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Cost-Effectiveness of Donanemab for Early Alzheimer Disease in Australia

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ABSTRACT

Objectives: To evaluate the cost-effectiveness of donanemab, an anti-amyloid-β monoclonal antibody recently approved in Australia, for treating early-stage Alzheimer disease with confirmed amyloid-β pathology from healthcare system and societal perspectives.

Design: A Markov microsimulation model simulating long-term Alzheimer disease progression, treatment costs and health outcomes for donanemab compared with standard care.

Setting, Participants: Australian healthcare context, applying published clinical and economic inputs. A hypothetical cohort of people with early symptomatic Alzheimer disease, consistent with TRAILBLAZER-ALZ eligibility criteria: mean age 75 years, amyloid-β-positive, with mild cognitive impairment or mild dementia because of Alzheimer disease and excluding individuals with *APOEE4* homozygotes, in line with the Australian labelling. Donanemab administered every 4 weeks with magnetic resonance imaging (MRI)-based amyloid-β-related imaging abnormalities monitoring and treatment suspension upon amyloid-β clearance or progression to severe Alzheimer disease, compared with standard care.

Main Outcome Measures: Incremental costs, quality-adjusted life years (QALYs) and incremental cost-effectiveness ratios (ICERs). Secondary analyses included sensitivity and distributional equity analyses.

Results: Donanemab increased total healthcare costs ($300,689 vs. $178,121) and societal costs ($389,113 vs. $283,618) compared with standard care per capita, while improving health outcomes (4.38 vs. 4.01 QALYs) per capita. The ICER was $342,424 per QALY from the healthcare perspective and $294,701 per QALY from the societal perspective, exceeding frequently cited Australian willingness-to-pay thresholds. Sensitivity analyses identified drug cost and efficacy as key drivers of uncertainty. Distributional analysis suggested inequitable health gains by remoteness because of differences in diagnostic and treatment infrastructure.

Conclusion: Donanemab provides clinical benefits but is unlikely to be cost-effective under current Australian thresholds. Policymakers should balance economic evidence with unmet need, equity considerations and healthcare sustainability when making reimbursement decisions. Further research using real-world evidence and disaggregated analyses by geography and socioeconomic status is warranted.

JEL Classification: Nervous system diseases, Health services administration

Plain Language Summary

The known: New Alzheimer disease drugs such as donanemab can slow disease progression, but the cost of their implementation raises affordability concerns for health systems.

The new: Our analysis shows that donanemab, at its current price, is not likely to be cost-effective in Australia. Even when accounting for broader societal costs, the benefits of the treatment do not justify its expense under typical thresholds.

The implications: Funding donanemab would require substantial investment and may widen inequities in access. Policymakers must weigh clinical benefits against cost, equity and sustainability before deciding on reimbursement.

1 | Introduction

Alzheimer disease—the most prevalent form of dementia—is a progressive neurodegenerative condi tion that impairs cognition, behaviour and daily functioning. Globally, dementia affects over 57 million people, projected to reach 139 million by 2050 as populations age [1]. In Australia, more than 411,100 people were living with dementia in 2023, with prevalence expected to double by 2054 without effective interventions [2].

The burden of dementia is considerable, both economically and socially. Dementia-related healthcare and aged care costs are projected to exceed $15 billion annually in Australia by 2036, with informal caregiving by family and community members comprising a significant portion of this burden [3]. The growing prevalence of dementia, therefore, presents a major challenge to the sustainability of Australia's health and aged care systems [4].

Alzheimer disease treatment options were previously limited to symptomatic therapies [5]. However, the treatment paradigm for Alzheimer disease has shifted recently with the development of disease-modifying therapies targeting amyloid-β accumulation, a hallmark pathological feature of the disease [6]. Monoclonal antibodies such as aducanumab, lecanemab and donanemab have been developed to reduce amyloid-β burden in the brain, with the aim of slowing cognitive decline in early-stage Alzheimer disease, and have received regulatory attention globally, but they differ in binding characteristics, clinical efficacy and safety profiles.

Aducanumab received accelerated approval in the United States based on amyloid-β plaque reduction but was later withdrawn because of uncertainty regarding clinical benefit and limited uptake [7, 8]. Lecanemab selectively binds soluble amyloid-β protofibrils and demonstrated a 27% reduction in clinical decline in the Clarity AD trial [9]. Donanemab targets pyroglutamate-modified deposited amyloid-β and showed a 35% reduction in disease progression among people with intermediate tau burden in the TRAILBLAZER-ALZ trial [10]. Donanemab was approved by Therapeutic Goods Administration (TGA) in May 2025 for use in early symptomatic Alzheimer disease with confirmed amyloid-β pathology.

