Project Alzheimer's Value Europe

White Paper: "Overcoming the Barriers to Value Assessment of New Innovations in Alzheimer's Disease"
October, 2022

Introduction

Health Technology Assessment (HTA) bodies advise payers and health governance organizations on the use, adoption, and reimbursement of new treatments and devices, with the aim to optimize allocation of public monies for public need through a full and fair assessment of value. The approach to value assessment varies by country, yet there are two common challenges all HTA bodies struggle to overcome: 1) how to assess the long-term impact of pharmaceutical therapies and diagnostic tools targeting slow-progressing diseases, when only short-term clinical trial data are available, and 2) how to assess these medicines when the majority of their impact lies in informal care costs. A disease that represents both challenges is Alzheimer's, which progresses over two to three decades and is characterized by enormous informal care costs, which are not adequately measured by traditional disease-related expenditure data. The lack of currently available treatment options for Alzheimer's disease, together with a high unmet patient need and a growing treatment pipeline adds urgency to the need to overcome barriers related to HTA. Alternative assessment methods, which place increased value on persons living with Alzheimer's (PLWA) and care partner quality of life and societal and economic impact, will be particularly important for assessing the value of emerging therapies and diagnostics for Alzheimer's disease (AD).

Project Alzheimer's Value Europe (PAVE), a coalition of clinical, regulatory, payer and HTA experts, reviewed the assessment methods currently employed by European HTA bodies through desk research and interviews to identify best practices aimed at supporting holistic value assessment, including those that consider the impact of the disease and potential new disease modifying treatments (DMTs) on PLWA, care partners, and society as a whole. The report focuses on lessons that can be taken from value-based healthcare implementation in UK and Sweden because of their progress on frameworks for value assessment and comprehensive health data collection to date. As part of this review, it was found that there remains a need for value assessment to adopt a broad perspective that considers the direct and indirect impacts of innovative treatments and diagnostics, including a treatment's benefits to the daily lives of PLWA and their care partners, as well as society over time. Based on our review, four areas of opportunity for improvement have emerged:

1. AD-Specific Frameworks are Needed to Assess New Treatments
    a. The burden of Alzheimer's disease is not only characterized by diminishing cognitive function of PLWA but also by a variety of behavioral problems and physical impairments, increasing the burden and costs related to the disease for people living with Alzheimer's and their care partners, economies and societies over time. Against a backdrop of an aging population and a shift towards value-based healthcare systems that place increased importance on outcomes that matter most to patients, there is a need for **assessment frameworks to capture the broad value of an AD intervention for PLWA, families, care partners and society, and allow for some degree of uncertainty around clinical outcomes**. Uncertainty, described as variability in the probabilities and outcomes associated with PLWA receiving treatment options, is inevitable as they are estimated from observing a sample of

people. To this end, qualitative and quantitative lived experience input from PLWA and care partners should supplement existing biomedical measurements assessing disease impact on PLWA daily lives. HTA bodies that give significant weight to PLWA and care partner input in formal models of assessment and factor in uncertainty of clinical and cost-effectiveness demonstrate optimal applicability of said frameworks. Sweden may be a good example of this, given its integration of the societal burden of disease (in terms of care partner quality of life and impact on employment) into assessment of candidate therapies. Germany, on the other hand, bases all therapy assessments on clinical trial evidence and does not consider societal impact more broadly. Such strict guidelines for clinical meaningfulness lend themselves to a limited applicability of any public value framework and create barriers to assessment in practice.

2. Long-Term Evidence Collection Should Allow for Some Uncertainty
    a. The burden of AD increases over the course of the disease and extends beyond the direct medical costs to PLWA, affecting care partners, healthcare systems, and society as a whole. Emerging disease-modifying therapies targeting the earlier stages of Alzheimer's disease will slow the progression of cognitive decline; currently available and approved therapies treat only the symptoms of Alzheimer's. The lack of long-term clinical data that will be available for DMTs to determine clinical effectiveness over time suggests a need to model long-term outcomes by using data from patient registries to supplement short-term clinical and biomarker data from clinical trials.[1] Also, **evidence requirements must allow for some degree of uncertainty for a new treatment to demonstrate its long-term positive risk-benefit profile given the limited scope of a PLWA sample treatment group**. To a degree, the data and registry infrastructure in place in Sweden and the UK can serve as an example for other HTA bodies to use. The UK and Sweden use patient registries and longitudinal, pre-treatment data to evaluate the effectiveness of future innovative therapies that deliver value to people with mild cognitive impairment[2], and early-stage disease over a long period of time by delaying cognitive, functional and/or behavioral decline.
3. Real-World Evidence Collection Must be Supported
    a. HTA agencies should also find ways to use PLWA input on lived experience in a valuable way and give proper weight to this dimension against clinical inputs from clinical trials and cost-effectiveness data. Additionally, real-world evidence can also help address the issues outlined in the above by helping to reduce uncertainty and provide long-term evidence over time. Real-world evidence can better characterize the impact of new treatments on PLWA, care partners, and healthcare systems when it includes evidence derived from PLWA and care partner data sources that are more reflective of PLWA lived experiences, preferences, and perspectives. As such, PLWA and care partner input should be given adequate weight and used in addition to the evidence prioritized today. Real-world evidence use requires progress on data collection methods and standardized determinations on leveraging data in value assessments. To support the application of holistic value frameworks, **alignment on practical data requirements are needed, including what type of data should be collected, for how long and for what purpose**. Data should be considered broadly

[1] Tahami Monfared AA, Tafazzoli A, Ye W, Chavan A, Zhang Q. Long-Term Health Outcomes of Lecanemab in Patients with Early Alzheimer's Disease Using Simulation Modeling. Neurol Ther. 2022 Jun;11(2):863-880. doi: 10.1007/s40120-022-00350-y. Epub 2022 Apr 25.

[2] Petersen RC, Smith GE, Waring SC, Ivnik RJ, Kokmen E, Tangelos EG. Aging, memory, and mild cognitive impairment. Int Psychogeriatr. 1997;9 Suppl 1:65-9. doi: 10.1017/s1041610297004717. PMID: 9447429.

as those outcomes which pose costs to society – economically and socially. Beginning steps to incorporate real-world evidence have been taken in Sweden. These include using population-based cohort data in value assessments. However, more must be done.

4. A Framework to Support Meaningful Input
    a. Most countries utilize a fairly limited input process without full representation of the stakeholder community. A framework that captures the full value of AD treatments will need to **duly consider input from all relevant stakeholders (e.g., PLWA, care partners, clinicians, industry, policymakers, payers)**. Experts agree that, while critical, the clinician's voice should not trump that of the PLWA and care partner.[3] To balance and facilitate meaningful stakeholder input, clear and transparent stakeholder involvement processes must be in place.

Conclusion

Innovative therapies and diagnostics may add value in ways not presently captured by current models for value assessment, which rely primarily on medical outcomes and cost-effectiveness data. This paper seeks to identify opportunities for new frameworks to address the challenges that exist in models presently used for value assessment. As demonstrated above, the practices of some European HTA bodies capture broad value that a therapy brings – to various stakeholders and with regard to the slow progression of Alzheimer's disease – and these can be built up and leveraged in the future. In the future, PAVE intends to update its evaluation of European countries' application of public value frameworks on a recurring basis to identify best practices for HTA bodies.

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[3] Bridges JF, Jones C. Patient-based health technology assessment: a vision of the future. Int J Technol Assess Health Care. 2007 Winter;23(1):30-5. doi: 10.1017/S0266462307051549. PMID: 17234014.