TECHNICAL REPORT

Cost-effectiveness of donanemab versus standard of care for adults with early Alzheimer's disease in the United Kingdom

Abstract

Objective: To determine the cost-effectiveness of donanemab compared to standard of care for adults with early symptomatic Alzheimer's disease (AD) in the United Kingdom from a healthcare payer perspective. **Methods:** A digital replica of a published health economic model (implemented as a patient-level microsimulation) was used to evaluate adults with early AD in the United Kingdom, comparing health and economic impacts of donanemab versus standard of care. The model tracked individual progression through four clinical states (MCI, mild dementia, moderate dementia, and severe dementia) plus death, and progression through these states could occur in community or institutional settings. Primary outcomes were direct cost of care per patient, quality-adjusted life-years (QALYs), and an incremental cost-effectiveness ratio (ICER). Secondary outcomes were life expectancy with AD, life-years lost to AD, AD-attributable mortality, mean time in MCI and mild dementia, median progression time from mild to moderate dementia, and median time to, as well as lifetime risk of, institutionalization. A lifetime horizon and 3.5% annual discount rate were applied, with half-cycle correction. **Results:** Donanemab was not cost-effective compared to standard of care, offering 0.32 more QALYs for GBP 63.7K more per patient (ICER: GBP 201.5K/QALY, above the GBP 35K/QALY threshold). Donanemab was also associated with changes in life expectancy (+0.38 years), average time in MCI (+11 months), average time in mild dementia (+7 months), and lifetime risk of institutionalization (−3.2 pp)—but does not represent good value at current pricing. **Conclusion: Based on these findings, coverage at current pricing is not supported.** Donanemab has an unfavorable ICER, though it is associated with improvements across some tracked health outcomes. Reconsideration may be warranted if prices decrease.

Objective

This is a technical report describing a health economic analysis intended to support treatment access decisions. The analysis used a health economic model to evaluate the cost-effectiveness of donanemab compared to standard of care for adults with early symptomatic Alzheimer's disease (AD) in the United Kingdom. This approach enables synthesis of data from individual studies to support adaptation to country-specific costs and demographics, and extrapolation of clinical outcomes over a lifetime horizon in an epidemiologically consistent manner — supporting decisions under uncertainty, particularly where direct real-world or observational evidence is limited.

Methods

Target Population

The target population comprised adults with early symptomatic Alzheimer's disease—specifically, mild cognitive impairment (MCI) or mild dementia due to AD—in the United Kingdom. This population corresponds to patients eligible for disease-modifying therapies.

Intervention and Comparator

The intervention evaluated was donanemab, an anti-amyloid monoclonal antibody indicated for treatment of early Alzheimer's disease. The comparator was standard of care, a symptomatic therapy comprising cholinesterase inhibitors and memantine, without disease modification.

Analytic Method

This analysis was conducted from a healthcare payer perspective over a lifetime time horizon with 100,000 simulated individuals. Costs and health outcomes were discounted at 3.5% per annum, using an annual cycle length and half-cycle correction (where indicated). Incremental cost-effectiveness was assessed using the ICER, which was evaluated against United Kingdom's willingness-to-pay threshold of GBP 35K/QALY.

Model Structure

Source Model

This analysis used a replicated version of the IPECAD (International Pharmaco-Economic Collaboration on Alzheimer's Disease) open-source model framework (Handels et al., 2025). IPECAD is a patient-level microsimulation designed for health technology assessment of early Alzheimer's disease treatments. The model tracks progression through mutually exclusive health states—MCI, mild dementia, moderate dementia, severe dementia, and death—using annual transition probabilities derived from the literature. Patients may transition forward (disease progression) or backward (improvement) between states. Institutionalization is modeled as an overlay on dementia states, with state-dependent transition probabilities. Mortality is

modeled using country-specific life tables modified by state-specific hazard ratios representing excess mortality associated with AD. Treatment effects are applied as hazard ratios on progression transitions while patients remain on therapy.

