Addressing nonpositivity using statistical and mathematical models

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Motivating Question

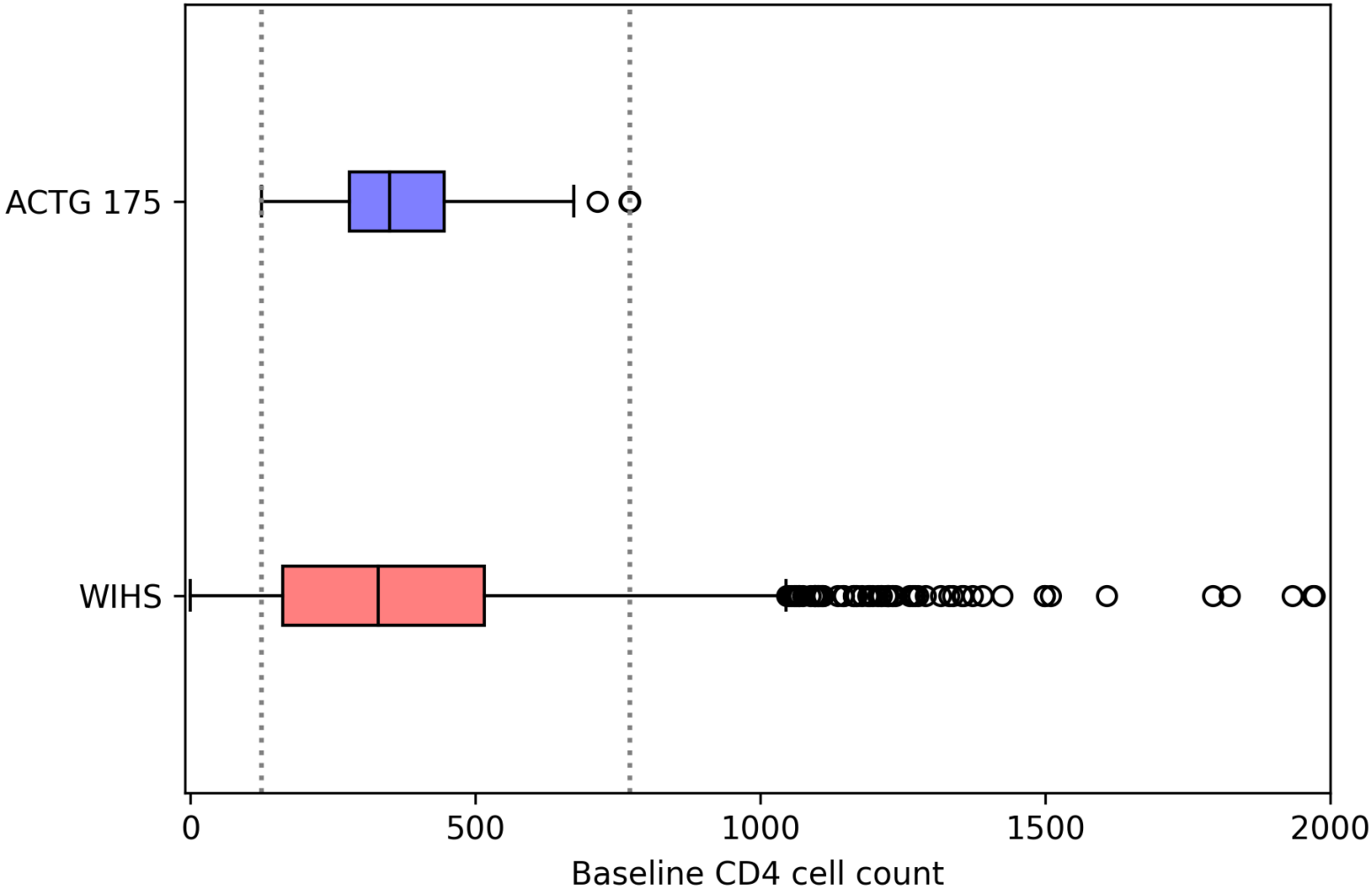
Teleporting to 1995, a colleague asks for help addressing a question

- **Question**: should women with HIV be treated with two-drug or one-drug antiretroviral therapy (ART)?
- **Parameter**: average causal effect of two-drug versus one-drug ART on 20-week CD4 T cell count (cells/mm^3)
  - CD4 is a continuous variable indicating immune function, higher is better

Two data sources

- AIDS Clinical Trial Group (ACTG) 175
- Women's Interagency HIV Study (WIHS)

