

Heterogeneous Treatment Effects of ARB versus ACEI initiation on Alzheimer's Disease and Related Dementias, Evidence from Target Trial Emulation of 2.5 Million US Veterans

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INTRODUCTION

- Hypertension is a modifiable risk factor for Alzheimer's disease (AD) and AD-related dementias (AD/ADRD)
- Mechanistic and observational evidence suggest angiotensin receptor blockers (ARBs) and angiotensin converting enzyme inhibitors (ACEIs) may differentially affect dementia risk

OBJECTIVE

Emulate a target trial with a new-user, active comparator design to compare the intention-to-treat effect of initiating ARBs vs. ACEIs on dementia risk across patient subgroups.

CONCLUSIONS

- Among US Veterans with incident hypertension, associations between ARB versus ACEI initiation and dementia risk varied across patient subgroups by age, sex, and statin use
- Future studies are needed to evaluate treatment effect heterogeneity across multiple patient characteristics to inform personalized antihypertensive therapy for dementia prevention

RESULTS

Figure 1. Five-Year Effects of ARB versus ACEI Initiation on Dementia across Subgroups.

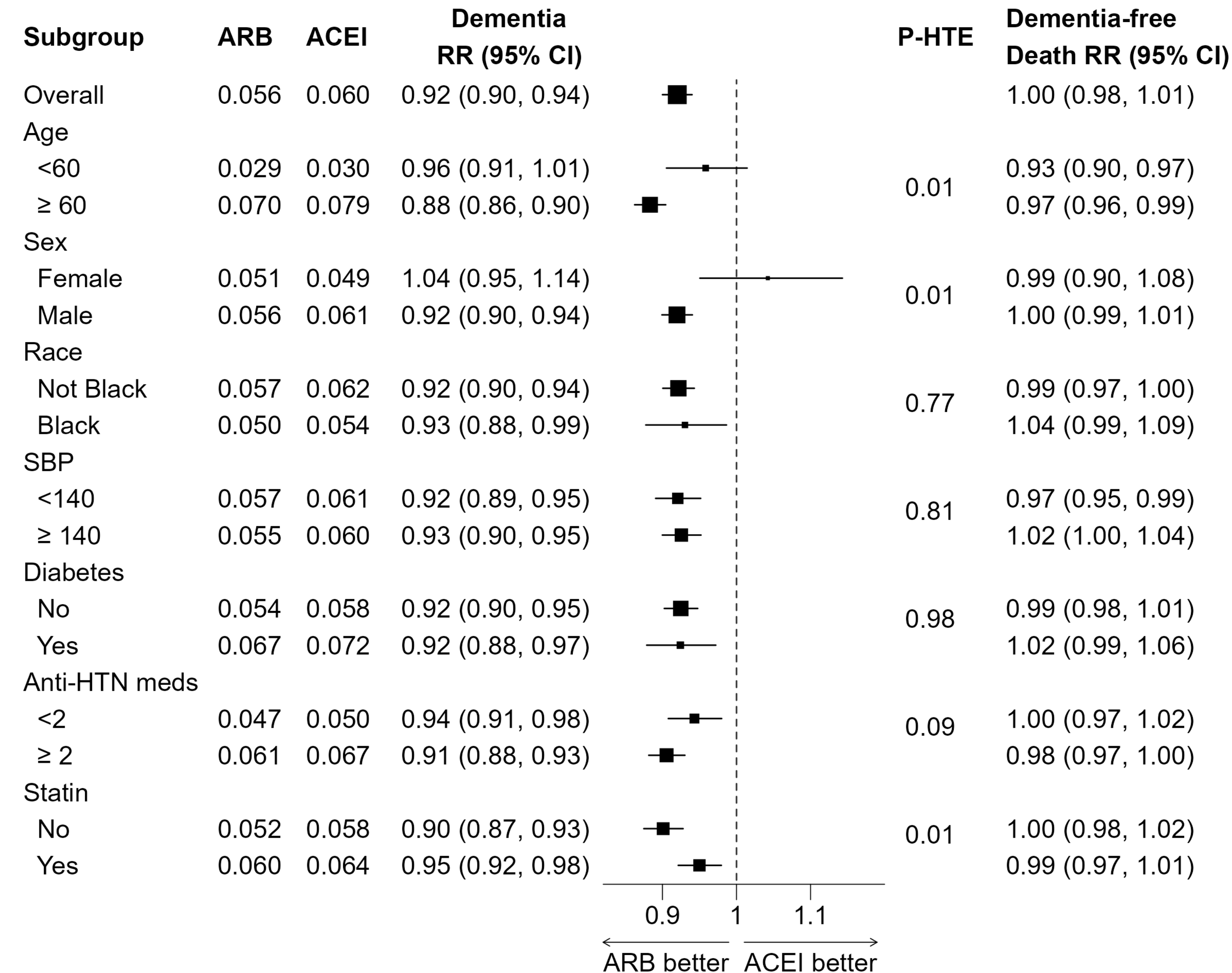
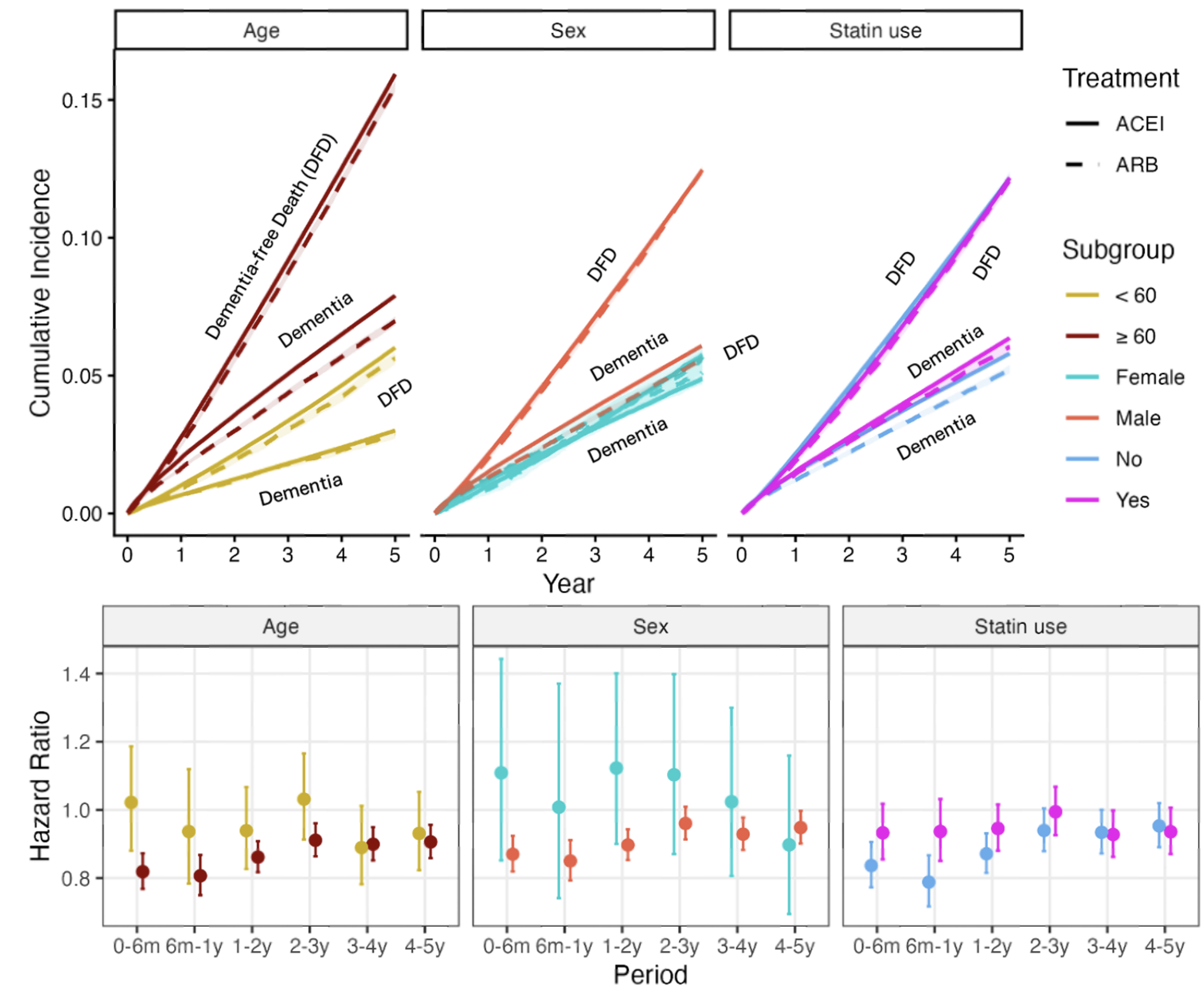


Figure 2. Weighted Cumulative Incidence Curves and Hazard Ratios Over Time across Subgroups. The error bars and shaded ribbon represent the 95% confidence intervals for hazard ratios and cumulative incidence, respectively.



METHODS

Data Source

- Using longitudinal electronic health records from >2.5 million US Veterans with incident hypertension who initiated ACEI or ARB between 1/1/2000 and 12/31/2017
- ACEI and ARB use was determined from pharmacy dispensing records

Target Trial Emulation

- Aligned the times of treatment initiation, patients' eligibility, and start of follow-up
- Minimized selection bias and immortal time bias

Outcomes: AD/ADRD were identified using natural language processing

Statistical Methods

- Over 60 baseline covariates were controlled using inverse probability weighting
- Wald tests were performed to assess differential treatment effects across subgroups
- A competing risk framework was applied to handle the competing event of death

CONNECT

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