

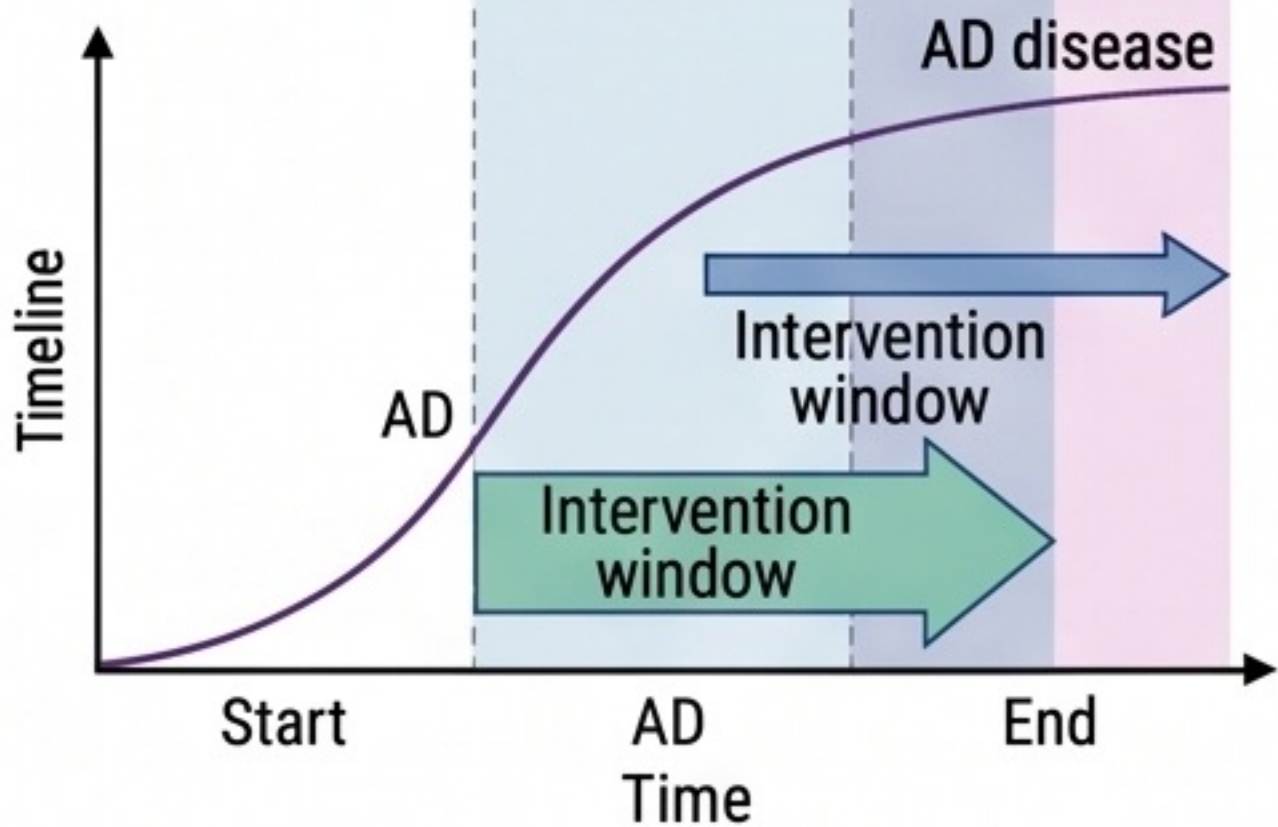
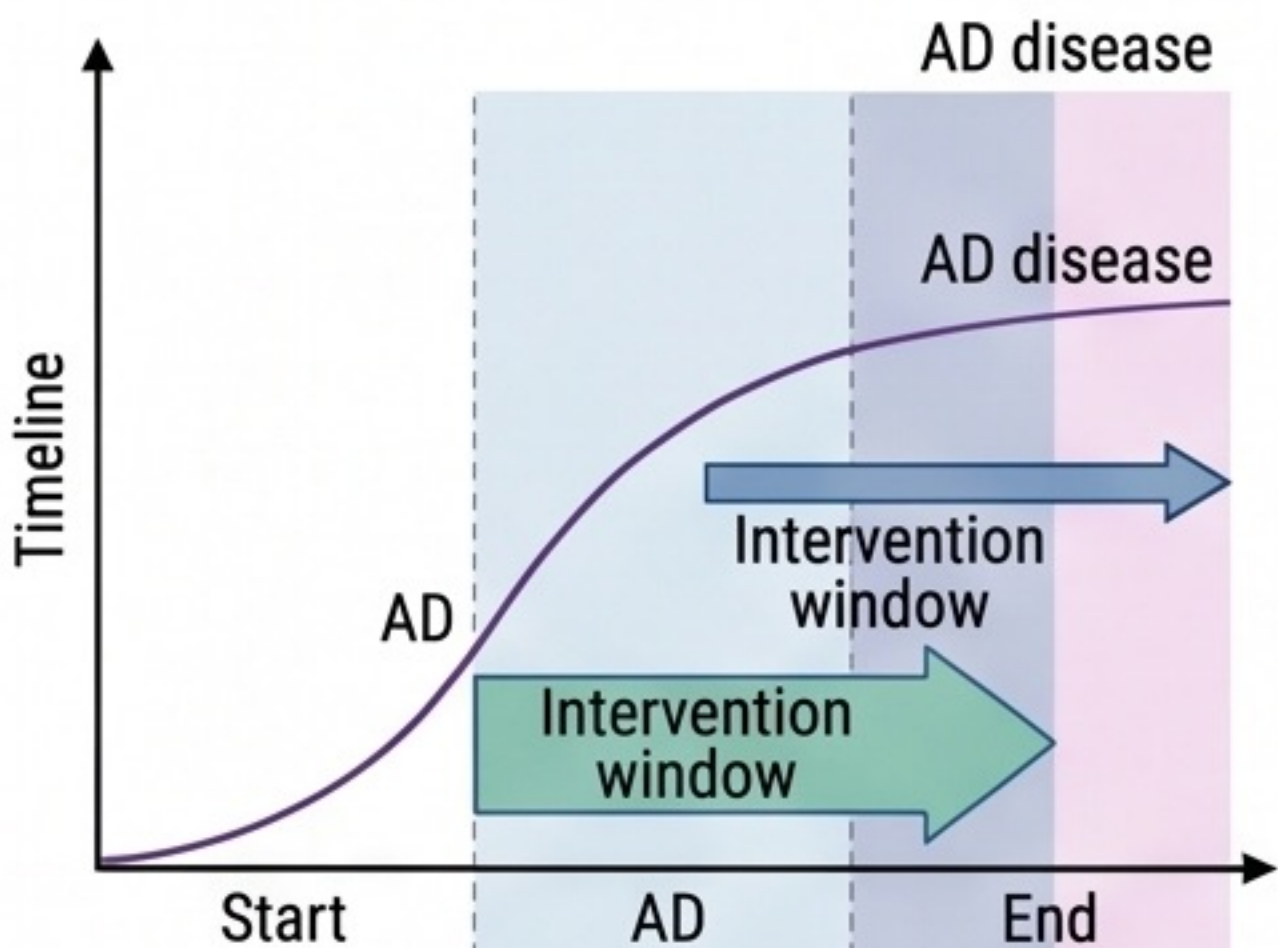
REINFORCEMENT LEARNING WITH WORLD MODELS FOR OPTIMIZING ALZHEIMER'S DISEASE TREATMENT TIMING AND DOSING

