

Cross-Validation of an Early Cost-Effectiveness Model for Spectris™ Therapy Using the Alzheimer's Disease Open-Source IPECAD Model Framework

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Background

- An estimated 7.2 million Americans live with Alzheimer's disease (AD), generating \$384 billion in annual healthcare costs.¹ Recent therapeutic innovations have increased the need for transparent, credible, and reproducible health economic models to support reimbursement decision-making.
- The International Pharmaco-Economic Collaboration on Alzheimer's Disease (IPECAD) model provides a transparent reference framework for evaluating economic models in Alzheimer's disease and has been recommended for cross-model evaluation due to its reproducibility and open-science principles.²
- Spectris™ is a clinical-stage non-invasive, at-home AD treatment that delivers visual and auditory stimulation, evoking gamma band oscillations in the brain. Brain gamma frequency oscillations are known to be disrupted in AD patients.^{3,4} Cognito Therapeutics previously developed an economic model to assess Spectris™, with early results suggesting favorable cost-effectiveness across a wide range of treatment effect assumptions.

Objectives

This study evaluates the performance of the previously developed Spectris™ economic model within the IPECAD framework and examines how structural and parameter differences impact cost-effectiveness outcomes

Methods

- The prior five-state Markov model (MCI, mild, moderate, severe AD, death) was mapped to IPECAD v2.3. Population characteristics, natural history, utilities, and medical costs were aligned.
- For Spectris, a range of relative risk (RR) efficacy scenarios between 0.3 (approximating the OVERTURE I results, where a 77% reduction in functional decline was observed) and 0.7 (consistent with available monoclonal antibodies) were applied to standard of care transition probabilities, within structural IPECAD constraints where and how treatment benefits can occur (Figure 1, 2).

- Acquisition cost inputs ranged from \$10,000- \$60,000 and were implemented as a one-off start cost in both models to align with the IPECAD input options.
- A cost-effective acquisition cost of Spectris™ was calculated at a willingness-to-pay (WTP) threshold of \$100,000. Scenario analyses explored the impact of structural and parameter differences.

