Causal Inference with Partial Interference

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Contents

Background and Motivation

Overview

- Standard causal inference methods often make use of the assumption of no interference, which states that an observation's treatment does not affect any other observation's outcome
- One area where this assumption may fail to hold is in vaccine trials, where a person's level of infection may depend on who else is vaccinated (i.e., herd immunity)
- Failure to account for this interference may result in traditional estimators being biased
- Today, we review methods for estimation and inference in the context of vaccine trials and present simulation results for commonly used estimators

Motivating Example

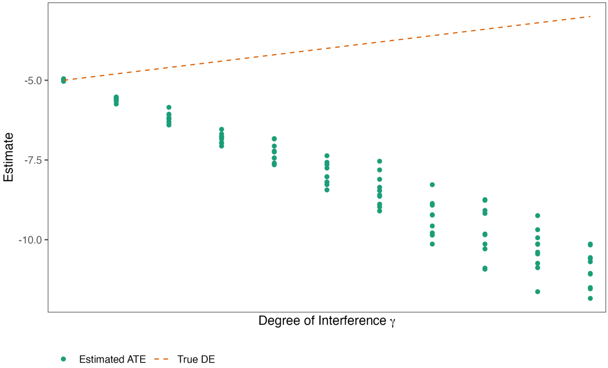
Consider the following (hypothetical) vaccine trial:

- We want to study the effectiveness of vaccination on the continuous outcome of infection level in a study population which consists of 5 geographically separate regions or groups
- In particular, we want to compare the effectiveness of two vaccination strategies, one in which 30% of individuals are vaccinated (ψ) and the other in which 50% of individuals are vaccinated (ϕ)
- 100 individuals are recruited to each group
- We randomize 3 of 5 groups to treatment strategy ψ and the other 2 groups to strategy ϕ
- Within each group, we randomly assign individuals vaccine vs. placebo depending on whether the group is assigned ψ vs. ϕ

Motivating Example

- We simulated data from this hypothetical trial, varying the level of interference within a group (to be formalized later)
- Individuals experience reduced levels of infection if other individuals in the same group receive vaccination
- This effect grows stronger as the level of interference increases!
- What happens if we analyze the data ignoring interference?

Motivating Example



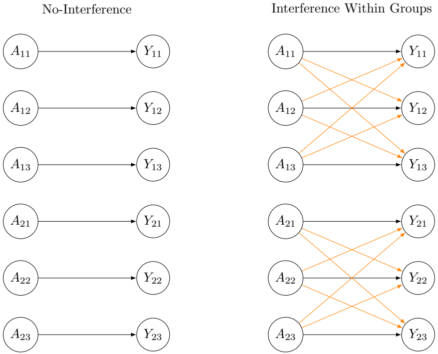
- Under no interference, the naive estimate of the ATE is unbiased for the true direct effect (to be formalized later)
- As degree of interference increases, these estimates become increasingly biased!

Definition, Notations, and Setup

Following the notation of Hudgens and Halloran [2008]:

- Suppose there are N groups of individuals
- Block i holds n_i individuals
- $\mathbf{A}_i = (A_{i1}, A_{i2}, ..., A_{in_i})$ is the vector of treatment assignments
- $\mathbf{A}_{i(j)}$ is the subvector of treatments in block i excluding observation j

Partial Interference



- We assume **partial interference**: treatment of one individual may affect the outcome of themselves and others in their block, but may not affect the outcomes of individuals outside of their block
- Violations of this assumption are known as contamination

Group (Two-Stage) Randomization

- Our setup assumes group (two-stage) randomization where the first stage randomizes each group to a treatment strategy and then the second stage randomizes $\mathbf{A}_i$ according to said treatment strategy
- Denote the treatment strategy assigned to group i as S_i, where $S_i \in \{\psi, \phi\}$
- Type A treatment strategies fix the number of treated individuals in a group (like in CREs), whereas Type B treatment strategies employ Bernoulli randomization
- In our hypothetical vaccine trial, ψ refers to the treatment assignment strategy where 30% of individuals in a group are randomized to vaccination, whereas ϕ refers to the strategy where 50% of individuals are randomzied to vaccination
- Group (two-stage) randomization is not to be confused with cluster randomization, where we cannot learn about direct and indirect effects

Potential Outcome Framework with Interference

- Assuming no interference, an individual typically has two potential outcomes, $Y_{ij}(a)$ for $a \in \{0, 1\}$
- With partial interference, we let an individual's potential outcomes depend on the treatment assignments of other units in the same block
- Denote $Y_{ij}(\mathbf{a}_i)$ as the potential outcome for observation j of block i when the treatment program for block i is set to $\mathbf{a}_i$
- Note: $Y_{ij}(\mathbf{a}_i) = Y_{ij}(\mathbf{a}_{i(j)}, A_{ij} = a_{ij})$
- Each individual in block i now has 2^{n_i} assuming partial interference!