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INTRODUCTION

Background: Recent evidence demonstrates advanced interventions can reverse advanced Alzheimer's disease (AD) phenotypes in vivo. However, specifying the therapeutic challenge from drug discovery to optimal deployment – determining when to start, how intensively to treat, and how to safely navigate complexity with cumulative drug burden and physiological safety – remains unresolved.

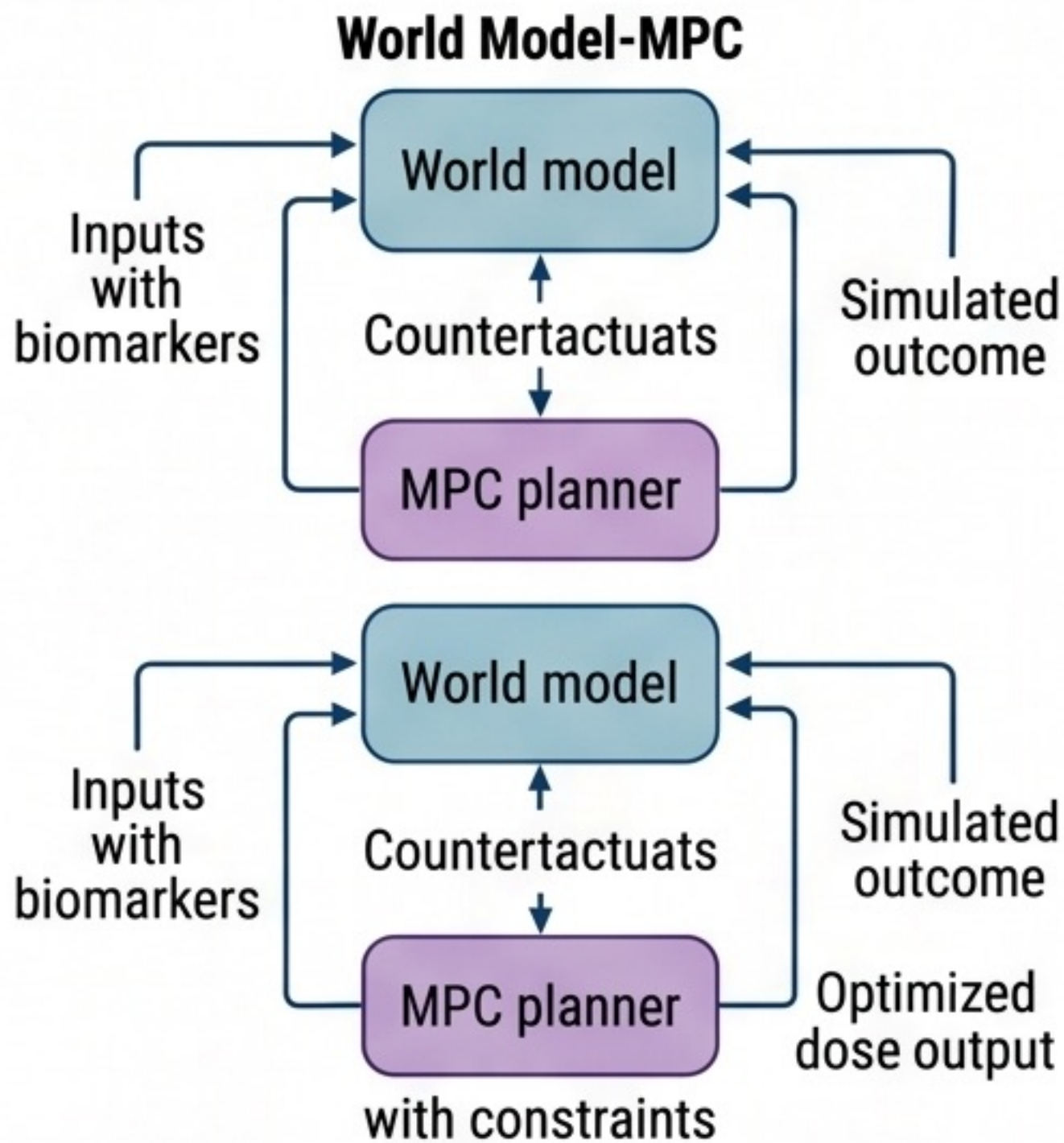
Objective: Frame AD treatment timing as a sequential decision problem and introduce an AI world model to optimize personalized intervention schedules.



