

Time is Up: The Need to Prepare People Impacted by Alzheimer’s Disease for Engagement in the Value Assessment Process

Project Alzheimer’s Value Europe

Abstract

This white paper is an outcome of PAVE’s Alzheimer Europe panel that delved into the gaps in the current assessment process for Alzheimer’s disease (AD) therapies within Health Technology Assessment (HTA) frameworks. Drawing from insightful discussion held during the panel, this paper advocates for substantial revisions to the evaluation methodologies in place. It highlights the imperative need to integrate the patient and care partner burden into assessments to achieve a more comprehensive and patient-centric approach. Furthermore, it explores practical strategies for engaging stakeholders, including patients, care partners (used interchangeably with caregivers, but defined herein as individuals providing support and/or assistance to loved ones with AD),¹ and advocacy groups, to collaboratively shape a more robust assessment framework for AD therapies.

Introduction: Contextualizing Health Technology Assessment

HTA is a systematic process used to evaluate the clinical, economic, social, and ethical implications of healthcare interventions such as medicinal products and medical equipment used for diagnosis, treatment, or prevention of disease.² HTA bodies inform healthcare policymakers on how these interventions can be used in health systems worldwide. In the context of AD therapies, HTA plays a pivotal role in determining the value and accessibility of treatments based on their clinical efficacy, safety, and cost-effectiveness.

Limitations of Current Assessment Frameworks for AD: Overlooked Patient and Care Partner Burden

From a lived experience perspective, the existing HTA methodologies often fall short of comprehensively capturing the multifaceted impact of chronic degenerative conditions such as AD. HTA bodies primarily rely on clinical effectiveness and cost-effectiveness measures, including budget impact analyses, to decide whether a treatment should be utilized. As a result,

¹ Alzheimer’s Association. Early Stage Caregiving. <https://www.alz.org/help-support/caregiving/stages-behaviors/early-stage>.

² European Commission. Health Technology Assessment Overview. https://health.ec.europa.eu/health-technology-assessment/overview_en.

conventional frameworks tend to overlook and undervalue broader societal implications. AD has far-reaching societal and economic implications, driven largely by the costs of informal care.³ Estimates of informal care costs typically stem from the amount of time devoted to aiding family members or loved ones with daily activities or overseeing their behavior. In 2019, caregivers collectively spent 133 billion hours providing informal dementia care.⁴ Beyond the time commitment, caregivers frequently encounter financial, social, and psychological stressors and would benefit from added training and support. To illustrate the gap in current assessment frameworks, please refer to the schematic representation in Figure 1 below.

Elements	HTA system in general	HTA system in each country		
		Japan	NICE (UK)	ICER (US)*
Patient QOL	++	++	++	++
Patient medical costs	++	++	++	++
Informal caregiver QOL	+	-	+	+*
Informal caregiver medical costs	-	-	-	+*
Public long-term care costs	+	-	+	+
Informal care costs/ informal caregiver productivity loss	-	-	-	+*

++, always included; +, possible, but not always included; -, not/almost not included.

Figure 1: Summary of current inclusion status of value assessment elements in health technology assessment system for Alzheimer’s disease dementia⁵

HTA frameworks predominantly focus on the clinical and cost-effectiveness measures mentioned above and, as a result, often overlook the burden on care partners and the wider societal implications of AD.

Importance of Incorporating Care Partner Burden in AD Value Assessments

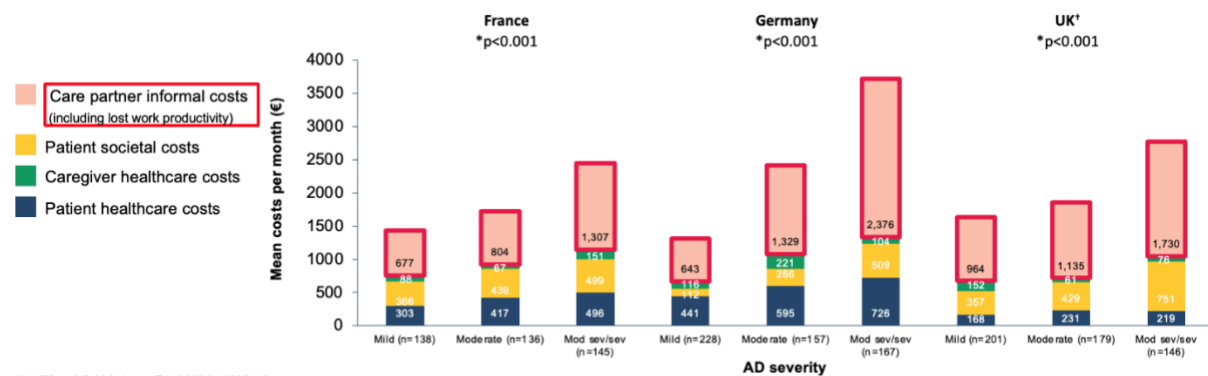
Informal care partners play a pivotal role in supporting individuals living with AD, but the cost of their contributions and sacrifices is not captured by existing assessment frameworks. As family, friends, or others with close relationships to a person living with AD, informal care partners a range of care services without pay, including assistance with daily living activities,

