

June 2, 2021

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

Dear Dr. Pearson,

The Partnership to Improve Patient Care (PIPC) appreciates this opportunity to comment on the Institute for Clinical and Economic Review's (ICER) draft evidence report regarding treatments for Alzheimer's Disease. More than six million Americans are living with Alzheimer's Disease and over eleven million Americans provide unpaid care for people with Alzheimer's Disease.<sup>1</sup> Given the huge toll that Alzheimer's Disease takes on patients, caregivers, and society writ large, treatments that improve quality of life and mitigate higher levels of care would mark a huge medical milestone. As we see more treatments in development and coming to market, there is a great responsibility to approach their assessment in a responsible and reliable manner using methods that capture outcomes that matter to patients. For this reason, we strongly urge ICER to postpone this assessment until after FDA approval of this drug. Should ICER choose to move forward at this premature phase, we submit to ICER the following comments on its current model.

**ICER is conducting this assessment far too early to produce accurate and useful results.**

A consistent concern PIPC and many others have presented to ICER is that it conducts assessments at too early a juncture to have accurate inputs for its models, and, as a result its results are often incomplete or incorrect. This assessment is particularly worrisome, as ICER's timeline is so condensed that it is requiring commenters to submit feedback prior to aducanumab being approved by the FDA. ICER already delayed the assessment once to align with FDA's changing timeline, and it would be prudent to delay the comment deadline until after approval. Conducting the assessment prior to approval, and requiring stakeholders to comment prior to the approval, forced both ICER and stakeholders to make inferences and deal in conjecture. This puts an undue burden on stakeholders and undermines the credibility of the assessment that will be referenced by payers.

In this case specifically, it is also very likely that we will have additional reliable data about this drug upon the conclusion of additional trials. Cognitive decline in mild

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<sup>1</sup> <https://www.alz.org/alzheimers-dementia/facts-figures>

cognitive impairment (MCI) and mild Alzheimer's Disease generally occurs over years. Because of this, longer-term follow-up data from patients enrolled in the ENGAGE and EMERGE trials are currently being collected in an open-label study, EMBARK, which is scheduled to be completed in 2023. The results from EMBARK will provide additional information about the longer-term efficacy and safety of aducanumab.

Therefore, we strongly suggest ICER delay this study, at a minimum until after FDA approval, and ideally until the conclusion of the EMBARK trial.

**ICER significantly underestimated the impact on caregiver burden in evaluating treatments for Alzheimer's Disease.**

Alzheimer's disease puts a particularly large burden on caregivers and accrues a multitude of societal care costs. The National Institute for Health and Care Excellence, NICE, which ICER leans heavily on for its approach to value assessment, has already included caregiver utility in its cost-effectiveness models for diseases such as Alzheimer's Disease, multiple sclerosis and Parkinson's disease.<sup>2</sup>

When ICER does look at caregiver burden, it appears to drastically underestimate it. More than 11 million family members and other caregivers provided an estimated 15.3 billion hours of unpaid care to patients with Alzheimer's Disease or other dementias, putting these caregivers at risk for negative mental, physical, and emotional outcomes.<sup>3</sup> For example, as patients moved from mild to severe Alzheimer's Disease, the financial, physical, psychosocial, social, and personal strain as measured by the Modified Caregiver Strain Index (MCSI) increased from an average score of 9.0 to 17.5, indicating a substantial increase in caregiver impact.<sup>4</sup> Despite this data, ICER assumes a very marginal impact on caregivers' utility.

Given the huge burden Alzheimer's Disease places on families and the assumption that ICER will continue to use this model to assess new treatments for Alzheimer's drugs as they come to market, we strongly encourage ICER to update its caregiver utilities.

**ICER continues to rely on the Quality-Adjusted Life Year (QALY), which is known to devalue the lives of older adults.**

As PIPC has consistently stated – the use of the QALY in ICER's models is inappropriate, as the QALY discriminates against older adults, patients,<sup>5</sup> and people

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<sup>2</sup> Afentou N, Jarl J, Gerdtham UG, Saha S. Economic evaluation of interventions in Parkinson's disease: a systematic literature review. *Movement disorders clinical practice*. 2019 Apr;6(4):282-90.

