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SHORT REPORT

Cost-effectiveness of aducanumab to prevent Alzheimer's disease progression at current list price

Pranay Sinha[1,2] | **Joshua A. Barocas**[3]

[1] Section of Infectious Diseases, Boston Medical Center (BMC), Boston, Massachusetts, USA

[2] Department of Medicine, Boston University School of Medicine (BUSM), Boston, Massachusetts, USA

[3] Divisions of General Internal Medicine and Infectious Diseases, University of Colorado Anschutz Medical Campus, Aurora, Colorado, USA

Correspondence
Pranay Sinha, Boston University Medical Campus, 801 Massachusetts Ave, 2nd Floor, Boston, MA 02131, USA.
E-mail: Pranay.Sinha@bmc.org

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Abstract

Introduction: An estimated 6 million Americans have Alzheimer's disease (AD). Aducanumab was recently approved by the Food and Drug Administration despite the lack of clinical effectiveness data.

Methods: We developed a Markov state transition model of AD to estimate the cost effectiveness of aducanumab compared to standard of care (SOC) over a 5-year time horizon for a cohort of persons aged 65 with mild AD. Outcomes included quality adjusted life years (QALYs), discounted costs, and incremental cost-effectiveness ratios (ICERs). We performed sensitivity analyses to address uncertainty.

Results: Over 5 years, the incremental cost of aducanumab compared to SOC was $179,890. Aducanumab resulted in 0.47 QALYs gained compared to SOC. The ICER for aducanumab compared to SOC was $383,080/QALY. In threshold analysis, aducanumab became cost-effective at $22,820/year.

Discussion: Aducanumab is not cost-effective at the estimated price of $56,000 even under ideal circumstances in which it completely halts AD progression.

KEYWORDS
aducanumab, Alzheimer's disease, cost-effectiveness, dementia

1 | INTRODUCTION

An estimated 5.8 million Americans have Alzheimer's disease (AD), a number that is likely to triple by 2060.[1] AD progression results in enormous morbidity and mortality and costs between $150 and $215 billion annually.[2] Aducanumab, a monoclonal antibody that binds to aggregated forms of amyloid beta (Aβ), has been shown in three randomized placebo-controlled trials to significantly reduce deposition of Aβ plaque in recipients. Based on this surrogate endpoint, the US Food and Drug Administration (FDA) approved aducanumab for AD using an accelerated pathway.[3] This step drew criticism given the unknown clinical benefits and high drug costs. We sought to determine the cost-effectiveness of aducanumab for the treatment of mild AD. Given the lack of efficacy data, we made the optimistic assumption that aducanumab completely arrests AD progression in mild disease.

2 | METHODS

2.1 | Analytic overview

We developed a Markov state-transition model of AD to project the incremental cost-effectiveness ratio (ICER) of aducanumab compared to standard of care (SOC) over a 5-year time horizon for a cohort of persons aged 65 years with mild AD. The model simulates the progression of patients with mild AD to moderate and, subsequently, severe AD (Figure S1 in supporting information). Each AD disease state carries distinct costs, disability weights, and mortality rates. We projected lifetime medical costs assuming a health-care system perspective and applied a 3% discount rate to costs and quality-adjusted life years (QALYs).[4] We interpreted ICERs using a willingness-to-pay (WTP) threshold of $100,000/QALY gained.

2.2 | Rates of progression and mortality

We derived rates of progression and mortality from the National Alzheimer's Coordinating Center Uniform Data Set (Table S1 in supporting information).[5] For the cohort receiving aducanumab, we assumed that patients did not transition beyond mild AD.

2.3 | Costs

We assumed aducanumab costs $56,000 (range: $33,600–84,000) annually.[6] We assumed that annual health costs for persons with mild AD were indistinct from those of average Americans older than 65 years: $7750 (range: $2480–16,000) whereas annual costs for those with moderate or severe AD were assumed to be $50,000 (range: $17,150–100,110).[2,7]

2.4 | QALYs

We assumed health utilities of 0.73, 0.69, and 0.27 for mild, moderate, and severe AD, respectively, based on a previous study.[8]

2.5 | Sensitivity analyses

We conducted one-way deterministic sensitivity analyses using a priori feasible ranges around core parameter values. We conducted a threshold analysis of aducanumab costs to assess the cost at which the drug would meet our WTP threshold. We also assessed the threshold of annual moderate–severe AD costs above which aducanumab would be favorable at a cost of $56,000. Last, we performed probabilistic sensitivity analysis (PSA) using probability density functions around each parameter value and used Monte Carlo simulation to repeat the analysis 10,000 times. We assumed beta distribution for state transition probabilities and gamma distributions for costs.[4] We represent uncertainty around base case results using 95% confidence intervals (CI) from PSA.

2.6 | Ethics

Consent was not necessary for this modeling study which did not make use of human subject data.

RESEARCH IN CONTEXT

1. **Systematic Review**: The authors reviewed the literature using traditional sources including PubMed and review of white paper literature. Little is known regarding the clinical effectiveness of aducanumab for the treatment of mild Alzheimer's disease (AD), yet it was approved by the Food and Drug Administration and carries with it a projected cost of $56,000/year.
2. **Interpretation**: Our model suggests that even under ideal circumstances in which aducanumab completely halts progression of AD, it may not be cost-effective at its current projected list price. Significant reductions in cost would be needed to make this cost-effective.
3. **Future Directions**: The threshold at which aducanumab would be cost-effective will need to be re-evaluated when data from a randomized clinical trial quantifies the clinical benefit.

