2020 SER Meeting Abstract

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Abstract

Causal inference has classically focused on the effect of static interventions, under which, for each unit, the magnitude of the treatment is set to a fixed, prespecified value. 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 of causal inference, by allowing for the counterfactual intervention distribution to be defined as a function of its natural (observed) 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 work around such constraints – unfortunately, their use produces side effects that require further adjustment when formal 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 estimated counterfactual means under stochastic interventions to construct a nonparametric working marginal structural model to summarize the effects of changes in 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.

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*Title: Efficient estimation of stochastic interventions effects under two-phase sampling for the analysis of vaccine efficacy trials

**Character count: 1976 (with spaces)

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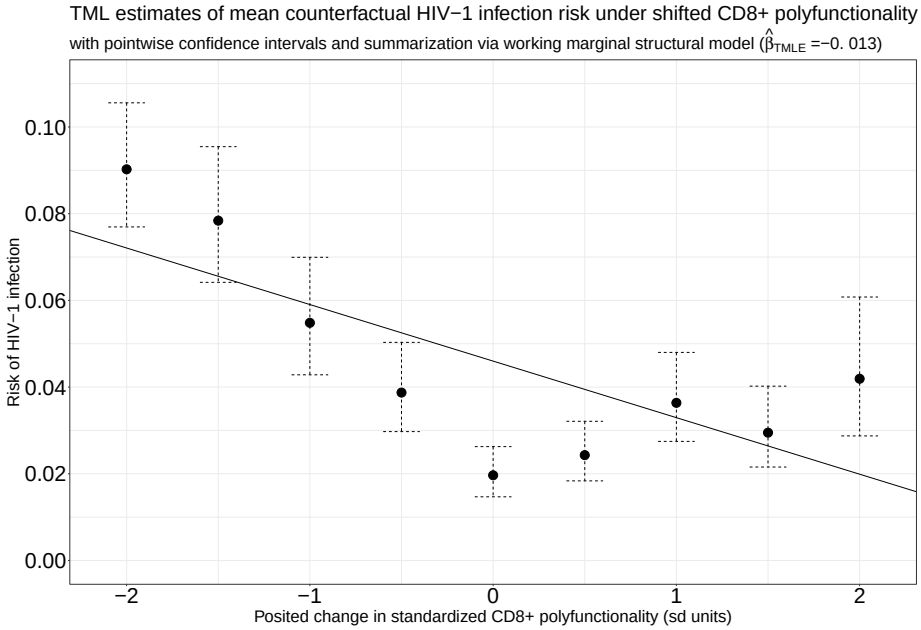
Key words: stochastic intervention, two-phase sampling, causal inference, targeted learning, vaccine efficacy trials


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)