
February 2, 2023

***Submitted electronically to:*** publiccomments@icer-review.org

Steven D. Pearson, MD, President
Institute for Clinical and Economic Review
Two Liberty Square, Ninth Floor
Boston, MA 02109

*Re: Draft Evidence Report: Beta-Amyloid Antibodies for Early Alzheimer's Disease*

Dear Dr. Pearson:

On behalf of the Institute for Patient Access, I thank you for the opportunity to provide comments regarding ICER's draft evidence report, "Beta-Amyloid Antibodies for Early Alzheimer's Disease," dated December 22, 2022.

**About the Institute for Patient Access**

The Institute for Patient Access (IfPA) is a physician-led policy research organization dedicated to maintaining the primacy of the physician-patient relationship in the provision of quality health care. To further that mission, IfPA produces educational materials and programming designed to promote informed discussion about patient-centered care. IfPA was established in 2012 by the leadership of the Alliance for Patient Access, a national network of health care providers committed to shaping a patient-centered health care system. IfPA is a 501(c)(3) public charity nonprofit organization.

**Draft Evidence Report Comments**

With respect to lecanemab, the report cites an inaccurate range regarding the treatment's efficacy, concluding that the impact could be "small" or "substantial." Such uncertainty regarding lecanemab's efficacy is inconsistent with the Phase III trial results and should not be used as justification to undervalue the drug's benefits.

The primary outcome for the lecanemab Phase III trial was the change from baseline in the Clinical Dementia Rating-Sum of Boxes (CDR-SB). The results of the trial demonstrated that the patients who received lecanemab performed better on this test than those who received a placebo. Further, the patients receiving lecanemab met the trial's secondary goals, which included reducing toxic plaques within the brain and a slower decline on three other memory and function measures.

These improvements in outcomes are not small. The Alzheimer's Association, in response to lecanemab's results, said that the treatment "has the potential to change the course of the disease in a clinically meaningful way."[1] Specific benefits for patients include more time at or near their full abilities, allowing them to remain independent and participate in future health care decision. The ability to maintain one's sense of self is also a critical benefit.

A University of Chicago working paper by Philipson and Ling (2022) quantifies the large value enabled by treatments that slow Alzheimer's progression. According to the authors, delaying the progression of Alzheimer's from mild to moderate by between six months and three years provides between $212 billion and $1.3 trillion in benefits over the next 10 years.[2] With respect to direct health care costs, delaying Alzheimer's progression can reduce expenditures by "$34,249 and non-market costs by caregivers by $7,882."

Despite both the positive results from the Phase III trial and the benefits in terms of reduced health care spending and improved patient and caregiver outcomes, the report rates lecanemab promising but inconclusive. This rating significantly understates lecanemab's efficacy in delaying disease progression and the tremendous value delayed progression offers patients, their caregivers and the broader community.

Beyond this fundamental flaw, IfPA urges ICER to reconsider several assumptions that bias its analysis results toward undervaluing the benefits of efficacious treatments.

***The Costs of Alzheimer's Are Higher Than the Estimates Cited in the Draft Evidence Report***

The draft evidence report states the "direct and indirect costs of health care related to AD are estimated to be around $500 billion annually." This is likely an understatement.

According to the Alzheimer's Association, the direct health care costs alone are projected at $321 billion in 2022.[3] A study in the AJMC confirms this estimate finding the direct health care costs for treating Alzheimer's in 2020 was $305 billion and expected to grow to over $1 trillion.[4] A substantial share of these costs, 49% according to a Milliman report, are related to long-term residential nursing care.[5]

In addition to these costs, caregivers provide nearly $271 billion in unpaid care to people living with Alzheimer's and other dementias.[6] These figures imply total annual costs around $600