Potential Outcome Framework with Interference

- With so many potential outcomes to consider, we may be interested in averaging over potential outcomes
- Denote the individual average potential outcome for individual j in block j under treatment a_{ij} and assignment strategy ψ as:

$$\begin{aligned}\bar{Y}_{ij}(a|\psi) &= E_{\psi}[Y_{ij}(\mathbf{a}_i)|A_{ij}=a] \\ &= \sum_{\omega \in \psi^{n_i-1}} Y_{ij}(\mathbf{A}_{i(j)}=\omega, A_{ij}=a) \cdot Pr_{\psi}(\mathbf{A}_{i(j)}=\omega|A_{ij}=a)\end{aligned}$$

  where ψ^{n_i-1} denotes all possible treatment assignments for $\mathbf{a}_{i(j)}$ that are consistent with treatment assignment strategy ψ
- Similarly, we can define group and population average potential outcomes:

$$\bar{Y}_i(a|\psi) = \frac{1}{n_i}\sum_{j=1}^{n_i}\bar{Y}_{ij}(a|\psi), \qquad \bar{Y}(a|\psi) = \frac{1}{N}\sum_{i=1}^{N}\bar{Y}_i(a|\psi)$$

Potential Outcome Framework with Interference

- Similarly, we can define marginal individual average potential outcomes:

$$\begin{aligned}\bar{Y}_{ij}(\psi) &= \mathbb{E}_\psi[Y_{ij}(\mathbf{a}_i)] \\ &= \sum_{\omega \in \psi^{n_i}} Y_{ij}(\omega) \cdot Pr_\psi(\mathbf{A}_i = \omega).\end{aligned}$$

  where ψ^{n_i} denotes all possible treatment assignments for $\mathbf{a}_i$ that are consistent with treatment assignment strategy ψ
- This is dependent solely as a function of the assigned group treatment strategy, and not the individual's treatment assignment as in $\bar{Y}_i(a|\psi)$
- Similarly, we can define group and population average potential outcomes:

$$\bar{Y}_i(\psi) = \frac{1}{n_i}\sum_{j=1}^{n_i} \bar{Y}_{ij}(\psi), \qquad \bar{Y}(\psi) = \frac{1}{N}\sum_{i=1}^{N} \bar{Y}_i(\psi)$$

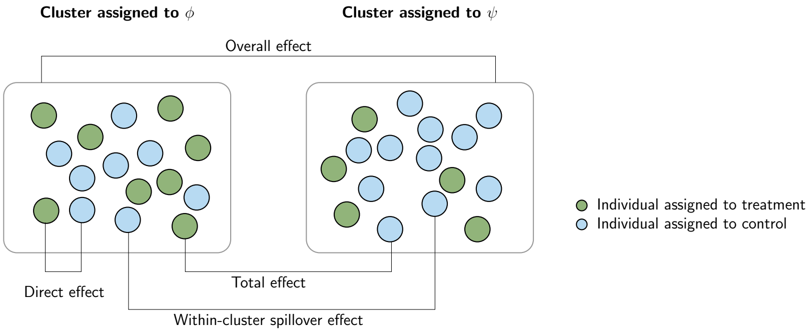
Causal Estimands

Causal Estimands

In interference, we are often interested in the following 4 causal estimands:

- Direct effects – effect of treatment of an individual on their own outcome holding other individuals' treatments at particular values
- Indirect effects – effect of other individuals' treatment assignments on the outcome of an untreated individual
- Total effects – the effect of both (1) changing an individual's own treatment and (2) changes in the treatments of other individuals in the same block on an individual's outcome
- Overall effects – the effect of changing the treatment assignment strategy of a block on an individual's outcome

Summary of causal estimands



Adapted from Halloran and Struchiner 1991, Benjamin-Chung et al 2018

Direct Effects

	Direct
Individual effects	$DE_{ij}(\boldsymbol{a}_{i(j)}) = Y_{ij}(\boldsymbol{a}_{i(j)}, A_{ij} = 1) - Y_{ij}(\boldsymbol{a}_{i(j)}, A_{ij} = 0)$
Individual average effects	$DE_{ij}(\psi) = \bar{Y}_{ij}(1\|\psi) - \bar{Y}_{ij}(0\|\psi)$
Group average effects	$DE_{i}(\psi) = \bar{Y}_{i}(1\|\psi) - \bar{Y}_{i}(0\|\psi)$
Population average effects	$DE(\psi) = \bar{Y}(1\|\psi) - \bar{Y}(0\|\psi)$

