaud C, Millan F, Salvador-Pascual A, García-Lucerga C, Blasco-Lafarga C, Garcia-Dominguez E, Carretero A, Correas AG, Viña J, Gomez-Cabrera MC. Physical exercise in the prevention and treatment of Alzheimer's disease. J Sport Health Sci. 2020 Sep;9(5):394-404. doi: 10.1016/j.jshs.2020.01.004. Epub 2020 Feb 4. PMID: 32780691; PMCID: PMC7498620.

Dumas A, Destrebecq F, Esposito G, Suchonova D, Steen Frederiksen K. Rethinking the detection and diagnosis of Alzheimer's disease: Outcomes of a European Brain Council project. Aging Brain. 2023 Sep 2;4:100093. doi: 10.1016/j.nbas.2023.100093. PMID: 37692977; PMCID: PMC10483037.

Eaglestone G, Gkaintatzi E, Jiang H, Stoner C, Pacella R, McCrone P. Cost-Effectiveness of Non-pharmacological Interventions for Mild Cognitive Impairment and Dementia: A Systematic Review of Economic Evaluations and a Review of Reviews. Pharmacoecon Open. 2023 Nov;7(6):887-914. doi: 10.1007/s41669-023-00440-z. Epub 2023 Sep 25. PMID: 37747616; PMCID: PMC10721583.

European Central Bank. Convergence Report 2024. Available from: https://www.ecb.europa.eu/press/other-publications/convergence/html/index.en.html

European Medicines Agency. Ginkgo folium - herbal medicinal product. Available from: https://www.ema.europa.eu/en/medicines/herbal/ginkgo-folium

Eurostat. (n.d.). Healthcare resource statistics - technical resources and medical technology. Retrieved September 11, 2024, from https://ec.europa.eu/eurostat/statistics-explained/index.php?oldid=452031

Eurostat. (n.d.). Availability of CT and MRI units in hospitals. Retrieved September 11, 2024, from https://ec.europa.eu/eurostat/web/products-eurostat-news/-/ddn-20210702-2

Eurostat. (n.d.). Ageing Europe - statistics on population developments. European Commission. Retrieved June 17, 2024, from https://ec.europa.eu/eurostat/statistics-explained/index.php?title=Ageing_Europe_-_statistics_on_population_developments#Older_people_.E2.80.94_population_overview

Eyre et al., (2023). "How Brain Capital Can Drive Progress on UN's Sustainable Development Goals" (Houston: Rice University's Baker Institute for Public Policy, November 21, 2023), https://doi.org/10.25613/E96R-EG11.

Frederiksen KS, Nielsen TR, Winblad B, Schmidt R, Kramberger MG, Jones RW, Hort J, Grimmer T, Georges J, Frölich L, Engelborghs S, Dubois B, Waldemar G. European Academy of Neurology/European Alzheimer's Disease Consortium position statement on diagnostic disclosure, biomarker counseling, and management of patients with mild cognitive impairment. Eur J Neurol. 2021 Jul;28(7):2147-2155. doi: 10.1111/ene.14668. Epub 2020 Dec 23. PMID: 33368924; PMCID: PMC8246881.

Gauthier S, Rosa-Neto P, Morais JA, & Webster C. 2021. World Alzheimer Report 2021: Journey through the diagnosis of dementia. London, England: Alzheimer's Disease International.

Gauthier S, Webster C, Servaes S, Morais JA, Rosa-Neto P. 2022. World Alzheimer Report 2022: Life after diagnosis: Navigating treatment, care and support. London, England: Alzheimer's Disease International.

Hajós M, Boasso A, Hempel E, Shpokayte M, Konisky A, Seshagiri CV, Fomenko V, Kwan K, Nicodemus-Johnson J, Hendrix S, Vaughan B, Kern R, Megerian JT, Malchano Z. Safety, tolerability, and efficacy estimate of evoked gamma oscillation in mild to moderate Alzheimer's disease. Front Neurol. 2024 Mar 6;15:1343588. doi: 10.3389/fneur.2024.1343588. PMID: 38515445; PMCID: PMC10957179.

