2020 SER Meeting Abstract

Nima S. Hejazi[a], Mark J. van der Laan[b], Holly E. Janes[c], Peter B. Gilbert[c], David C. Benkeser[d]

[a] *Graduate Group in Biostatistics, University of California, Berkeley*
[b] *Division of Epidemiology and Biostatistics, University of California, Berkeley*
[c] *Vaccine and Infectious Disease Division, Fred Hutchinson Cancer Research Center*
[d] *Department of Biostatistics and Bioinformatics, Emory University*

Abstract

Causal inference has traditionally focused on the effects of static interventions, under which the magnitude of the treatment is set to a fixed, prespecified value for each unit. The evaluation of such interventions faces a host of issues, among them non-identification, violations of the assumption of positivity, and inefficiency. Stochastic interventions provide a promising solution to these fundamental issues by allowing for the target parameter to be defined as the mean counterfactual outcome under a hypothetically shifted version of the observed exposure distribution. Despite the promise of such approaches, real data analyses are often further complicated by economic constraints, such as when the primary variable of interest is far more expensive to collect than auxiliary covariates. Two-phase sampling schemes are often used to bypass such limitations – unfortunately, their use produces side effects that require further adjustment when formal statistical inference is the principal goal of a study. We present a novel approach for use in such settings: augmented targeted minimum loss and one-step estimators for the causal effects of stochastic interventions, with guarantees of consistency, efficiency, and multiple robustness even in the presence of two-phase sampling. We further propose a technique that utilizes the estimated causal effects of stochastic interventions to construct a nonparametric working marginal structural model to summarize the effect of shifting an exposure variable on the outcome of interest, analogous to a dose-response analysis. Using data from the recent HVTN 505 HIV vaccine efficacy trial, we demonstrate this technique by assessing the effects of changes in post-vaccination immunogenicity on HIV-1 acquisition across a range of possible shifts, outlining a highly interpretable variable importance measure for ranking multiple immune responses based on their utility as immunogenicity study endpoints in future HIV-1 vaccine trials.

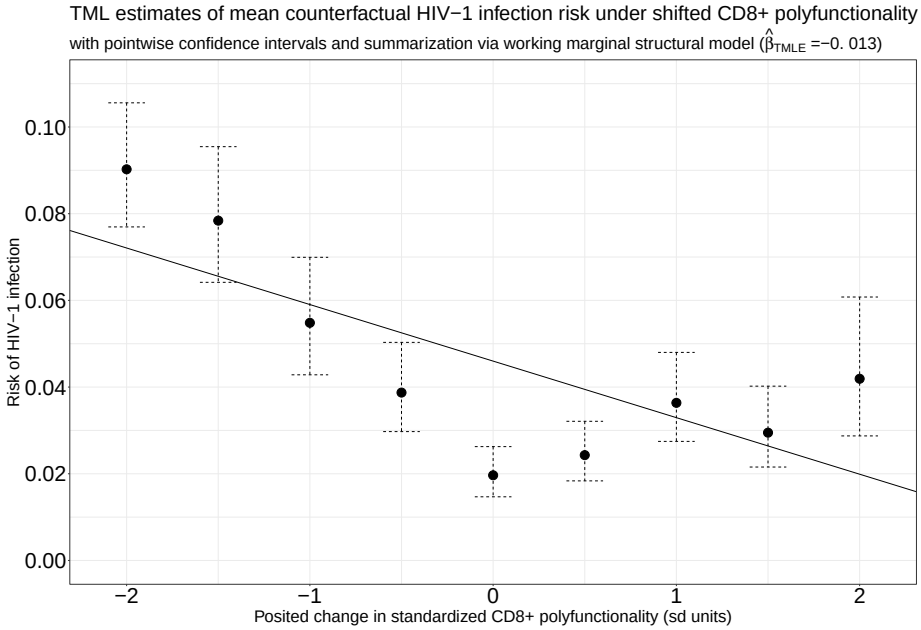
---

*Character count: 1990 (with spaces)

**Corresponding author: nhejazi@berkeley.edu

Key words: causal inference, two-phase sampling, stochastic intervention, targeted learning, vaccine efficacy

Title: Assessing the causal effects of stochastic interventions in vaccine efficacy trials with two-phased designs


TML estimates of mean counterfactual HIV−1 infection risk under shifted CD8+ polyfunctionality
with pointwise confidence intervals and summarization via working marginal structural model ($\hat{\beta}_{TMLE}$ =−0. 013)
Risk of HIV−1 infection
0.00
0.02
0.04
0.06
0.08
0.10
−2
−1
0
1
2
Posited change in standardized CD8+ polyfunctionality (sd units)