Nonpositivity



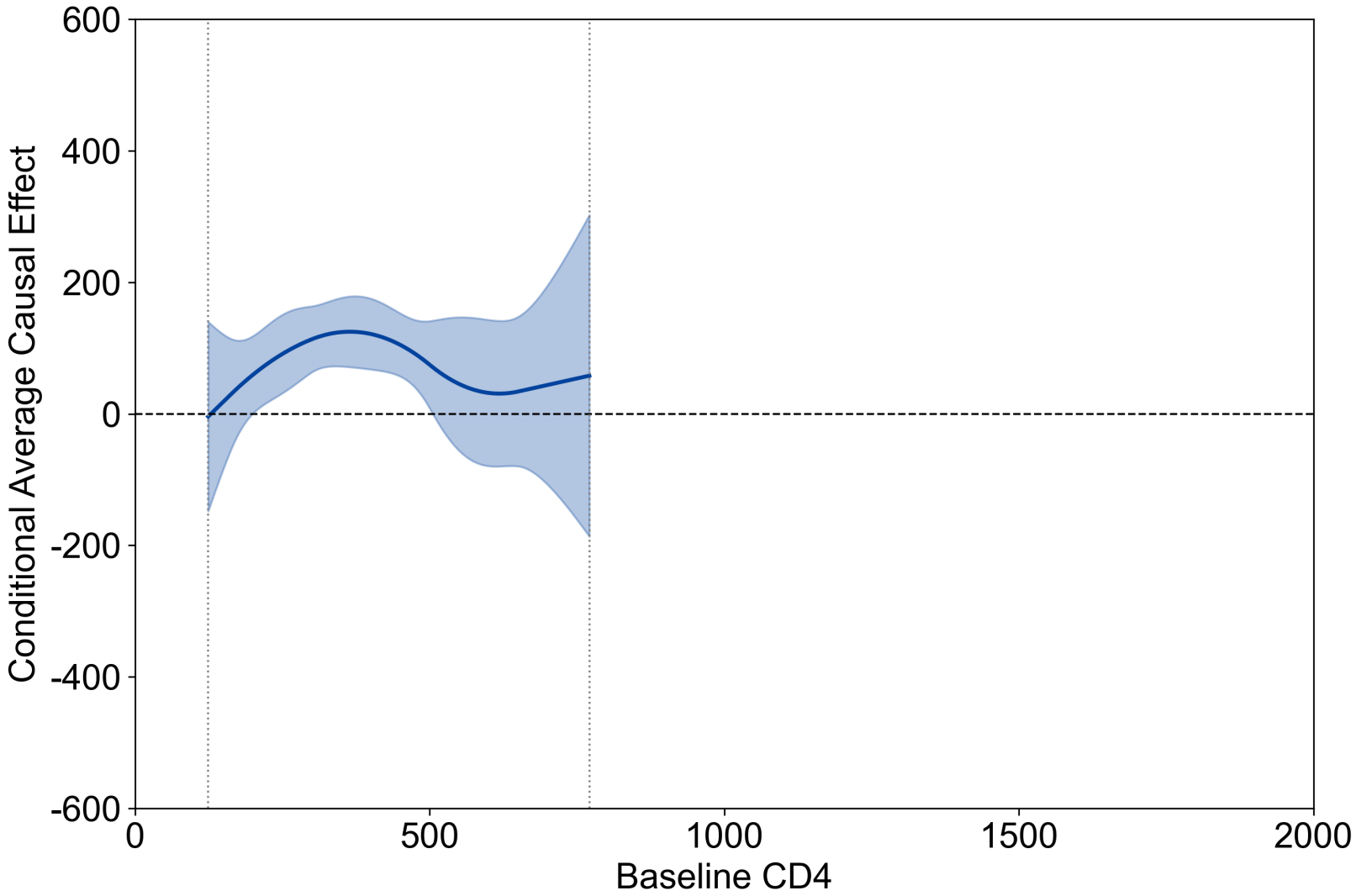
A Brief Aside

Average causal effect can be viewed as an average of the *conditional average causal effect* over the distribution of the covariate.[1]

