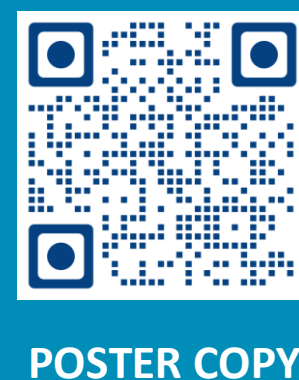


ESTIMATING THE ECONOMIC IMPACT OF DELAYED ALZHEIMER'S DISEASE PROGRESSION WITH LECANEMAB

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Introduction

- Alzheimer's disease (AD) is associated with substantial and increasing medical and societal costs that rise sharply with disease progression¹
- Lecanemab significantly slowed AD progression at 18 months compared to placebo in the Clarity AD trial²
- Benefits of lecanemab treatment continued to expand through 48 months in the open-label extension (OLE), relative to a matched control from the Alzheimer's Disease Neuroimaging Initiative (ADNI)³
- An analysis of time to disease progression revealed delay of progression from Mild Cognitive Impairment (MCI) to Mild AD and from Mild AD to Moderate AD⁴
- The trends from the trials were compared to the natural progression of ADNI to project benefits for 10 years
- The goal of this analysis was to estimate the 10-year medical and societal cost savings associated with delayed progression of early AD in patients treated with lecanemab