³ WHO. Global Status Report on the Public Health Response to Dementia (5). <https://iris.who.int/bitstream/handle/10665/344701/9789240033245-eng.pdf?sequence=1>.

⁴ Ibid, 55.

⁵ Igarashi, A., & Ikeda, S. (2022). Value assessment of new interventions for Alzheimer’s disease dementia in Japan based on literature review and group interview. *Expert Review of Pharmacoeconomics & Outcomes Research*, 22(8), 1163—1170. <https://doi.org/10.1080/14737167.2022.211811>.

transportation, medical care, and emotional support. Many care partners are forced to reduce their working hours or forego employment altogether to provide around-the-clock care, resulting in lost income. Research suggests that informal care accounts for the highest overall cost associated with AD (Figure 2).⁶ Care partner burden is evident across the disease continuum of Alzheimer’s, with a particularly heavy burden in the advanced stages.⁷ Consequently, the economic impact over time is substantial. In the UK, informal carers collectively spend 1.1 billion hours looking after their loved ones, costing the UK economy €10.2 billion a year.⁸ By comparison, the UK health service spends €1.7 billion annually on dementia.⁹



*Tu JY et al. J Alzheimers Dis 2022;86:1527-43
 *p value for comparison between severity groups (ANOVA) of total monthly societal costs (value in italics above each column); †UK costs were converted from pounds sterling to euros using the conversion rate £1 = €1.1661.
 AD, Alzheimer’s disease; ANOVA, analysis of variance; mod sev/sev, moderately severe/severe.

Figure 2: Monthly baseline costs for components associated with AD by severity: GERAS study¹⁰

There is a pressing need to reform HTA methodologies to more effectively capture the broader societal impacts of AD. To do so, payers should consider incorporating input from care partners via an assessment tool that comprehensively measures the nuanced challenges care partners experience in their role supporting individuals affected by AD. Measuring QoL with a standard generic tool such as EQ-5D not only for patients but also caregivers makes it possible in principle to incorporate the benefit of alleviating the burden for both in the value assessment

⁶ Wimo, Anders et al. (2013, Jan. 1). ‘The GERAS Study: A Prospective Observational Study of Costs and Resource Use in Community Dwellers with Alzheimer’s Disease in Three European Countries – Study Design and Baseline Findings’.

⁷ Reed, C. et al. (2019, May 28). Factors associated with long-term impact on informal caregivers during alzheimer’s disease dementia progression: 36-month results from Geras: International psychogeriatrics. Cambridge Core. <https://www.cambridge.org/core/journals/international-psychogeriatrics/article/factors-associated-with-longterm-impact-on-informal-caregivers-during-alzheimers-disease-dementia-progression-36month-results-from-geras/1686386239EB0D8805925FA464AB353D>.

⁸ Alzheimer’s Research UK. ‘The Economic Impact of Dementia.’ <https://dementiastatistics.org/statistics/the-economic-impact-of-dementia/>.

⁹ Ibid.

¹⁰ Wimo, Anders et al. (2013, Jan. 1). ‘The GERAS Study: A Prospective Observational Study of Costs and Resource Use in Community Dwellers with Alzheimer’s Disease in Three European Countries – Study Design and Baseline Findings’.

based on QALYs (Quality Adjusted Life Years). However, not all HTA reviewers do consider this type of data, and even if so, may be reluctant to incorporate it in their final analysis because their mission is primarily to assess the value from the payer perspective. Similar restrictions may take place when considering the indirect economic benefits such as a reduction of income loss for patients and caregivers. Furthermore, generic QoL tools may not be sufficiently sensitive to capture comprehensively the benefits and HTA bodies could give more consideration to the development of a disease-specific value set for AD that reflects the unique changes associated with quality of life in people living with AD as well as their preferences. Arguments for derogating the general principle of addressing value across diseases in a fully standardized manner is the frequency of AD in aging populations across the world and some precedent for another frequent disease such as cancer.