<sup>3</sup> Deb A, Thornton JD, Sambamoorthi U, Innes K. Direct and indirect cost of managing alzheimer's disease and related dementias in the United States. *Expert Rev Pharmacoecon Outcomes Res*. 2017;17(2):189-202

<sup>4</sup> UsAgainstAlzheimer's. AD PACE. [usaagainstalzheimer.org/UsAgainstAlzheimer's/7/29/2020](https://usaagainstalzheimer.org/UsAgainstAlzheimer's/7/29/2020) 2020.

<sup>5</sup> Paulden M. Recent amendments to NICE's value-based assessment of health technologies: implicitly inequitable?. *Expert review of pharmacoeconomics & outcomes research*. 2017 May 4;17(3):239-42.

with disabilities.<sup>6</sup> This is widely recognized as a problem with the QALY. In fact, in 2019, the National Council on Disability, an independent federal agency, published a report finding that the use of the QALY would be contrary to United States civil rights laws and disability policy.<sup>7</sup> The use of this metric is particularly concerning in an assessment of treatments for Alzheimer's disease, as it is a condition that generally impacts older adults.

In recognition of the fact that QALYs are innately discriminatory, health economists have begun investigating ways to repair this problem and have been actively developing new metrics, from healthy year totals<sup>8</sup> to risk-adjusted QALYs.<sup>9</sup> The most recent work shows that due to diminishing returns, traditional cost utility methods overvalue treatments for mild illnesses and undervalue treatments for highly severe illnesses, like Alzheimer's disease. ICER should be evolving away from use of the QALY, toward use of outcome measures based on the most up to date science.

**ICER's model underestimates the probability of patients being admitted to long-term care facilities, which is a major driver of costs and burden related to Alzheimer's Disease.**

Transition into long-term care facilities is a very common outcome for patients and people with disabilities with Alzheimer's Disease. The set of probabilities used in the ICER model seems quite conservative compared to other data points. As ICER's source is over twenty years old, we would posit it is now out of date. A more recent study suggests that the probability of transitioning to long-term care is much higher than those estimates used in the ICER model. Examples of this discrepancy include 16% a year in moderate Alzheimer's Disease as compared to 11% used in ICER's model and over 32% in severe Alzheimer's Disease as compared to just 23% used in the ICER model.<sup>10</sup> Since admission into long-term care facilities is such a large driver of costs and burden of this disease, updating these numbers is essential for the model to accurately describe the long-term cost savings of an effective treatment for Alzheimer's Disease.

**Conclusion**

We highly encourage ICER to postpone this assessment until after FDA approval. If ICER does move forward, we encourage it to fix some of the obvious shortcomings in

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<sup>6</sup> Nord E, Pinto JL, Richardson J, Menzel P, Ubel P. Incorporating societal concerns for fairness in numerical valuations of health programmes. *Health economics*. 1999 Feb;8(1):25-39.

<sup>7</sup> [https://www.ncd.gov/sites/default/files/NCD\\_Quality\\_Adjusted\\_Life\\_Report\\_508.pdf](https://www.ncd.gov/sites/default/files/NCD_Quality_Adjusted_Life_Report_508.pdf)

<sup>8</sup> Basu A, Carlson J, Veenstra D. Health years in total: a new health objective function for cost-effectiveness analysis. *Value in Health*. 2020 Jan 1;23(1):96-103.

<sup>9</sup> Lakdawalla DN, Phelps CE. Health Technology Assessment With Diminishing Returns to Health: The Generalized Risk-Adjusted Cost-Effectiveness (GRACE) Approach. *Value in Health*. 2021 Feb 1;24(2):244-9.

<sup>10</sup> Davis M, O'Connell T, Johnson S, Cline S, Merikle E, Martenyi F, Simpson K. Estimating Alzheimer's disease progression rates from Normal cognition through mild cognitive impairment and stages of dementia. *Current Alzheimer Research*. 2018 Jul 1;15(8):777-88.

its model to paint a more accurate picture of Alzheimer's disease and the individuals impacted by it.

Sincerely,



Tony Coelho  
Chairman  
Partnership to Improve Patient Care