Figure 1: IPECAD Key Structural Constraints In Capturing Treatment Benefits

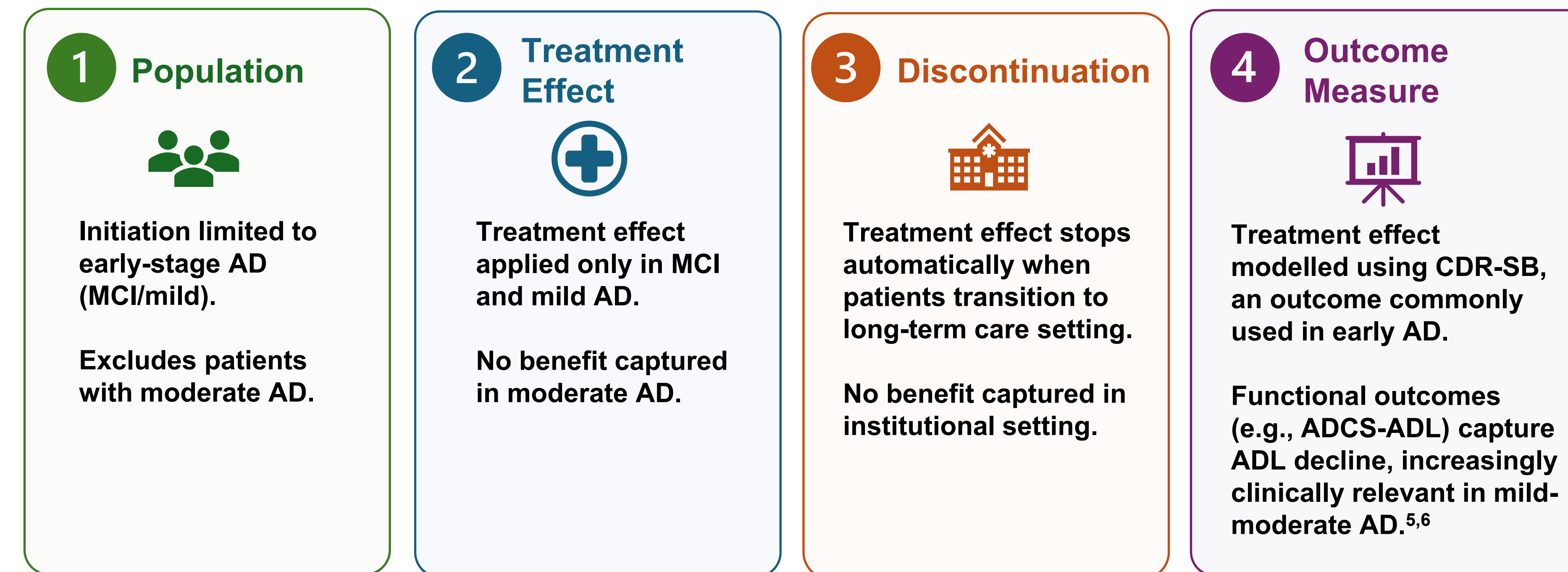
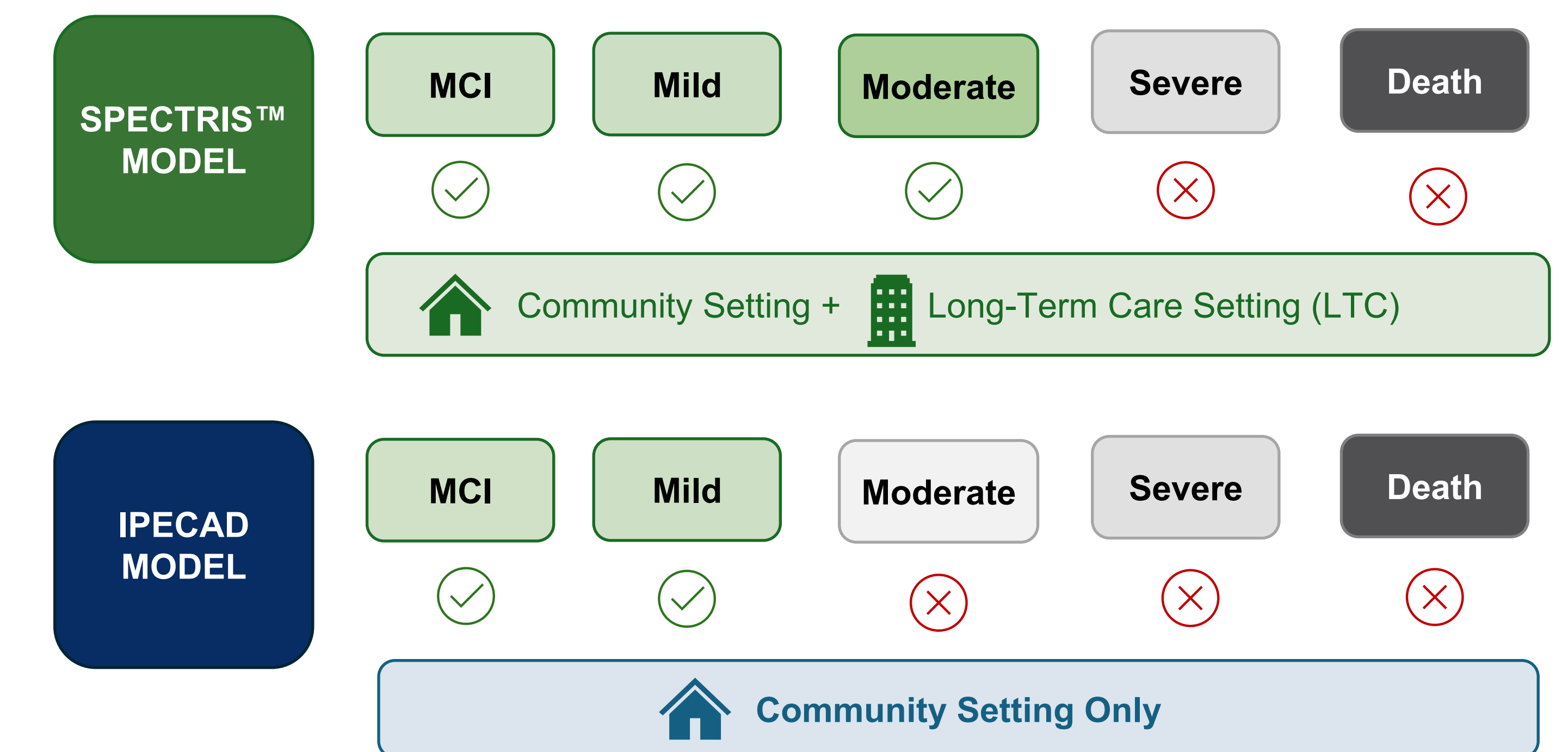