A Case Study: Lessons Learned from MS

Multiple sclerosis (MS) is a chronic, progressive disease that affects the central nervous system with an early onset in young adults. However, since the 1990s, several innovative treatments have proved they modify the disease progression and are made available to patients in need in many countries. Patient advocacy groups have been effective in promoting their perception of the value of such treatments, including the risk-benefit ratio appraisal that may differ from the one of the regulatory agencies or payers. Furthermore, similarly to Alzheimer's, there are significant indirect costs resulting from informal care such as lost productivity, out-of-pocket expenses, and emotional and physical stress. MS value assessment frameworks are increasingly taking into account these costs of informal care, acknowledging that the disease can have a significant impact on the quality of life and economic status of people with MS and their families.

Utilization of Clinical Data and Patient-Reported Outcomes

HTA bodies heavily rely on clinical data to assess the efficacy and safety of AD therapies. While clinical data provide valuable information about the effectiveness of a treatment in a specific population under controlled conditions, they focus on objective measures of efficacy (i.e., changes in disease severity or survival rates) and do not capture the full spectrum of a patient's experience with a treatment. Patient-reported outcomes (PROs), which are measures of a patient's health and well-being, can identify treatment benefits not captured by clinical data, such as one's experiences with symptoms and overall quality of life. For example, some treatments may improve a patient's quality of life without significantly changing the trajectory of the disease. PROs provide a complementary perspective on treatment outcomes that is essential to effective decision-making over treatment decisions.

ROADMAP Project

The ROADMAP (Real-world Outcomes across the Alzheimer's Disease Spectrum for better care: Multi-modal data Access Platform) project aimed to improve understanding of real-world outcomes in AD.¹¹ To do so, researchers engaged people living with AD, their care partners and healthcare providers in public involvement consultations to collect input on meaningfulness of treatment outcomes. They identified that people living AD were most interested in outcomes that reflected their ability to participate in daily living activities and maintain their sense of self. Conversely, care partners prioritized a patients' overall well-being and need for support, and healthcare providers emphasized more traditional clinical outcomes and signs of disease progression.^{12,13} Consultations ultimately informed a new outcomes measurement tool for AD, titled the ROADMAP Outcomes Questionnaire, which assesses meaningfulness of a range of outcomes such as physical and cognitive function, emotional well-being and social participation.

The ROADMAP project is an example of how comprehensive measurements (i.e., those that incorporate diverse perspectives) can ensure that new treatments are not only effective but also meaningful to the people who will use them. Some HTA bodies (such as NICE (UK), IQWiG (Germany) or HAS (France)) do consider patient quality of life to an extent. However, there is much work to be done to better understand what constitutes meaningfulness for individuals with AD, care partners, and healthcare providers. In 2019, Alzheimer's Research UK commissioned researchers at the University of Edinburgh to conduct a nationwide study on what treatment outcomes matters to people living with AD with a focus on those at the pre-dementia stage of disease. A survey of 5,800 participants identified family connections, driving, socializing, reading and friendships to be the top five most important things people would want treatments to help them keep in their everyday lives.¹⁴ Notably, none of these outcomes are

¹¹ Alzheimer Europe. (2018, February). *Dementia in Europe Magazine*, 26. https://issuu.com/alzheimer-europe/docs/dementia_in_europe_issue_26_-_february_2018.

¹² Tochel, C., Smith, M., Baldwin, H., Gustavsson, A., Ly, A., et al. ROADMAP consortium. What outcomes are important to patients with mild cognitive impairment or Alzheimer's disease, their caregivers, and health-care professionals? A systematic review. *Alzheimers Dement (Amst)*. 2019 Mar 7;11:231-247. doi: 10.1016/j.dadm.2018.12.003. PMID: 30906845; PMCID: PMC6411507.