Under no interference, the direct effect has the ATE interpretation

Indirect effects

	Direct	Indirect
Individual effects	$DE_{ij}(\boldsymbol{a}_{i(j)})$ $= Y_{ij}(\boldsymbol{a}_{i(j)}, A_{ij} = 1)$ $- Y_{ij}(\boldsymbol{a}_{i(j)}, A_{ij} = 0)$	$IE_{ij}(\boldsymbol{a}_{i(j)}, \boldsymbol{a'}_{i(j)})$ $= Y_{ij}(\boldsymbol{a}_{i(j)}, A_{ij} = 0)$ $- Y_{ij}(\boldsymbol{a'}_{i(j)}, A_{ij} = 0)$
Individual average effects	$DE_{ij}(\psi)$ $= \bar{Y}_{ij}(1\|\psi) - \bar{Y}_{ij}(0\|\psi)$	$IE_{ij}(\phi, \psi)$ $= \bar{Y}_{ij}(0\|\phi) - \bar{Y}_{ij}(0\|\psi)$
Group average effects	$DE_{i}(\psi)$ $= \bar{Y}_{i}(1\|\psi) - \bar{Y}_{i}(0\|\psi)$	$IE_{i}(\phi, \psi)$ $= \bar{Y}_{i}(0\|\phi) - \bar{Y}_{i}(0\|\psi)$
Population average effects	$DE(\psi)$ $= \bar{Y}(1\|\psi) - \bar{Y}(0\|\psi)$	$IE(\phi, \psi)$ $= \bar{Y}(0\|\phi) - \bar{Y}(0\|\psi)$

Under no interference, all IE's are equal to 0

Total effects

	Direct	Indirect	Total
Individual effects	$DE_{ij}(\boldsymbol{a}_{i(j)}) = Y_{ij}(\boldsymbol{a}_{i(j)}, A_{ij} = 1) - Y_{ij}(\boldsymbol{a}_{i(j)}, A_{ij} = 0)$	$IE_{ij}(\boldsymbol{a}_{i(j)}, \boldsymbol{a}'_{i(j)}) = Y_{ij}(\boldsymbol{a}_{i(j)}, A_{ij} = 0) - Y_{ij}(\boldsymbol{a}'_{i(j)}, A_{ij} = 0)$	$TE_{ij}(\boldsymbol{a}_{i(j)}, \boldsymbol{a}'_{i(j)}) = Y_{ij}(\boldsymbol{a}_{i(j)}, A_{ij} = 1) - Y_{ij}(\boldsymbol{a}'_{i(j)}, A_{ij} = 0)$
Individual average effects	$DE_{ij}(\psi) = \bar{Y}_{ij}(1 \vert \psi) - \bar{Y}_{ij}(0 \vert \psi)$	$IE_{ij}(\phi, \psi) = \bar{Y}_{ij}(0 \vert \phi) - \bar{Y}_{ij}(0 \vert \psi)$	$TE_{ij}(\phi, \psi) = \bar{Y}_{ij}(1 \vert \phi) - \bar{Y}_{ij}(0 \vert \psi)$
Group average effects	$DE_i(\psi) = \bar{Y}_i(1 \vert \psi) - \bar{Y}_i(0 \vert \psi)$	$IE_i(\phi, \psi) = \bar{Y}_i(0 \vert \phi) - \bar{Y}_i(0 \vert \psi)$	$TE_i(\phi, \psi) = \bar{Y}_i(1 \vert \phi) - \bar{Y}_i(0 \vert \psi)$
Population average effects	$DE(\psi) = \bar{Y}(1 \vert \psi) - \bar{Y}(0 \vert \psi)$	$IE(\phi, \psi) = \bar{Y}(0 \vert \phi) - \bar{Y}(0 \vert \psi)$	$TE(\psi) = \bar{Y}(1 \vert \phi) - \bar{Y}(0 \vert \psi)$

