



HAL
open science

Reweighting the RCT for generalization: finite sample analysis and variable selection

Bénédicte Colnet, Julie Josse, Gaël Varoquaux, Erwan Scornet

► **To cite this version:**

Bénédicte Colnet, Julie Josse, Gaël Varoquaux, Erwan Scornet. Reweighting the RCT for generalization: finite sample analysis and variable selection. 2022. hal-03822662v1

HAL Id: hal-03822662

<https://hal.science/hal-03822662v1>

Preprint submitted on 20 Oct 2022 (v1), last revised 4 Nov 2022 (v2)

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Reweighting the RCT for generalization: finite sample analysis and variable selection

Bénédicte Colnet ^{*} Julie Josse[†] Gaël Varoquaux[‡] Erwan Scornet [§]

October 20, 2022

Abstract

The limited scope of Randomized Controlled Trials (RCT) is increasingly under scrutiny, in particular when samples are unrepresentative. Indeed, some RCTs over- or under- sample individuals with certain characteristics compared to the target population, for which one wants to draw conclusions on treatment effectiveness. Re-weighting trial individuals to match the target population helps to improve the treatment effect estimation. Such procedures require an estimation of the ratio of the two densities (trial and target distributions). In this work, we establish the exact expressions of the bias and variance of such reweighting procedures - also called Inverse Propensity of Sampling Weighting (IPSW) - in presence of categorical covariates for any sample size. Such results allow us to compare the theoretical performance of different versions of IPSW estimates. Besides, our results show how the performance (bias, variance and quadratic risk) of IPSW estimates depends on the two sample sizes (RCT and target population). A by-product of our work is the proof of consistency of IPSW estimates. A refined analysis also shows that IPSW performances are improved when the trial probability to be treated is estimated (rather than using its oracle counterpart). In addition, we study how including covariates that are unnecessary to a proper estimation of the weights may impact the asymptotic variance. We illustrate all the takeaways twice: in a toy and didactic example, and on a semi-synthetic simulation inspired from critical care medicine.

Keywords: Average treatment effect (ATE); Sampling bias; External validity; Transportability; Distributional shift; IPSW.

1 Introduction

Motivation Modern *evidence-based* medicine puts Randomized Controlled Trial (RCT) at the core of most, if not all clinical evidence. Indeed, randomization enables to estimate the average treatment effect (called ATE) by avoiding any confounding effect of spurious or undesirable associated factors. But more recently, concerns have been raised on the limited scope of RCTs: stringent eligibility criteria, unrealistic real-world compliance, short timeframe, limited sample size, etc. All these drawbacks hint to a possible lack of external validity of these studies to other situations or populations (Rothwell, 2007; Gatsonis and Sally, 2017; Deaton and Cartwright, 2018). The usage of complementary non-randomized data, referred to as *observational* or from the *real world*, is bringing many promises as being future additional sources of evidence, in particular when combined to trials (Kallus et al., 2018; Athey et al., 2020; Liu et al., 2021). For example, assume a policy maker is reading the results from a newly published RCT which comes with great promises about a new treatment. But when reading the report, he/she may discover that the RCT is composed of substantially younger people than the target population of interest. Such a situation can be deduced when discovering the so-called *Table 1* of this newly published trial. In case of treatment effect heterogeneities, for e.g. if the younger individuals respond better to the treatment, the ATE estimated from the trial is over-estimated and then biased. Now, assume this policy maker has also at disposal a sample of the actual patients in the district, being a representative sample of the true distribution of age in this population (with, most of the time, no information on the outcome or the treatment). Can we use this representative sample of the target population of interest to *re-weight* or to *generalize* the trial's findings? The answer is *yes*, while the exact strategy has been formalized and popularized recently (Stuart et al., 2011; Pearl and Bareinboim, 2011; Bareinboim and Pearl, 2012a,b; Tipton, 2013; O'Muircheartaigh and Hedges, 2013; Hartman et al., 2015; Kern et al., 2016; Dahabreh et al., 2020) (reviewed in Colnet et al. (2020); Degtiar and Rose (2021)) and can come under many

^{*}Soda project-team, Premedical project-team, INRIA (email: benedicte.colnet@inria.fr).

[†]Premedical project team, INRIA Sophia-Antipolis, Montpellier, France.

[‡]Soda project-team, INRIA Saclay, France.

[§]Centre de Mathématiques Appliquées, UMR 7641, École polytechnique, CNRS, Institut Polytechnique de Paris, Palaiseau, France.

variants named *generalization*, *transportability*, *recoverability*, and *data-fusion*. In fact, the idea of re-weighting a trial can be traced back before the 2010’s. Several books of epidemiology had already presented the idea of trial re-weighting under the name *standardization* (Rothman and Greenland, 2000; Rothman, 2011). In this work, we exclusively focus on this question, and more particularly on one estimator: the *Inverse Propensity of Sampling Weighting* (IPSW) (Cole and Stuart, 2010; Stuart et al., 2011), also named *Inverse Odds of Sampling Weights* (IOSW) (Westreich et al., 2017; Josey et al., 2021). Despite an increasing number of contributions about *generalization*, open practical and important questions remain (Kern et al., 2016; Tipton et al., 2016; Stuart and Rhodes, 2017; Ling et al., 2022). For instance, which covariates – for e.g. age, and others – should be used to build the weights? Are some covariates increasing or lowering the overall precision? What is the impact of the size of the two samples (trial and representative sample) on the IPSW’s properties?

Outline We start by illustrating the principles of trial re-weighting and some of the key results of this article on a toy example (Section 2). Section 2 ends with related works. Mathematical notations, assumptions, and the precise definition of the IPSW estimator are introduced in Section 3. In particular, we present several versions of the IPSW estimator: whether the covariates probability the trial or the target population are estimated from the data or assumed as an oracle. This allows to link our results with seminal works in causal inference and previous work in epidemiology. Section 4 contains all the theoretical results, such as finite sample bias, variance, bounds on the risk, consistency, and large sample variance. We also detail why another version of the IPSW, where the probability of treatment assignment in the trial is also estimated, has a lower variance. Finally, we discuss in Section 4 how additional and non-necessary covariates can either improve or damage precision, depending on their status, whether they are only shifted between the two populations or only treatment-effect modifiers. Section 5 completes the toy example and illustrates all theoretical results on an extensive semi-synthetic example inspired from the medical domain. In this semi-synthetic simulation, the data are taken from an application in critical care medicine, and only the outcome generative model is simulated, such that the covariate distribution and in particular the distribution shift between populations is inherited from a real situation. Finally, Section 6 summarizes all practical takeaways of this research work and proposes a discussion.

2 Problem setting

2.1 Toy example

2.1.1 Context and intuitive estimation strategy

Assume that we would like to measure the average effect of a treatment (ATE) A on a outcome Y in a target population of interest \mathcal{P}_T (for **t**arget). Consider the situation where an existing Randomized Controlled Trial (RCT) has already been conducted on $n = 150$ individuals, sampled from a population \mathcal{P}_R (for **r**andomized), to assess the average effect of A on Y . Usually, the average treatment effect is estimated from a trial via an Horvitz-Thomson estimator (Horvitz and Thompson, 1952),

$$\hat{\tau}_{\text{HT},n} = \frac{1}{n} \sum_{i \in \text{Trial}} \left(\frac{Y_i A_i}{\pi} - \frac{Y_i (1 - A_i)}{1 - \pi} \right), \quad (1)$$

where π is the probability of treatment allocation in the trial (in most applications, $\pi = 0.5$). Results of a simulated trial are presented on Figure 1 with an average treatment effect around 8.2. In addition, assume that the trial puts in evidence that the treatment effect is heterogeneous with respect to a certain genetic mutation denoted X (with $X = 1$ for the mutation, and $X = 0$ if no mutation). More specifically, the average treatment effect conditional to X is larger for individuals with $X = 1$ than for those with $X = 0$. This situation is illustrated on Figure 1 where the average effect per strata X is also represented. We have at hand a representative sample of $m = 1000$ individuals from the target population we are interest in (for example from an existing observational data base). We observe that individuals with the genetic mutation ($X = 1$) are over-represented in the trial compared to the target population of interest (see Figure 2). As a direct consequence, the trial overestimates the target population’s ATE we are interested in.

