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Introduction

- Plasma phosphorylated tau (p-tau) is a promising blood-based biomarker for prescreening in Alzheimer's disease (AD) clinical trials.
- Incorporating plasma p-tau measurements before confirmatory amyloid- β (A β) PET imaging may enrich enrollment, reduce PET utilization, and lower recruitment costs.

Aim: to assess the cost-effectiveness of plasma p-tau217 prescreening across the AD continuum

Results

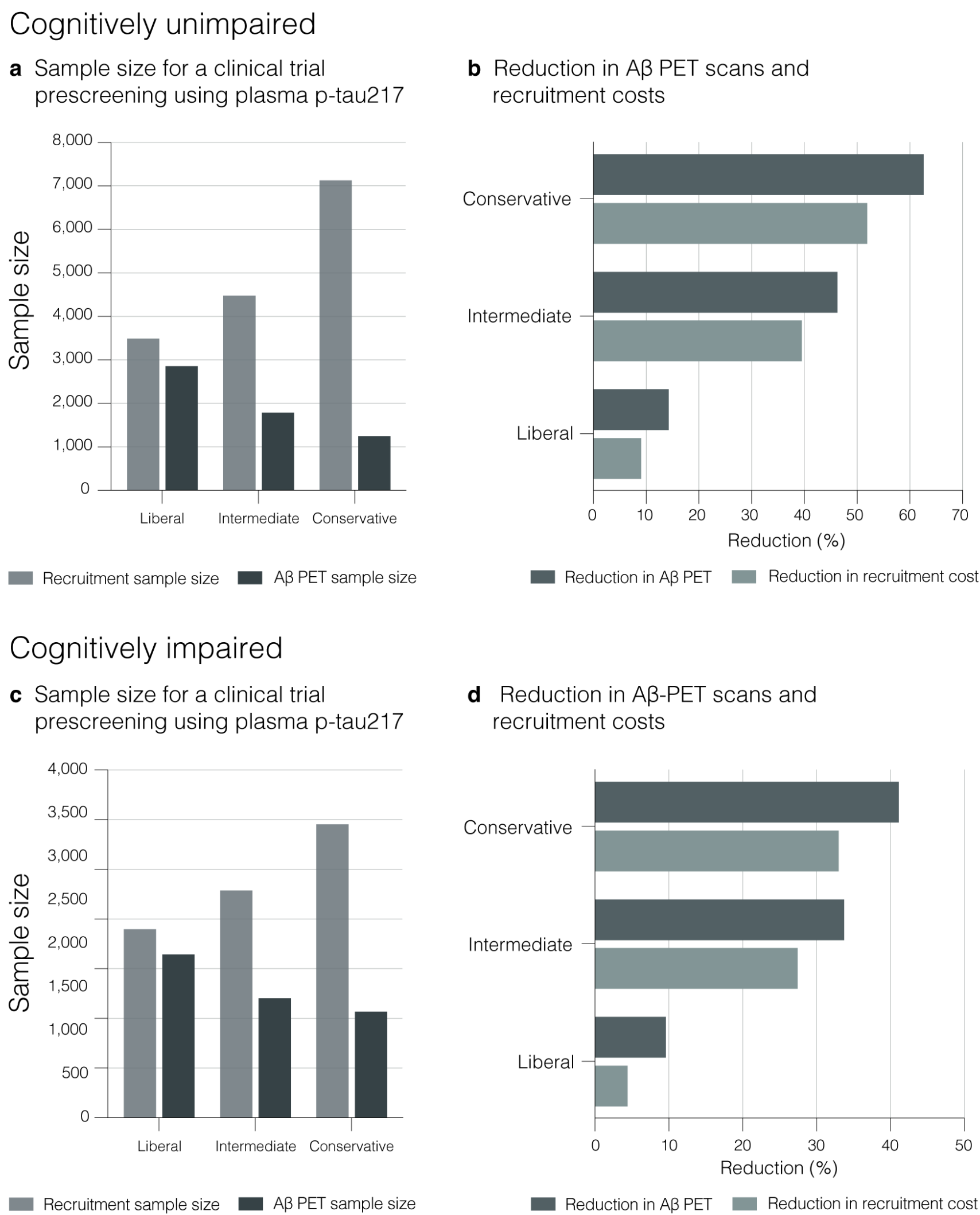


Figure 1. Intermediate plasma p-tau217 threshold streamline recruitment for AD clinical trials. Results for the CU (a-b) and CI (c-d) populations. **a,c**, Total number of individuals undergoing plasma p-tau217 prescreening and the corresponding number of confirmatory A β PET scans using liberal, intermediate, and conservative thresholds. **b,c**, Reduction in A β PET scans and overall recruitment costs compared with A β PET-only screening. Final enrollment was fixed at a target sample size of 1,000 participants. A β PET-positivity prevalence was assumed to be 30% for CU and 55% for CI. Cost assumptions were as follows: A β PET, \$3,000 per scan; plasma biomarker, \$200 per participant; recruitment, consenting, and clinical assessment, \$1,000 per participant. A β , amyloid- β ; CU, cognitively unimpaired; CI, cognitively impaired; PET, positron emission tomography.