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[1] "Alzheimer's Association Statement on Lecanemab Phase 3 Topline Data Release." Alzheimer's Association September 27, 2022, https://www.alz.org/news/2022/alzheimers-association-statement-on-lecanemab-phas.
[2] Philipson TJ and Ling Y "The Value of Innovation Delaying the Progression of Alzheimer's Disease in the US." The University of Chicago, November 28, 2022, https://bpb-us-w2.wpmucdn.com/voices.uchicago.edu/dist/d/3128/files/2022/12/Value-of-Delaying-Alzheimers-Progression-Final-Dec-12.pdf.
[3] https://www.jec.senate.gov/public/index.cfm/democrats/issue-briefs?id=02F4CADC-954F-4E3B-8409-A4213E3C0759#:~:text=Over%206%20million%20Americans%20are,%24271%20billion%20in%20unpaid%20caregiving.
[4] Wong W. Economic burden of Alzheimer disease and managed care considerations. Am J Manag Care. 2020 Aug;26(8 Suppl): S177-S183. doi: 10.37765/ajmc.2020.88482. PMID: 32840331. https://pubmed.ncbi.nlm.nih.gov/32840331/.
[5] Pyenson B, Pelizzari P, Smith R, and Latimer H "Assessing the Value of Therapies in Alzheimer's Disease: Considerations to create a practical approach to value" Milliman Report, May 12, 2021, https://www.milliman.com/-/media/milliman/pdfs/2021-articles/5-12-21-assessing-the-value-of-therapies-in-alzheimers.ashx.
[6] https://www.jec.senate.gov/public/index.cfm/democrats/issue-briefs?id=02F4CADC-954F-4E3B-8409-A4213E3C0759#:~:text=Over%206%20million%20Americans%20are,%24271%20billion%20in%20unpaid%20caregiving.

billion, approximately 20% more than the number cited in the report. And this cost estimate is still incomplete because it does not account for the many costs that are difficult to quantify.

According to a survey from the Alzheimer's Association, 64% of respondents caring for someone with Alzheimer's or dementia felt "isolated or alone," and more than four in every five (84%) said they needed more help with caregiving, especially from other family members."[7] These stresses impact caregivers' health, with surveys showing that caregivers experience higher rates of stress, depression and even report declines in cognition themselves.

Importantly, Alzheimer's caregivers endure a larger burden compared to caregivers for other diseases. According to a survey by Home Care Assistance, "dementia caregivers were seven times more likely to experience daily physical, emotional and mental exhaustion from caregiving than non-dementia caregivers." Dementia caregivers were also three times more likely to "feel extreme stress from their caregiving responsibilities than other types of caregivers."[8]

As Alzheimer's patients will often have multiple caregivers,[9] these caregiver burdens significantly expand the number of people experiencing negative consequences from this disease. The severity and pervasiveness of these burdens demonstrates that it is essential for a cost-effectiveness model to incorporate the full costs borne by caregivers despite the difficulty in quantifying them. Without an accurate assessment of these burdens, ICER's model will significantly undervalue the benefits from any efficacious treatment.

The cost estimates reviewed look at the disease's cost from an annual basis. However, when discussing the financial burden of a degenerative disease, it's necessary to recognize that the costs are incurred for many years and will increase over time as degeneration worsens. Consequently, an accurate understanding of the costs is incomplete without considering the lifetime burden of the disease (appropriately discounted into the present value).

According to Jutkowitz et al., "the discounted cost of care for a person with dementia was $321,780 (2015 dollars)" over each patient's lifetime.[10] The Alzheimer's Association estimates that in 2020 dollars, lifetime costs that cover just the direct care expenditures equate to $373,527.

Of course, people not living with Alzheimer's or other forms of dementia will also require direct health care expenditures over their lifetimes. For this reason, the study also accounted for the additional discounted lifetime costs of an Alzheimer's patient compared to someone not living with dementia. Evaluated on this "additional cost basis," the excess lifetime health care costs of an Alzheimer's patient are $184,500 higher than a patient not living with dementia. Again, these are direct health care costs only, and do not include the impacts on caregivers. Across the 6.2

[7] https://alzheimersnewstoday.com/2017/06/01/alzheimers-dementia-caregivers-emotional-toll-need-support-surveys/.
[8] "Study Reveals Toll of Dementia Care on Caregivers." HomeCare, June 1, 2017, https://www.homecaremag.com/news/study-reveals-toll-dementia-care-caregivers.
[9] As evidence to this reality, the CDC estimates there are more than "16 million Americans providing unpaid care" to patients with Alzheimer's and other dementia (https://www.cdc.gov/aging/caregiving/alzheimer.htm) compared to 6.2 million living with the disease.
[10] Jutkowitz E, Kane RL, Gaugler JE, MacLehose RF, Dowd B, Kuntz KM. Societal and family lifetime cost of dementia: Implications for policy. J Am Geriatr Soc 2017;65(10):2169-75.

million people currently living with Alzheimer's, these additional costs imply that the present value of Alzheimer's excessive direct health care costs are over $1.1 trillion.