3 | RESULTS

Over 5 years, costs with aducanumab were $255,440 (95% CI: $161,460–$375,340) and $75,550 (95% CI: $34,790–$136,610) with SOC. Aducanumab was associated with 2.93 (95% CI: 2.33–3.42) QALYs compared to 2.46 (95% CI: 2.06–2.82) QALYs with SOC. The ICER for aducanumab compared to SOC was $383,080/QALY (95% CI: 14,110–1,082,060; Table 1).

In one-way deterministic sensitivity analysis, the two parameters with the greatest impact on the ICER were the time horizon and the cost of aducanumab (Figure S2 in supporting information). At a time horizon of 30 years, the ICER was $128,520/QALY and at a time horizon of 3 years, the ICER was $731,660/QALY. At the upper bound of cost ($84,000) the ICER was $622,000/QALY and at the lower bound of cost ($33,600) it was $191,940/QALY. In threshold analysis, we estimate that the ICER for aducanumab would meet the WTP threshold at a drug cost of $22,820 (Figure 1). Annual costs for moderate–severe AD would have to be greater than $209,720 for aducanumab to be the favorable strategy at an annual cost of $56,000. Cost-effectiveness conclusions were robust in PSA. The cost-effectiveness acceptability curve shows that aducanumab was favored 0.76% of the time at the

TABLE 1 Base case analysis for cost-effectiveness of aducanumab

Strategy	Cost ($US)	Incremental cost ($US)	QALY (years)	Incremental QALY (years)	ICER ($US/QALY)
SOC	75,550(34,790–136,610)	REF	2.46(2.06–2.82)	REF	REF
Aducanumab	255,440(161,460·375,340)	179,890(74,450–304,090)	2.93(2.33–3.42)	0.47(0.18–0.75)	383,080(141,110–1,082,060)

Abbreviations: ICER, incremental cost-effectiveness ratio; SOC, standard of care; QALY, quality-adjusted life year.

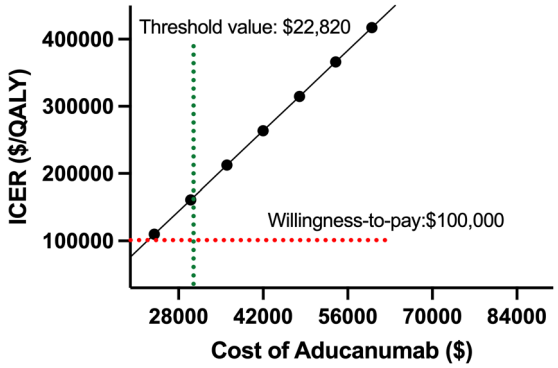

FIGURE 1 Threshold analysis for cost of aducanumab. ICER, incremental cost-effectiveness ratio

WTP threshold of 100,000/QALY (Figure S3 in supporting information).

4 | DISCUSSION

Aducanumab is a potentially promising treatment for the 6 million Americans with AD, most of whom are 65 years or older and eligible for Medicare. As of 2017, at least 2 million of these individuals used one or more treatments for AD, which were largely covered under Medicare Part D. A recent analysis by the Kaiser Family Foundation determined that total annual spending for aducanumab at this price would be nearly $57 billion per year.[9] Cost concerns aside, the FDA approved this agent for use in people with mild AD though clinical efficacy data are noticeably absent. Our analysis suggests that aducanumab may not be cost-effective at this price even though we modeled a best-case scenario in which aducanumab completely halted AD progression. In our model, aducanumab met the WTP threshold of $100,000 when the price was decreased to $22,820 annually. Given that few therapeutics achieve 100% effectiveness, this threshold will need to be re-evaluated when data from an ongoing randomized clinical trial quantifies the clinical benefit of aducanumab.

Our analysis is limited by lack of available clinical effectiveness data and by uncertainty around parameters. As such, we incorporated data that would skew toward the cost-effectiveness of aducanumab and accounted for uncertainty using both deterministic and probabilistic sensitivity analyses.

Of the estimated 6 million Americans with AD, if even 50% are categorized as having mild disease, we would expect annual aducanumab cost to approach $162 billion, grossly inflating Medicare costs.[2] Our findings add to the nascent economic literature regarding aducanumab. The Institute for Clinical and Economic Review estimated a price of between $2500 and $8300, which is lower than our estimates.[10] That analysis did not assume 100% effectiveness and modeled the population based on several clinical trials whereas we evaluated the cost-effectiveness in a general cohort of 65-year-old individuals with mild AD, the population for whom this agent is approved. Another analysis of a hypothetical disease-modifying treatment for AD by Green et al. found that such a treatment with a 40% risk reduction in disease progression at an annual cost of $10,000 would have an ICER of $52,029.[11] Taken together, these studies suggest that regardless of the clinical efficacy, it is the cost of drug that is likely to limit its use and access. It will be particularly difficult to convince providers and payors of its value at the current price if it is no more effective than donepezil or memantine, which cost $80 and $250 annually, respectively.[12,13]

In conclusion, our model suggests that aducanumab is likely not cost-effective at an annual price of $56,000.

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CONFLICT OF INTEREST

This manuscript was not funded by any grants or external entities. In the last 36 months, the authors have not received royalties, licenses, honoraria for lectures, presentations, speakers bureaus, manuscript writing, or educational events. In the last 36 months, the authors have not received payment or support for expert testimony, attending meetings, or travel. The authors do not have any patents planned, issued, or pending. The authors have not held a leadership or fiduciary role in any other board, society committee, or advocacy group and have not held any stock or stock options in entities related to the current manuscript or area of research. The authors have not received equipment, materials, drugs, medical writing, gifts, or other services.

ORCID

Pranay Sinha https://orcid.org/0000-0002-4233-0871
Joshua A. Barocas https://orcid.org/0000-0002-4155-4697

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SUPPORTING INFORMATION

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