Under no interference, the TE is equal to the DE

Overall effects

	Direct	Indirect	Total	Overall
Individual effects	$DE_{ij}(\boldsymbol{a}_{i(j)})$ $= Y_{ij}(\boldsymbol{a}_{i(j)}, A_{ij} = 1)$ $- Y_{ij}(\boldsymbol{a}_{i(j)}, A_{ij} = 0)$	$IE_{ij}(\boldsymbol{a}_{i(j)}, \boldsymbol{a}'_{i(j)})$ $= Y_{ij}(\boldsymbol{a}_{i(j)}, A_{ij} = 0)$ $- Y_{ij}(\boldsymbol{a}'_{i(j)}, A_{ij} = 0)$	$TE_{ij}(\boldsymbol{a}_{i(j)}, \boldsymbol{a}'_{i(j)})$ $= Y_{ij}(\boldsymbol{a}_{i(j)}, A_{ij} = 1)$ $- Y_{ij}(\boldsymbol{a}'_{i(j)}, A_{ij} = 0)$	$OE_{ij}(\boldsymbol{a}_i, \boldsymbol{a}'_i)$ $= Y_{ij}(\boldsymbol{a}_i) - Y_{ij}(\boldsymbol{a}'_i)$
Individual average effects	$DE_{ij}(\psi)$ $= \bar{Y}_{ij}(1\vert\psi) - \bar{Y}_{ij}(0\vert\psi)$	$IE_{ij}(\phi, \psi)$ $= \bar{Y}_{ij}(0\vert\phi) - \bar{Y}_{ij}(0\vert\psi)$	$TE_{ij}(\phi, \psi)$ $= \bar{Y}_{ij}(1\vert\phi) - \bar{Y}_{ij}(0\vert\psi)$	$OE_{ij}(\phi, \psi)$ $= \bar{Y}_{ij}(\phi) - \bar{Y}_{ij}(\psi)$
Group average effects	$DE_i(\psi)$ $= \bar{Y}_i(1\vert\psi) - \bar{Y}_i(0\vert\psi)$	$IE_i(\phi, \psi)$ $= \bar{Y}_i(0\vert\phi) - \bar{Y}_i(0\vert\psi)$	$TE_i(\phi, \psi)$ $= \bar{Y}_i(1\vert\phi) - \bar{Y}_i(0\vert\psi)$	$OE_i(\phi, \psi)$ $= \bar{Y}_i(\phi) - \bar{Y}_i(\psi)$
Population average effects	$DE(\psi)$ $= \bar{Y}(1\vert\psi) - \bar{Y}(0\vert\psi)$	$IE(\phi, \psi)$ $= \bar{Y}(0\vert\phi) - \bar{Y}(0\vert\psi)$	$TE(\psi)$ $= \bar{Y}(1\vert\phi) - \bar{Y}(0\vert\psi)$	$OE(\phi, \psi)$ $= \bar{Y}(\phi) - \bar{Y}(\psi)$

$OE_{ij}(\mathbf{a}_i, \mathbf{a}'_i)$ will equal $TE_{ij}(\mathbf{a}_{i(j)}, \mathbf{a}'_{i(j)})$ if $A_{ij} = 1$ in $\mathbf{a}_i$ and $A_{ij} = 0$ in $\mathbf{a}'_i$

Interpretations

In our hypothetical vaccine trial:

- $\overline{DE}(\psi)$ is the expected difference in level of infection when an individual is vaccinated versus unvaccinated, assuming all groups are assigned to randomization strategy ψ
- $\overline{IE}(\phi, \psi)$ is the expected difference in level of infection of an unvaccinated individual comparing the world where treatment mechanism ϕ was used to the world where treatment mechanism ψ was used.
- $\overline{TE}(\phi, \psi)$ is the expected difference in level of infection in an individual comparing the worlds where (1) they are treated and treatment mechanism ϕ was used and (2) they are untreated and treatment mechanism ψ was used
- $\overline{OE}(\phi, \psi)$ is the expected difference in level of infection in an individual comparing the worlds where (1) treatment mechanism ϕ was used and (2) treatment mechanism ψ was used

Identification, Estimation, and Inference

Intuition

	Direct	**Indirect**	**Total**	**Overall**
Individual effects	$DE_{ij}\big(\boldsymbol{a}_{i(j)}\big) = Y_{ij}\big(\boldsymbol{a}_{i(j)}, A_{ij} = 1\big) - Y_{ij}\big(\boldsymbol{a}_{i(j)}, A_{ij} = 0\big)$	$IE_{ij}\big(\boldsymbol{a}_{i(j)}, \boldsymbol{a'}_{i(j)}\big) = Y_{ij}\big(\boldsymbol{a}_{i(j)}, A_{ij} = 0\big) - Y_{ij}\big(\boldsymbol{a'}_{i(j)}, A_{ij} = 0\big)$	$TE_{ij}\big(\boldsymbol{a}_{i(j)}, \boldsymbol{a'}_{i(j)}\big) = Y_{ij}\big(\boldsymbol{a}_{i(j)}, A_{ij} = 1\big) - Y_{ij}\big(\boldsymbol{a'}_{i(j)}, A_{ij} = 0\big)$	$OE_{ij}(\boldsymbol{a}_i, \boldsymbol{a'}_i) = Y_{ij}(\boldsymbol{a}_i) - Y_{ij}(\boldsymbol{a'}_i)$
Individual average effects	$DE_{ij}(\psi) = \bar{Y}_{ij}(1\|\psi) - \bar{Y}_{ij}(0\|\psi)$	$IE_{ij}(\phi, \psi) = \bar{Y}_{ij}(0\|\phi) - \bar{Y}_{ij}(0\|\psi)$	$TE_{ij}(\phi, \psi) = \bar{Y}_{ij}(1\|\phi) - \bar{Y}_{ij}(0\|\psi)$	$OE_{ij}(\phi, \psi) = \bar{Y}_{ij}(\phi) - \bar{Y}_{ij}(\psi)$

