

June 4, 2021

Institute for Clinical and Economic Review  
Two Liberty Square  
Ninth Floor  
Boston, MA 02109

To Whom It May Concern,

On behalf of the [Alliance for Aging Research](http://www.agingresearch.org) (Alliance), and the millions of older adults whose health and access to care we advocate for, we appreciate the opportunity to provide comment on the Institute for Clinical and Economic Review (ICER)'s draft evidence report on aducanumab for the treatment of Alzheimer's disease (AD).

### **Do Not Ignore the Value of Alzheimer's Innovation**

The development of effective therapies to prevent, delay, and better manage AD and related dementias is one of the most pressing and complex public health challenges facing our nation. Alzheimer's disease is the only top-ten cause of death in the United States without a cure. [One in three older adults who die have ADRD](#), and over six million Americans suffer from AD. According to NIH-sponsored research, the total healthcare and caregiving costs for a person with probable dementia are [\\$287,000 in the last five years of life](#), compared to \$173,000 for someone with cancer and \$175,000 for someone with heart disease. In 2020, [Medicare and Medicaid spent \\$206 billion](#) on the total cost of care for AD.

The human cost of not finding a cure for Alzheimer's disease is astronomical. An AD drug development program's [total cost is estimated at \\$5.7 billion](#), with an expected study time of 13 years from preclinical studies to market approval. However, due to the clinical complexity of ADRD, the failure rate for test therapies in the clinical pipeline to treat AD is [98 percent](#). Between January 2008 and February 2019, [87 clinical programs investing and researching Alzheimer's disease closed](#). The clinical trial success rates for AD candidates are lower than observed for all other disease areas combined. Ensuring that assessments reflect the value of a treatment to patients and society is vital to support continued investment in treatments for AD.

### **ICER's Made-Up "Modified Societal Perspective" Does Not Cut It**

In May 2021, the Alliance for Aging Research released a report, "[Assessing the Value of Therapies in Alzheimer's Disease: Considerations to create a practical approach to value](#)," which the Alliance

commissioned from the actuarial firm Milliman. The report outlines a new framework for assessing the value of Alzheimer’s treatments and describes how the traditional approach to value assessment for therapeutics fails to address the challenges posed by AD and suggests principles to create an alternative, equitable value assessment framework.

To evaluate the effectiveness of established value assessment approaches in terms of a disease’s true impact on family caregivers, communities, and social service needs, the report authors analyzed publicly available financial and public health data specific to AD. The authors explain that total costs for AD care exist disproportionately beyond medical costs, with an extensive burden on families and residential long-term care. In fact, the status quo of AD care consists of systems of care that depend on low-paid workers or family caregivers, create multi-generational family burdens, and exacerbate existing racial disparities. Available public health data show Alzheimer’s has immeasurable and intangible effects on both the patient and caregiver, including unintended job loss, reduction in income, behavioral and psychiatric consequences, and much more.

However, ICER’s method of disease burden analysis incorporates direct medical costs into its model and relegates the costs of health effects to family caregivers or work loss for family members related to care needs for loved ones with AD to its subjective “modified societal perspective” as a “co-base-case analysis.” ICER states that the rationale for this additional analysis is due to “the large impact of AD on caregivers,” which makes it seem as though it would better account for the caregiver perspective. Instead, the modified societal perspective that ICER invented *penalizes* the caregiver for the productivity and economic impacts of keeping a loved one at home, as captured in report summary and comment: “In addition, keeping a patient in earlier AD states longer, which delays the transition to long-term care, can increase productivity losses for the caregiver... This highlights the complexities of capturing caregiver perspectives in the modified societal perspective in that caregivers may prefer to keep loved ones at home, rather than in a long-term care facility, although doing so may increase the negative financial impact on the caregiver.”

This statement illustrates the tension inherent in the assumptions underlying ICER’s value assessment framework, even under the modified societal perspective proposal, illustrating its inherent weakness and inability to truly account for the family caregiver perspective. From a patient, family caregiver, and societal perspective, there is significant value to prolonging independence and identity that is not reflected in medical costs or solely captured in caregiving burden. Slowing the progression of AD means prolonging independence and identity, both lowering caregiver burden in earlier stages of the disease and providing immense intrinsic value to patients and their families that outweighs opportunity costs lost elsewhere. **If this value is not reflected in the value assessment, that is a shortcoming of the model in accurately capturing and incorporating value, not of patients and caregivers in valuing non-monetary outcomes.** If value assessment fails to accurately capture value to those who benefit from the therapeutic, then the exercise is incomplete.