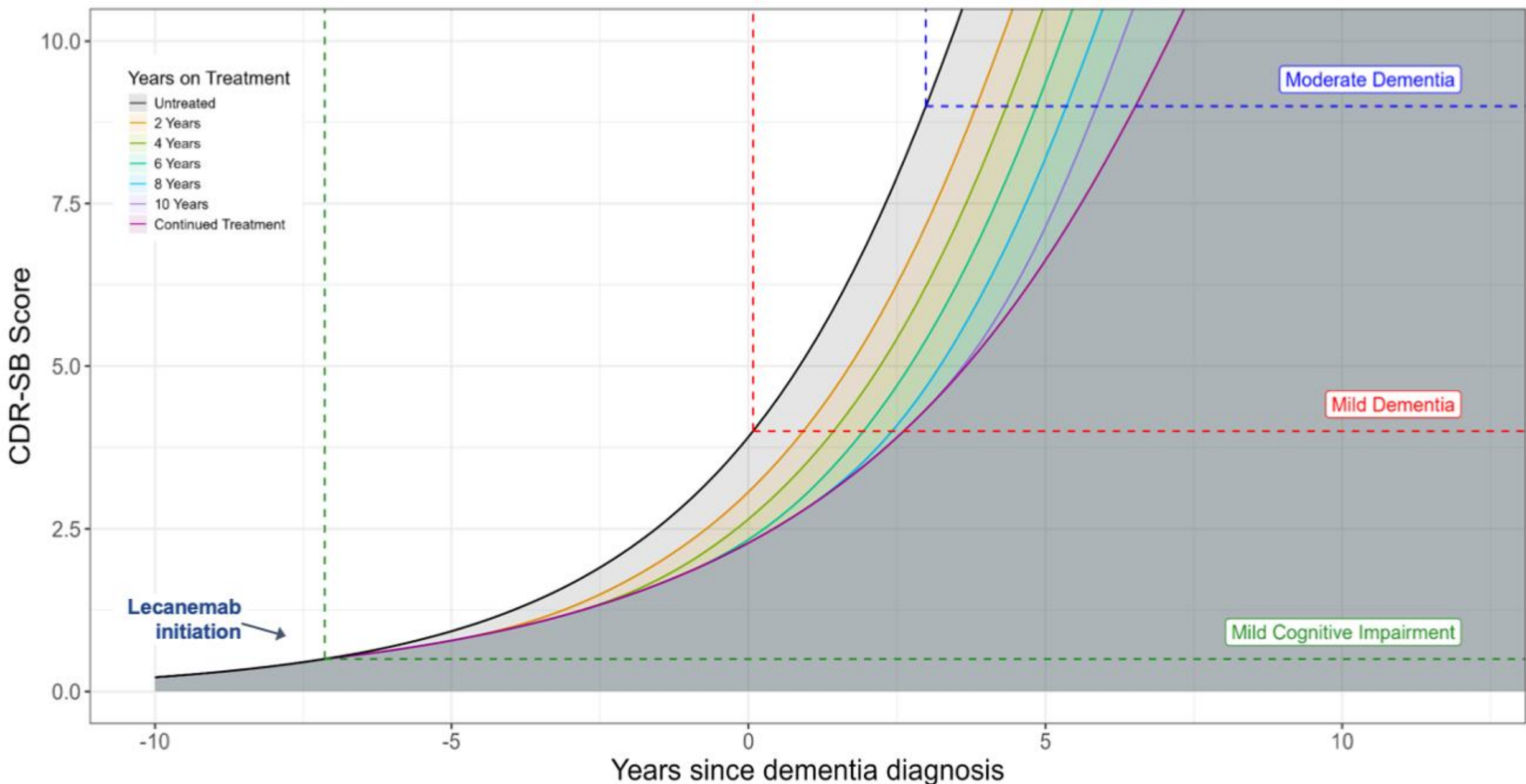
Methods

- The 10-year projections were used to quantify patients in each disease stage over time, to which costs were applied
- Disease progression was modeled using transition probabilities based on CDR-SB data from Clarity AD, including the open-label extension, and natural transition benchmarks based on ADNI
- The analysis began at the mild cognitive impairment (MCI) stage, defined by a CDR-SB score of 0.5, which aligns with the overall mean baseline CDR-SB score indicating MCI for the Clarity AD population
- Lacking the details implied by the Whetten et al.,⁴ simple linear progressions were developed for the two cases of
 - progression from MCI to mild delayed by 2.5 years and
 - progression from Mild to moderate delayed by 3.5 years
- Published studies reporting medical and societal costs with consideration of disease stage were reviewed for this analysis
- Medical costs included home health, nursing home, and other medical service; lecanemab costs were not included
- Societal costs included unpaid caregiving as well as market and non-market productivity losses, were generated from an average of available sources⁵⁻⁶
- Scenarios for the distribution of costs by measure, by state, by year using existing sources⁵⁻⁶ was developed
- Medical cost inflation from government projections (5.5%) and a discount rate (3.5%) were used to present results in 2025 US dollars (\$USD)⁷
- Linear progressions were developed with a Markov model using 1,000 random simulated baseline CDR-SB values and a normal distribution to reproduce the observed baseline stage distribution via iterative draws without half-cycle corrections

Results (continued)

- Estimated disease progressions are presented in **Figure 1**
 - Untreated patients could progress from MCI to mild AD in 7.2 years, and to moderate AD in 10.1 years
- With ongoing lecanemab treatment initiated when CDR-SB = 0.5:
 - Patients could progress from MCI to mild AD in 9.7 years; an estimated delay of 2.5 years to mild AD
 - Patients could progress from MCI to moderate AD in 13.6 years; an estimated delay of 3.5 years to moderate AD

Figure 1. Estimated Progression in CDR-SB Over 10 Years of Alzheimer's Disease for Clarity AD Full Population⁴



- Cost measures are presented in **Table 1**
 - Progression from MCI to mild AD implies health care costs increasing from 11,956 to 16,692 per patient year and further progression to moderate AD implies health care costs increasing to 29,292 per patient per year
 - Progression from MCI to mild AD implies societal costs increasing from 45,844 to 79,276 per patient per year and further progression to moderate AD implies societal costs increasing to 131,295 per patient per year
 - The sum of healthcare and societal costs, presented as the average over 10 years, exhibit a difference of 42,141 between MCI and mild AD and 71,312 between mild AD and moderate AD

Table 1. Healthcare and Societal Costs by AD Stage

Cost Measure	MCI	Mild	Moderate
Healthcare Costs (\$)⁵			
Community medical provider costs	15,048	17,652	23,496
Residential care costs	134,460	143,712	155,280
Percent Residential	0.0%	3.8%	11.0%
Health Care Costs	15,048	22,442	37,992
Inflated to 2025*	18,449	27,514	46,578
Less, Out-of-pocket ^{†4}	6,493	10,822	17,316
Unique Health Care Costs	11,956	16,692	29,262
Societal Costs (\$)⁴			
Simple Average	45,844	79,276	131,295
Total Costs (\$)⁴			
Healthcare Costs + Societal Costs	57,799	95,968	160,557
10 Year net inflated and discounted	63,815	105,956	177,268

*Cost inflated from source data using the medical component of the Consumer Price Index from the U.S. Bureau of Labor Statistics.
[†] Out-of-pocket costs were included in societal costs; deducted from healthcare costs to avoid double counting

- A simple analysis involves simply multiplying the number of years of delayed disease progression by the costs saved per patient per year from delayed disease progression.
- Using the distribution of patients starting in the Clarity AD trial (61.5% MCI and 38.5% mild dementia), total savings per person, a quick analysis results in savings of 16,088 per person per year. (**Table 2**)
- The more sophisticated Markov model of disease progression results in savings of \$17,750 annually, or \$177,500 over 10 years (**Table 2**)

Table 2. Cost-Savings from Delayed Disease Progression

Cost Measure	MCI to Mild	Mild to Moderate
Simple Analysis (\$)		
Years of Delayed Progression Saved	2.50	3.50
Progression of Costs (Savings)	(42,141)	(71,312)
Total Costs (Savings)	(105,352)	(249,591)
Distribution of Starting Stages	61.5%	38.5%
Costs (Savings) by Stage	(64,792)	(96,093)
Total Cost (Savings) per Person per Year	(16,088)	
Markov Model (\$)*		
Total Cost (Savings) per Person per Year	(17,750)	
Total Cost (Savings) per Person over 10 Years	(177,500)	

*Markov model uses random values generated for starting CDR-SB values, linear control, and delayed disease progression and without half-cycle correction.

Conclusions

- Delayed progression of Alzheimer's disease offers clear economic benefits to both medical and social support
- Published studies report similar annual per-patient costs, though not all included both healthcare and societal costs⁸⁻¹⁰
- Findings align with a Tysinger et al.'s microsimulation, showing meaningful long-term value for lecanemab over 10 years through improved quality of life and reduced medical and caregiving costs¹¹
- This analysis estimates total per-person savings of \$17,750 annually (\$177,500 over 10 years)

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