GENESIS Implementation

The digital replica is a patient-level microsimulation within GENESIS (Global Engine for Navigating Economic Simulations of Intervention Scenarios), a web-based platform that enables rapid adaptation of published health economic models to any country. The replicated model preserves IPECAD's Markov-microsimulation framework. The replica also has the following capabilities: (1) it includes a catalog of preloaded anti-amyloid therapies (e.g., lecanemab, donanemab) with trial-derived effects and unit costs, plus a custom-drug builder for any other agent; (2) it can be rapidly adapted to any country using local or regional data on patient demographics, background mortality, and care costs (including nursing-home placement); (3) it captures patient-level heterogeneity by drawing baseline age and sex from country-specific distributions, producing the spectrum of fast and slow progressors observed clinically; (4) it explicitly reports lifetime risk and median years to nursing-home admission as outcomes; and (5) it tracks amyloid-related imaging abnormalities (ARIA) as adverse events. The structure of the replicated model is presented in Figure 1.

Clinical Inputs

Clinical input parameters, including baseline characteristics, treatment effects, state transition probabilities, institutionalization rates, mortality hazard ratios, and ARIA event rates, are summarized in Table 1 and discussed below.

Baseline Characteristics

Simulated patients were assigned characteristics representative of real-world patients with early symptomatic Alzheimer's disease eligible for disease-modifying therapy. These included age at diagnosis, sex, and initial disease state (MCI or mild dementia). Baseline characteristics are presented in Table 1.

Transition Probabilities

Each cycle, simulated patients could remain stable, progress, or improve based on transition probabilities (Potashman et al., 2021), and faced state-specific risk of institutionalization (Tate et al., 2025). Age- and sex-specific baseline mortality was derived from the UK-specific life tables (UN WPP 2024), with excess mortality applied as state-specific hazard ratios (Handels et al., 2025). All parameters except life tables are presented in Table 1.

Treatment Effects

Treatment efficacy was modeled as a hazard ratio that slowed progression from treatment-eligible states (MCI and mild dementia) to more severe states while patients remained on treatment, derived from published clinical trial data.

Treatment was discontinued at a published rate or upon progression to moderate or severe dementia. Post-discontinuation, patients reverted to unmodified transition probabilities. Treatment parameters for each arm are summarized in Table 1.

Utilities

State-specific health utility values (EQ-5D) were applied for each of the four clinical states (MCI, mild dementia, moderate dementia, and severe dementia), with separate values for community and institutional settings. Disutility adjustments were applied for institutionalization in moderate and severe dementia (Handels et al., 2025) and for symptomatic ARIA among patients on donanemab (Lin et al., 2023). All utility values are summarized in Table 1.

Costs

Costs included disease state-specific annual healthcare costs (with state-specific multipliers and pharmacy add-ons), institutional care costs, and treatment-related costs comprising drug acquisition, administration, and monitoring. Costs were converted to local currency using purchasing power parity factors (World Bank, World Development Indicators). Cost inputs and sources are summarized in Table 1.

Outcomes of Interest

Primary outcomes included direct cost of care, quality-adjusted life-years (QALYs), and the incremental cost-effectiveness ratio (ICER). Secondary outcomes included life expectancy with AD, life-years lost to AD, AD-attributable mortality, mean time in MCI and mild dementia, median progression time from mild to moderate dementia, and median time to, as well as lifetime risk of, institutionalization.

Assumptions

Key assumptions: (1) treatment effects on disease progression were assumed sustained while on treatment, with no waning;

(2) treatment efficacy is transportable from trial populations to the United Kingdom; (3) treatment was discontinued upon progression to moderate or severe dementia; (4) treatment has no direct effect on mortality, only indirect effects via slowing disease progression; (5) background mortality rates at the time of analysis remain constant over simulated patients' lifetime; (6) the model is agnostic to the United Kingdom's healthcare infrastructure and assumes patients receive care as needed.