Although all three agents reduce amyloid-β burden, clinical outcomes and adverse event profiles vary [7, 9, 10]. Amyloid-β-related imaging abnormalities are a class-wide safety concern, with higher rates reported for aducanumab and donanemab than for lecanemab in pivotal trials [7, 10]. These abnormalities may be asymptomatic or symptomatic and often require treatment interruption and close magnetic resonance imaging (MRI) monitoring, with associated healthcare costs [11].

Early cost-effectiveness analyses in the United States and Europe indicate that these therapies may be economically viable only under specific conditions, such as price discounts or rebates and long-term benefit assumptions [11–14]. Their high costs, monitoring requirements and diagnostic infrastructure needs (e.g., MRI, positron emission tomography [PET] and infusion capacity) pose additional implementation challenges. In Australia, none of these therapies are reimbursed under the Pharmaceutical Benefits Scheme (PBS), and Pharmaceutical Benefits Advisory Committee (PBAC) evaluation requires robust local evidence on cost-effectiveness.

This study aimed to address a critical evidence gap by evaluating the cost-effectiveness of donanemab compared with standard care in early Alzheimer disease in Australia and examining the distributional impacts across population groups. Using a lifetime modelling approach, this analysis will provide important insights into the value proposition of donanemab and support future funding and policy decisions regarding Alzheimer disease treatment in Australia.

2 | Methods

2.1 | Model Structure

A Markov model was adapted based on a prior cost-effectiveness analysis of disease-modifying agents for Alzheimer disease compared with usual care [11–14] (Section S1). Briefly, we modelled people entered the Markov model from the mild cognitive impairment or mild Alzheimer disease state. People can subsequently remain unchanged or progress to the next disease stage (i.e., from mild cognitive impairment to mild Alzheimer disease or from mild to moderate Alzheimer disease) or death from any cause (Figure S1). Within each monthly cycle, people may continue the treatment or discontinue because of adverse events. The microsimulation model tracked individual age, disease stage occurrence of amyloid-β-related imaging abnormalities and treatment suspension. Trackers were used to apply discontinuation due to amyloid-β-related imaging abnormalities and treatment suspension because of amyloid-β clearance.

At 24 and 52 weeks, treatment suspension because of amyloid-β clearance was also modelled as allowed in the pivotal trial. Donanemab treatment was also discontinued upon progression to the severe Alzheimer disease state in the model.

We followed the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement for reporting this

economic evaluation [15] (Section S2). The model was developed using TreeAge Pro 2025, R1.

2.2 | Model Inputs

2.2.1 | Modelled Population

To reflect the Australian population eligible for donanemab, the modelled cohort was aligned with both the TRAILBLAZER-ALZ trial and the TGA-approved indication. Consistent with the Australian label, *APOEE4* homozygous individuals were excluded from treatment eligibility because of elevated risk of amyloid-β-related imaging abnormalities.

All individuals entered the model at a fixed starting age of 75 years, reflecting the mean age of cohort of participants from the Australian Imaging, Biomarkers and Lifestyle (AIBL) study [16, 17]. The proportional distribution of people with mild cognitive impairment and Alzheimer disease was matched to the TRAILBLAZER-ALZ trial, and the likelihood of transitioning across health states under usual care was sourced from the National Alzheimer's Coordinating Center (NACC) in the United States [18].

Because AIBL does not report mortality hazard ratios (HRs) by Alzheimer disease severity stage, stage-specific mortality estimates were obtained from the NACC dataset, which includes a larger and more clinically heterogeneous cohort spanning the full Alzheimer disease spectrum and provides validated stage-specific mortality HRs [19]. These NACC-derived HRs for mild, moderate and severe Alzheimer disease were applied multiplicatively to Australian age- and sex-specific baseline mortality rates from the Australian Institute of Health and Welfare (AIHW) [20, 21], ensuring that stage-dependent mortality gradients from NACC were anchored to Australian absolute mortality levels.

2.3 | Transition Probabilities

2.3.1 | Treatment Eligibility and Efficacy

In line with the TRAILBLAZER-ALZ trial, people undergo screening for eligibility to receive donanemab within the model [10, 11]. The screening procedure for donanemab includes an initial amyloid-β PET with ^{18}F-florbetapir to quantify amyloid-β levels [10] while cerebrospinal fluid (CSF) analysis can be accepted when the former is not available. In line with the Australian label, screening also included genetic testing for the *APOEE4* homozygote genotype (which is an exclusion).

Based on data from the TRAILBLAZER-ALZ trial, donanemab slowed the decline in Integrated Alzheimer disease Rating Scale Score by 32% (HR, 0.68; 95% confidence interval [CI], 0.44–0.99) [10]. This treatment effect was applied only to early-stage transitions—progression from mild cognitive impairment to mild Alzheimer disease and from mild to moderate Alzheimer disease. No treatment effect was applied to the transition from moderate to severe Alzheimer disease.