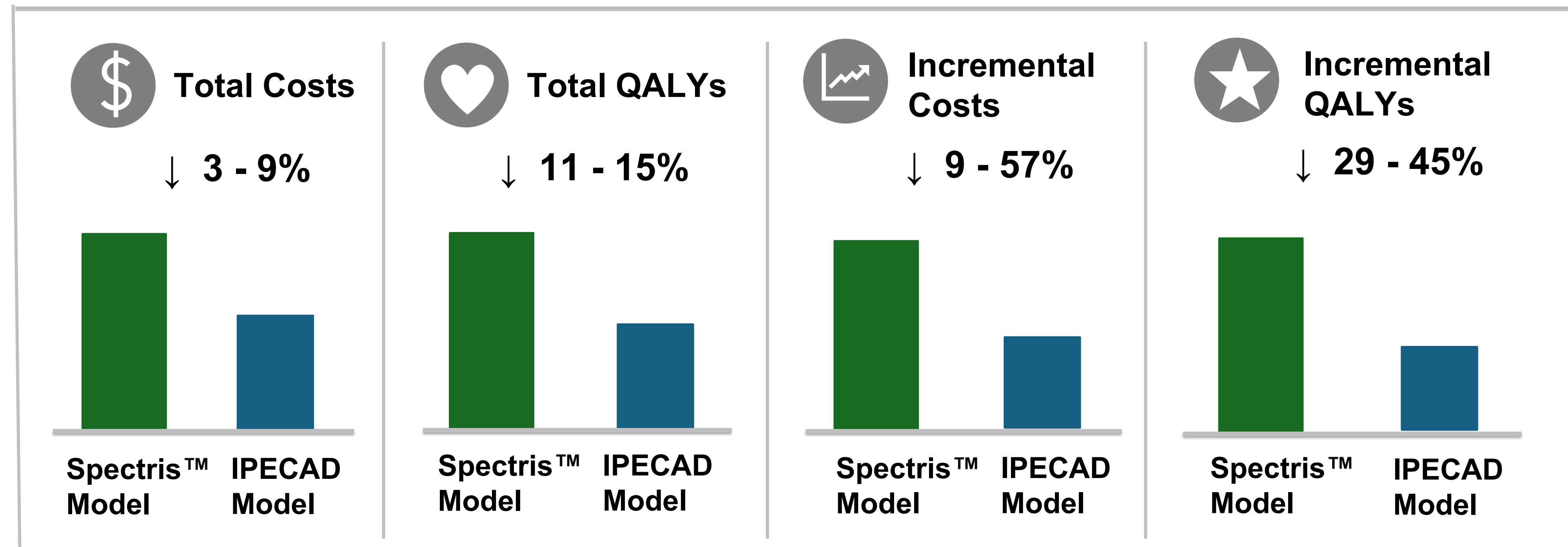
Figure 2: Where Treatment Benefit is Captured