Several of these assumptions — particularly the use of trial-derived efficacy and the idealization of care delivery — reflect a deliberate portability design: by holding these dimensions to standardized forms, the model isolates the comparative effect of the intervention itself, leaving access realities such as memory-clinic referral, diagnostic and biomarker confirmation, drug availability and reimbursement, infusion-center capacity, and long-term care availability to be layered in through GENESIS's parameter interface. This produces a result interpretable across jurisdictions without re-specification, since access constraints vary by setting and over time.

Sensitivity Analyses

Multiple one-way deterministic sensitivity analyses were used to identify key ICER drivers. Price threshold analysis examined how cost-effectiveness varies with treatment price. Probabilistic sensitivity analysis used Monte Carlo simulations (1,000 iterations) to assess the impact of parameter uncertainty.

Model Validation

Cross validation was assessed by comparing economic outcomes between the digital replica and Handels et al.'s IPECAD implementation (Handels et al., 2025) under matched inputs. Comparable outcomes included standard-of-care lifetime cost ($469,637 vs $484,963), standard-of-care QALYs (3.20 vs 2.94), standard-of-care life-years (6.32 vs 6.15), incremental cost ($95,292 vs $95,370), incremental QALYs (0.29 vs 0.35), incremental life-years (0.31 vs 0.34), and the ICER ($325,298 vs $272,131/QALY).

External validity was assessed by comparing secondary outcomes under the standard-of-care assumption with published epidemiological targets. These include: life expectancy with AD (6.1 vs 2–10 years; Garcia-Ptacek et al., 2021) and life-years lost to AD (7.9 vs 8–11 years; Strand et al., 2018); AD-attributable mortality (79.5% vs 45–75%); average time in MCI (3.6 vs 2.9–7.1 years) and mild dementia (2.2 vs 0.1–3.1 years) (Tate et al., 2025); median progression time from mild to moderate dementia (2.0 vs 3.0 years) (Tate et al., 2025); median time to institutionalization (3.0 vs 1.9–4.0 years) and lifetime risk of needing institutionalization (53.9% vs 43–92%) (Brück et al., 2025). Targets are drawn from international literature. Life-years lost are bounded by remaining life expectancy in the target population, so values can fall below the international range in settings with lower background life expectancy. Deviations for the United Kingdom reflect these demographic and healthcare-system differences.

Results

Over a lifetime horizon, standard of care cost GBP 193.2K per patient and yielded 3.2 QALYs, while donanemab cost GBP 256.9K and yielded 3.5 QALYs. The ICER was GBP 201.5K/QALY, exceeding the GBP 35K/QALY threshold, indicating donanemab is not cost-effective at current pricing. Beyond cost-effectiveness, donanemab was also associated with changes in life expectancy (+0.38 years), time in MCI (+11 months), time in mild dementia (+7 months), and lifetime institutionalization risk (−3.2 pp). Primary and secondary outcomes are detailed in Tables 2 and 3. Figure 2 illustrates state distributions over the model horizon. Under standard of care, patients progress relatively quickly through disease states, spending limited time in MCI and mild dementia before advancing to moderate and severe stages. Donanemab shifts this trajectory, extending time in earlier disease states and delaying institutionalization. Deterministic sensitivity analysis identified treatment effect on disease progression, mild-to-moderate dementia transition, and moderate-to-severe dementia transition as the three most influential drivers of the ICER (Figure 3). Price threshold analysis indicated that no price within the tested range achieved cost-effectiveness for donanemab at the GBP 35K/QALY threshold. Probabilistic sensitivity analysis yielded a ratio-of-means ICER of GBP 205.3K/QALY with less than 1% probability of cost-effectiveness at the GBP 35K/QALY threshold. Further details are provided in Tables 2–3 and Figures 3–5.

Conclusion

Based on these findings, coverage at current pricing is not supported. Donanemab has an unfavorable ICER, though it is associated with improvements across some tracked health outcomes. Reconsideration may be warranted if prices decrease.