METHODS

Action-Conditioned Disease Simulator (a world model) learns latent disease dynamics from longitudinal multimodal biomarkers (e.g., tau pathology, cognitive scores) to predict future clinical trajectories under hypothetical treatment sequences.

Model Predictive Control (MPC), with planning capabilities, drives adaptive treatment schedules, model is penalized for uncertainty and strictly constrained by physiological safety thresholds.



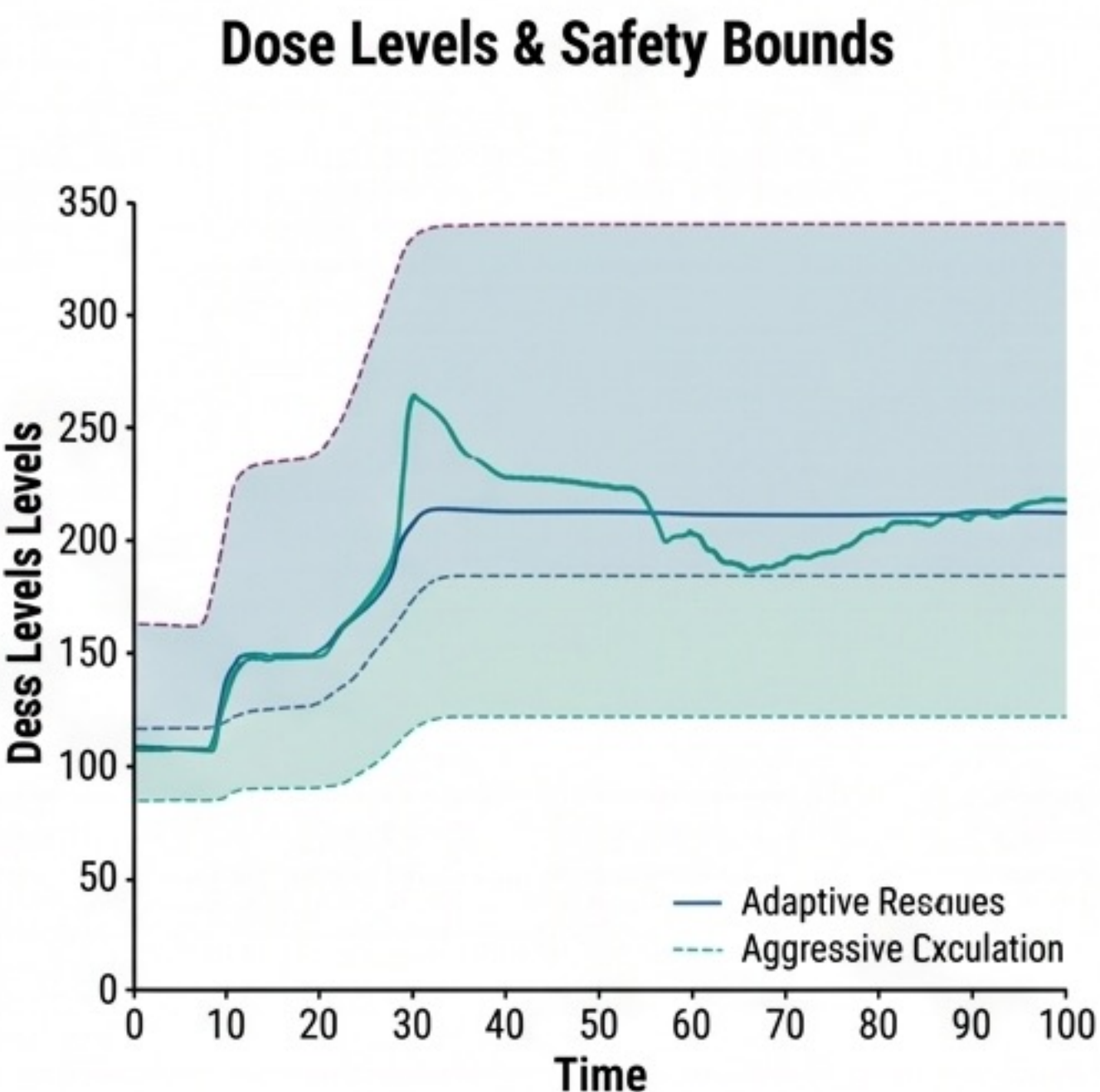
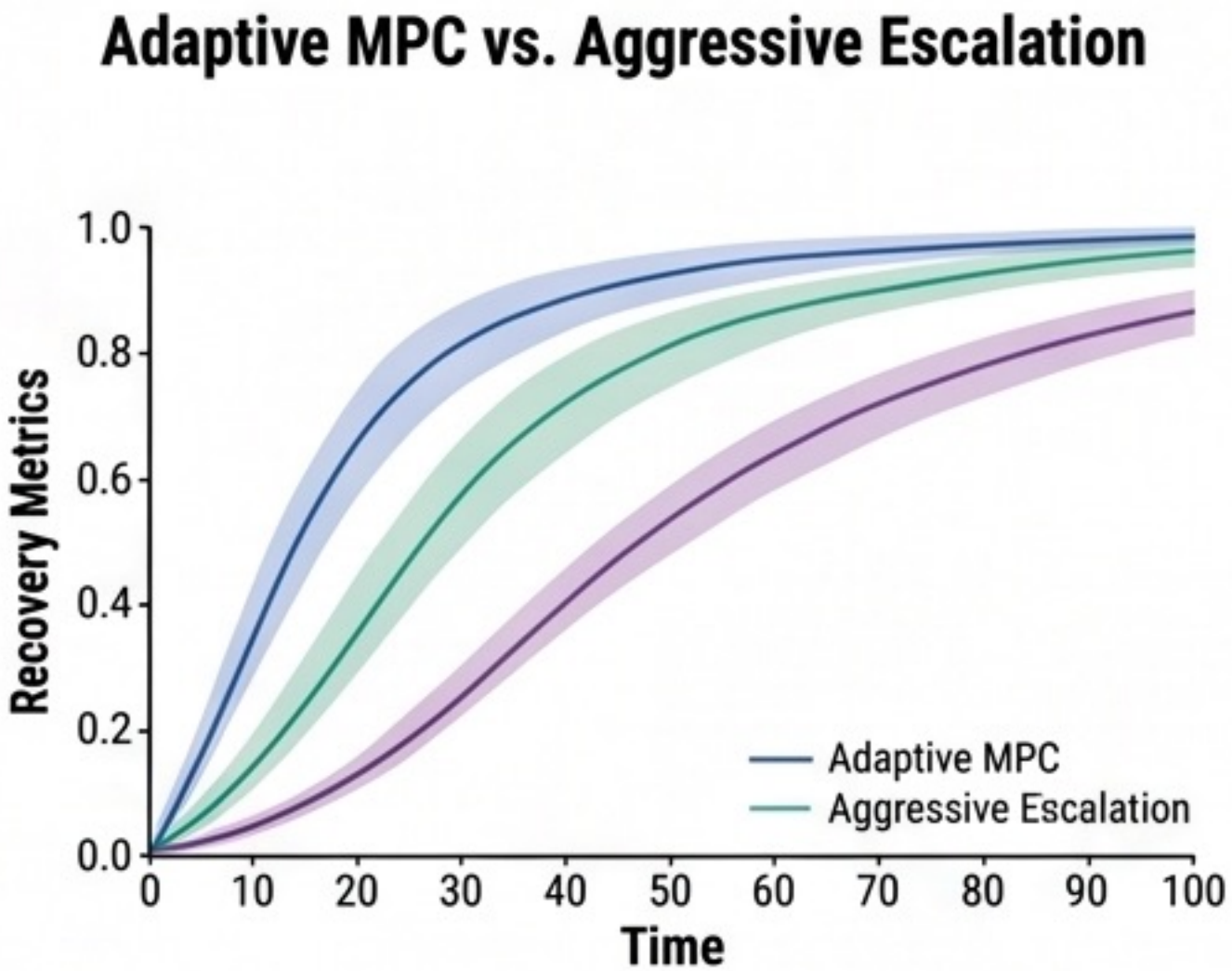
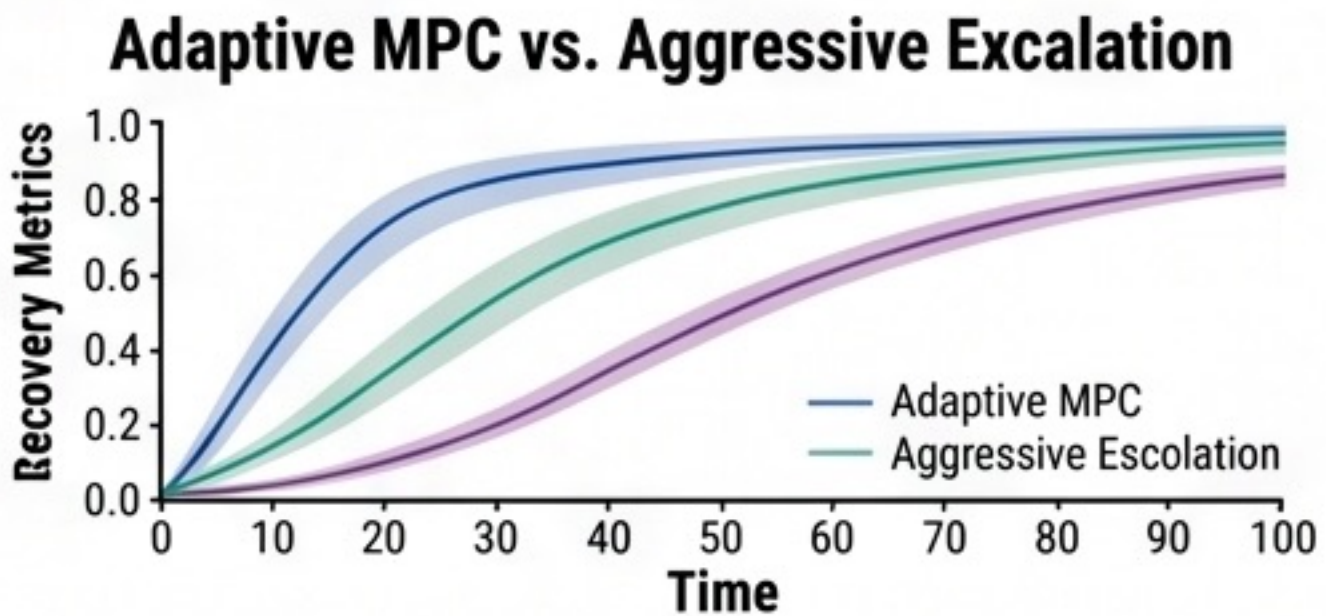
PHYSIOLOGICAL SAFETY CONSTRAINTS & BIOMARKERS