Similar to the case with no interference, we cannot identify / estimate individual effects, as we only observe one of many potential outcomes

Intuition

	Direct	Indirect	Total	Overall
Individual effects	$DE_{ij}\big(\boldsymbol{a}_{i(j)}\big) = Y_{ij}\big(\boldsymbol{a}_{i(j)}, A_{ij}=1\big) - Y_{ij}\big(\boldsymbol{a}_{i(j)}, A_{ij}=0\big)$	$IE_{ij}\big(\boldsymbol{a}_{i(j)}, \boldsymbol{a'}_{i(j)}\big) = Y_{ij}\big(\boldsymbol{a}_{i(j)}, A_{ij}=0\big) - Y_{ij}\big(\boldsymbol{a'}_{i(j)}, A_{ij}=0\big)$	$TE_{ij}\big(\boldsymbol{a}_{i(j)}, \boldsymbol{a'}_{i(j)}\big) = Y_{ij}\big(\boldsymbol{a}_{i(j)}, A_{ij}=1\big) - Y_{ij}\big(\boldsymbol{a'}_{i(j)}, A_{ij}=0\big)$	$OE_{ij}(\boldsymbol{a}_i, \boldsymbol{a'}_i) = Y_{ij}(\boldsymbol{a}_i) - Y_{ij}(\boldsymbol{a'}_i)$
Individual average effects	$DE_{ij}(\psi) = \bar{Y}_{ij}(1\vert\psi) - \bar{Y}_{ij}(0\vert\psi)$	$IE_{ij}(\phi,\psi) = \bar{Y}_{ij}(0\vert\phi) - \bar{Y}_{ij}(0\vert\psi)$	$TE_{ij}(\phi,\psi) = \bar{Y}_{ij}(1\vert\phi) - \bar{Y}_{ij}(0\vert\psi)$	$OE_{ij}(\phi,\psi) = \bar{Y}_{ij}(\phi) - \bar{Y}_{ij}(\psi)$
Group average effects	$DE_i(\psi) = \bar{Y}_i(1\vert\psi) - \bar{Y}_i(0\vert\psi)$	$IE_i(\phi,\psi) = \bar{Y}_i(0\vert\phi) - \bar{Y}_i(0\vert\psi)$	$TE_i(\phi,\psi) = \bar{Y}_i(1\vert\phi) - \bar{Y}_i(0\vert\psi)$	$OE_i(\phi,\psi) = \bar{Y}_i(\phi) - \bar{Y}_i(\psi)$

$DE_i(\psi)$ may be identified / estimated as long a group assigned to ψ has individuals assigned to both treatment and control – likewise for $DE_i(\phi)$

Intuition

	Direct	**Indirect**	**Total**	**Overall**
Individual effects	$DE_{ij}(\boldsymbol{a}_{i(j)})$ $= Y_{ij}(\boldsymbol{a}_{i(j)}, A_{ij}=1)$ $- Y_{ij}(\boldsymbol{a}_{i(j)}, A_{ij}=0)$	$IE_{ij}(\boldsymbol{a}_{i(j)}, \boldsymbol{a}'_{i(j)})$ $= Y_{ij}(\boldsymbol{a}_{i(j)}, A_{ij}=0)$ $- Y_{ij}(\boldsymbol{a}'_{i(j)}, A_{ij}=0)$	$TE_{ij}(\boldsymbol{a}_{i(j)}, \boldsymbol{a}'_{i(j)})$ $= Y_{ij}(\boldsymbol{a}_{i(j)}, A_{ij}=1)$ $- Y_{ij}(\boldsymbol{a}'_{i(j)}, A_{ij}=0)$	$OE_{ij}(\boldsymbol{a}_i, \boldsymbol{a}'_i)$ $= Y_{ij}(\boldsymbol{a}_i) - Y_{ij}(\boldsymbol{a}'_i)$
Individual average effects	$DE_{ij}(\psi)$ $= \bar{Y}_{ij}(1\|\psi) - \bar{Y}_{ij}(0\|\psi)$	$IE_{ij}(\phi,\psi)$ $= \bar{Y}_{ij}(0\|\phi) - \bar{Y}_{ij}(0\|\psi)$	$TE_{ij}(\phi,\psi)$ $= \bar{Y}_{ij}(1\|\phi) - \bar{Y}_{ij}(0\|\psi)$	$OE_{ij}(\phi,\psi)$ $= \bar{Y}_{ij}(\phi) - \bar{Y}_{ij}(\psi)$
Group average effects	$DE_i(\psi)$ $= \bar{Y}_i(1\|\psi) - \bar{Y}_i(0\|\psi)$	$IE_i(\phi,\psi)$ $= \bar{Y}_i(0\|\phi) - \bar{Y}_i(0\|\psi)$	$TE_i(\phi,\psi)$ $= \bar{Y}_i(1\|\phi) - \bar{Y}_i(0\|\psi)$	$OE_i(\phi,\psi)$ $= \bar{Y}_i(\phi) - \bar{Y}_i(\psi)$
Population average effects	$DE(\psi)$ $= \bar{Y}(1\|\psi) - \bar{Y}(0\|\psi)$	$IE(\phi,\psi)$ $= \bar{Y}(0\|\phi) - \bar{Y}(0\|\psi)$	$TE(\psi)$ $= \bar{Y}(1\|\phi) - \bar{Y}(0\|\psi)$	$OE(\phi,\psi)$ $= \bar{Y}(\phi) - \bar{Y}(\psi)$