This analysis replicated the IPECAD framework (Handels et al., 2025) within GENESIS as a patient-level microsimulation and adapted it to the United Kingdom. Several limitations warrant consideration. The model was not calibrated to the United Kingdom-specific epidemiology, so absolute per-arm outcomes approximate local reality while relative differences between arms — which drive decisions — are accurate. Treatment efficacy from registration trials may not fully transport to the United Kingdom. Treatment effects are assumed sustained while on treatment, with no within-treatment waning, which may overestimate long-term benefit. The age-sex baseline utility curve and state-specific utilities are derived from published

studies and assumed transportable to the United Kingdom; country-specific HRQoL norms, where available, would refine absolute QALY estimates without materially affecting incremental comparisons. The payer perspective excludes indirect costs and caregiver burden — a particularly material limitation in AD, where caregiver time and lost productivity often exceed direct medical costs. Re-implementing the IPECAD framework as a patient-level microsimulation within GENESIS, rather than the source's cohort Markov formulation, could introduce structural divergences; cross-validation against Handels et al.'s implementation (using lecanemab as the test case) yielded the same coverage decision (not cost-effective at the $100,000/QALY threshold) with incremental cost matching within 0.1% under matched inputs, suggesting any residual divergence is unlikely to materially affect the coverage decision. Additionally, institutional care is modeled as a payer-funded long-term care pathway, which may overstate realized payer expenditure — and understate caregiver burden — in settings where formal nursing-home care is rare. Cost and utility inputs were sourced from published studies and adapted to the United Kingdom, but may not fully capture current local care patterns or quality-of-life weights. Results reflect the input configuration documented in Table 1, and findings may not generalize to patients with more advanced disease or those ineligible for anti-amyloid therapy.

Cost-effectiveness conclusions are typically robust to plausible variation in individual parameters, as shown in the sensitivity analyses. The result also has a useful diagnostic property: an intervention not cost-effective under idealized care is unlikely to become so under real-world constraints, which generally erode rather than amplify margins. When cost-effectiveness does hold, the relevant local question shifts from whether the intervention is worth doing to how much implementation friction would erode the margin in the local context. Absolute magnitudes — including incremental costs, outcomes, and price headroom — are conditional on the inputs as configured.

Table 1: Model Input Parameters

Parameter	Value (Uncertainty)	Distribution	Source
Demographics			
Age at AD diagnosis (years)	73	—	Kansal et al., 2018
Sex distribution (% male)	47.2%	—	UN WPP, 2024
Baseline Severity Distribution			
Mild Cognitive Impairment	28.0%	—	Xu et al., 2024
Mild AD	72.0%	—	Xu et al., 2024
Moderate AD	0.0%	—	Xu et al., 2024
Severe AD	0.0%	—	Xu et al., 2024
Mortality Hazard Ratios			
MCI	1.82	Log-normal	Handels et al., 2025
Mild AD	2.92	Log-normal	Handels et al., 2025
Moderate AD	3.85	Log-normal	Handels et al., 2025
Severe AD	9.52	Log-normal	Handels et al., 2025
Annual Transition Probabilities			
MCI → Mild AD	0.18	Dirichlet	Potashman et al., 2021
MCI → Moderate AD	0.06	Dirichlet	Potashman et al., 2021
MCI → Severe AD	0.00	Dirichlet	Potashman et al., 2021
Mild → Moderate AD	0.35	Dirichlet	Potashman et al., 2021
Mild → Severe AD	0.05	Dirichlet	Potashman et al., 2021
Mild → MCI	0.03	Dirichlet	Potashman et al., 2021
Moderate → Severe AD	0.42	Dirichlet	Potashman et al., 2021
Moderate → Mild	0.03	Dirichlet	Potashman et al., 2021
Moderate → MCI	0.00	—	Potashman et al., 2021
Severe → Moderate	0.02	Dirichlet	Potashman et al., 2021
Severe → Mild	0.00	—	Potashman et al., 2021
Severe → MCI	0.00	—	Potashman et al., 2021
Need for Institutionalization			
MCI	0.00	—	Tate et al., 2025
Mild AD	0.09	Beta	Tate et al., 2025
Moderate AD	0.20	Beta	Tate et al., 2025
Severe AD	0.29	Beta	Tate et al., 2025
Treatment Effects (HR disease progression) and Discontinuation			
Treatment effect (HR disease progression)			
Donanemab	0.65 (0.07)	Log-normal	Sims et al., 2023
Standard of Care	1.00	—	Birks et al., 2018
Discontinuation rate	6.9%	Beta	Lin et al., 2023
Utilities/Disutilities			
Mild Cognitive Impairment	0.7900	Beta	Landeiro et al., 2020
Mild AD	0.6800	Beta	Bryan et al., 2005
Moderate AD	0.6100	Beta	Orgeta et al., 2015
Severe AD	0.3000	Beta	Sheehan et al., 2012
Symptomatic ARIA event rate (Year 1)	0.0350	Beta	Lin et al., 2023
Expected ARIA QoL loss (Year 1)	-0.0012	Normal	Lin et al., 2023
Institutionalization disutility (MCI)	0.0000	—	Handels et al., 2025
Institutionalization disutility (Mild)	0.0000	—	Handels et al., 2025
Institutionalization disutility (Moderate)	-0.0600	Normal	Handels et al., 2025
Institutionalization disutility (Severe)	-0.0600	Normal	Handels et al., 2025
Healthcare Costs (GBP)			
MCI annual cost	4.9K	Gamma	Lin et al., 2023
Mild dementia annual cost	7.1K	Gamma	Lin et al., 2023
Moderate dementia annual cost	9K	Gamma	Lin et al., 2023
Severe dementia annual cost	9.2K	Gamma	Lin et al., 2023