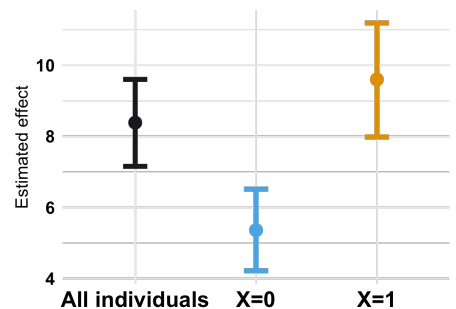


Figure 1: Treatment effect estimates (absolute difference) measured on a simulated trial of size $n = 150$ sampled according to the trial population \mathcal{P}_R . On the left the estimate on **all individuals**, and on the right the two estimate stratified ($X = 0$ and $X = 1$) showing treatment effect heterogeneities along the genetic mutation X .

Fortunately, the representative sample of the target population can be used to learn weights, and re-weight the trial data in the following way,

$$\hat{\tau}_{n,m} = \frac{1}{n} \sum_{i \in \text{Trial}} \underbrace{\hat{w}_{n,m}(X_i)}_{\text{Weights}} \underbrace{\left(\frac{Y_i A_i}{\pi} - \frac{Y_i(1 - A_i)}{1 - \pi} \right)}_{\text{Horvitz-Thomson}}. \quad (2)$$

As detailed later on, the weights $\hat{w}_{n,m}$ aims at estimating the probability ratio $\frac{p_T(x)}{p_R(x)}$, where $p_T(x)$ (resp. $p_R(x)$) is the probability of observing an individual with characteristics $X = x$ in the target (resp. randomized) population. The weights $\hat{w}_{n,m}$ depend on the sizes of the randomized **and** observational data sets, namely n and m . Consequently, the ATE estimator $\hat{\tau}_{n,m}$ depends on the size of two data sets, which questions how this estimator behaves (bias and variance) as function of n and m .

Figure 2: Covariate shift along the genetic mutation X between the trial population \mathcal{P}_R and target population \mathcal{P}_T , highlighting the distributional shift between the two data sources. Such population’s difference questions what is named the external validity of a trial.

	Target (\mathcal{P}_T)	Trial (\mathcal{P}_R)
$X = 1$	30%	75%
$X = 0$	70%	25%

2.1.2 Simulations and first observations

To empirically investigate how $\hat{\tau}_{n,m}$ behaves, we perform simulation following the Data Generative Process (DGP) described in Section 2.1.1. Results are depicted in Figure 3. More precisely, the DGP is presented in Figure 3a. Figure 3b shows the different estimators in action, showing that the re-weighted trial allows to compensate for the distribution shift as expected. Figure 3b also shows that estimating π from the data and plugging it in Equation 2 leads to a clear gain in variance. This phenomenon is linked to seminal works in causal inference, and is further demonstrated in Corollary 3. Finally, Figure 3c shows that if m remains small while n increases, at some point continuously increasing n will not further reduce the asymptotic variance (see Proposition 2 for a formal statement).

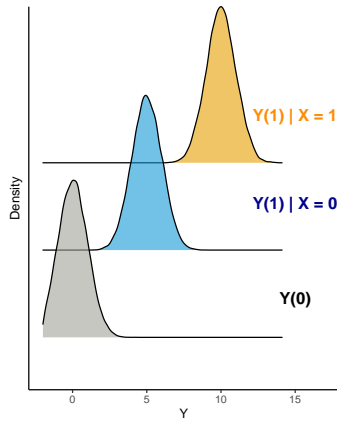
For correct trial generalization, all shifted treatment effect modifier baseline covariates, such as the genetic mutation X , are necessary (Stuart et al., 2011). But, in practice one may be tempted to add as many covariates V as available to take into account all possible sources of external validity bias. Doing so, we may add covariates V that are not needed to properly estimates the weights. This is the case if (i) V is shifted between the two data sets, but in reality is not a treatment effect modifier or if (ii) V is a treatment effect modifier, but not shifted between the two data sets. Figure 4a shows that in (i), the covariate V should not be added, as it can considerably inflate the variance and therefore damage the precision (see Corollary 4 for a formal statement); while in (ii), Figure 4b highlights that the covariate V should be added as the precision can be augmented by adding such covariates (see Corollary 5 for a formal statement).

In Section 4, we prove these phenomenons, deriving explicit finite sample and asymptotic results to characterize the re-weighting process.

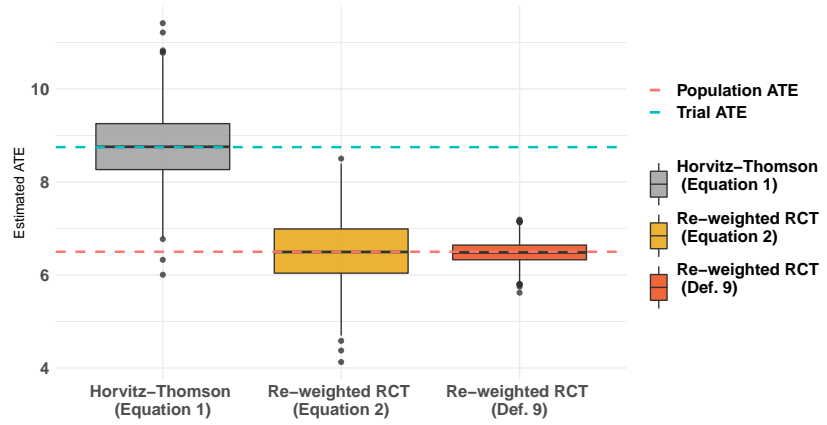
2.2 Related work

The estimator $\hat{\tau}_{n,m}$ introduced in the toy example (Equation 2) is an exact implementation of the so-called *Inverse Propensity of Sampling Weighting* (IPSW) where the word *sampling* comes from the popular habit of modeling the problem as the one of a randomized trial suffering from selection bias (Cole and Stuart, 2010; Bareinboim and Pearl, 2012a; Tipton, 2013; Dahabreh et al., 2019). Beyond trial re-weighting, other estimation strategies can be chosen when it comes to generalization, for example stratification (Tipton, 2013; O’Muircheartaigh and Hedges, 2013), modeling the response (G-formula or Outcome Modeling) (Kern et al., 2016; Dahabreh et al., 2019), using both strategies in a so-called doubly-robust approach (AIPSW) (Dahabreh et al., 2019, 2020), or entropy balancing (Lee et al., 2022; Josey et al., 2021).

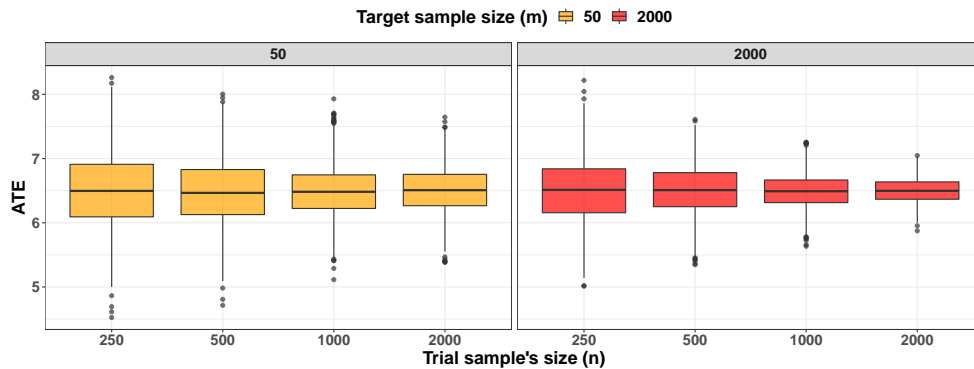
Link with IPW Note that the IPSW can be compared – at least to a certain extent – to the well-known *Inverse Propensity Weighting* (IPW) estimator in the context of one single observational data set (Hirano et al., 2003). Indeed, this corresponds to a mirroring situation, where the weights are no longer the probability ratio, but the probability to be treated (propensity score, Rosenbaum and Rubin, 1983). Hahn (1998) and Hirano et al. (2003) both showed that IPW is more efficient when weights are estimated, rather than relying on oracle weights. This curious phenomenon can even be found in other areas of statistics (Efron and Hinkley, 1978). Beyond efficient estimation with a minimal adjustment set, it is known that additional and non-necessary



(a) **Toy example's data generative model:** where individuals with $X = 1$ have a higher average treatment effect compared to individuals with $X = 0$. The baseline, centered on 0, is the same for both stratum.



(b) **Re-weighting in action:** Simulations's results with a trial of size $n = 150$, a target sample of size $m = 1,000$ with 1,000 repetitions, where the naive trial estimate corresponds Equation 1, and re-weighted trial to Equation 2. As expected re-weighting allows to recover the ATE of the target population (red dashed line). It is also possible to estimate π from the data, giving another re-weighting estimator with lower variance (later introduced in Definition 9).