2.3.2 | Treatment Discontinuation and Adverse Events

To capture patient discontinuation from donanemab therapy, the rate of discontinuation from adverse events was sourced from the TRAILBLAZER-ALZ donanemab trial [10]. In line with the pivotal trial, this rate was applied in the first year of treatment commencement only. Furthermore, the likelihood of treatment cessation with donanemab because of amyloid-β clearance was sourced from the TRAILBLAZER-ALZ trial [10, 11] between 0–6 months and 6–12 months. Lastly, the models captured the occurrence of amyloid-β-related imaging abnormalities [11], and treatment costs associated with amyloid-β-related imaging abnormalities were considered in the model.

2.4 | Utility Values

Utility values for people with mild cognitive impairment and Alzheimer disease were sourced from a systematic literature review exploring the health-related quality of life for persons with mild cognitive impairment or dementia [22]. The utility values were assigned to the life years lived in a corresponding health state to calculate the quality-adjusted life years (QALYs). To capture the temporary reduction in quality of life associated with treatment-related adverse events, a disutility of −0.065 was applied for individuals experiencing amyloid-β-related imaging abnormalities [23].

2.5 | Costs

2.5.1 | Treatment Costs

In the absence of data on the price of donanemab in Australia, we assumed a base-case price of $40,000 for comparability [11, 13]. Infusions were assumed to cost $657.15, guided by the costs of admission as a day surgery patient or outpatient setting for chemotherapy intravenous infusions, and Medicare Benefits Schedule (MBS) items 14,245 and 13,950 [11, 24]. The cost per MRI scan was sourced from the MBS ($375), and it was assumed that the cost of a CSF assay was $350 [25]. As amyloid-β PET scans are not currently publicly funded in Australia, we assumed a cost per amyloid-β PET scan to be $3000 to examine the amyloid-β clearance [11, 13]. People treated with donanemab received regular MRI scans before the 2nd, 3rd, 4th and 7th doses and amyloid-β PET scans twice a year, and infusions administered every 4 weeks while ceasing the treatment upon progression to severe Alzheimer disease [10].

2.5.2 | Cost of Amyloid-β-Related Imaging Abnormalities

People with amyloid-β-related imaging abnormalities incurred costs of one additional outpatient physician consult, and three MRI scans until resolution [11, 13]. For people with hospitalisations associated with amyloid-β-related imaging abnormalities, the mean cost of hospitalisation for delirium was sourced from the AIHW [2].

2.5.3 | Cost of Standard of Care for Alzheimer Disease

The annual costs of Alzheimer disease per-person were sourced from a study exploring the cost burden attributed to dementia in Australia [26]. These were stratified based on Alzheimer disease severity and whether or not a patient required residential care [26]. All model inputs are summarised in Table 1.

2.6 | Cost-Effectiveness Analysis

The cost-effectiveness of donanemab for the treatment of Alzheimer disease was evaluated from both Australian healthcare system and societal perspectives. Under the societal perspective, costs included healthcare-related and informal caregiving time and travel associated with diagnosis and monitoring. Productivity losses were not included, as the modelled cohort is beyond retirement age. Informal care hours for each Alzheimer disease severity level were valued using the opportunity cost approach, applying mean hourly earnings [31]. The microsimulation model tracked individual age, disease stage, amyloid-β-related imaging abnormalities occurrence and treatment suspension. Trackers were used to apply discontinuation due to amyloid-β-related imaging abnormalities and treatment suspension because of amyloid-β clearance. Given the typical age of Alzheimer disease onset (75 years) and the mean life expectancy (81 and 85 years for males and females, respectively) in Australia [16, 17, 32], a 15-year period was adopted to capture both costs and health outcomes in the long-term, specifically QALYs. The incremental cost-effectiveness ratio (ICER) was calculated to assess the value of donanemab relative to standard care. Both costs and benefit outcomes were discounted at 5% per annum [27]. A willingness-to-pay threshold of $50,000 per QALY was used to determine cost-effectiveness. In addition to QALYs, life years gained were also examined as an alternative health outcome.

2.7 | Sensitivity Analysis

To assess the robustness of the base-case findings, both one- and two-way deterministic analyses were conducted. In the one-way deterministic sensitivity analysis, key model parameters were varied within their 95% CIs or within plausible ranges to evaluate their impact on the ICER. Results were summarised using a tornado diagram. A two-way deterministic sensitivity analysis was conducted to examine the variations in both donanemab costs and efficacy simultaneously. Furthermore, a scenario analysis incorporating the mortality associated with amyloid-β-related imaging abnormalities (0.0035) over the trial period was performed to assess the potential impact of treatment-related deaths.