Table 1: Model Input Parameters (continued)

Parameter	Value (Uncertainty)	Distribution	Source
Institutional care annual cost	60.3K	Gamma	Lin et al., 2023
ARIA event management cost (per event)	120	Gamma	Lin et al., 2023
Donanemab annual treatment cost	23,240 (2,320)	Gamma	Net price estimate

Abbreviations: AD, Alzheimer's disease; ARIA, amyloid-related imaging abnormalities; HR, hazard ratio; MCI, mild cognitive impairment. Uncertainty reported as standard error, standard deviation, 95% confidence interval, or ±% range, depending on source.

HR = 1.00 denotes the reference (comparator) arm; intervention HRs are from trial data.

Table 2: Cost-Effectiveness Results

Analyses/Strategy	Lifetime Cost	Lifetime QALYs	Inc. Cost	Inc. QALYs	ICER
Base case					
– Standard of Care	GBP 193,240	3.18185	—	—	—
– Donanemab	GBP 256,900	3.49779	GBP 63,660	0.31594	GBP 201,500/QALY
Probabilistic sensitivity analysis					
– Standard of Care	GBP 211,850	3.18681	—	—	—
– Donanemab	GBP 275,860	3.49855	GBP 64,010	0.31174	GBP 205,400/QALY

Abbreviations: Inc., incremental; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life-year; GBP, British Pound.

Table 3: Secondary Outcomes

Outcome	Standard of Care	Donanemab
Life Expectancy (years)	6.13	6.51
Life-years lost (years)	7.93	7.55
Average Disease State Duration (years)		
– MCI	3.6	4.5
– Mild Dementia	2.2	2.8
Median Progression Time (years)		
– Mild to Moderate Dementia	2.0	2.0
Median Time to Institutionalization (years)	3.0	3.0
Lifetime Risk of Institutionalization (%)	53.9	50.7

Figure 1. Health state transition diagram showing Alzheimer's disease progression through cognitive stages with mortality.