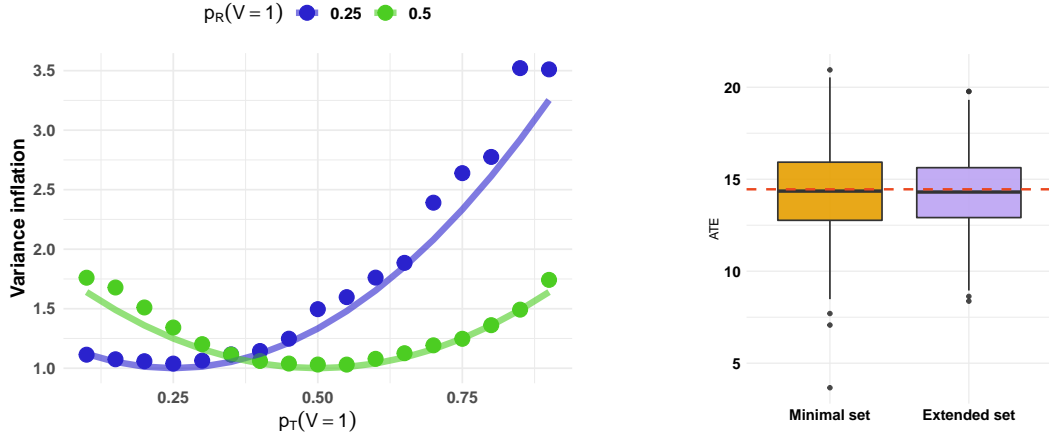


(c) **Two data sets leading to two asymptotic regimes:** where two situations are considered, one with a large target sample ($m = 2000$) or a small target sample ($n = 50$). Then, increasing n leads to a variance stagnation if m is small, while increasing n allows to further gain in precision if $n \leq m$.

Figure 3: Toy example's simulations - Minimal adjustment set.

baseline covariates in the adjustment set of the IPW can either increase the variance (the so-called instruments) (Velentgas et al., 2013; Schnitzer et al., 2015; Wooldridge, 2016), while another class of covariates (the ones linked only to the outcome – and also called *outcome-related covariates* or *risk factors* or *precision covariates*) improves precision (Hahn, 2004; Lunceford and Davidian, 2004; Brookhart et al., 2006; Lefebvre et al., 2008; Witte and Didelez, 2018). A recent crash-course about good and bad controls recalls this phenomenon (Cinelli et al., 2022). Finally, another very recent line of research consists in determining - given a Directed Acyclic Graph (DAG) - the asymptotically efficient adjustment set for ATE estimation. This is also named ‘optimal’ valid adjustment set (O-set), that is the smallest asymptotic variance compared to other adjustment sets assuming causal linear models (Henckel et al., 2019), or non parametric graphical models and any non-parametrically adjusted estimator (Rotnitzky and Smucler, 2020). Such methods are meant for complex DAGs where several possible adjustment sets can be used.

Theoretical results on IPSW Expression of the variance have been proposed for an estimator related to the IPSW one: the stratification estimator (O’Muircheartaigh and Hedges, 2013; Tipton, 2013). These results only consider the situation of an infinite target sample. Close expressions can also be found in Rothman and Greenland (2000), also assuming an infinite target sample compared to the trial sample size. Buchanan et al. (2018) has proposed theoretical properties such as asymptotic variance of a variant of IPSW under a parametric model, using M-estimation methods for the proof (Stefanski and Boos, 2002). *Why variant?* Because this proof is under the situation of a so-called nested design, that is a trial embedded in a larger observational population, so that there is only one single big data set to consider and not two. In addition, we have found no discussion - neither empirical nor theoretical - about the impact of adding non-necessary covariates on the IPSW (or any other generalization’s estimator) properties (e.g., bias, variance). Egami and Hartman (2021) propose a method



(a) Adding shifted covariate not being a treatment effect modifier leads to a variance inflation. Simulation represents the situation of a binary shifted covariate V added or not in the adjustment set. The y -axis represents how much the variance with the minimal set is multiplied compared to a situation with this additional shifted covariate. The plain lines come from the Theory (see Corollary 4) while dots are empirical variance (obtained from 1,000 repetitions with $n = 150$ and $m = 1,000$). The more shifted the covariate, the higher the inflation. The phenomenon is amplified if the covariate is **imbalanced** in the trial (in opposition with a **balanced**).

(b) Adding non-shifted treatment effect modifier leads to a gain in precision compared to a situation with only the necessary covariate. In this plot DGP from Figure 3a is adapted to add one non-shifted treatment effect modifier. Adding such covariate (**extended set**) compared to an adjustment set with only X (**minimal set**) lowers the variance.

Figure 4: Toy example's simulations - Extended adjustment set.

to estimate a separating set - that is a set of variables affecting both the sampling mechanism and treatment effect heterogeneity - and in particular when the trial contains many more covariates than the target population sample. However, their work focus on identification. Huitfeldt et al. (2019) also consider covariate selection for generalization, but focus on which covariates are necessary depending on the causal measure chosen (ratio, difference, or other). Note that some existing practical recommendations advocate to add as many covariates as possible (Stuart and Rhodes, 2017).

Contributions This work considers several variants of the IPSW, whether or not the weights are oracle, semi-oracle, or completely estimated. In this context, we derive the asymptotic variance of all the variants of IPSW and we show that several asymptotic regimes exist, depending on the relative size of the RCT compared to the target sample. We also provide finite sample expression of the bias and variance for all the IPSW variants introduced, allowing to bound the risk on this estimator for any samples sizes (trial and target population). We link our work to seminal works in causal inference, showing that semi-oracle estimation outperforms a completely oracle estimation, while the exact result of Hahn (1998) on efficient estimation can not be directly extended to the case of generalization. Indeed, we show that a completely estimated IPSW is not more efficient than the semi-oracle version of it. Such discussions lead to our proposal of a completely estimated IPSW, also estimating from the data the propensity to be treated in the trial.

From these theoretical results, we explain why the addition of some additional but non-necessary covariates in the adjustment set has a big impact on precision, for the best or the worst. Indeed, while non-shifted treatment effect modifiers improve precision by lowering the variance, adding shifted covariates that are not predictive of the outcome considerably reduce the statistical power of the analysis by inflating the variance. For this latter situation, we provide an explicit formula of the variance inflation when the additional covariate set is independent of the necessary one. These results have important consequences for practitioners because they allow to give precise recommendations about how to select covariates. All our results are neither assuming any parametric form of the outcome nor the sampling process, at the cost of restricting the scope to categorical covariates for adjustment. Within the medical domain, scores or categories are often used to characterize individuals, which leads us to believe that our work can be of practical interest, at least in this field.

3 Notations and assumptions for causal identifiability

3.1 Notations

3.1.1 Problem setting

The notations and assumptions used in this work are grounded in the potential outcome framework (Imbens and Rubin, 2015). We assume to have at hand two data sets,

1. A randomized controlled trial, denoted \mathcal{R} (for randomized), assessing the efficacy of a binary treatment A on an outcome Y (ordinal, binary, or continuous) conducted on n *iid* observations. Each observation i is labelled from 1 to n and can be modelled as sampled from a distribution $P_{\mathcal{R}}(X, Y^{(1)}, Y^{(0)}, A) \in \mathbb{X} \times \mathbb{R}^2 \times \{0, 1\}$, where \mathbb{X} is a categorical support. For any observation i , A_i denotes the binary treatment assignment (with $A_i = 0$ if no treatment and $A_i = 1$ if treated), and $Y_i^{(a)}$ is the outcome had the subject been given treatment a (for $a \in \{0, 1\}$), which is assumed to be squared integrable. Y_i denotes the observed outcome, defined as $Y_i = A_i Y_i^{(1)} + (1 - A_i) Y_i^{(0)}$. In addition, this trial is assumed to be a Bernoulli trial with a constant probability of treatment assignment for all units and independence of treatment allocation between units¹. We denote $\mathbb{P}_{\mathcal{R}}[A_i = 1] = \pi$. X_i is a p -dimensional vector of categorical covariates accounting for individual characteristics on the observation i ;
2. A sample of the target population of interest, denoted \mathcal{T} (for target), containing m *iid* individuals samples drawn from a distribution $P_{\mathcal{T}}(X, Y^{(1)}, Y^{(0)}, A) \in \mathbb{X} \times \mathbb{R}^2 \times \{0, 1\}$, labelled from $n+1$ to $n+m$. In this data set, we only observe individual categorical characteristics X_i . For simplicity, we further use the notation $P_{\mathcal{T}}(X)$ for the marginal of X on distribution $P_{\mathcal{T}}$.