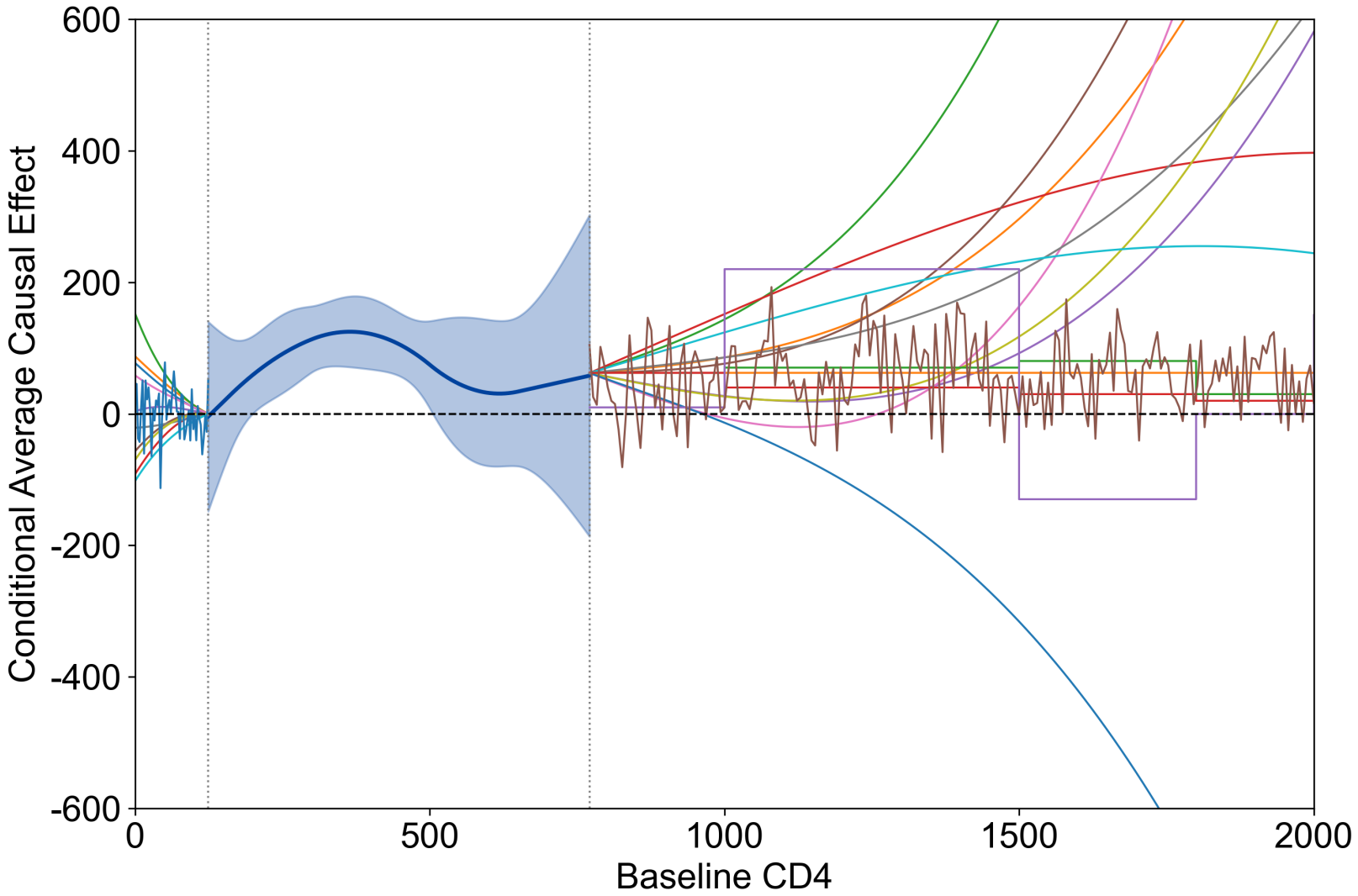
So, examine nonpositivity through the *conditional average causal effect* of two-drug vs. one-drug ART on **20-week CD4** by **baseline CD4**

[1] $E[Y^a \mid R = 1] = E[E[Y^a \mid V, R = 1] \mid R = 1]$ via iterated expectation