Results

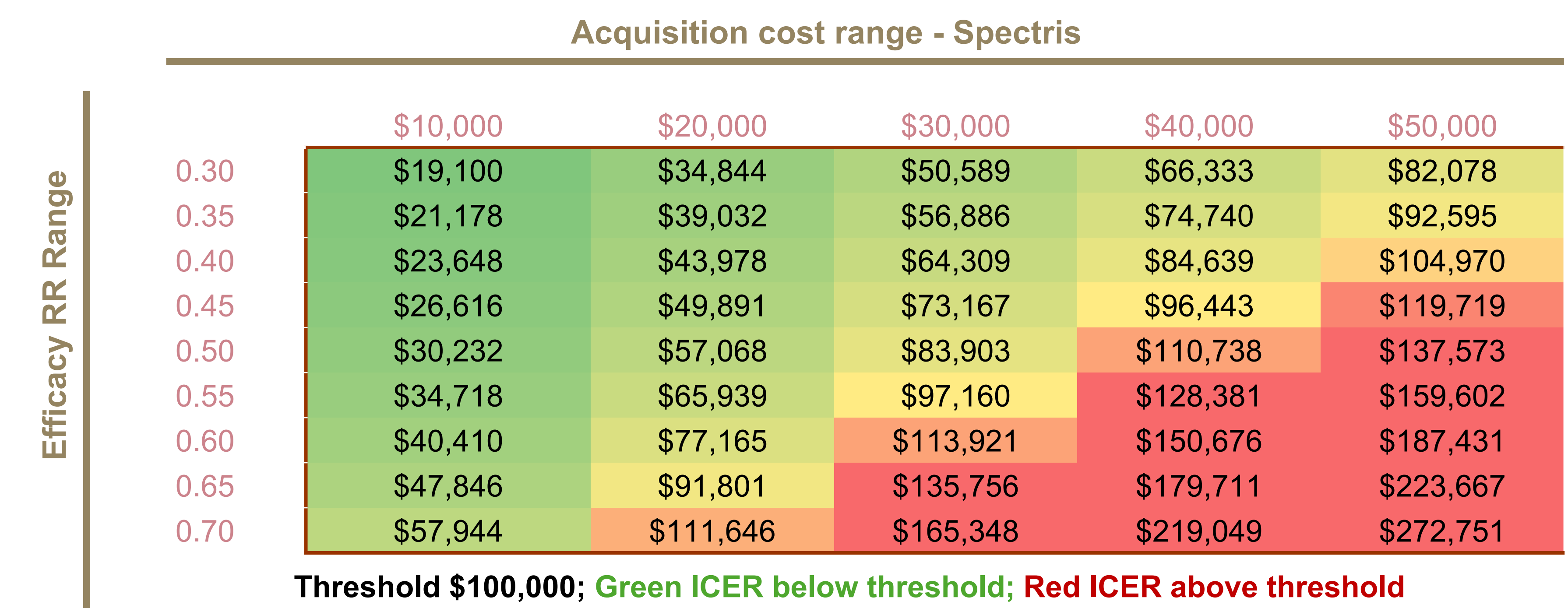
- IPECAD produced more conservative estimates. Compared to the prior model, the IPECAD-Spectris replication yielded lower Total Costs (3-9%) and Total QALYs (11-15%), lower Incremental Costs (9-57%) and Incremental QALYs (29-45%) versus standard-of-care treatment. (Figure 3)

Figure 3: Comparing IPECAD and Spectris™ Model Outcomes



- These difference are expected given structural constraints on who can benefit (population), when benefit occurs (disease stage), how long it persists (setting), and how it is measured (outcomes). This results in a systematic underestimation of treatment benefit.
- Differences also arose from variations in model structure (excess mortality calculations, half cycle correction implementation), and from differing parameter inputs, such as simplified cost assumptions.
- Findings largely align with IPECAD replication of ICER's lecanemab model. However, unlike lecanemab—where total QALYs were similar across models—QALYs were lower in the IPECAD-Spectris analysis, likely reflecting that Spectris™ targets mild-moderate AD, where structural constraints limit captured benefit.⁷
- Using a \$100,000/QALY threshold, Spectris™ demonstrated potential cost-effectiveness with total acquisition costs between \$17,831 (RR = 0.7) and \$61,383 (RR = 0.3), with the IPECAD model. (Figure 4)

Figure 4: Treatment Effect vs Spectris™ Costs in IPECAD model



Conclusions

- Cross-validation using IPECAD shows that, based on OVERTURE pilot inputs, Spectris™ appears potentially cost-effective across a wide range of assumptions within a conservative, structurally restrictive framework.
- These constraints limit where and how treatment benefits are captured and may underestimate value for therapies targeting mild-moderate Alzheimer's disease, including high unmet need populations. While IPECAD provides a transparent and reproducible reference framework, it is primarily suited to early-stage disease and does not fully capture treatment effects in moderate AD.
- Future reference models should be fit-for-purpose, aligned with therapy mechanism, target population, and outcomes across disease stages. In particular, models should ensure that outcome measures are appropriate to the stage of disease and capture clinically meaningful changes across the full spectrum of Alzheimer's disease progression.**

References

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