Finally, the probability of X in the target population (resp. trial population) is denoted $p_{\mathcal{T}}(x)$ (resp. $p_{\mathcal{R}}(x)$). Mathematically, a covariate shift between the two populations occurs when there exists $x \in \mathbb{X}$ such that $p_{\mathcal{R}}(x) \neq p_{\mathcal{T}}(x)$. The situation and notations are summarized on Figure 5.

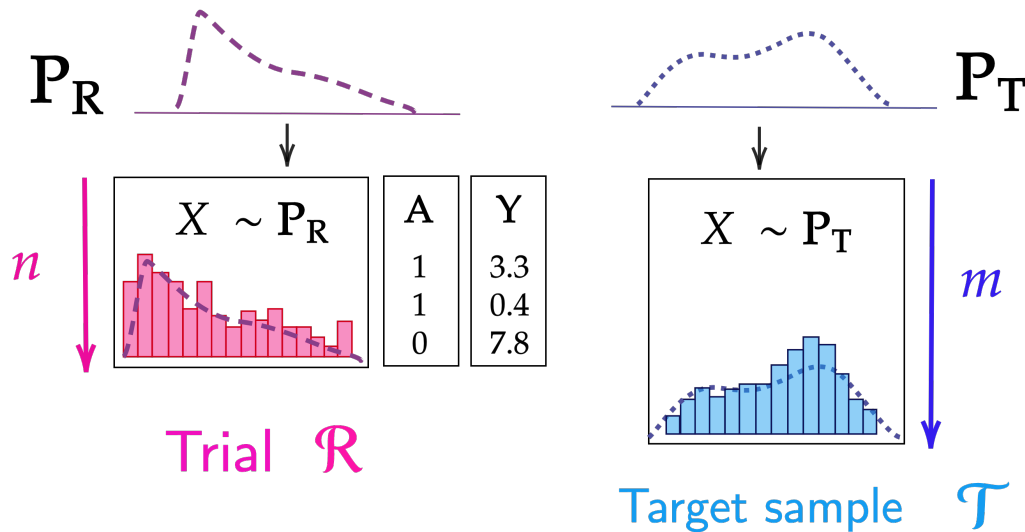


Figure 5: Summary of the data at hand: on the left, a randomized controlled trial \mathcal{R} of size n sampled according to $P_{\mathcal{R}}$ and informing about the effect of a treatment A on the outcome Y . On the right, a sample \mathcal{T} of size m sampled from the target population of interest $P_{\mathcal{T}}$, containing only information on covariates X . As suggested on the drawing, n is expected to be smaller than m , as trials are usually of limited size compared to large national data base or cohort.

Comments on the notations Note that a large part of the literature models the problem with a sampling mechanism from a super population. Doing so, the target and the trial samples are assumed sampled from this super population, with different mechanisms leading to a distributional shift of the trial (for e.g. see how the problem is framed in Stuart et al. (2011); Hartman (2021)). Still, as soon as we are not working with a nested-trial (that is a trial embedded in the target sample) and if only baseline covariates are considered for adjustment, the framing with a sampling model is equivalent to the problem setting introduced above (Colnet et al., 2020). Note that framing the problem as done in this work has started to spread in the literature recently (Kern et al., 2016; Nie et al., 2021; Chattopadhyay et al., 2022).

¹For a review of trial designs, in particular explaining the difference between a Bernoulli and a completely randomized design, we refer the reader to Chapter 2 of Imbens and Rubin (2015).

3.1.2 Target quantity of interest

Recall that two distributions, indexed by R and T are involved in our problem setting (Section 3.1.1). Therefore, we will use these indices to denote quantities (expectations, probabilities) taken with respect to these distributions, for example $\mathbb{E}_R[\cdot]$ (resp. $\mathbb{E}_T[\cdot]$) for an expectation on P_R (resp. P_T).

We define the target population average treatment effect ATE (sometimes called TATE):

$$\tau := \mathbb{E}_T \left[Y^{(1)} - Y^{(0)} \right]. \quad (3)$$

Because the randomized controlled data \mathcal{R} are not sampled from the target population of interest, the sample average treatment effect τ_R (sometimes called SATE) estimated from this sample

$$\tau_R := \mathbb{E}_R \left[Y^{(1)} - Y^{(0)} \right],$$

may be biased, that is $\tau_R \neq \tau$. While not being the target quantity of interest, we also introduce the so-called Conditional Average Treatment Effect (CATE), as

$$\forall x \in \mathbb{X}, \tau(x) := \mathbb{E}_T \left[Y^{(1)} - Y^{(0)} \mid X = x \right].$$

3.2 Identification assumptions

When willing to generalize the findings from the population data P_R toward the population P_T , assumptions are needed. In particular we first need to ensure the validity of the trial, also called *internal validity*. These assumptions are the usual ones formulated in causal inference, and in particular for randomized controlled trials within the potential outcomes framework (Imbens and Rubin, 2015; Hernan, 2020).

Assumption 1 (Representativity of the randomized data). *For all $i \in \mathcal{R}$, $X_i \sim P_R(X)$ where P_R is the population distribution from which the RCT was sampled.*

Assumption 2 (Trial’s internal validity). *The RCT at hand \mathcal{R} is assumed to be internally valid, such that*

- (i) *Consistency and no interference hold, that is: $\forall i \in \mathcal{R}, Y_i = A_i Y_i^{(1)} + (1 - A_i) Y_i^{(0)}$;*
- (ii) *Treatment randomization holds, that is: $\forall i \in \mathcal{R}, \{Y_i^{(1)}, Y_i^{(0)}\} \perp A_i$;*
- (iii) *Positivity of trial treatment assignment holds, that is: $0 < \pi < 1$ (usually $\pi = 0.5$).*

Assumption (i) is often termed SUTVA. The two following assumptions are specific to generalization or transportability.

Assumption 3 (Transportability). $\forall x \in \mathbb{X}, \mathbb{P}_R(Y^{(1)} - Y^{(0)} \mid X = x) = \mathbb{P}_T(Y^{(1)} - Y^{(0)} \mid X = x)$.

The transportability assumption (Stuart et al., 2011; Pearl and Bareinboim, 2011), also called *sample ignorability for treatment effects* (Kern et al., 2016) or *Conditional Ignorability* (Hartman, 2021), is probably the most important assumption to generalize or transport the trial findings to the target population, as this requires to have access to all shifted covariates being treatment modifiers. In other words, it assumes that all the systematic variations in the treatment effect are captured by the covariates X (O’Muircheartaigh and Hedges, 2013). The covariates X are usually named the adjustment or separating set (Egami and Hartman, 2021; Hartman, 2021). Note that the concept of treatment effect modifiers depends on the chosen causal-measure; in this paper, we only consider the absolute difference most common for a continuous outcome as detailed in Equation 3. Would we have chosen the (for e.g.) log-odd-ratio, then the covariates being treatment effect modifiers could be different. Finally, note that Pearl and Bareinboim (2011) introduces *selection* diagram to formalize this assumption relying on causal diagrams. Pearl (2015) details why diagrams can contain more identification scenarii. But in this work, we only consider baseline covariates for the transportability assumption (i.e no *front-door* adjustment).

Assumption 4 (Support inclusion). $\forall x \in \mathbb{X}, p_R(x) > 0$, and $\text{supp}(P_T(X)) \subseteq \text{supp}(P_R(X))$.

Note that this last assumption is sometimes referred as the positivity of trial participation and can also be viewed as a sampling process with non-zero probability for all individuals (Hartman, 2021). This assumption is restrictive because RCT inclusion and exclusion criteria can be strict as the goal of RCTs (at least in early stages) is to show a clear effect even on a restricted population. In particular, restriction to a limited population also helps avoiding sanitary issues. Still, whenever Assumption 4 does not hold, it is still possible to generalize as soon as we consider a different target population. The question asked would rather be “What would have been the estimated treatment effect in a situation where the trial has sampled individuals from the target population with trial’s eligibility criteria?”.

3.3 Estimators

In this work, we denote any estimator targeting a quantity τ as $\hat{\tau}_{n,m}$ with in index the symbol n or m to characterise which data were used in the estimation strategy. For example an estimator $\hat{\tau}_n$ (resp. $\hat{\tau}_m$) only uses the trial data (resp. observational data) whereas $\hat{\tau}_{n,m}$ uses both data sets.

3.3.1 Within-trial estimators of ATE

Two classical estimators targeting τ_R from trial data are the Horvitz-Thomson and Difference-in-means estimators.