In addition, the threshold analysis was performed to identify the value-based pricing for donanemab in Australia using the often-quoted willingness-to-pay per QALY threshold. Lastly, probabilistic sensitivity analysis was conducted to quantify joint parameter uncertainty. Probability distributions were assigned to key parameters, including treatment efficacy (reported as HRs), utilities, costs and onset age of Alzheimer disease (Table S1). Monte Carlo simulations were run, generating distributions of incremental costs and QALYs. Results were summarised using a cost-effectiveness plane and acceptability curve.

2.8 | Distributional Impact

Access to donanemab may be limited by the requirement for specialist access and diagnostic imaging, such as PET and MRI scans, which are less accessible in regional and rural areas of Australia. To explore potential equity implications, an exploratory distributional analysis was conducted. This scenario analysis varied access rates to donanemab according to levels of geographic remoteness, while maintaining the same model structure. A 20% reduction in access was assumed with each increasing level of remoteness. This approach enabled the assessment of potential differences in cost-effectiveness outcomes arising from differential access across population subgroups. Although AIBL provides high-quality biomarker and cognitive data [17], it does not report socioeconomic information stratified by Alzheimer disease stage, limiting its suitability for socioeconomic status-based distributional modelling in this analysis.

2.9 | Model Validation

To ensure credibility of model outputs, we undertook a structured validation process. Internal validation included checking the consistency of transition probabilities, life-table mortality calculations and cohort flow. External validation compared modelled survival and disease progression trajectories against published estimates from systematic reviews. Particularly, a literature search was conducted to identify real-world survival estimates for people with Alzheimer disease. If the simulated survival was broadly comparable to the real-world observations, we considered the modelled results to be valid. Face-validity checks were conducted with clinical experts to confirm the plausibility of disease-state transitions, treatment pathways and model assumptions.

2.10 | Ethics Statement

Ethics approval was not required for this study because it involved secondary analysis of published data and did not include human participants.

3 | Results

3.1 | Cost-Effectiveness Analysis

In the base case, donanemab was associated with both higher costs ($300,698 vs. $178,121 from the healthcare system perspective or $389,113 vs. $283,618 from the societal perspective) and benefits (4.38 vs. 4.03 QALYs) per capita compared with standard care in Alzheimer disease, resulting in an incremental cost-effectiveness ratio of $ 342,424 per QALY from healthcare system or $294,701 per QALY gained from societal perspectives (Table 2). These costs exceed the often cited willingness-to-pay per QALY threshold in Australia. Particularly, the higher costs

TABLE 1 | Inputs used in the cost-effectiveness models.

Parameter	Value (range in one-way SA)	Source
Discount rate	5% (0% to 6%)	PBAC [27]
Proportional distribution of mild cognitive impairment/mild Alzheimer disease		Ross et al. [11]
Mild cognitive impairment	65%	
Mild Alzheimer disease	35%	
Probability of progression from stage (annual)		Tariot et al. [18]
Mild cognitive impairment to mild Alzheimer disease	0.201	
Mild-to-moderate Alzheimer disease	0.266	
Moderate-to-severe Alzheimer disease	0.311	
HR of donanemab for disease progression	0.68 (0.44 to 0.99)	Mintun et al. [10]
Likelihood of mortality	Age- and sex-specific	AIHW [20]
Mortality (HR, 95% CI)		
Mild cognitive impairment	1.61 (1.49 to 1.74)	Stokes et al. [28]
Mild Alzheimer disease	2.23 (1.77 to 2.82)	Villarego et al. [29]
Moderate Alzheimer disease	3.10 (2.47 to 3.89)	Crowell et al. [21]
Severe Alzheimer disease	6.19 (4.36 to 8.80)	
Discontinuation due to AE		
Donanemab	31%	Ross et al. [11]
Discontinuation due to clearance (donanemab)		Ross et al. [11]
0–6 months	27%	
6–12 months	55%	
Likelihood of amyloid-β-related imaging abnormality		
Donanemab	36.8%	Ross et al. [11]
Hospitalisation due to amyloid-β-related imaging abnormality	4%	Assumption
Utilities		
Mild cognitive impairment	0.8 (0.64 to 0.96)	Landeiro et al. [22]
Mild Alzheimer disease	0.74 (0.59 to 0.89)	
Moderate Alzheimer disease	0.59 (0.47 to 0.71)	
Severe Alzheimer disease	0.36 (0.29 to 0.43)	
Disutility from amyloid-β-related imaging abnormality	−0.065 (−0.078 to −0.052)	Pitkala et al. [23]
Cost inputs		
Cost of infusion	$657.15	Assumption
Cost of transportation		
Usual care	$907	Brown et al. [26]
Donanemab	$1088	Assumption
Annual drug cost	$40,000 ($5200 to $208,000)	Assumption

(Continues)