### **ICER’s Use of QALYs to Value Alzheimer’s Disease Presents a Moral Quandary**

The use of cost-effectiveness assessment to judge therapeutic value from a payer’s perspective, and technical issues using quality-adjusted life years (QALYs) renders the approach problematic. The

QALY has significant limitations when dealing with complex diseases such as AD, as they do not recognize value driven by public health improvement, transformation, or even societal value. These issues are not unique to AD, although the characteristics of AD and the ecology of care around people with AD highlight these issues.

Use of QALY-based cost-effectiveness analysis is a significant issue for people with Alzheimer's disease since the majority of those with dementia are the oldest old—of the estimated 6 million people with Alzheimer's disease who are age 65 and older, 80 percent are 75 years or older, and more than a third are 85 years or older.<sup>1</sup> Also, people aged 65 years and older with Alzheimer's disease [are likely to have a comorbid condition](#) such as coronary artery disease (38 percent), diabetes (37 percent), chronic kidney disease (29 percent), congestive heart failure (28 percent), and chronic pulmonary disease (25 percent). When applied to healthcare decision-making by insurance companies, this can mean that treatments for these more vulnerable people are deemed "too expensive" and therefore "not cost-effective" to cover.

Objections about reliance upon QALY-based methodologies also extend to race. For example, [Black Americans have an average life expectancy lower than whites](#). As such, treatments for conditions that disproportionately affect Black individuals may be assessed as lower value. Furthermore, Black and Latino communities experience Alzheimer's disease at higher rates than the general population. Data from the CHAP study shows that 18.6 percent of Black Americans and 14 percent of Hispanic Americans age 65 and older have Alzheimer's disease compared to 10 percent of White Americans.<sup>2</sup> ICER should not use measures that are unable to incorporate equity considerations, which may inadvertently promote structural discrimination.

### **ICER Pooled Clinical Trial Data with No Adjustments for Exposure**

The Alliance for Aging Research is also the convening organization of the [Accelerate Cures/Treatments for All Dementias](#) (ACT-AD) coalition, which started in 2005 to be a point of advocacy to share updates and bring the perspectives of patients, family caregivers, health professionals, academic researchers, industry, and senior representatives from federal research and regulatory agencies with the Food and Drug Administration (FDA). In this role, we closely follow the clinical development paths of Alzheimer's disease and related dementia therapies.

ICER's evaluation of the cost-effectiveness of aducanumab in the draft evidence report inappropriately pooled the data of the ENGAGE and EMERGE trials without adjusting for the number of people titrated to a higher dose for the different time periods. Fewer trial participants had the opportunity in ENGAGE to receive high-dose treatment than the patients in EMERGE. By not adjusting, ICER's approach provides an inaccurate picture of the value of the treatment. In its July 2021 public meeting on aducanumab, we request that ICER address why it selected this approach instead of properly analyzing the updated sponsor data submitted to the FDA.

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<sup>1</sup> Rajan KB, Weuve J, Barnes LL, McAninch EA, Wilson RS, Evans DA. Population estimate of people with clinical AD and mild cognitive impairment in the United States (2020-2060). *Alzheimers Dement* 2021;17. In press.

<sup>2</sup> Ibid.

## Next Steps Along a Better Path

To accurately assess the value of Alzheimer's disease treatments, Milliman's report outlines an alternative, equitable value assessment framework for use in AD that accounts for the ecosystem that surrounds people with AD, including the impact treatments may have on ameliorating social ills such as racial disparities. The principles include that such a framework should:

- utilize metrics that, when appropriate, apply the same standards regardless of age or socioeconomics,
- capture the health-related value of AD treatments not only for patients but also for their family caregivers, and
- appropriately account for changes in non-health outcomes and issues of community value related to AD patients and their caregivers.

Dr. Gillian Leng, the new chief executive for the UK's National Institute for Health and Care Excellence (NICE), recently wrote that dealing with COVID-19 has brought [a new lens to the use of QALYs](#) in cases where people are suffering from a life-threatening condition, but not yet dying. Her sentiments sound familiar. It is frustrating that ICER continues to espouse the QALY as other countries that have been using it for decades may be moving away from it.

The Alliance will be working in the coming months with leading experts in health economics to further expand upon an alternative value framework for Alzheimer's therapies. The question of whether ICER will modernize and take steps along a better path is in their hands.

If you have questions, please contact me at [speschin@agingresearch.org](mailto:speschin@agingresearch.org). Thank you for considering our comment.

Sincerely,



Susan Peschin, MHS  
President and CEO