Definition 1 (Horvitz-Thomson - [Horvitz and Thompson \(1952\)](#)). *The Horvitz-Thomson estimator is denoted $\hat{\tau}_{HT,n}$ and defined as,*

$$\hat{\tau}_{HT,n} = \frac{1}{n} \sum_{i=1}^n \left(\frac{A_i Y_i}{\pi} - \frac{(1 - A_i) Y_i}{1 - \pi} \right).$$

Previous works (for e.g. [Hirano et al. \(2003\)](#)) show that the Horvitz-Thomson estimator $\hat{\tau}_{HT,n}$ is an unbiased and consistent estimator of τ_R , and its variance satisfies, for all n ,

$$n \text{Var} [\hat{\tau}_{HT,n}] = \mathbb{E}_R \left[\frac{(Y^{(1)})^2}{\pi} \right] + \mathbb{E}_R \left[\frac{(Y^{(0)})^2}{1 - \pi} \right] - \tau_R^2 := V_{HT}. \quad (4)$$

Derivations to obtain such variance are recalled in Appendix (see Section D).

Definition 2 (Difference-in-means). *The Difference-in-means estimator is denoted $\hat{\tau}_{DM,n}$ and defined as*

$$\hat{\tau}_{DM,n} = \frac{1}{n_1} \sum_{A_i=1} Y_i - \frac{1}{n_0} \sum_{A_i=0} Y_i, \quad \text{where } n_a = \sum_{i=1}^n \mathbb{1}_{A_i=a}.$$

The Difference-in-means estimator can be viewed as a variant of the Horvitz-Thomson estimator, where the probability to be treated π (or propensity score) is estimated, that is,

$$\hat{\tau}_{DM,n} = \frac{1}{n} \sum_{i=1}^n \left(\frac{A_i Y_i}{\hat{\pi}} - \frac{(1 - A_i) Y_i}{1 - \hat{\pi}} \right), \quad \text{where } \hat{\pi} = \frac{\sum_{i=1}^n A_i}{n}.$$

As recalled in [Imbens and Rubin \(2015\)](#), the Difference-in-means estimator $\hat{\tau}_{DM,n}$ is an unbiased and consistent estimator of τ_R , and its asymptotic variance satisfies,

$$n \text{Var} [\hat{\tau}_{DM,n}] = \frac{\text{Var}_R [Y^{(1)}]}{\pi} + \frac{\text{Var}_R [Y^{(0)}]}{1 - \pi} := V_{DM}, \quad (5)$$

Counter-intuitively, the interest of estimating π is to lower the variance. Even if the true probability is $\pi = 0.5$, the actual treatment allocation in the sample can be different (e.g., $\hat{\pi} = 0.48$), and using $\hat{\pi}$ rather than π leads to a smaller variance by adjusting to the exact observed probability to be treated in the trial. In particular, it is possible to observe this phenomenon by comparing the two variances (see Subsection D.3 for derivations),

$$V_{DM} = V_{HT} - \left(\sqrt{\frac{1 - \pi}{\pi}} \mathbb{E}_R [Y^{(1)}] + \sqrt{\frac{\pi}{1 - \pi}} \mathbb{E}_R [Y^{(0)}] \right)^2 \leq V_{HT}. \quad (6)$$

3.3.2 Re-weighting estimator for generalizing the trial findings

As mentioned in Subsection 2.2, in this work we focus on the reweighting strategy, that is the *Inverse Propensity of Sampling Weighting* (IPSW) estimator ([Cole and Stuart, 2010](#)). In this section, we introduce several variants of this estimator.

Definition 3 (Completely oracle IPSW). *The completely oracle IPSW estimator is denoted $\hat{\tau}_{\pi,T,R,n}^*$ and defined as*

$$\hat{\tau}_{\pi,T,R,n}^* = \frac{1}{n} \sum_{i=1}^n \frac{p_T(X_i)}{p_R(X_i)} Y_i \left(\frac{A_i}{\pi} - \frac{1 - A_i}{1 - \pi} \right), \quad (7)$$

where $\frac{p_T(X_i)}{p_R(X_i)}$ are called the weights or the nuisance components.

Definition 3 corresponds to a completely oracle IPSW, where p_T , p_R , and the trial allocation probability π are known.

3.3.3 Probability ratio estimation

In practice neither p_R nor p_T are known, and therefore one needs to estimate these probabilities. As explained in Subsection 3.1.1, we consider the case where X is composed of categorical covariates only. In such a situation, a practical IPSW estimator can be built from Definition 3 by estimating each probability p_T and p_R by their empirical counterpart (that is counting how many observations fall in each categories in the trial and target samples).

Definition 4 (Probability estimation). *Under the setting defined in Subsection 3.1.1,*

$$\forall x \in \mathcal{X}, \hat{p}_{T,m}(x) := \frac{1}{m} \sum_{i \in \mathcal{T}} \mathbb{1}_{X_i=x} \quad \text{and,} \quad \hat{p}_{R,n}(x) := \frac{1}{n} \sum_{i \in \mathcal{R}} \mathbb{1}_{X_i=x}.$$

Having defined a method for probability estimation, one can build practical IPSW variants.

Definition 5 (Semi-oracle IPSW). *The semi-oracle IPSW estimator $\hat{\tau}_{\pi,T,n}^*$ is defined as*

$$\hat{\tau}_{\pi,T,n}^* = \frac{1}{n} \sum_{i=1}^n \frac{p_T(X_i)}{\hat{p}_{R,n}(X_i)} Y_i \left(\frac{A_i}{\pi} - \frac{1 - A_i}{1 - \pi} \right), \quad (8)$$

where $\hat{p}_{R,n}$ is estimated according to Definition 4.

Note that this semi-oracle estimator corresponds to the so-called standardization procedure described in Rothman and Greenland (2000) and Rothman (2011).

Definition 6 (IPSW). *The (completely estimated) IPSW estimator $\hat{\tau}_{\pi,n,m}$ is defined as*

$$\hat{\tau}_{\pi,n,m} = \frac{1}{n} \sum_{i=1}^n \frac{\hat{p}_{T,m}(X_i)}{\hat{p}_{R,n}(X_i)} Y_i \left(\frac{A_i}{\pi} - \frac{1 - A_i}{1 - \pi} \right), \quad (9)$$

where $\hat{p}_{R,n}$ and $\hat{p}_{T,m}$ are estimated according to Definition 4.

Definition 6 corresponds to the classical implementation of the IPSW since, practically, the probabilities $\hat{p}_{R,n}$ and $\hat{p}_{T,m}$ are not known and must be estimated.

The completely and the semi-oracle estimators are not used in practice, as usually none of the true probabilities are known. Still, they both correspond to some asymptotic situations that are of interest to understand the IPSW. For instance:

- Studying $\hat{\tau}_{\pi,T,R,n}^*$ allows us to observe the effect of averaging over the trial sample \mathcal{R} , without the variability due to covariates probability estimation;
- Studying $\hat{\tau}_{\pi,T,n}^*$ allows to understand the situation where the target sample \mathcal{T} is infinite ($m \rightarrow \infty$).

In addition, studying these estimators allows us to link our results with seminal works in causal inference showing that the estimated propensity score can lead to better properties than an oracle one (Hahn, 1998; Hirano et al., 2003). Note that we could introduce another semi-oracle estimator, where p_R is known but not p_T . This specific estimator does not correspond to a limit situation helping understanding the results, as it is as if the covariates probabilities in the trial are learned on a infinite data sample, but where the treatment effect estimate is still averaged on a finite sample.

Finally, since all covariates are assumed to be categorical in our framework, trial and observational densities (continuous covariates) turn into trial and observational probabilities (categorical covariates). Oracles and semi-oracles will be different when considering continuous covariates as the weights will be replaced by density estimation, sometimes directly estimating the ratio by binding the two data sources and therefore making the notion of semi-oracle outdated.

4 Theoretical results

In this section, we prove our main theoretical results on the three variants of IPSW estimator (Definition 3, 5 and 6).

4.1 Estimators' properties

The following results rely on variance of each strata of the Horvitz-Thomson estimator (see Definition 1), denoted $V_{HT}(x)$, and corresponding to,

$$V_{HT}(x) = \mathbb{E}_R \left[\frac{(Y^{(1)})^2}{\pi} \mid X = x \right] + \mathbb{E}_R \left[\frac{(Y^{(0)})^2}{1 - \pi} \mid X = x \right] - \tau(x)^2. \quad (10)$$

In this equation, we removed the index R of $\tau(x)$ as $\tau_R(x) = \tau_T(x) = \tau(x)$, according to Assumption 3. Removing the indices of the conditional expectations on the right-hand side would require to go beyond the classical transportability assumption, by assuming that

$$\forall a \in \{0, 1\}, P_R(Y^{(a)} \mid X = x) = P_T(Y^{(a)} \mid X = x),$$

i.e. assuming that X contains all the covariates being shifted and predictive of the outcome, which is stronger than Assumption 3.