Category	Example
Toxicity	Prevents excessive biomarker levels (e.g., Max. Tau protein) or dosage cap.
Function	Ensures normal physiological function (e.g., Cognitive Scores, Quality of Life Index).
Cumulative Burden	Limits multi-drug interactions and cumulative drug load.

Validation: Framework validated on ALZWORLD, a synthetic longitudinal cohort dataset.

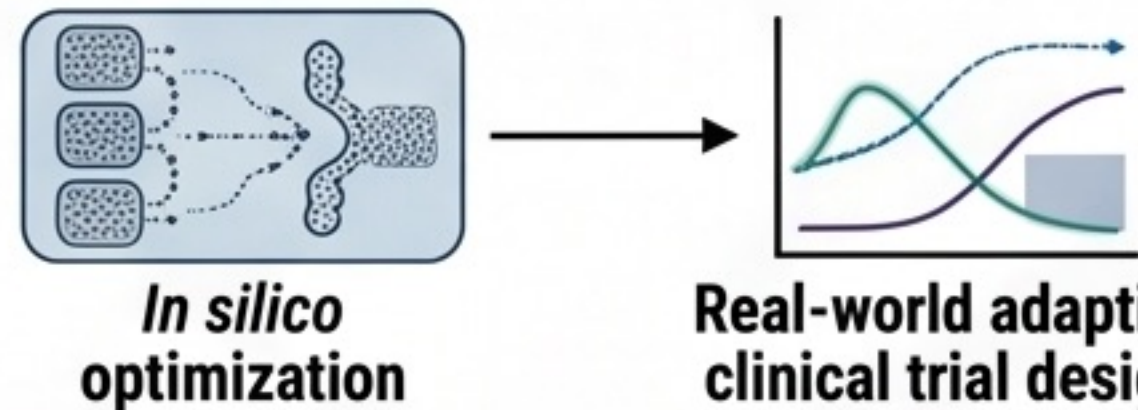
RESULTS

Discovered Policies: In simulated cohorts, the world model MPC discovered adaptive front-load and taper policies to achieve near-maximum recovery compared to aggressive, continuously escalating dosing baselines ($p=0.801$). By enforcing strict homeostatic bounds and uncertainty calibration, the planner safely incorporated personalized dosages without recommending toxic dose levels.

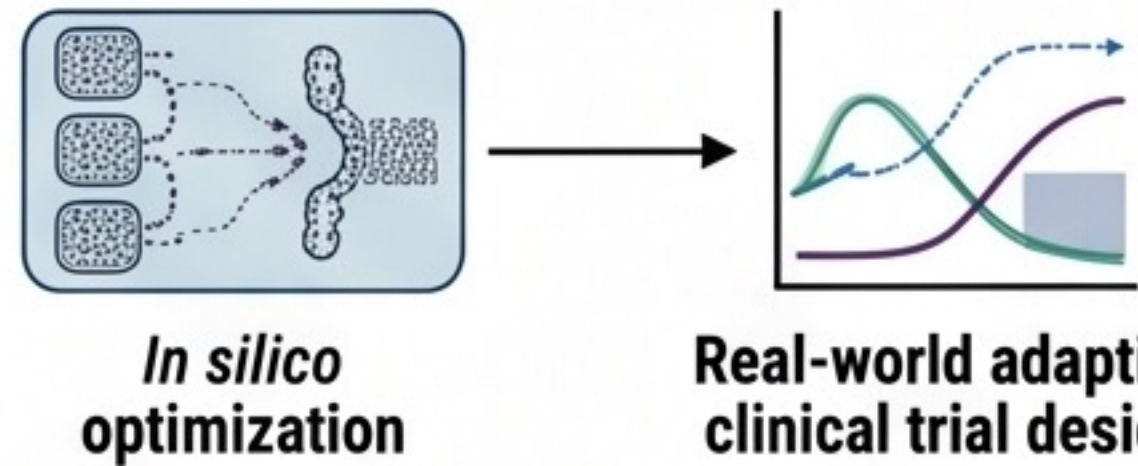


CONCLUSIONS

Summary: AI-driven world models function as digital twins, allowing researchers to accotote long-term AD progression and counterfactual treatment responses. By optimizing dosing schedules in silico to minimize efficacy while mathematically guaranteeing safety constraints, this approach provides a robust decision-support hioocrint for designing adaptive, personalized AD clinical trials.



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★ **KEY TAKEAWAY: ADAPTIVE, IN SILICO-OPTIMIZED DOSING SCHEDULES DISCOVERED BY AY AD WORLD MODELS OUTPERFORM STANDARD ESCALATION WHILE SOLVING PHYSIOLOGICAL SAFETY CHALLENGES IN PERSONALIZED TREATMENT.**