Hampel H, Au R, Mattke S, van der Flier WM, Aisén P, Apostolova L, Chen C, Cho M, De Santi S, Gao P, Iwata A, Kurzman R, Saykin AJ, Teipel S, Vellas B, Vergallo A, Wang H, Cummings J. Designing the next-generation clinical care pathway for Alzheimer's disease. Nat Aging. 2022 Aug;2(8):692-703. doi: 10.1038/s43587-022-00269-x. Epub 2022 Aug 19. PMID: 37118137; PMCID: PMC10148953.

Hampel H, Elhage A, Cho M, Apostolova LG, Nicoll JAR, Atri A. Amyloid-related imaging abnormalities (ARIA): radiological, biological and clinical characteristics. Brain. 2023 Nov 2;146(11):4414-4424. doi: 10.1093/brain/awad188. PMID: 37280110; PMCID: PMC10629981.

Hampel H, Hu Y, Cummings J, Mattke S, Iwatsubo T, Nakamura A, Vellas B, O'Bryant S, Shaw LM, Cho M, Batrla R, Vergallo A, Blennow K, Dage J, Schindler SE. Blood-based biomarkers for Alzheimer's disease: Current state and future use in a transformed global healthcare landscape. Neuron. 2023 Sep 20;111(18):2781-2799. doi: 10.1016/j.neuron.2023.05.017. Epub 2023 Jun 8. PMID: 37295421; PMCID: PMC10720399.

Herr M, Ankri J, Diard C, Hiance-Delahaye A. Removal of Drugs for Alzheimer's Disease from the List of Reimbursable Drugs in France: Analysis of Change in Drug Use, Disease Management and Cognition Using the National Alzheimer Data Bank (BNA). Drugs Aging. 2021 Jan;38(1):63-74. doi: 10.1007/s40266-020-00817-3. Epub 2021 Jan 7. PMID: 33410119.

Hlavka JP, Mattke S, Liu JL. Assessing the Preparedness of the Healthcare System Infrastructure in Six European Countries for an Alzheimer's Treatment. Rand Health Q. 2019 May 16;8(3):2. PMID: 31205802; PMCID: PMC6557037.

Jack CR Jr, Andrews SJ, Beach TG, Buracchio T, Dunn B, Graf A, Hansson O, Ho C, Jagust W, McDade E, Molinuevo JL, Okonkwo OC, Pani L, Rafii MS, Scheltens P, Siemers E, Snyder HM, Sperling R, Teunissen CE, Carrillo MC. Revised criteria for the diagnosis and staging of Alzheimer's disease. Nat Med. 2024 Aug;30(8):2121-2124. doi: 10.1038/s41591-024-02988-7. PMID: 38942991.

Jessen, F., Kramberger, M.G., Angioni, D. et al. Progress in the Treatment of Alzheimer’s Disease Is Needed – Position Statement of European Alzheimer’s Disease Consortium (EADC) Investigators. J Prev Alzheimers Dis (2024). https://doi.org/10.14283/jpad.2024.153

Jia J, Ning Y, Chen M, Wang S, Yang H, Li F, Ding J, Li Y, Zhao B, Lyu J, Yang S, Yan X, Wang Y, Qin W, Wang Q, Li Y, Zhang J, Liang F, Liao Z, Wang S. Biomarker Changes during 20 Years Preceding Alzheimer's Disease. N Engl J Med. 2024 Feb 22;390(8):712-722. doi: 10.1056/NEJMoa2310168. PMID: 38381674.

Lee J, Howard RS, Schneider LS. The Current Landscape of Prevention Trials in Dementia. Neurotherapeutics. 2022 Jan;19(1):228-247. doi: 10.1007/s13311-022-01236-5. Epub 2022 May 19. PMID: 35587314; PMCID: PMC9130372.

Leroi I, Dolphin H, Dinh R, Foley T, Kennelly S, Kinchin I, O'Caoimh R, O'Dowd S, O'Philbin L, O'Reilly S, Trepel D, Timmons S. Navigating the future of Alzheimer's care in Ireland - a service model for disease-modifying therapies in small and medium-sized healthcare systems. BMC Health Serv Res. 2024 Jun 5;24(1):705. doi: 10.1186/s12913-024-11019-7. PMID: 38840115; PMCID: PMC11151472.