4.1.1 Properties of the completely oracle IPSW

Theorem 1 (Properties of the completely oracle IPSW). *Under the general setting defined in Subsection 3.1.1, granting Assumptions 1-4, the completely oracle IPSW is unbiased and has an explicit variance expression, that is, for all n ,*

$$\mathbb{E} [\hat{\tau}_{\pi, T, R, n}^*] = \tau, \text{ and } \text{Var} [\hat{\tau}_{\pi, T, R, n}^*] = \frac{V_o}{n},$$

where

$$V_o := \text{Var}_R \left[\frac{p_T(X)}{p_R(X)} \tau(X) \right] + \mathbb{E}_R \left[\left(\frac{p_T(X)}{p_R(X)} \right)^2 V_{HT}(X) \right].$$

As a consequence, for all n , the quadratic risk of the completely oracle IPSW is given by,

$$\mathbb{E} \left[(\hat{\tau}_{\pi, T, R, n}^* - \tau)^2 \right] = \frac{V_o}{n},$$

which implies its L^2 -consistency as n tends to infinity, that is,

$$\hat{\tau}_{\pi, T, R, n}^* \xrightarrow{L^2} \tau.$$

The results presented in Theorem 1 can be found in the literature in various forms. They don't constitute our main contribution but they will be of primary importance when trying to compare the different IPSW variants and the impact of sample sizes. Besides, we provide in the Appendix (Subsection A.1) a very detailed proof of all these results, which can help the reader to understand the more complex derivations of our next results. In the literature, the consistency of the oracle IPSW is well-acknowledged, for example in Egami and Hartman (2021) (see their appendix, Section SM-2). The asymptotic variance both depends on the probability ratio. In particular if for some category x , the $p_T(x)$ and $p_R(x)$ are very different, this leads to a large variance when generalizing the trial's findings.

4.1.2 Properties of the semi-oracle IPSW

In this section, we study the behaviour of the semi-oracle IPSW (Definition 5), for which the probability p_T is known but the probability p_R is estimated. One can obtain $p_R(x) = 0$ for some $x \in \mathbb{X}$, even if $p_R > 0$. This phenomenon, occurring when no observations in the trial correspond to the covariate vector x , creates a bias of the IPSW estimate. To analyze it in our next results, we need to introduce $Z_n(x) = \sum_{i=1}^n \mathbb{1}_{X_i=x}$.

Proposition 1. *Under the general setting defined in Subsection 3.1.1, granting Assumptions 1-4, the bias of the semi-oracle IPSW satisfies, for all n ,*

$$\mathbb{E} [\hat{\tau}_{\pi, T, n}^*] - \tau = - \sum_{x \in \mathbb{X}} p_T(x) \tau(x) (1 - p_R(x))^n.$$

and

$$|\mathbb{E} [\hat{\tau}_{\pi, \tau, n}^*] - \tau| \leq (1 - \min_x p_R(x))^n \tau.$$

Moreover, under the same set of assumptions, the variance of the semi-oracle IPSW satisfies, for all n ,

$$n \operatorname{Var} [\hat{\tau}_{\pi, \tau, n}^*] = \sum_{x \in \mathbb{X}} p_T(x)^2 V_{HT}(x) \mathbb{E}_R \left[\frac{\mathbb{1}_{Z_n(x) > 0}}{\frac{1}{n} \sum_{i=1}^n \mathbb{1}_{X_i = x}} \right],$$

and

$$\operatorname{Var} [\hat{\tau}_{\pi, \tau, n}^*] \leq \frac{2V_{so}}{n+1},$$

with

$$V_{so} := \mathbb{E}_R \left[\left(\frac{p_T(X)}{p_R(X)} \right)^2 V_{HT}(X) \right].$$

The proof is detailed in Subsection A.2.1. Proposition 1 presents novel results with the explicit finite-sample bias and variance. In particular, for small trials (*i.e.* small n), the semi-oracle IPSW is biased (which can be understood by undercoverage of some categories in the trial). As shown in Proposition 1, this bias is upper-bounded by a quantity, which exponentially decreases as n increases. Still, in case of a poor overlap (intrinsic small probability $p_R(x)$ for at least one category x or in a high-dimensional setting), the bias vanishes slowly. Note that, as soon as $\tau(x)$ is of constant sign, the sign of the bias is known. Finally, the variance can also be bounded, with a larger bound if the probability ratio takes some extreme values as expected. Finite-sample expressions can be studied asymptotically, and results are provided in Corollary 1.

Corollary 1. *Under the same assumptions as in Proposition 1, the semi-oracle IPSW is asymptotically unbiased, and its asymptotic variance satisfies,*

$$\lim_{n \rightarrow \infty} \mathbb{E} [\hat{\tau}_{\pi, \tau, n}^*] = \tau, \quad \text{and} \quad \lim_{n \rightarrow \infty} n \operatorname{Var} [\hat{\tau}_{\pi, \tau, n}^*] = V_{so}.$$

The proof is detailed in Subsection A.2.2. The semi-oracle IPSW was introduced by Rothman and Greenland (2000) under the name *standardization* in a different context. Although the quantity V_{so} was mentioned in Rothman and Greenland (2000), it did not come with a general theoretical justification. Corollary 1 is the first theoretical result establishing the asymptotic variance of the semi-oracle IPSW.

One can observe from the explicit derivations that the semi-oracle estimator $\hat{\tau}_{\pi, \tau, n}^*$ has a lower asymptotic variance than the oracle IPSW $\hat{\tau}_{\pi, \tau, R, n}^*$, as detailed in Theorem 1. In particular,

$$\forall n, \operatorname{Var}[\hat{\tau}_{\pi, \tau, R, n}^*] = \underbrace{\frac{1}{n} \mathbb{E}_R \left[\left(\frac{p_T(X)}{p_R(X)} \right)^2 V_{HT}(X) \right]}_{\text{Semi-oracle asymptotic variance}} + \underbrace{\frac{1}{n} \operatorname{Var}_R \left[\frac{p_T(X)}{p_R(X)} \tau(X) \right]}_{\text{Always positive}}.$$

This phenomenon has similar explanations with the common (and always surprising!) result stating that an estimated propensity score allows to lower the variance when re-weighting observational data compared to using an oracle propensity score (Hahn, 1998; Hirano et al., 2003; Lunceford and Davidian, 2004) (IPW estimator). Intuitively, we only need to generalize from the actual sample to the target population, and not from a source trial population to a target population. In fact, similar considerations are not specific to causal inference (Efron and Hinkley, 1978).

The new finite-sample bounds in Proposition 1 yields upper bounds on the risk of the semi-oracle IPSW.

Theorem 2 (Properties of the semi-oracle IPSW). *Under the general setting defined in Subsection 3.1.1, granting Assumptions 1-4, the quadratic risk of the completely oracle IPSW satisfies,*

$$\mathbb{E} \left[(\hat{\tau}_{\pi, \tau, n}^* - \tau)^2 \right] \leq \left(1 - \min_x p_R(x) \right)^{2n} \tau^2 + \frac{2V_{so}}{n+1},$$

which implies its L^2 -consistency as n tends to infinity, that is,

$$\hat{\tau}_{\pi, \tau, n}^* \xrightarrow{L^2} \tau.$$

The proof is detailed in Subsection A.2.3. The bound on the risk is also a novel result, opening doors to guarantees even on small sample sizes, and in particular all the terms in the bound can be estimated from the data. Note that this is hard to compare the bound on the risk of the semi-oracle IPSW to the completely oracle IPSW as the former has an additional term due to the bias, and the later due to a larger asymptotic variance. However, the bias decreases exponentially faster with n , whereas the additional variance term decreases at rate $1/n$. Consequently, the risk of the semi-oracle estimate is lower than that of the completely oracle estimate for large and moderate values of n .

4.1.3 Properties of the (completely estimated) IPSW

Previous results on IPSW are valid when the size of the target population tends to infinity. In this context, the only remaining asymptotic analysis is to dissect the behaviour of the IPSW estimate as a function of n . In this subsection, we establish theoretical guarantees for the completely estimated IPSW in a more complex setting: we consider finite trial and target population datasets and establish bounds depending on both sample sizes (n and m).