- Liberal p-tau217 thresholds yielded minimal PET and trial cost savings (**Figure 1** and **2**).
- Conservative thresholds maximized recruitment efficiency but markedly prolonged enrollment.
- Intermediate thresholds achieved an optimal balance, reducing costs by up to 46% while maintaining acceptable timelines compared with PET-only screening.
- We developed a freely accessible online tool to calculate sample size, recruitment cost, and time for clinical trials using plasma p-tau217 prescreening (**Figure 3**).

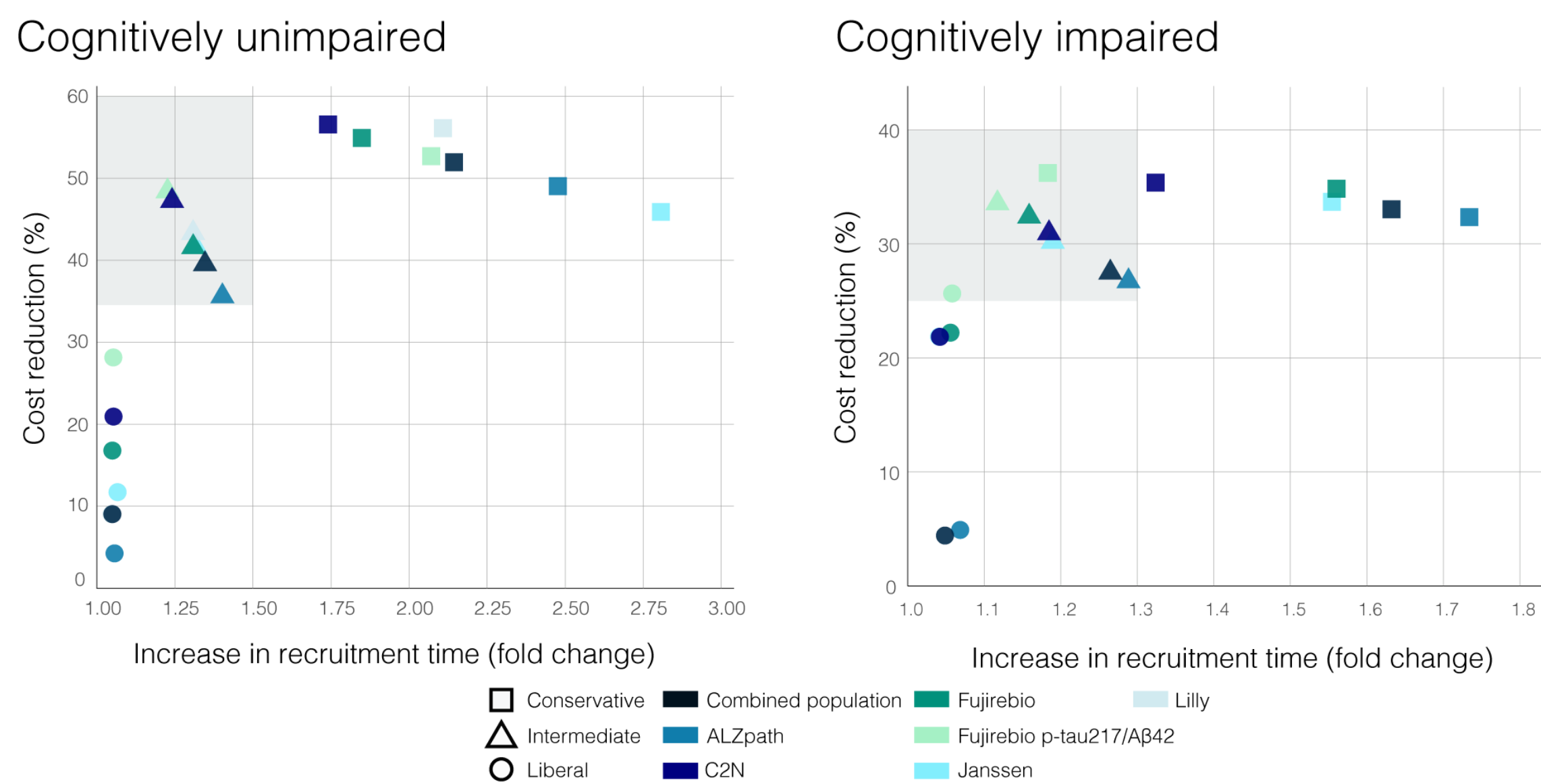


Figure 2. Trade-off between cost reduction and recruitment time. The plot shows the increase in recruitment time (expressed as fold change relative to A β PET-only screening) for each plasma p-tau217 assay and threshold.

Methods

- Multicohort study including 4,749 individuals (3,303 cognitively unimpaired [CU] and 1,446 cognitively impaired [CI]).
- Available plasma p-tau217 and A β PET imaging .
- Compared three p-tau217 thresholding strategies - liberal (95% sensitivity), intermediate (Youden index), and conservative (95% specificity) - to identify individuals more likely to be A β PET positive.