All population average effects may be identified / estimated as long as the population has groups assigned to both ψ and ϕ, and all groups have individuals assigned to both treatment and control

Estimation

Let

$$\hat{Y}_i(a|\psi) = \frac{\sum_{j=1}^{n_i} I(A_{ij} = a) Y_{ij}}{\sum_{j=1}^{n_i} I(A_{ij} = a)} \text{ for groups assigned to } \psi,$$

$$\hat{Y}(a|\psi) = \frac{\sum_{i=1}^{N} \hat{Y}_i(a|\psi) I(S_i = \psi)}{\sum_{i=1}^{N} I(S_i = \psi)}$$

$$\hat{Y}_i(\psi) = \frac{\sum_{j=1}^{n_i} Y_{ij}}{n_i}, \text{ for groups assigned to } \psi$$

$$\hat{Y}(\psi) = \frac{\sum_{i=1}^{n_i} \hat{Y}_i(\psi) I(S_i = \psi)}{\sum_{i=1}^{N} I(S_i = \psi)}.$$

and analogously for $\hat{Y}_i(a|\phi)$, $\hat{Y}(a|\phi)$ and $\hat{Y}(\phi)$.

Estimation

Hudgens and Halloran [2008] propose the following estimators

$$\widehat{DE}_i(\psi) = \hat{Y}_i(0|\psi) - \hat{Y}_i(1|\psi),$$

$$\widehat{DE}(\psi) = \hat{Y}(0|\psi) - \hat{Y}(1|\psi),$$

$$\widehat{IE}(\phi, \psi) = \hat{Y}(0|\phi) - \hat{Y}(0|\psi),$$

$$\widehat{TE}(\phi, \psi) = \hat{Y}(1|\phi) - \hat{Y}(0|\psi),$$

$$\widehat{OE}(\phi, \psi) = \hat{Y}(\phi) - \hat{Y}(\psi),$$

Under the assumption that a Type A treatment strategy is used to assign groups and individuals, they show that these estimators are unbiased for the true causal estimands

Inference

- For inference, most methods make the assumption of stratified interference
- **Assumption (Stratified interference)**: For any treatment assignment ψ, $Y_{ij}(\mathbf{A}_{i(j)} = \mathbf{a}_{i(j)}, A_{ij} = a'_{ij}) = Y_{ij}(\mathbf{A}_{i(j)} = \mathbf{a}'_{i(j)}, A_{ij} = a'_{ij})$ for all $\mathbf{a}_{i(j)}, \mathbf{a}'_{i(j)} \in \psi^{n_i - 1}$. This means that the potential outcome doesn't depend on *who* else in a group is assigned treatment, just *how many* are assigned treatment
- Hudgens and Halloran [2008] propose conservative variance estimators for proposed estimators
- Liu and Hudgens [2014] propose confidence intervals based on asymptotic distributions under two regimes: one where the size of each group n_i grows large and the other where the number of groups N grows large
- Rigdon and Hudgens [2015] propose exact confidence intervals by inverting permutation tests when the outcome is binary
- Tchetgen and VanderWeele [2012] do not rely on this assumption and propose conservative confidence intervals based on a Hoeffding-type inequality

Towards observational studies...