Proposition 2. *Under the general setting defined in Subsection 3.1.1, granting Assumptions 1-4, the bias of the completely estimated IPSW is the same as that of the semi-oracle IPSW, that is, for all n, m ,*

$$\mathbb{E}[\hat{\tau}_{\pi, n, m}] - \tau = - \sum_{x \in \mathbb{X}} p_T(x) \tau(x) (1 - p_R(x))^n.$$

Moreover, under the same set of assumptions, the variance of the completely estimated IPSW satisfies, for all n, m ,

$$\begin{aligned} \text{Var}[\hat{\tau}_{\pi, n, m}] &= \text{Var}[\hat{\tau}_{\pi, \tau, n}^*] + \frac{1}{m} \text{Var}_T[\tau(X) \mathbb{1}_{Z_n(X) \neq 0}] + \left(1 - \frac{1}{m}\right) \text{Var}_T[\mathbb{E}[\mathbb{1}_{Z_n(X)=0} | \mathbf{X}_n]] \\ &\quad + \frac{1}{nm} \sum_{x \in \mathbb{X}} V_{HT}(x) p_T(x) (1 - p_T(x)) \mathbb{E}_R \left[\frac{\mathbb{1}_{Z_n(x) \neq 0}}{\hat{p}_{R, n}(x)} \right], \end{aligned}$$

and

$$\text{Var}[\hat{\tau}_{\pi, n, m}] \leq \frac{\text{Var}_T[\tau(X)]}{m} + \sum_{x \in \mathbb{X}} p_T(x) (1 - p_R(x))^n + \frac{2}{n+1} \left(V_{so} + \frac{1}{m} \mathbb{E}_R \left[\frac{p_T(X) (1 - p_T(X))}{p_R(X)^2} V_{HT}(X) \right] \right).$$

Proof is detailed in Subsection A.3.1. Note that the term $\text{Var}_T[\tau(X)]$ can be replaced by $\text{Var}[\tau(X)]$ thanks to Assumption 3. Proposition 2 contains new results, linking the semi-oracle results to a more complex estimator. A first observation is that the bias of the (completely estimated) IPSW is the same as the semi-oracle, showing that only a limited trial sample size can explain a finite sample bias. On the other side, the variance is inflated compared the semi-oracle IPSW, due to the estimation of the target probability p_T . Indeed the variance equals the semi-oracle and two additional terms depending on m . One of this term is vanishing faster: only one sample size has to tend to infinity to make it disappear, as the term is $\propto 1/(nm)$. In addition, as soon as $m \rightarrow \infty$ then the finite sample variance of the completely estimated IPSW converges toward the semi-oracle one, following the intuition.

Similarly to previous results, the asymptotic expression of the bias and the variance can be deduced from the previous proposition.

Corollary 2. *Under the same assumptions as in Proposition 2, the completely estimated IPSW is asymptotically unbiased when n tends to infinity, that is*

$$\lim_{n \rightarrow \infty} \mathbb{E}[\hat{\tau}_{\pi, n, m}] = \tau.$$

Besides, letting $\lim_{n, m \rightarrow \infty} m/n = \lambda \in [0, \infty]$, the asymptotic variance of completely estimated IPSW satisfies

$$\lim_{n, m \rightarrow \infty} \min(n, m) \text{Var}[\hat{\tau}_{\pi, n, m}] = \min(1, \lambda) \left(\frac{\text{Var}[\tau(X)]}{\lambda} + V_{so} \right).$$

Proof is detailed in Subsection A.3.2. As highlighted in Corollary 2, there is not a unique asymptotic variance for the completely estimated IPSW. Its asymptotic variance depends on how the sample sizes n and m compare to each other. For example,

- If $m/n \rightarrow \infty$, (i.e., $\lambda = \infty$) then the asymptotic variance of the completely estimated IPSW corresponds to the semi-oracle's one;
- If we consider an asymptotic regime where the observational sample is about ten times bigger than the trial ($\lambda = 10$), then the asymptotic variance is equal to $\lim_{n,m \rightarrow \infty} n \text{Var} [\hat{\tau}_{\pi,n,m}] = \text{Var} [\tau(X)] / 10 + V_{so} > V_{so}$;
- Finally, if $m/n \rightarrow 0$, (i.e., $\lambda = 0$) then the asymptotic variance of the completely estimated IPSW has no more link to that of the semi-oracle IPSW, and $\lim_{n,m \rightarrow \infty} m \text{Var} [\hat{\tau}_{\pi,n,m}] = \text{Var} [\tau(X)]$.

Upper bound on the risk of the completely estimated IPSW can be established, based on Proposition 2.

Theorem 3 (Properties of the IPSW). *Under the general setting defined in Subsection 3.1.1, granting Assumptions 1-4, the quadratic risk of the completely estimated IPSW satisfies,*

$$\mathbb{E} \left[(\hat{\tau}_{\pi,n,m} - \tau)^2 \right] \leq \left(1 - \min_x p_R(x) \right)^n (\tau^2 + 1) + \frac{\text{Var} [\tau(X)]}{m} \quad (11)$$

$$+ \frac{2V_{so}}{n+1} + \frac{2}{m(n+1)} \mathbb{E}_R \left[\frac{p_T(X)(1-p_T(X))}{p_R(X)^2} V_{HT}(X) \right], \quad (12)$$

which implies its L^2 -consistency as m, n tends to infinity, that is,

$$\hat{\tau}_{\pi,n,m} \xrightarrow{L^2} \tau.$$

Proof is detailed in Subsection A.3.3. The first and third terms in inequality (12) correspond to the bound of the semi-oracle estimator (see Theorem 2). Following the intuition, the bound on the risk of the completely estimated IPSW is larger than the one for the semi-oracle. This is due to the cost of estimating p_T from a finite sample (of size m). In particular, if m tends to infinity, it is possible to retrieve the bound of the semi-oracle IPSW. Note that if at least $n \rightarrow \infty$, while m remains small, the bounds can lower up to a certain extent. Indeed, in this situation the risk is still bounded by a term depending only on m and the variance of the CATE.

Finally, note that if consistency of the (completely estimated) IPSW for continuous covariates has been proven in the literature (Colnet et al., 2021) (assuming uniform convergence of the probability ratio under a cross-fitting procedure), our results are the first to establish the bias and the variance of the completely estimated IPSW in finite and asymptotic regimes, with an explicit dependence on both sample sizes.

4.2 Estimating the probability to be treated in the trial?

So far, we have considered an estimation procedure where π , the probability to be treated in the trial, is plugged-in in the formula. Still, one may want to estimate it, for the purpose of precision. This idea follows the same spirit of what can be done with the Horvitz-Thomson (Definition 1) and the Difference-in-means (Definition 2) estimators on a single trial. The gain in efficiency for a trial when estimating $\hat{\pi}$ is recalled in Equation (6). The same phenomenon can also be observed when re-weighting a trial through a IPSW procedure, adapting the weights estimation strategies. To our knowledge, such a version of the IPSW estimator where all quantities are estimated is not present in the generalization literature, except in recent works (Josey et al., 2021; Chattopadhyay et al., 2022). In particular Chattopadhyay et al. (2022) also advocate what they call a one-step re-weighting procedure, for generalizing from an observational sample to another observational sample using balancing. Note that if Cole and Stuart (2010) present IPSW with an oracle π as done in Definitions 3, 5, and 6, other estimation procedure can be considered. For example, Buchanan et al. (2018) introduce IPSW where $\hat{\pi}$ is estimated once on the whole trial sample. In our work, we estimate π per strata, and then adapt the semi-oracle IPSW (Definition 5) and the completely estimated IPSW (Definition 6).

Definition 7 (Estimation of $\hat{\pi}$ for each strata). *Under the setting defined in Subsection 3.1.1,*

$$\forall x \in \mathbb{X}, \hat{\pi}_n(x) = \frac{\sum_{i \in \mathcal{R}} \mathbb{1}_{X_i=x} \mathbb{1}_{A_i=1}}{\sum_{i \in \mathcal{R}} \mathbb{1}_{X_i=x}}.$$

Definition 8 (Semi-oracle IPSW with $\hat{\pi}$). *The semi-oracle IPSW estimator $\hat{\tau}_{T,n}^*$ with estimated propensity scores $\hat{\pi}_n$ is defined as*

$$\hat{\tau}_{T,n}^* = \frac{1}{n} \sum_{i=1}^n \frac{p_T(X_i)}{\hat{p}_{R,n}(X_i)} Y_i \left(\frac{A_i}{\hat{\pi}_n(X_i)} - \frac{1-A_i}{1-\hat{\pi}_n(X_i)} \right), \quad (13)$$

with $\hat{p}_{R,n}(x)$ and $\hat{\pi}_n(x)$ defined in Definitions 4 and 7.