TABLE 1 | (Continued)

Parameter	Value (range in one-way SA)	Source
Amyloid-β-related imaging abnormality costs		
Cost of additional physician visit (outpatient)	$244	AIHW [2]
Cost of amyloid-β-related imaging abnormality hospitalisation	$16,050	AIHW [2]
MRI	$1125	MBS [25]
Cost of Alzheimer disease (community setting)		Brown et al. [26]
Mild	$21,017 (14,712 to 27,322)	
Moderate	$22,201 (15,541 to 28,861)	
Severe	$92,961 (65,073 to 120,849)	
Cost of Alzheimer disease (residential aged care setting)		Brown et al. [26]
Mild	$29,692 (20,784 to 38,600)	
Moderate	$32,712 (22,898 to 42,526)	
Severe	$103,473 (72,431 to 134,515)	
Hours of informal care (per week)		Langa et al. [30]; AIHW [2]
Mild cognitive impairment	0	
Mild Alzheimer disease	8.5	
Moderate Alzheimer disease	17.4	
Severe Alzheimer disease	60	
Proportion of Alzheimer disease in care		Brown et al. [26]
Mild	6%	
Moderate	62%	
Severe	31%	

Abbreviations: ABS, Australian Bureau of Statistics; AIBL, Australian Imaging, Biomarkers and Lifestyle; AIHW, Australian Institute of Health and Welfare; MBS, Medicare Benefits Schedule; PBAC, Pharmaceutical Benefits Advisory Committee.

were attributed to the drug costs and dementia long-term management. Because of the delay in progression for people treated with donanemab, the informal care costs were lowered in the intervention group compared with the standard care group ($17,083).

3.2 | Sensitivity Analysis

The one-way sensitivity analysis identified that the base-case ICER was sensitive to variations in the cost and efficacy of donanemab (i.e., HR of donanemab), age at Alzheimer disease diagnosis, utility weights for the mild cognitive impairment health state and the discount rate (Figure 1).

In the two-way sensitivity analysis, results showed that if the HR of donanemab improved to 0.1 and the monthly cost was reduced to $1075 simultaneously, the ICER would fall to $47,414 per QALY gained. The scenario analysis by incorporating the mortality associated with amyloid-β-related imaging abnormalities generated consistent results with the base case.

In the threshold analysis, if the cost of donanemab were reduced to $3333 per annum, it could become cost-effective within the Australian context with the often-quoted $50,000 per QALY cut-off value.

The probabilistic sensitivity analysis, incorporating uncertainty in all key parameters, produced results consistent with the base case. For donanemab and standard care, mean costs were $411,662 (95% prediction interval [PI], $408,963–$414,361) vs. $182,602 (95% PI, $180,663–$184,541), respectively, and mean health benefits were 4.19 QALYs (95% PI, 4.17–4.21) vs. 3.84 QALYs (95% PI, 3.82–3.85) from the healthcare system perspective. These results indicate that donanemab exceeding often-quoted willingness-to-pay thresholds in 100% of simulations within the Australian setting, corresponding to a 0% of probability to be cost-effective at a $50,000 per QALY threshold (Figure 2). The cost-effectiveness acceptability curve from probabilistic sensitivity analysis is provided in Figure S2.

3.3 | Distributional Impact

Assuming a gradual reduction in access to donanemab by remoteness levels, the exploratory cost-effectiveness analysis revealed the difference in access to donanemab by geographic locations would generate a difference in health outcomes,

TABLE 2 | Results of base case cost-effectiveness analysis.

	Donanemab	Standard care	Difference
Quality-adjusted Life Years	4.38	4.03	0.36
Life years	6.35	6.07	0.28
Costs			
Screening	$3759	$0	$3759
Drug treatment	$103,434	$0	$103,434
Adverse events	$1488	$0	$1488
Management	$192,016	$178,121	$13,896
Informal care	$88,415	$105,498	-$17,083
Healthcare system perspective	$300,698	$178,121	$122,577
ICER			$342,424
Societal perspective	$389,113	$283,618	$105,494
ICER			$294,701

Abbreviation: ICER, incremental cost-effectiveness ratio.