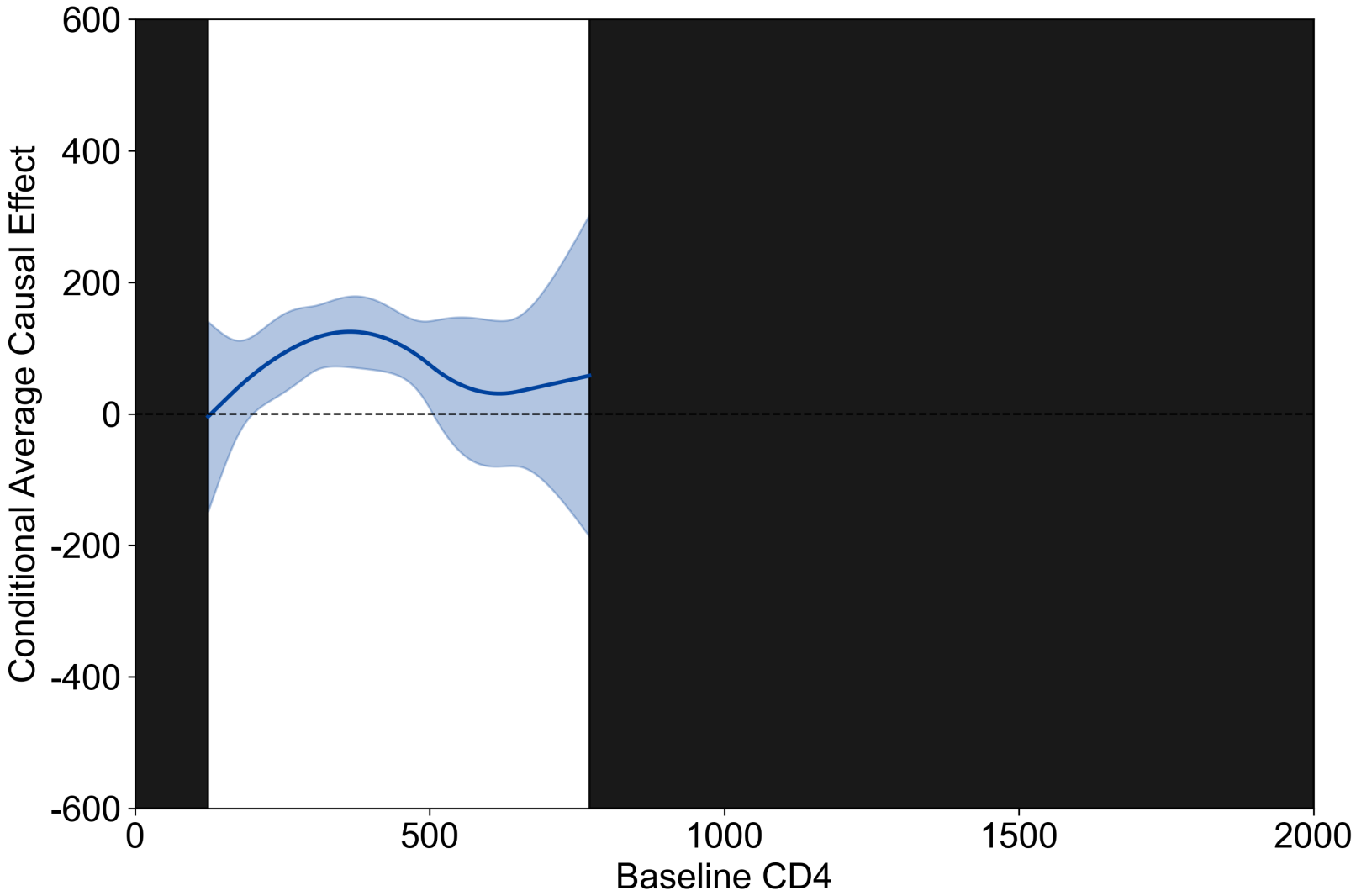
Conditional Average Causal Effect



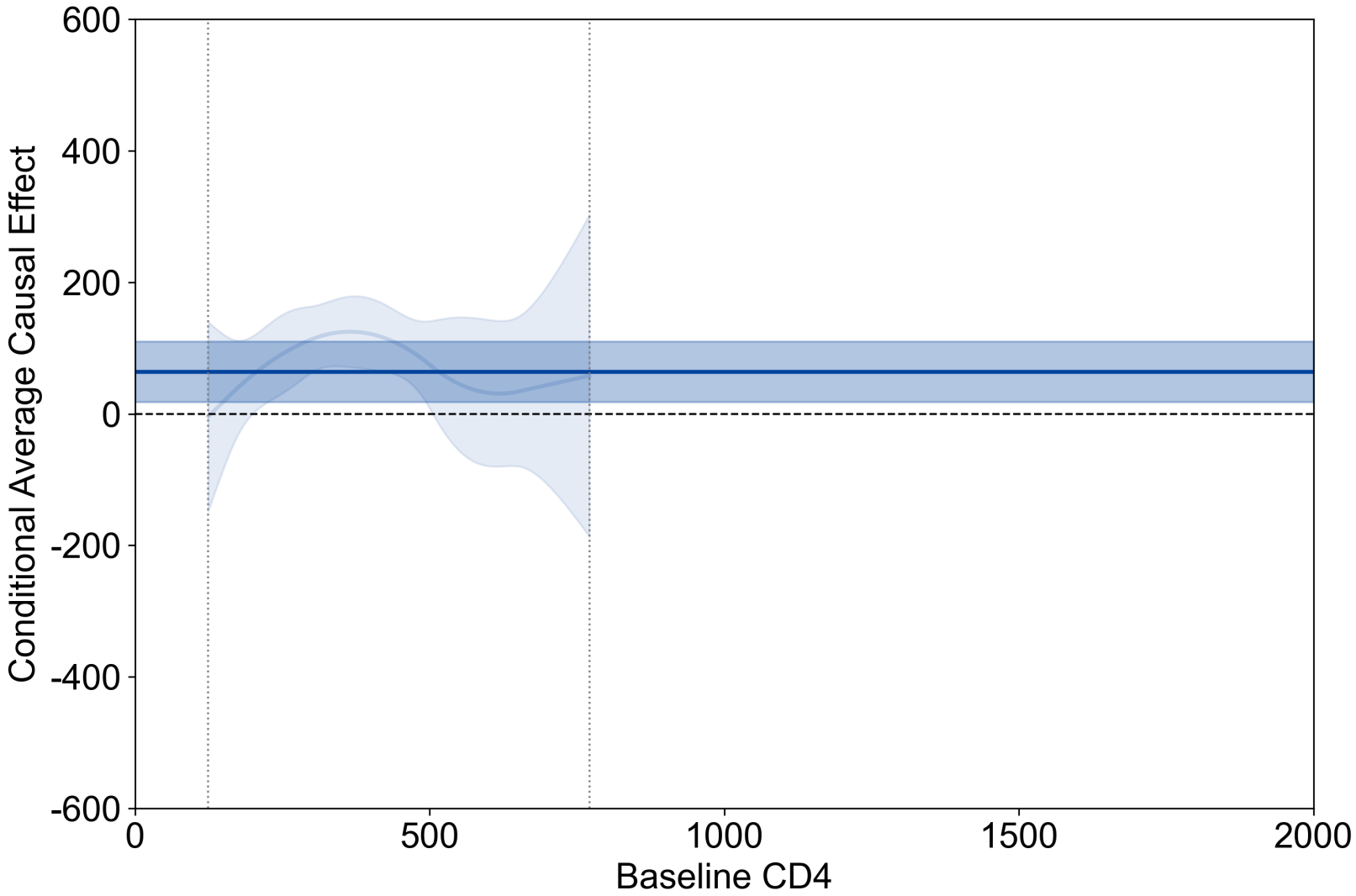
Challenge of Nonpositivity



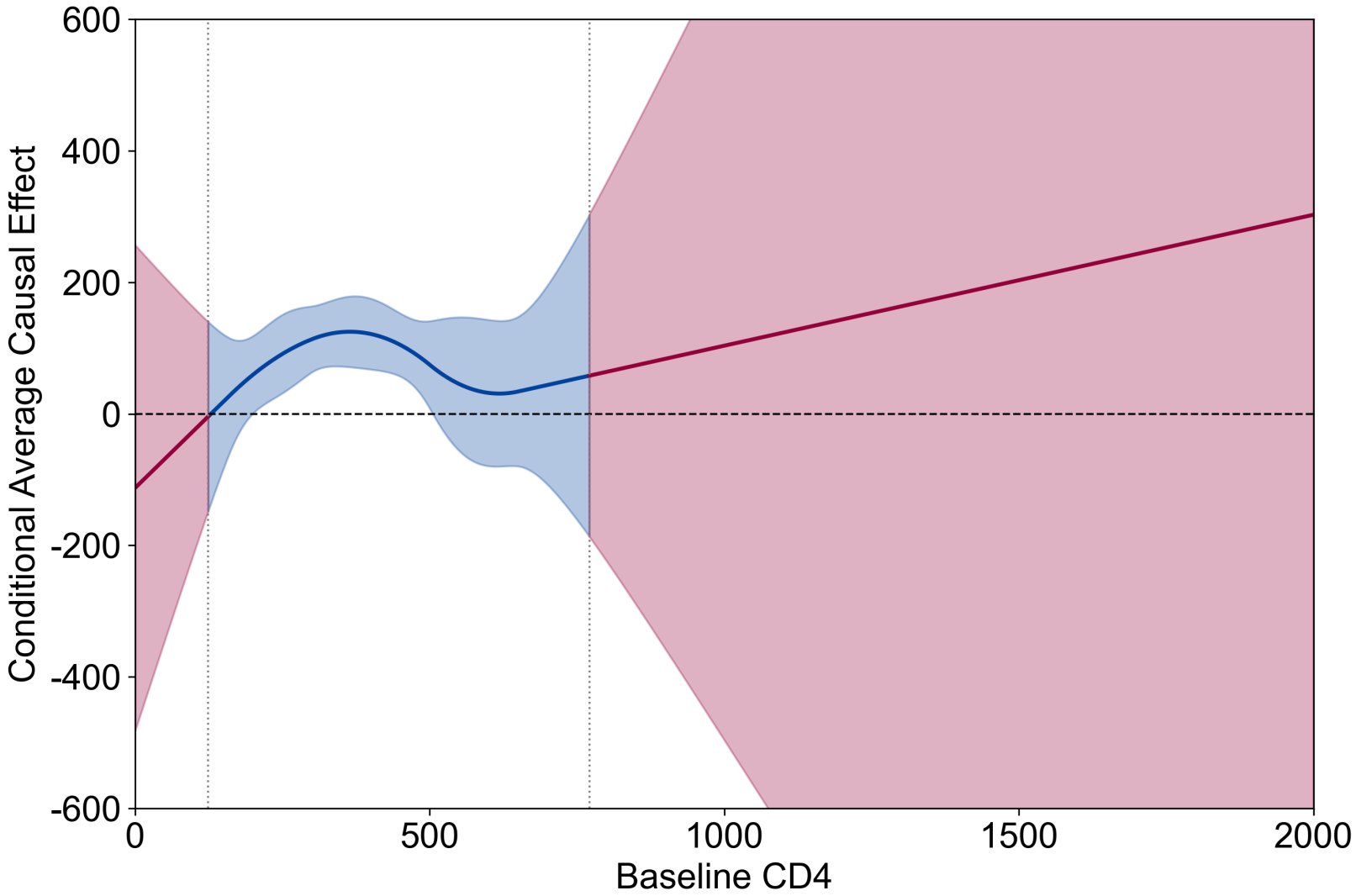