A disproportionate share of the financial burden from this disease will be directly borne by families. Families will incur 70% of the total cost burden ($225,140), compared to Medicaid, which will incur 14% ($44,090) and Medicare, which will incur 16% ($52,540).[11]

In light of these costs, IfPA fears that the $500 billion cost estimate cited in the report may be an inaccurate basis from which to judge the benefits of effective treatments.

***Accounting for Patients' "Loss of Self" and Alzheimer's Less Tangible Costs***

Loss of identity is one of the more devastating and terrifying aspects of Alzheimer's and other forms of dementia. The ability to maintain one's self-worth while having to accept the inevitable cognitive decline, along with the realization that you will become a burden on your loved ones, is a common struggle for patients diagnosed with Alzheimer's.

According to the aforementioned Alzheimer's Association survey, "a full 70% of the 1,502 adult participants feared being unable to care for themselves and live independently as they aged...."[12] Alzheimer's patients also commonly experience depression, have thoughts of suicide and experience a poorer quality of life even before the disease robs them of their memories.[13, 14]

The methodologies to accurately quantify these subjective impacts are underdeveloped. Nevertheless, when it comes to Alzheimer's and dementia, not incorporating these impacts will lead to a vast underestimation of the benefits provided by efficacious treatment.

***Explicitly Accounting for Alzheimer's Disproportionate Impact on Communities of Color is Essential***

As the draft evidence report mentions, Alzheimer's imposes a disproportionate impact on communities of color. According to the Alzheimer's Association, "African Americans are about two times more likely than whites to have Alzheimer's and other dementias, [but] they are only 34% more likely to have a diagnosis. Hispanics are about one and one-half times more likely than whites to have Alzheimer's and other dementias, but they are only 18% more likely to be diagnosed."[15] Communities of color have a higher risk of developing this devastating disease and, because it is discovered later, have higher average medical costs.

Even still, racial and ethnic minorities are underrepresented in clinical trials – for Alzheimer's drugs specifically and across disease states broadly. Of studies that reported ethno-racial

[11] Jutkowitz E, Kane RL, Gaugler JE, MacLehose RF, Dowd B, Kuntz KM. Societal and family lifetime cost of dementia: Implications for policy. J Am Geriatr Soc 2017;65(10):2169-75.
[12] https://alzheimersnewstoday.com/2017/06/01/alzheimers-dementia-caregivers-emotional-toll-need-support-surveys/.
[13] https://www.webmd.com/alzheimers/alzheimers-depression.
[14] https://bmcgeriatr.biomedcentral.com/articles/10.1186/s12877-018-0831-2.
[15] https://www.alz.org/aaic/downloads2020/2020_Race_and_Ethnicity_Fact_Sheet.pdf.

information, according to a systematic review, the participation rate for racial and ethnic minorities in dementia prevention clinical trials was only 25.6%.[16] This disproportionately low participation translates to lack of knowledge, risks associated with generalizability of findings and also lost benefits associated with clinical trials participation. Despite these shortcomings, ICER's review heavy relies on clinical trials data – as opposed to waiting for FDA approval and real-world patient experience. As a result, ICER's results inadequately capture the benefit effective treatments could have on communities of color.

The disproportionate burden of Alzheimer's born by communities of color means that an efficacious treatment will be particularly valuable for these demographic groups. Such a benefit cannot be understated.

**Assessment Timeline and Scope Comments**

IfPA would also like to comment about the structure of this assessment of Alzheimer's disease interventions. IfPA has previously commented about the pitfalls associated with ICER initiating an assessment ahead of the FDA – as the designated federal agency – completing its drug review, yet those concerns are worth reiterating.

Without the Phase III trial results, the efficacy of any drug cannot be determined – either positively or negatively. Further, without federal approval, a final indication and a manufacturer list price, any determination of value can only be based on assumptions – not facts. Timing aside, ICER has redefined the scope of this review multiple times since it was first announced over a year ago. Multiple edits to both the timeline and the interventions of interest make meaningful participation in the process difficult. In short, this assessment, which spurred a prolonged investment of time and resources by stakeholders, was premature.

**Conclusion**

If IfPA can provide further detail or aid the Institute for Clinical and Economic Review in addressing the concerns related to this draft evidence report, please contact us at 202-964-2624.

Sincerely,

Michelle M. D. Winokur, DrPH
Executive Director
Institute for Patient Access

[16] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8804327/.