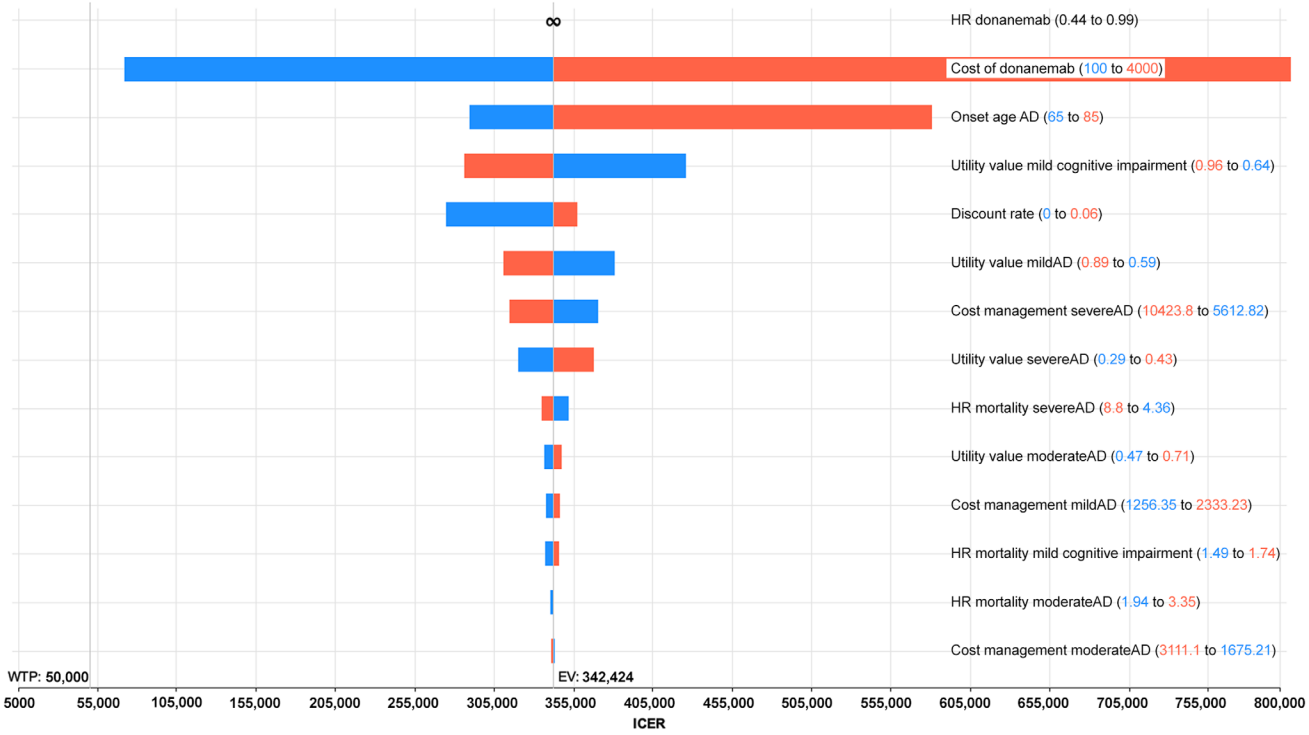

FIGURE 1 | Tornado diagram showing the results of one-way deterministic sensitivity analysis. AD, Alzheimer disease; EV, expected value (referring to the base-case ICER from the healthcare system perspective); HR donanemab, hazard ratio for the treatment efficacy of donanemab; ICER, incremental cost-effectiveness ratio; WTP, willingness-to-pay. The blue bar represents the variable value decreases from the base case; the red bar marks the variable value increases from the base case. For example, when the cost of donanemab increases from the base-case value, the ICER further increases. The numbers in the bracket refer to the low and high entry values examined in the sensitivity analysis. ∞ indicates that when the HR for donanemab approaches 0.99, the ICER becomes extremely large in the sensitivity analysis.

leading to further difference in QALY and life year gains for people with Alzheimer disease. Specifically, the resulted QALYs and life years would be 4.38 and 6.35, 4.30 and 6.31, 4.25 and 6.27 in the metropolitan, regional and rural areas, respectively.

3.4 | Model Validation

External validation was conducted using a systematic review and meta-analysis of cross-sectional and cohort studies of people involving people with dementia internationally, which reported

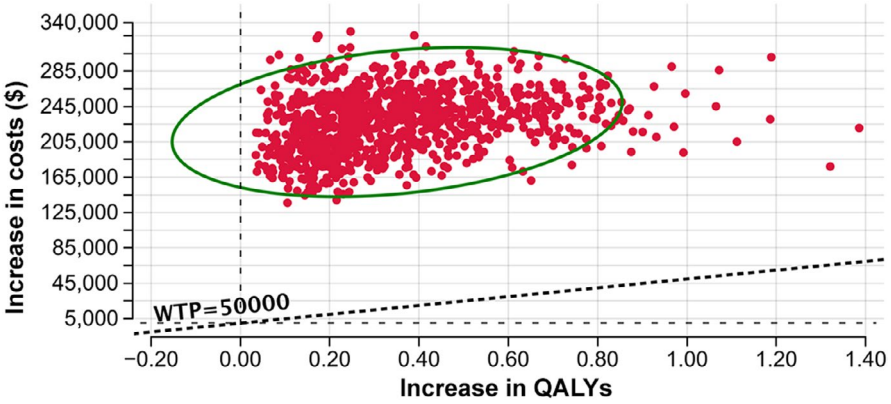

FIGURE 2 | Cost-effectiveness plane from the probabilistic sensitivity analysis. QALYs, quality-adjusted life years; WTP, willingness-to-pay. Donanemab has 0% of probability being cost-effective at the $50,000/QALY threshold.

a mean survival time following an Alzheimer disease diagnosis was 5.8 years (standard deviation, 2.0) [33]. In comparison, our modelled results estimated a mean survival of 6.07 years after the diagnosis in the usual care group, which was considered broadly consistent with the findings reported in international literature.