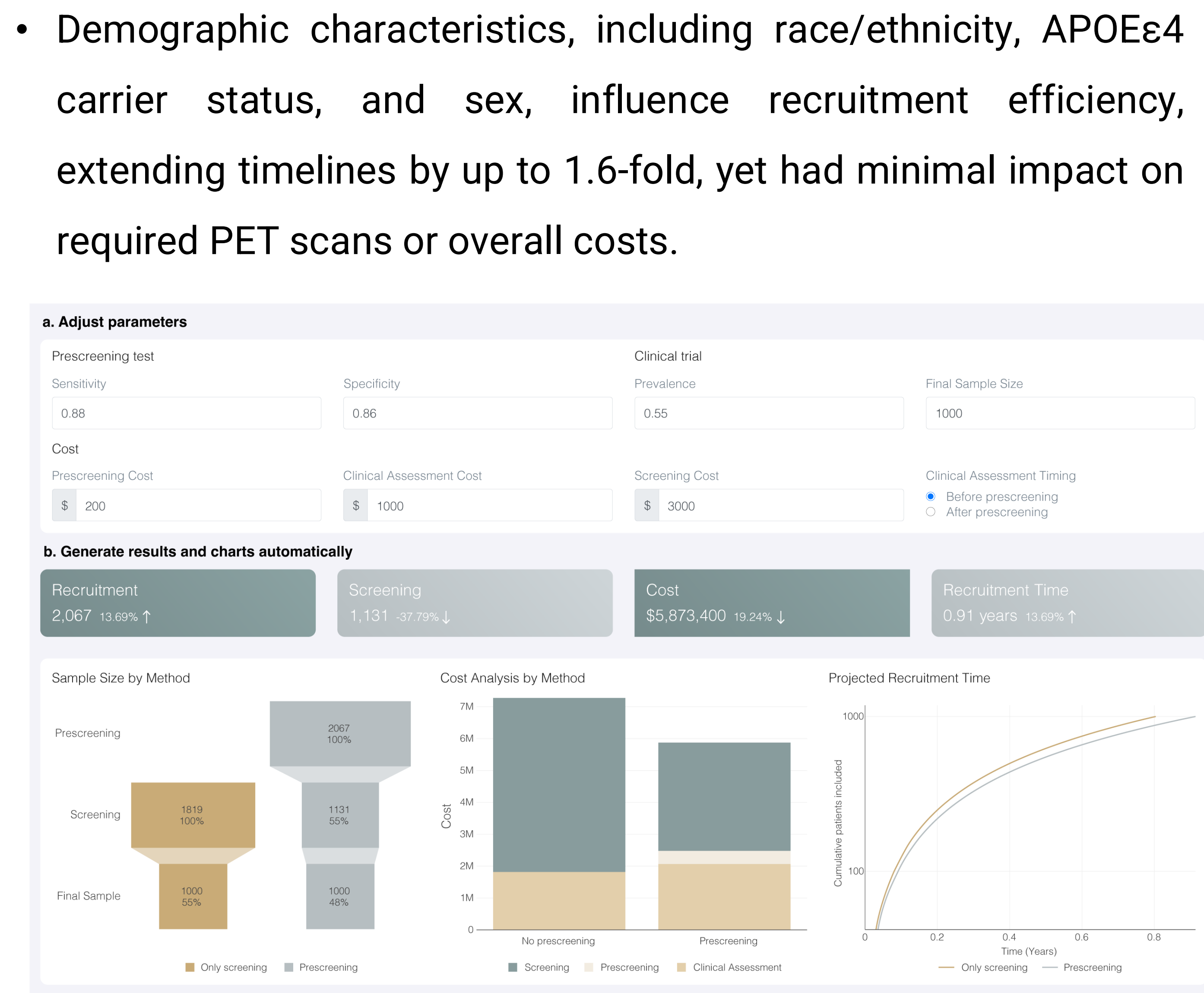


Fig. 3. Online modeling tool for estimating clinical trial recruitment with plasma-based prescreening. **a**, Users adjust input parameters, including prescreening test sensitivity, specificity, and population prevalence, as well as trial characteristics such as final sample size and cost estimates for clinical assessment and screening procedures. **b**, The tool automatically generates recruitment projections and visualizations, including the number of individuals required for recruitment and confirmatory screening, total projected costs, and estimated recruitment time. Graphical outputs display sample size requirements, cost distributions, and projected recruitment time curves, enabling comparison between strategies with and without prescreening.

Conclusion

The findings of this study support plasma p-tau217 intermediate thresholding as an efficient and broadly applicable prescreening biomarker, providing a framework to accelerate AD trial enrollment, reduce costs, and expand access, with demonstrated applicability across populations and clear advantages over the extreme conservative and liberal thresholding strategies.

Acknowledgments



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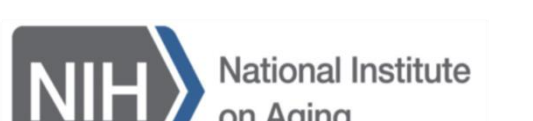
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