Letta Report "Much More Than a Market" (April 2024)

Liu Z, Qiu X, Mak S, Guo B, Hu S, Wang J, Luo F, Xu D, Sun Y, Zhang G, Cui G, Wang Y, Zhang Z, Han Y. Multifunctional memantine nitrate significantly protects against glutamate-induced excitotoxicity via inhibiting calcium influx and attenuating PI3K/Akt/GSK3beta pathway. Chem Biol Interact. 2020 Jul 1;325:109020. doi: 10.1016/j.cbi.2020.109020. Epub 2020 Feb 21. PMID: 32092300.

Livingston G, Huntley J, Liu KY, Costafreda SG, Selbæk G, Alladi S, Ames D, Banerjee S, Burns A, Brayne C, Fox NC, Ferri CP, Gitlin LN, Howard R, Kales HC, Kivimäki M, Larson EB, Nakasujja N, Rockwood K, Samus Q, Shirai K, Singh-Manoux A, Schneider LS, Walsh S, Yao Y, Sommerlad A, Mukadam N. Dementia prevention, intervention, and care: 2024 report of the Lancet standing Commission. Lancet. 2024 Aug 10;404(10452):572-628. doi: 10.1016/S0140-6736(24)01296-0. Epub 2024 Jul 31. PMID: 39096926.

Long, S, Benoist, C, Weidner, W, 2023. World Alzheimer Report 2023: Reducing dementia risk: never too early, never too late. London, England: Alzheimer's Disease International.

Majdi A, van Boekholdt L, Sadigh-Eteghad S, Mc Laughlin M. A systematic review and meta-analysis of transcranial direct-current stimulation effects on cognitive function in patients with Alzheimer's disease. Mol Psychiatry. 2022 Apr;27(4):2000-2009. doi: 10.1038/s41380-022-01444-7. Epub 2022 Feb 3. PMID: 35115703.

Marucci G, Buccioni M, Ben DD, Lambertucci C, Volpini R, Amenta F. Efficacy of acetylcholinesterase inhibitors in Alzheimer's disease. Neuropharmacology. 2021 Jun 1;190:108352. doi: 10.1016/j.neuropharm.2020.108352. Epub 2020 Oct 6. PMID: 33035532.

National Library of Medicine. A Pivotal Study of Sensory Stimulation in Alzheimer's Disease (Hope Study, CA-0011) (Hope). Available from: https://clinicaltrials.gov/study/NCT05637801

Ng CKM, Leung DKY, Cai X, Wong GHY. Perceived Help-Seeking Difficulty, Barriers, Delay, and Burden in Carers of People with Suspected Dementia. Int J Environ Res Public Health. 2021 Mar 13; 18(6):2956. doi: 10.3390/ijerph18062956. PMID: 33805808; PMCID: PMC7999253.

Pardo-Moreno T, González-Acedo A, Rivas-Domínguez A, García-Morales V, García-Cozar FJ, Ramos-Rodríguez JJ, Melguizo-Rodríguez L. Therapeutic Approach to Alzheimer's Disease: Current Treatments and New Perspectives. Pharmaceutics. 2022 May 24;14(6):1117. doi: 10.3390/pharmaceutics14061117. PMID: 35745693; PMCID: PMC9228613.

Saragih ID, Tonapa SI, Saragih IS, Lee BO. Effects of cognitive stimulation therapy for people with dementia: A systematic review and meta-analysis of randomized controlled studies. Int J Nurs Stud. 2022 Apr;128:104181. doi: 10.1016/j.ijnurstu.2022.104181. Epub 2022 Jan 22. PMID: 35149325.

Schmachtenberg T, Monsees J, Thyrian JR. Structures for the care of people with dementia: a European comparison. BMC Health Serv Res. 2022 Nov 18;22(1):1372. doi: 10.1186/s12913-022-08715-7. PMID: 36401262; PMCID: PMC9673874.