4 | Discussion

This study assessed the cost-effectiveness of donanemab for individuals with early symptomatic Alzheimer disease within the Australian healthcare system. Although donanemab was associated with greater clinical benefits in terms of extended QALYs and life years, our base-case analysis suggests an ICER of $342,424 from the healthcare system perspective, or $294,701 from the societal perspective, which are unlikely to be cost-effective under the frequently cited willingness-to-pay threshold of $50,000 per QALY.

These findings carry substantial policy implications as Australia prepares to evaluate and potentially fund disease-modifying therapies for Alzheimer disease. A finding of non-cost-effectiveness does not necessarily warrant exclusion from public reimbursement. Precedents exist within the Australian context where novel medicines for cancer or other conditions with ICERs above conventional thresholds have been listed on the PBS. In such cases, decisions were influenced by considerations such as disease severity, unmet need and societal value (i.e., non-health-related outcomes valued by society, such as well-being, hope and reduced caregiver burden). Donanemab may follow a similar pathway, particularly given the absence of effective disease-modifying options for Alzheimer disease and the substantial clinical and economic burden the condition imposes. A similar trend is evident in the United Kingdom, where National Institute for Health and Care Excellence (NICE) recently announced a reconsideration of the reimbursement decisions for lecanemab and donanemab, following their initial rejection 6 months earlier [34, 35].

The PBAC may consider multiple factors beyond cost-effectiveness in its funding recommendations, including clinical benefit, severity of disease and lack of alternative treatments. For example, the PBAC has recommended funding for nivolumab for melanoma [36], pembrolizumab for breast cancer [37] and brentuximab for relapsed or refractory systemic anaplastic large cell lymphoma [38], each with ICERs (between $75,000 and $135,000) exceeding the often-quoted willingness-to-pay per QALY threshold in Australia.

In many such cases, these drugs were reimbursed under a Special Pricing Arrangement (SPA). SPAs are confidential agreements between the Australian Government and pharmaceutical sponsors, which allow for a reduced effective price—either through rebates, price–volume agreements or risk-sharing schemes. Performance-based SPAs, in particular, tie reimbursement to real-world effectiveness outcomes. If a therapy does not achieve the expected benefits (e.g., in disease progression or survival), the sponsor may offer rebates or refunds. A performance-based SPA may be particularly suitable for donanemab, enabling reimbursement to be contingent upon demonstrating meaningful outcomes in real-world Australian settings. This could involve establishing a patient registry to monitor clinical effectiveness, although such infrastructure would require additional resources to implement. In Italy, between 2013 and 2018, 26 registries linked to performance-based agreements were set up to track high-cost drugs across oncology and rare diseases. They even introduced a novel success-fee model where the government only pays for people who benefited from the treatment [39]. For example, pirfenidone to treat idiopathic pulmonary fibrosis was reimbursed using a success-fee model, where the Italian National Health Service pays only for people achieving pre-defined clinical outcomes collected using a dedicated registry that captures clinical data [39].

It is estimated that around 10% of people with Alzheimer disease would be eligible for donanemab treatment (based on people seen in memory clinics), translating to about 30,000 people nationwide. These people tend to be younger, healthier and more engaged with specialist services than the broader Alzheimer disease population. As real-world people are often older and have more comorbid conditions, eligibility and treatment effectiveness may be lower in routine practice, meaning our modelled results may represent a lower bound on real-world cost-effectiveness. In addition, the availability of donanemab is likely to stimulate substantially greater diagnostic activity, as clinicians investigate a larger pool of people for potential eligibility. This expanded use of PET scans and CSF testing—despite only

a minority ultimately qualifying for treatment—would increase the overall budget impact of implementation beyond what is implied by the 10% eligibility estimate. Alternatively, a volume-based SPA could contain financial risk if large-scale uptake occurs following approval. These mechanisms help manage uncertainty and budget impact while facilitating patient access to promising therapies that may not otherwise meet conventional cost-effectiveness thresholds. If donanemab is ultimately considered for PBS reimbursement, an SPA could serve as a viable pathway to mitigate its high upfront cost.