Aforementioned estimators are for finite sample, fixed number of treatment assignment strategies, which do not hold in observational studies. Tchetgen and VanderWeele [2012] propose the following assuming ϕ and ψ are Bernoulli randomization strategies:

$$\hat{Y}_i^{ipw}(a|\psi) \equiv \frac{\sum_{j=1}^{n_i} Pr_\psi(\mathbf{A}_{i(j)} = \mathbf{A}_{i(j)}|L_i) I(A_{ij} = a) \mathbf{Y}_{ij}(\mathbf{A}_i)}{n_i Pr_\psi(A_i = 1|L_i)}, \qquad \text{and}$$

$$\hat{Y}_i^{ipw}(\psi) \equiv \frac{\sum_{j=1}^{n_i} Pr_\psi(\mathbf{A}_{i(j)} = \mathbf{A}_{i(j)}|L_i) \mathbf{Y}_{ij}(\mathbf{A}_i)}{n_i Pr_\psi(A_i = 1|L_i)}.$$

Under assumptions resembling conditional exchangeability and positivity, Tchetgen and VanderWeele [2012] demonstrate that our population average causal estimands are identified and that these estimators are unbiased

Simulation Study

Redefining the Direct Effect

- Is the direct effect really “direct”?

$$\begin{aligned}\bar{Y}_{ij}(a|\psi) &= E_\psi[Y_{ij}(\mathbf{a}_i)|A_{ij} = a] \\ &= \sum_{\omega \in \psi^{n_i - 1}} Y_{ij}(\mathbf{A}_{i(j)} = \omega, A_{ij} = a) \cdot Pr_\psi(\mathbf{A}_{i(j)} = \omega | A_{ij} = a)\end{aligned}$$

- In the finite sample setting, $\overline{DE}_i(\psi) = \bar{Y}_i(1|\psi) - \bar{Y}_i(0|\psi)$ includes the effect of an individual's own treatment as well as *one fewer other individuals being treated*.
- This is not a problem in the Bernoulli setting where $Pr_\psi(\mathbf{A}_{i(j)}|A_{ij}) = Pr_\psi(\mathbf{A}_{i(j)})$.

Redefining the Direct Effect

- VanderWeele and Tchetgen Tchetgen [2011] suggest a new definition of individual average counterfactuals to combat this.

$$\bar{Y}_{ij}^{*}(a|\psi, a') = \sum_{\omega \in \psi^{n_i - 1}} Y_{ij}(\mathbf{A}_{i(j)} = \omega, A_{ij} = a) Pr_{\psi}(\mathbf{A}_{i(j)} = \omega | A_{ij} = a')$$

$$\bar{Y}_{ij}^{*}(a|\psi) = \sum_{\omega \in \psi^{n_i}} Y_{ij}(\mathbf{A}_{i(j)} = \omega_{(j)}, A_{ij} = a) Pr_{\psi}(\mathbf{A}_{i} = \omega)$$

- New direct effect $\overline{DE}_i^*(\psi) = \bar{Y}_i^*(1|\psi) - \bar{Y}_i^*(0|\psi)$ only includes the effect of an individual's own treatment.
- Unfortunately, $\bar{Y}_i^*(a|\psi)$ is only identifiable under the Bernoulli setting, in which case the two versions of direct effect are identical.

Simulation Study: Setup

For our simulation, we assume a linear outcome model with an effect due to individual treatment and interference from the group. The coefficient on interference is ‘gamma‘, ranging from 0 to 2.

$$Y_{ij}(\mathbf{a}) = \beta_0 + \beta_1 a_j + \gamma \sum_{k \neq j} \beta_2 a_k + \epsilon_{ij}$$

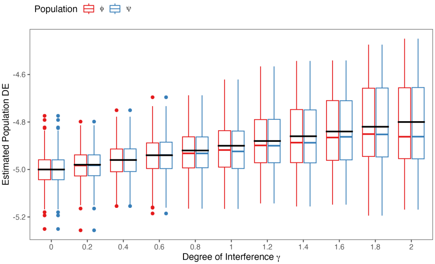
$$\epsilon_{ij} \sim N(0, \sigma^2 = 0.1)$$

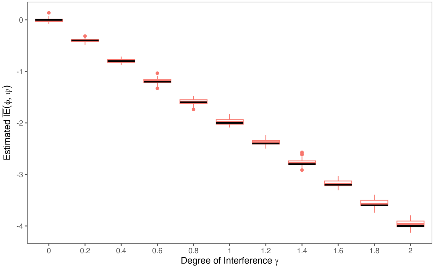
We set $\beta_0 = 10$ (baseline severity of infection with everyone unvaccinated), $\beta_1 = -5$ (a protective effect due to an individual's own vaccination) and $\beta_2 = -0.1$ (protection due to the vaccination of others, subject to the size of γ).