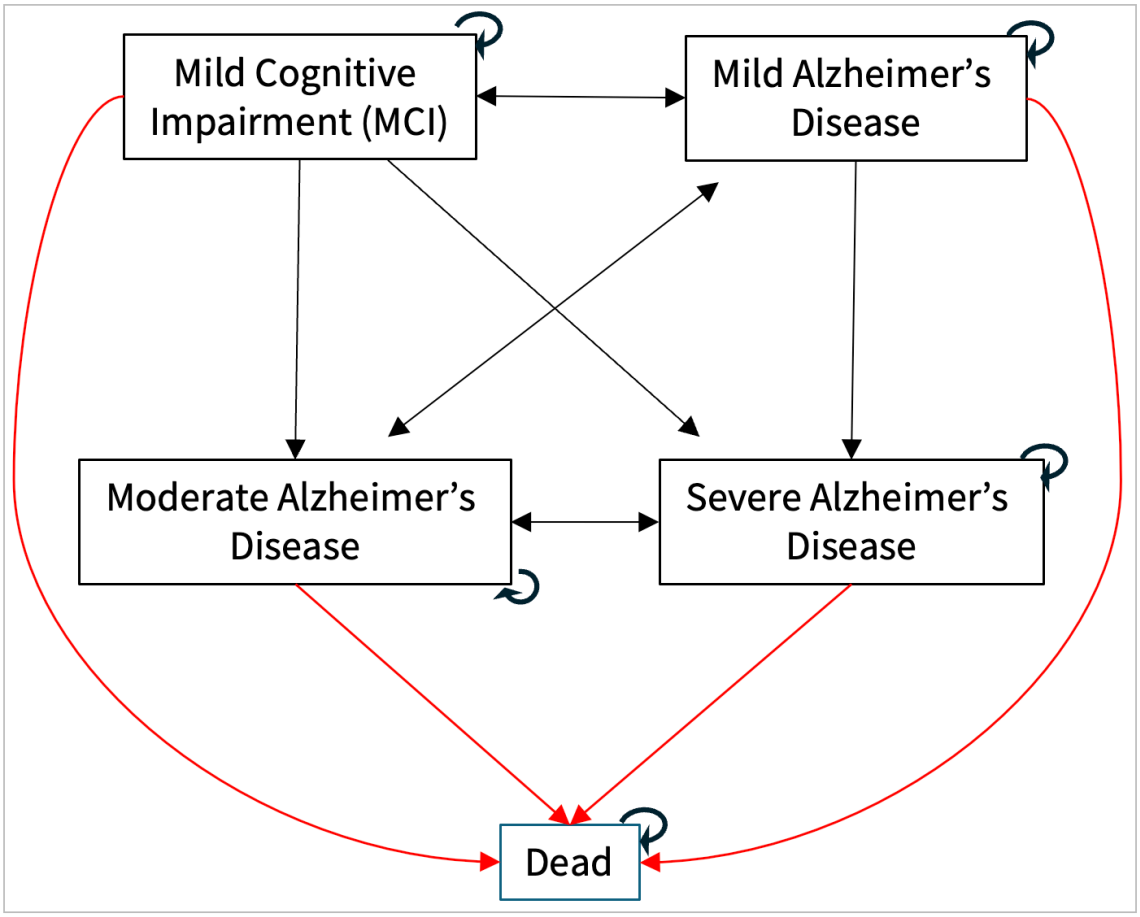


Figure 2. Health State Distribution Over Time (Markov Traces)