Our findings are broadly consistent with international cost-effectiveness analyses of amyloid-β-targeting monoclonal antibodies. In the United States, ICERs for aducanumab have ranged from US$383,000 to more than US$1.3 million per QALY gained, even when optimistic assumptions about long-term efficacy, discontinuation and pricing were applied [14], while lecanemab has been estimated at about US$200,000–US$300,000 per QALY [13]. Similarly, a US-based analysis reported that donanemab would require substantial price reductions to achieve value-based pricing thresholds, with ICERs exceeding US$300,000 per QALY at current pricing assumptions [11]. In the United Kingdom, the NICE reached comparable conclusions, determining that donanemab is not cost-effective at list price because of high drug costs, treatment infrastructure requirements and uncertainty around long-term benefits [35]. Taken together, international evidence consistently indicates that, at current prices and with available efficacy data, disease-modifying therapies for early Alzheimer disease are unlikely to meet conventional willingness-to-pay thresholds—aligning with our Australian findings. Although the potential for donanemab design for treatment discontinuation following amyloid-β clearance could reduce long-term costs, such assumptions require further validation with real-world evidence.

Equity concerns emerged from our scenario analysis, which highlighted potential differences in access to donanemab treatment because of variability in availability of diagnostic infrastructure, particularly PET and MRI scans required for confirming eligibility and monitoring treatment continuation. People in rural and remote areas will likely have decreased access or prolonged waiting time to access these diagnostic tools, potentially limiting the reach and impact of donanemab in these communities. This geographic inequity raises broader ethical and policy considerations about fair access to high-cost therapies and reinforces the importance of health system planning to address structural barriers. To address the access difference, hub and spoke models with partnerships with major metropolitan services, such as those that have been successfully applied to acute stroke care in Australia, could be a potential solution.

5 | Limitations

There are several limitations that should be considered in interpreting our results. First, long-term efficacy data for donanemab are still evolving, and assumptions regarding disease progression, discontinuation rates and health utilities may not fully capture real-world dynamics. Second, the decreased probability of Alzheimer disease progression was assumed as equal to the relative improvement in mean score on a cognitive and functional scale observed in the TRAILBLAZER-ALZ trial, which may not equate to the real-world scenario. However, this assumption was also adopted by other economic evaluation in this regard and was considered reasonable [11]. Third, the cost of donanemab was not publicly available in Australia. A further limitation is the potential for amyloid-β-related imaging abnormalities to contribute to partial unblinding in the pivotal trials. Emerging evidence indicates that such unblinding could lead to an overestimation of treatment effects in trials [40]. Consequently, our modelled estimates may overstate the real-world effectiveness of donanemab. In addition, the long-term consequences of amyloid-β-related imaging abnormalities and disease modification remain uncertain. Although most amyloid-β-related imaging abnormalities episodes resolve, there is limited evidence on whether they have lasting neurological or functional effects that could alter longer term disease trajectories. However, any sustained neurological impact of amyloid-β-related imaging abnormalities, if present, could reduce these gains and diminish the overall effectiveness of treatment in real-world settings. As long-term data are not yet available, our model does not incorporate these potential effects, representing an additional source of uncertainty. Furthermore, our modelled cohort reflects the highly selected TRAILBLAZER-ALZ population, who were younger, healthier and with Alzheimer disease confirmed by biomarkers, unlike the more diverse real-world Alzheimer disease population. As real-world people are typically older, treatment eligibility and effectiveness may differ from those observed in the trial population, meaning our analysis may not fully reflect real-world cost-effectiveness. Lastly, although AIBL provides high-quality biomarker and cognitive data, it does not report socioeconomic information stratified by Alzheimer disease stage, limiting its suitability for distributional modelling based on socioeconomic status in this analysis. As a result, we were unable to examine distributional cost-effectiveness by socioeconomic status.

6 | Conclusion

Donanemab did not meet conventional cost-effectiveness thresholds based on the modelled assumptions. Despite this, the drug and others in its class represents a promising advance in the treatment of people with early Alzheimer disease, and policymakers may need to weigh economic evidence alongside considerations of unmet need, access equity and long-term system sustainability when evaluating public reimbursement. Further research incorporating real-world outcomes and disaggregated analyses by geography and socioeconomic status will be essential to inform equitable and evidence-based policy decisions in this space.

Author Contributions

Lan Gao: conceptualisation, methodology, formal analysis, writing – original draft. **Rosie Watson:** conceptualisation, methodology, writing – review and editing. **Nawaf Yassi:** conceptualisation, methodology, writing – review and editing.

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Conflicts of Interest

Nawaf Yassi has received honoraria for educational activities from Eli Lilly and Novo Nordisk. Lan Gao and Rosie Watson have no relevant disclosures.

Data Availability Statement

This study did not generate original data.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section. **Data S1:** mja270186-sup-0001-supinfo.pdf.