1. Restrict Target Population



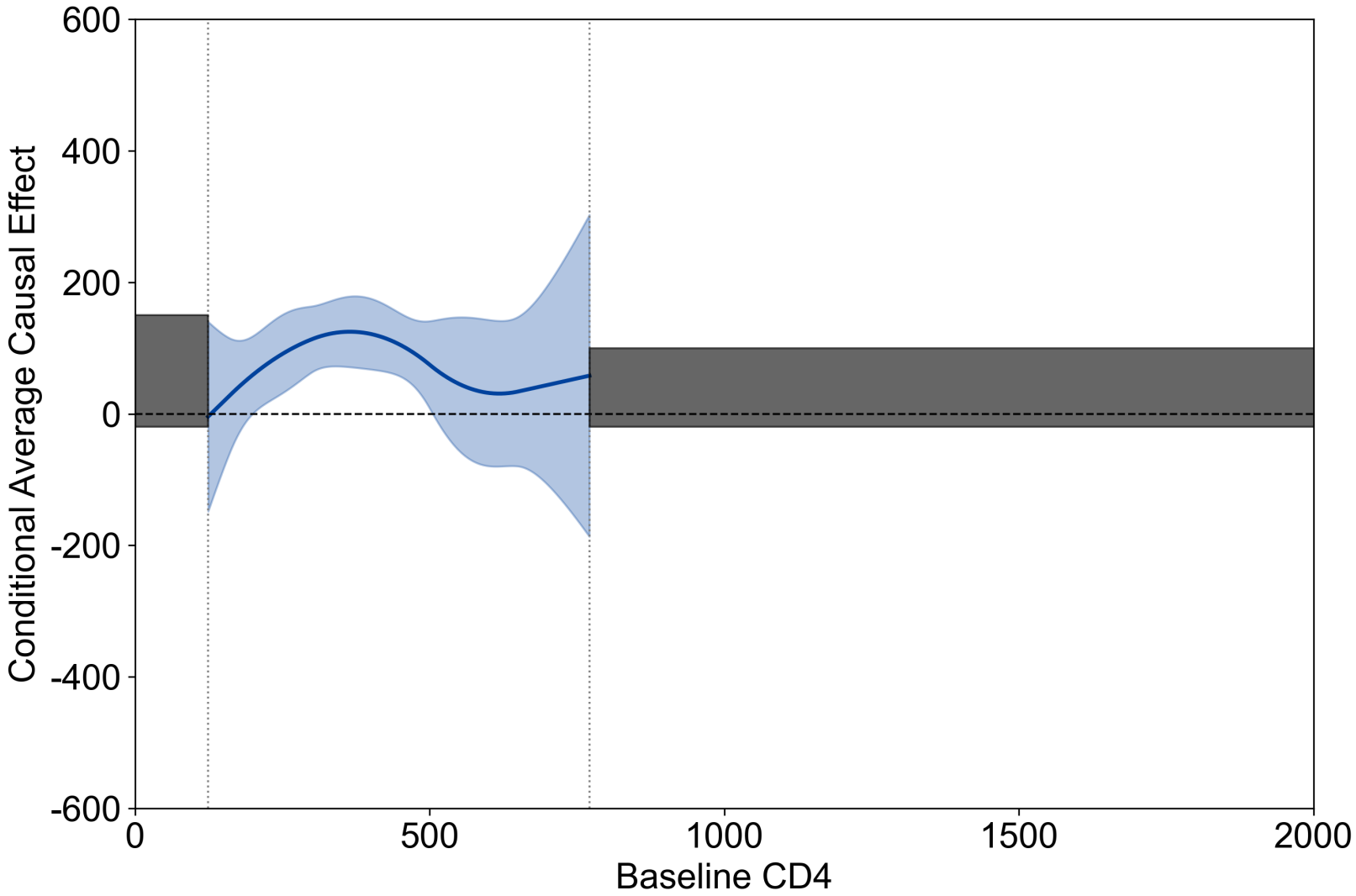
2. Restrict Covariate Set



3. Extrapolate



4. Synthesis of Statistical and Mathematical Model