Simulation Setup: Finite Sample (Type A) Randomization

$S_i \sim$ finite sample from $\{\psi, \psi, \psi, \phi, \phi\}$

$$A_{ij} \sim \begin{cases} \text{finite sample from 30 treated, 70 untreated, w/o replacement if } S_i = \psi \\ \text{finite sample from 50 treated, 50 untreated, w/o replacement if } S_i = \phi \end{cases}$$



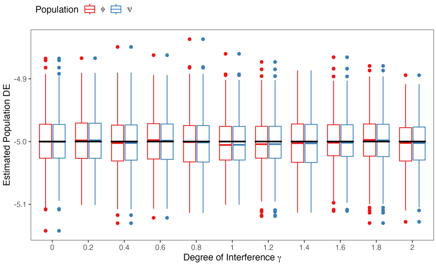


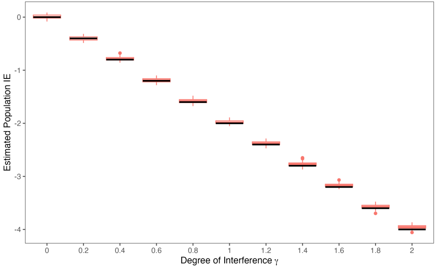
True $DE(\phi) = DE(\psi) = \beta_1 - \gamma\beta_2$, $\quad IE(\phi, \psi) = \gamma\beta_2(K_{\phi,n_i} - K_{\psi,n_i})$

Simulation Setup: Bernoulli (Type B) Randomization

Here, Bernoulli randomization means that the A_{ij}s are sampled independently rather than from a finite population.

$$S_i \sim \text{finite sample from } \{\psi, \psi, \psi, \phi, \phi\}, \quad A_{ij} \sim \begin{cases} \text{Bernoulli}(0.3) & \text{if } S_i = \psi \\ \text{Bernoulli}(0.5) & \text{if } S_i = \phi. \end{cases}$$





$$\text{True } DE^*(\phi) = DE^*(\psi) = \beta_1, \quad IE^*(\phi, \psi) = \gamma \beta_2 n_i (p_\phi - p_\psi)$$

Limitations, Current Research, Discussion

Limitations

A potentially non-exhaustive list:

- **Standard assumptions apply**. As usual, we need a version of positivity and consistency (this time at the group-level), and conditional randomization.
- **Partial and Stratified Interference**.
- **Group-Randomized Design**. Our data must resemble or be resultant from a *group-randomized design*.
- **Contamination**. Though these methods do construct unbiased estimators when interference is limited to within groups, if there is interference across groups that is either unknown or ignored and these estimators are applied as if such contamination does not exist, they will be biased.
- **Assumption of Homogeneous Mixture**. One assumption directly implied by stratified interference is that the effect of interference from other units only goes through the overall proportion of treated within groups.
- **Covariate Shift**. I.e., situations where the distribution of covariates differs between the treated and untreated groups in ways that can result in positivity violations or in residual confounding between the treatment assignment mechanism and outcome.

Current Research

We looked at works from 2020 or later on spillover effects in randomized trials:

- Aronow et al. [2021] in their book chapter *Spillover Effects in Experimental Data* present examples (anti-bullying school programs, unconditional cash-transfer programs, and get-out-the-vote efforts), present a Horvitz-Thompson style estimator, and the `interference` R package for dealing with network interference.
- Sävje et al. [2021] investigate the large-sample properties of estimators under unknown levels of interference in randomized experiments, deriving rates of convergence.
- Buchanan et al. [2022] estimate the effects of an HIV intervention among people who inject drugs using marginal structural models with the `interference` package.
- Jiang et al. [2022] describe a framework for conducting power analysis in two-stage randomized experiments.
- Vazquez-Bare [2023a] analyzes the identification of causal direct and spillover effects under one-sided noncompliance and show that causal effects can be estimated by 2SLS as in instrumental variables.
- Vazquez-Bare [2023b] proposes nonparametric estimators for average direct and spillover effects that are consistent, asymptotically normal, and illustrated using data from a conditional cash transfer program and via simulation.
- Hernández-Ramírez et al. [2024] report on a peer-education intervention among people who inject drugs, presenting overall, direct, spillover, and composite effects.

Discussion

- We introduced and motivated the estimation of direct and spillover effects in randomized trials.
- While total and overall effects can be validly estimated without taking spillover into account, disaggregation of total effects into direct effects and those due to spillover effects remains relevant in vaccine trials, epidemiology, and economics.
- To formalize spillover effects, we had to introduce Type A vs. Type B randomization.
- Our simulation study demonstrated the more intuitive nature of Tchetgen Tchetgen and VanderWeele's redefined direct effect, showing that spillover (indirect) effects can be estimated under the assumptions listed.
- Finally, we provide several limitations to the methods presented for handling interference in partially randomized settings.

Thank you!

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