¹³ Janssen O, Vos SJB, García-Negredo G, Tochel C, Gustavsson A, Smith M, Ly A, Nelson M, Baldwin H, Sudlow C, Bexelius C, Jindra C, Vaci N, Bauermeister S, Gallacher J, Ponjoan A, Dufouil C, Garre Olmo J, Pedersen L, Skoog I, Hottgenroth A, Visser PJ, van der Lei J, Diaz C. Real-world evidence in Alzheimer's disease: The ROADMAP Data Cube. *Alzheimers Dement*. 2020 Mar;16(3):461-471. doi: 10.1016/j.jalz.2019.09.087. Epub 2020 Jan 6. PMID: 32157788.

¹⁴ Saunders, S., Muniz-Terrera, G., Sheehan, S. *et al.* A UK-Wide Study Employing Natural Language Processing to Determine What Matters to People about Brain Health to Improve Drug Development: The Electronic Person-Specific Outcome Measure (ePSOM) Programme. *J Prev Alzheimers Dis* 8, 448–456 (2021). <https://doi.org/10.14283/jpad.2021.30>.

presently included in the Clinical Dementia Rating scale, a tool used to determine dementia stage in research settings.¹⁵

Measuring Cost Effectiveness of New Treatments

As described above, extended quality of life is invaluable, not only to patients but also to their care partners, improving patient outcomes and alleviating the burden of disease management. Interventions that not only slow disease progression but also sustain cognitive function and preserve independence over extended periods could significantly enhance quality of life, reducing the burden for individuals living with AD and their families. Traditional assessments tend to prioritize short-term clinical efficacy and immediate cost savings, often underestimating the long-term benefits and societal savings that novel treatments could bring. Interventions that slow disease progression not only benefit people living with AD by extending the period of milder disease, and keeping individuals healthier for longer, but reduce the financial burden on healthcare systems by mitigating the need for long-term care. As a result, they may prove cost-effective in the broader context. Indirect, long-term benefits must be integrated into cost-effectiveness assessments to more accurately depict the true value of AD therapies.

Effective Engagement with HTA Bodies: Key Takeaways

I. A Call for Stakeholder Involvement

It is imperative to adopt a patient-centric and comprehensive approach to HTA to address existing limitations. Empowering patients, care partners, and advocacy groups to actively be involved in the assessment process is crucial. Their insights can provide valuable perspectives that better reflect the true impact of AD and the benefits of interventions. Initiatives such as patient-led research, public consultations, and stakeholder education on HTA decision-making processes would facilitate engagement in health technology discussions and ensure that perspectives of those directly affected by the decisions are considered.

II. Proposal for a Holistic Assessment Framework

This paper proposes a holistic assessment framework that integrates traditional clinical endpoints with care partner burden measurements and PROs. Aligning on

¹⁵ Radford, Isole. "Holding on to what matters and risking a lot to do so – What do people want from new dementia treatments?" Alzheimer's Research UK. September 28, 2023. <https://www.alzheimersresearchuk.org/blog/holding-on-to-what-matters-and-risking-a-lot-to-do-so-what-do-people-want-from-new-dementia-treatments/>.

key evidentiary components and then building a robust evidence base, is essential. This involves prioritizing the collection of real-world evidence that supports the medical and social needs and conducting long-term impact assessments when disease modifying drugs become available. A uniform and comprehensive approach to value assessment ensures equitable evaluations, facilitates informed decision-making and ultimately leads to more effective healthcare interventions for conditions like AD.

III. Advancing Research: The Role of Registries and Standardized Clinical Trials

Finally, enhancing the value assessment process of complex conditions like AD requires robust registries and standardized clinical trials. Registries serve as critical repositories of real-world data, offering insights into disease progression, treatment outcomes, and patient experiences over extended periods. By pooling diverse patient and care partner information, registries enable a more comprehensive understanding of the disease landscape and aid in the identification of potential biomarkers and the patients who could benefit most from specific treatments. Standardized clinical trials, with uniform methodology and established endpoints, facilitate comparisons across studies. Together, these initiatives enhance the reliability of research findings and support transparent, evidence-based decision-making processes.

Conclusion: Embracing Change for Improved Assessment of AD Therapies

Enhancing the evaluation process for AD therapies within HTA frameworks requires a paradigm shift towards a more inclusive, patient and care partner-centric approach. By fostering stakeholder engagement and incorporating the patient and care partner burden and benefits into assessments, HTA bodies can create a more robust evaluation framework that better reflects the true value of treatments and improves outcomes for individuals living with AD and their care partners. Through this white paper, PAVE calls for a holistic approach to the assessment of AD therapies, ultimately driving towards more compassionate and effective healthcare solutions.