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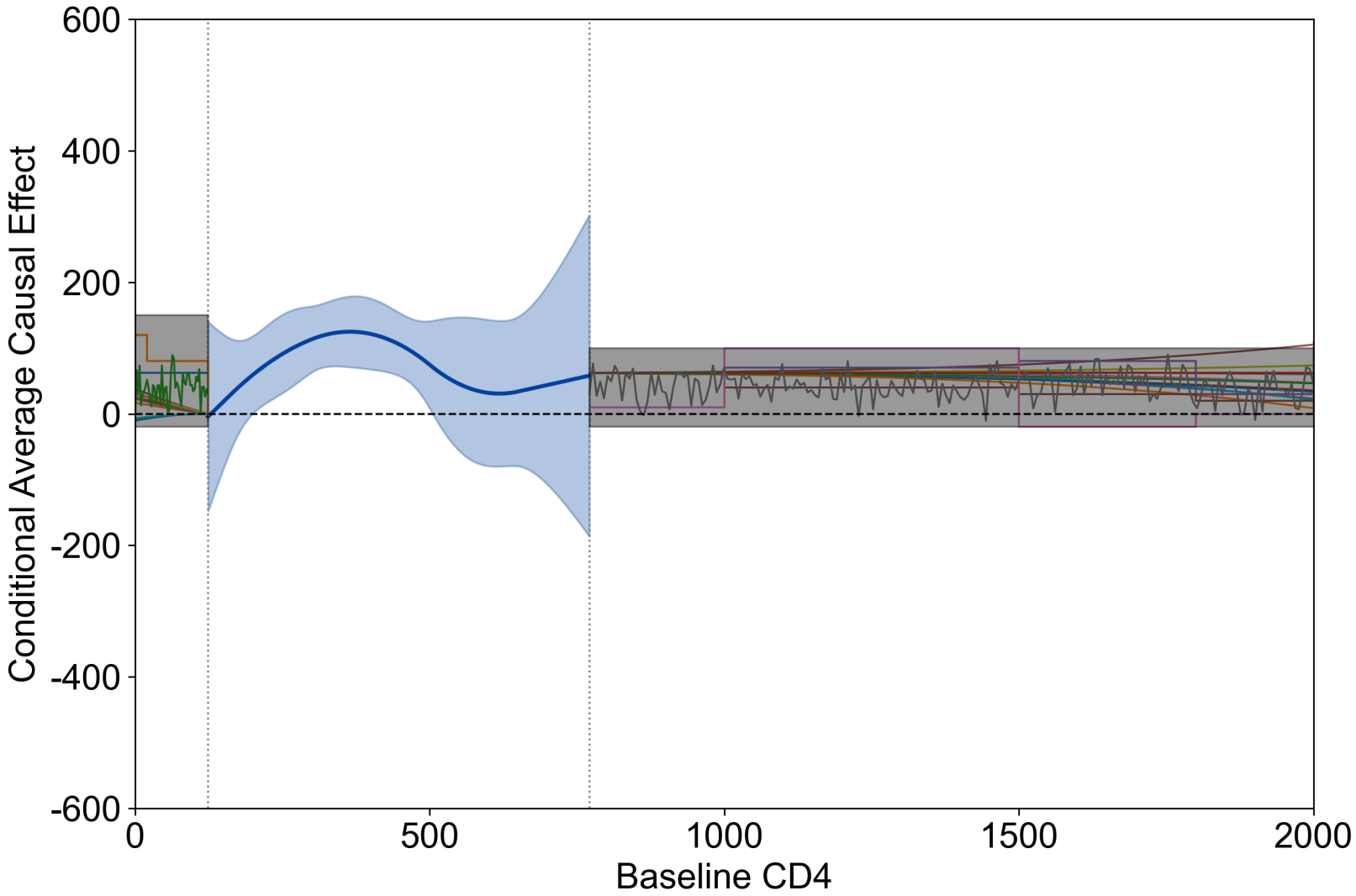
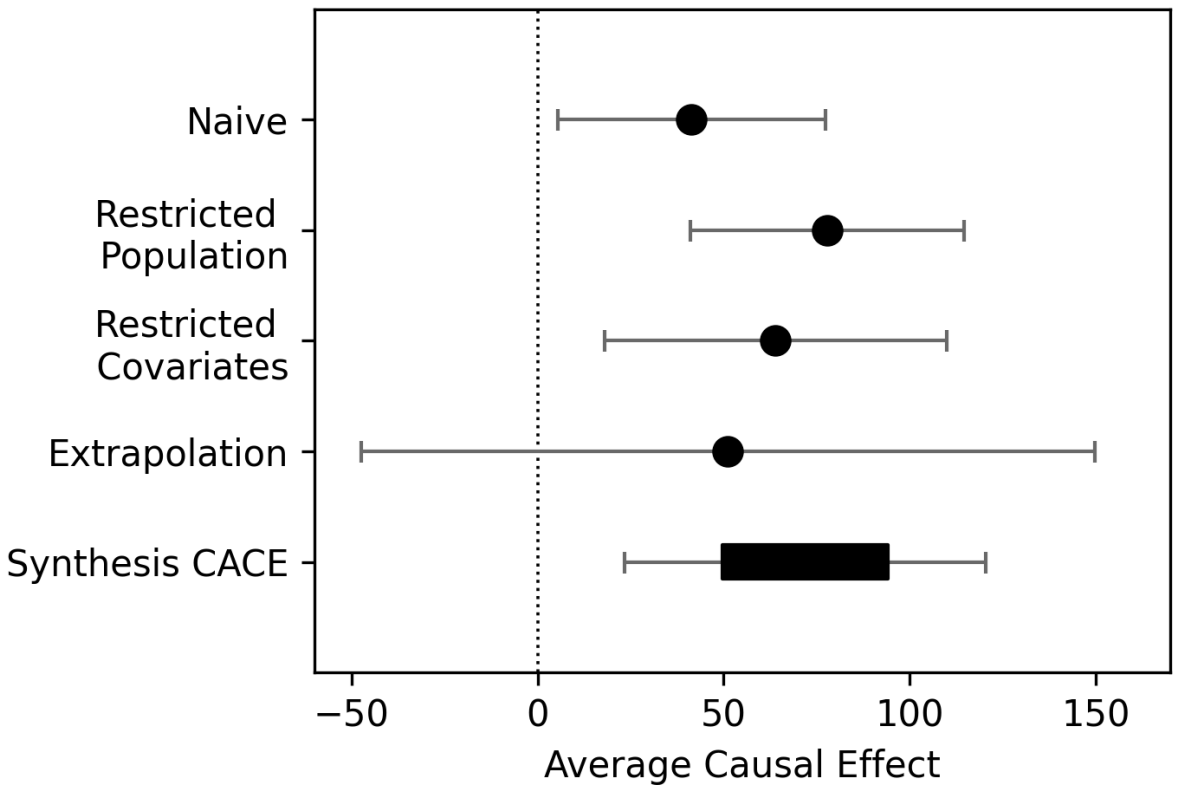


Estimated Average Causal Effect



	Estimate	95% CI
Naive	41	(5, 77)
Restricted Population	78	(41, 115)
Restricted Covariates	64	(18, 110)
Extrapolation	51	(-47, 150)
Synthesis CACE	[50, 94]	(23, 120)

Thank you!

Zivich PN et al. "Synthesis estimators for transportability with positivity violations by a continuous covariate". *arXiv*:2311.09388, under revision at the *Journal of the Royal Statistical Society Series A*

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