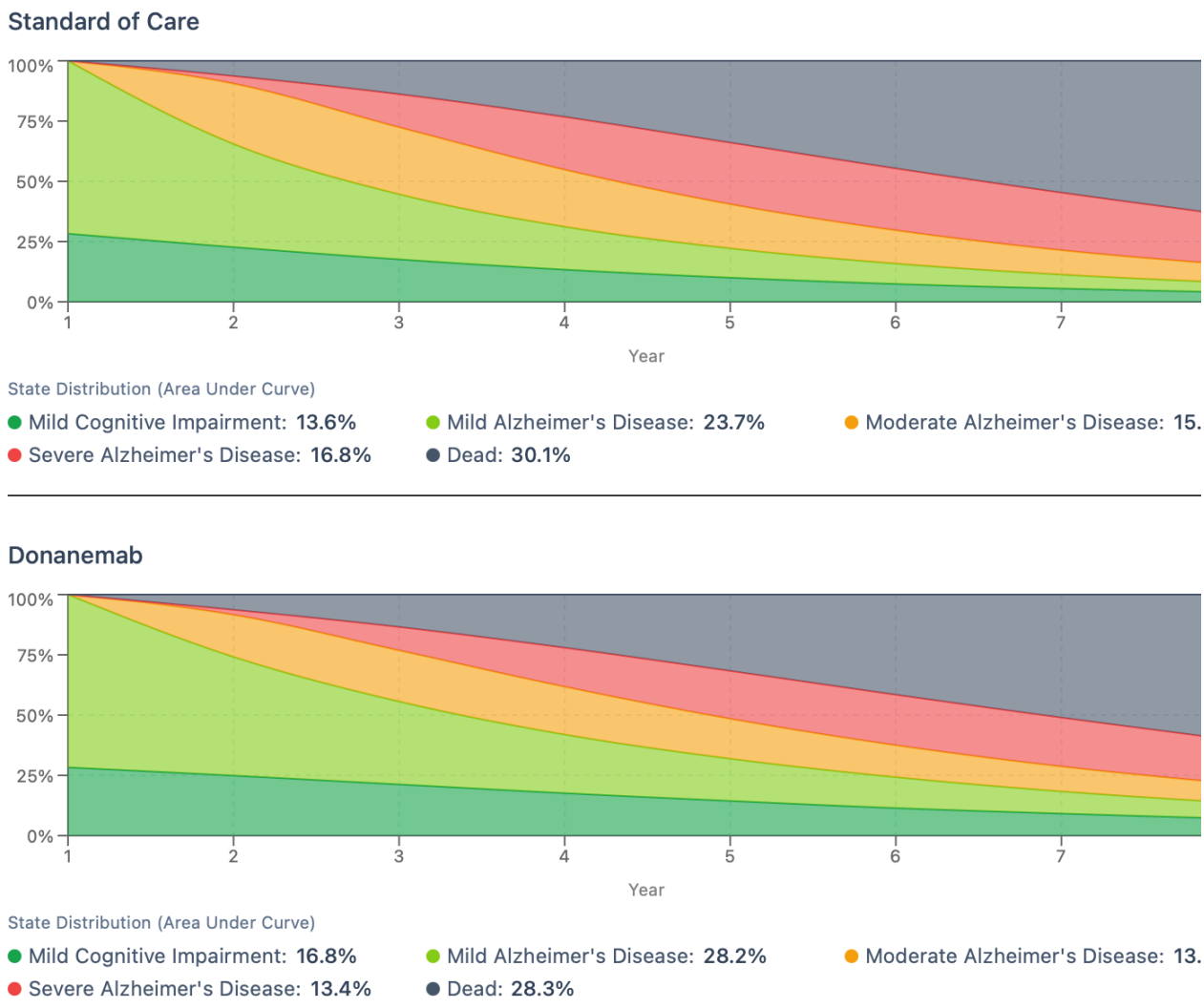


Figure 3. Tornado Diagram (Deterministic Sensitivity Analysis)