Sims JR, Zimmer JA, Evans CD, Lu M, Ardayfio P, Sparks J, Wessels AM, Shcherbinin S, Wang H, Monkul Nery ES, Collins EC, Solomon P, Salloway S, Apostolova LG, Hansson O, Ritchie C, Brooks DA, Mintun M, Skovronsky DM; TRAILBLAZER-ALZ 2 Investigators. Donanemab in Early Symptomatic Alzheimer Disease: The TRAILBLAZER-ALZ 2 Randomized Clinical Trial. JAMA. 2023 Aug 8; 330(6):512-527. doi: 10.1001/jama.2023.13239. PMID: 37459141; PMCID: PMC10352931.

Thompson T. How CRISPR gene editing could help treat Alzheimer's. Nature. 2024 Jan;625(7993): 13-14. doi: 10.1038/d41586-023-03931-5. PMID: 38082131.

Smith E, Ali D, Wilkerson B, Dawson WD, Sobowale K, Reynolds C 3rd, Berk M, Lavretsky H, Jeste D, Ng CH, Soares JC, Aragam G, Wainer Z, Manji HK, Licinio J, Lo AW, Storch E, Fu E, Leboyer M, Tarnanas I, Ibanez A, Manes F, Caddick S, Fillit H, Abbott R, Robertson IH, Chapman SB, Au R, Altimus CM, Hynes W, Brannelly P, Cummings J, Eyre HA. A Brain Capital Grand Strategy: toward economic reimagination. Mol Psychiatry. 2021 Jan;26(1):3-22. doi: 10.1038/s41380-020-00918-w. Epub 2020 Oct 26. PMID: 33100330; PMCID: PMC8244537.

United Nations (2024). The 17 goals. United Nations. https://sdgs.un.org/goals.

van der Flier WM, Kunneman M, Bouwman FH, Petersen RC, Smets EMA. Diagnostic dilemmas in Alzheimer's disease: Room for shared decision making. Alzheimers Dement (N Y). 2017 May 9; 3(3):301-304. doi: 10.1016/j.trci.2017.03.008. PMID: 29067336; PMCID: PMC5651445.

van der Flier WM, de Vugt ME, Smets EMA, Blom M, Teunissen CE. Towards a future where Alzheimer's disease pathology is stopped before the onset of dementia. Nat Aging. 2023 May;3(5):494-505. doi: 10.1038/s43587-023-00404-2. Epub 2023 May 18. PMID: 37202515.

van Dyck CH, Swanson CJ, Aisen P, Bateman RJ, Chen C, Gee M, Kanekiyo M, Li D, Reyderman L, Cohen S, Froelich L, Katayama S, Sabbagh M, Vellas B, Watson D, Dhadda S, Irizarry M, Kramer LD, Iwatsubo T. Lecanemab in Early Alzheimer's Disease. N Engl J Med. 2023 Jan 5;388(1):9-21. doi: 10.1056/NEJMoa2212948. Epub 2022 Nov 29. PMID: 36449413.

Walsh S, King E, Brayne C. France removes state funding for dementia drugs. BMJ. 2019 Dec 30; 67:l6930. doi: 10.1136/bmj.l6930. PMID: 31888870.

Wessels AM, Dennehy EB, Dowsett SA, Dickson SP, Hendrix SB. Meaningful Clinical Changes in Alzheimer Disease Measured With the iADRS and Illustrated Using the Donanemab TRAILBLAZER-ALZ Study Findings. Neurol Clin Pract. 2023 Apr;13(2):e200127. doi: 10.1212/CPJ.0000000000200127. Epub 2023 Feb 16. PMID: 36891463; PMCID: PMC9987204.

Wimo A, Seeher K, Cataldi R, Cyhlarova E, Dielemann JL, Frisell O, Guerchet M, Jönsson L, Malaha AK, Nichols E, Pedroza P, Prince M, Knapp M, Dua T. The worldwide costs of dementia in 2019. Alzheimers Dement. 2023 Jul;19(7):2865-2873. doi: 10.1002/alz.12901. Epub 2023 Jan 8. PMID: 36617519; PMCID: PMC10842637.

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