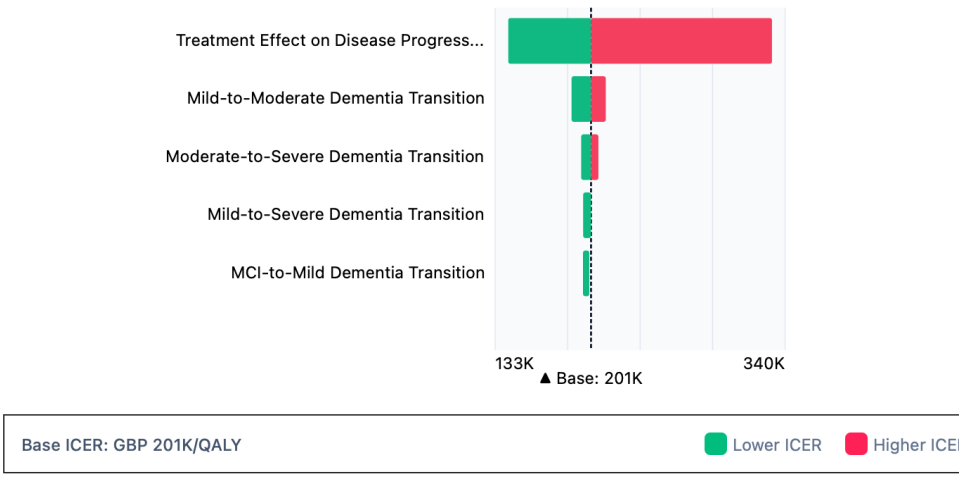
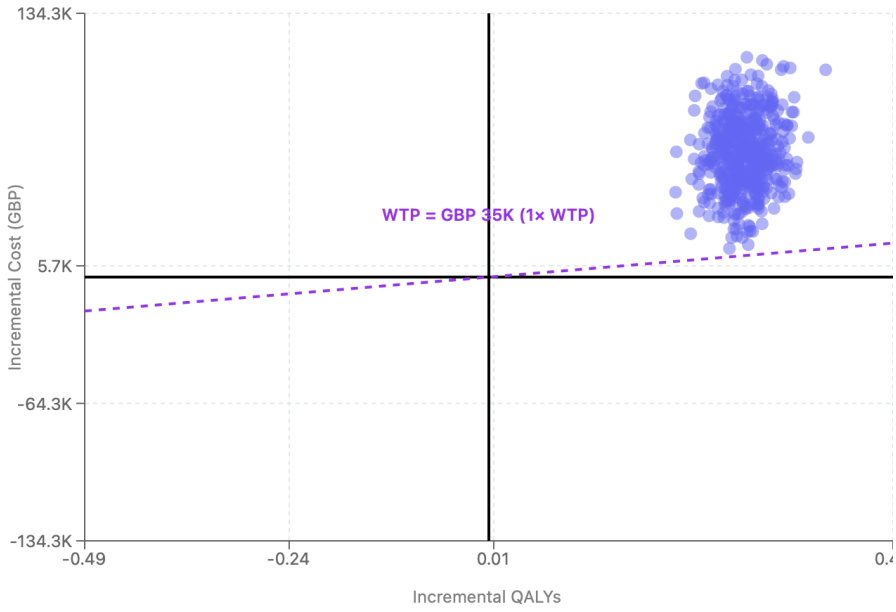
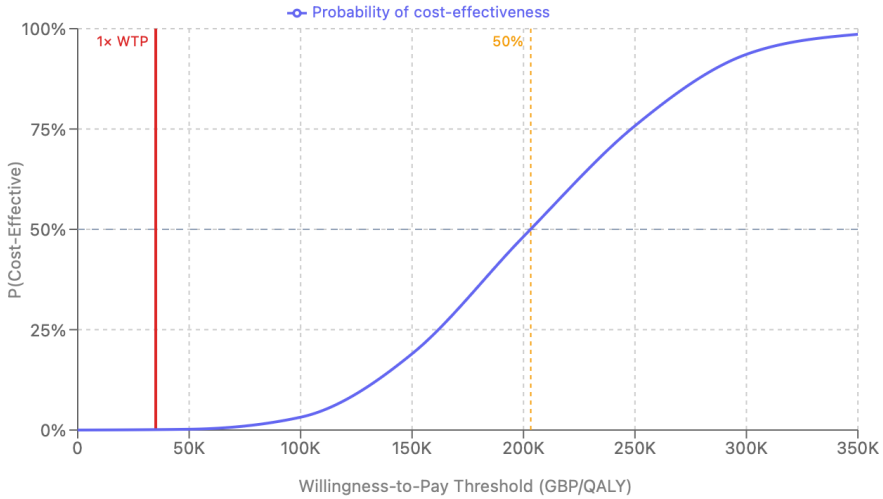


Figure 4. Cost-Effectiveness Plane (Probabilistic Sensitivity Analysis)



Iterations	Mean ICER	Median ICER	P(CE) at 1× WTP
1,000	GBP 201K	GBP 203K	0.0%

Figure 5. Cost-Effectiveness Acceptability Curve



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