Definition 9 (IPSW with $\hat{\pi}$). *The semi-oracle IPSW estimator $\hat{\tau}_{n,m}$ with estimated propensity scores $\hat{\pi}_n$ is defined as*

$$\hat{\tau}_{n,m} = \frac{1}{n} \sum_{i=1}^n \frac{\hat{p}_{T,m}(X_i)}{\hat{p}_{R,n}(X_i)} Y_i \left(\frac{A_i}{\hat{\pi}_n(X_i)} - \frac{1 - A_i}{1 - \hat{\pi}_n(X_i)} \right), \quad (14)$$

where $\hat{p}_{T,m}(x)$, $\hat{p}_{R,n}(x)$, and $\hat{\pi}_n(x)$ defined in Definitions 4 and 7.

Corollary 3 (Properties when also estimating π). *Under the general setting defined in Subsection 3.1.1, granting Assumptions 1-4, the bias of the completely estimated IPSW with estimated $\hat{\pi}$ is given by*

$$\mathbb{E}[\hat{\tau}_{n,m}] - \tau = - \sum_{x \in \mathbb{X}} p_T(x) \tau(x) \left(1 - \frac{p_R(x)}{2} \right)^n - \sum_{x \in \mathbb{X}} p_T(x) \tau(x) (1 - p_R(x))^n.$$

Proof is detailed in Subsection A.4.

Conjecture 1. *Under the general setting defined in Subsection 3.1.1, granting Assumptions 1-4, the asymptotic variance of the completely estimated IPSW is the same as in Corollary 2, but replacing $V_{HT}(x)$ by $V_{DM}(x)$, where*

$$V_{DM}(x) = \frac{\text{Var}_R[Y^{(1)} | X = x]}{\pi} + \frac{\text{Var}_R[Y^{(0)} | X = x]}{1 - \pi}.$$

As a consequence, because $\forall x \in \mathbb{X}$, $V_{DM}(x) \leq V_{HT}(x)$, the large sample variance of the semi-oracle and completely estimated IPSW are smaller. The finite-sample bounds are also shrunk. This is why this estimator is recommended in practice.

4.3 Extended adjustment set

In this section, we detail the impact of adding covariates that are not necessary for adjustment – for example being only shifted or only treatment effect modifiers – on the IPSW performances. Indeed, in the literature, one of the common approach is to adjust on all shifted covariates, also named the *sampling set* (Cole and Stuart, 2010; Tipton, 2013). Another adjustment set is also possible, being the *heterogeneity set* comprising all the treatment effect modifiers (Hartman, 2021), even if, knowing which covariate is treatment effect modifier is harder. As mentioned in the related work (Subsection 2.2), there is an important literature about optimal adjustment set for precision in the causal inference literature, but to our knowledge the topic has not been tackled yet when it comes to efficiency in generalization. Egami and Hartman (2021) discuss extensively the usage of these two sets for identification but do not study their impact on the asymptotic variance.

Formalization Consider that the user has at disposal an external set of baseline categorical covariates denoted V . We assume that Assumptions 3 and 4 are preserved when adding V to the adjustment set X previously considered². As mentioned above, this external covariates set can be of two different natures.

Definition 10 (V is not a treatment effect modifier). *V does not modulate treatment effect modifier, that is*

$$\forall v \in \mathbb{V}, \forall s \in \{T, R\}, \mathbb{P}_s(Y^{(1)} - Y^{(0)} | X = x, V = v) = \mathbb{P}_s(Y^{(1)} - Y^{(0)} | X = x).$$

Definition 11 (V is not shifted). *V is not shifted, that is*

$$\forall v \in \mathbb{V}, p_T(v) = p_R(v).$$

To distinguish estimator using the set X or the extended set X, V , we denote $\hat{\tau}(X)$ and $\hat{\tau}(X, V)$ the two estimations strategies. In this section, we only provide results for the semi-oracle estimator (Definition 8), that is a situation where the target sample is infinitely large compared to the trial sample size. One can show that adding only shifted covariates V leads to a loss of precision, when the set V is independent of the set X .

Corollary 4 (Adding shifted and independent covariates). *Consider the semi-oracle IPSW estimator $\hat{\tau}_{T,n}^*$ (Definition 8), and a set of additional shifted covariates V (Definition 10) independent of X , which are not treatment effect modifiers. Then,*

$$\lim_{n \rightarrow \infty} n \text{Var}_R[\hat{\tau}_{T,n}^*(X, V)] = \left(\sum_{v \in \mathbb{V}} \frac{p_T(v)^2}{p_R(v)} \right) \lim_{n \rightarrow \infty} n \text{Var}_R[\hat{\tau}_{T,n}^*(X)].$$

²Note that if preserving transportability is pretty straightforward as V is a baseline covariate too (for e.g. no collider bias), the support inclusion's assumption can be more challenging when adding too many covariates (see D'Amour et al. (2017) for a discussion).

Proof is detailed in Subsection B.1. This results states that the asymptotic variance of the semi-oracle estimator is always bigger if an additional independent shifted covariate set V is added in the adjustment. Moreover, the stronger the shift, the bigger the variance inflation. Note that this specific rule was retrieved in the toy example, where the plain line (corresponding to Corollary 4) matches the empirical dots on Figure 4a.

On the contrary, adding an additional treatment effect modifier covariate set leads to a gain in precision.

Corollary 5 (Adding non-shifted treatment effect modifiers). *Consider the semi-oracle IPSW estimator $\hat{\tau}_{T,n}^*$ (Definition 8). Consider an additional non-shifted treatment effect modifier set (Definition 11) independent of X . Then,*

$$\lim_{n \rightarrow \infty} n \text{Var}_R [\hat{\tau}_{T,n}^*(X, V)] = \lim_{n \rightarrow \infty} n \text{Var}_R [\hat{\tau}_{T,n}^*(X)] - \mathbb{E}_R \left[\frac{p_T(X)}{p_R(X)} \text{Var} [\tau(X, V) | X] \right].$$

In particular,

$$\lim_{n \rightarrow \infty} n \text{Var}_R [\hat{\tau}_{T,n}^*(X, V)] \leq \lim_{n \rightarrow \infty} n \text{Var}_R [\hat{\tau}_{T,n}^*(X)].$$

Proof is detailed in Subsection B.2. More particularly, the variance diminution is related to how much the additional covariates V can explain $\text{Var} [Y^{(a)} | X = x, V = v]$ compared to $\text{Var} [Y^{(a)} | X = x]$. Proof is detailed in Subsection B.2. This result follows a similar spirit as Rotnitzky and Smucler (2020) due to the comparison of two asymptotic variances, even though the context and the theoretical tools are different.

5 Synthetic and semi-synthetic simulations

In this section, one additional analysis based on the toy example is provided to illustrate the different asymptotic regimes from Section 4. In addition, results are also illustrated on a semi-synthetic simulation aiming to mimic a medical scenario. The code to reproduce the simulations and the different figures is available on Github³.

5.1 Synthetic: additional experiment from the toy example

While most of the results are illustrated at the beginning of the article through the toy example, we complete this section investigating experimentally the different asymptotic regimes of the IPSW and its variants. In particular we complete Figure 3c that is only raising attention to the phenomenon of different asymptotic regimes, with a complete visualization of risks and variances. More precisely, the quadratic risk is depicted in Figure 6b, while the variance via $\min(n, m) \text{Var} [\hat{\tau}_{n,m}]$ is displayed in Figure 6a. In both figures, different estimators (oracle or not) are considered with different regimes for m , as n grows to infinity. In particular, this simulation confirms that

- (i) all IPSW variants are consistent, even though their convergence speeds depend on the regime (Figure 6b),
- (ii) the completely oracle IPSW has a bigger variance than the semi-oracle one (Figure 6a),
- (iii) the asymptotic variance depends on the asymptotic regime (Figure 6a),
- (iv) the completely estimated IPSW reaches the variance of the semi-oracle one if the target population sample is bigger than the trial (Figure 6a).

5.2 Semi-synthetic

5.2.1 Design

Two data-sets are used to generate two sources:

1. A randomized controlled trial (RCT), called CRASH-3 (Dewan et al., 2012), aiming to measure the effect of Tranexamic Acide (TXA) to prevent death from Traumatic Brain Injury (TBI). A total of 175 hospitals in 29 different countries participated to the RCT, where adults with TBI suffering from intracranial bleeding were randomly administrated TXA (CRASH-3, 2019). The inclusion criteria of the trial are patients with a Glasgow Coma Scale (GCS)⁴ score of 12 or lower or any intracranial bleeding on CT scan, and no major extracranial bleeding.

³BenedicteColnet/IPSW-categorical.

⁴The Glasgow Coma Scale (GCS) is a neurological scale which aims to assess a person's consciousness. The lower the score, the higher the gravity of the trauma.

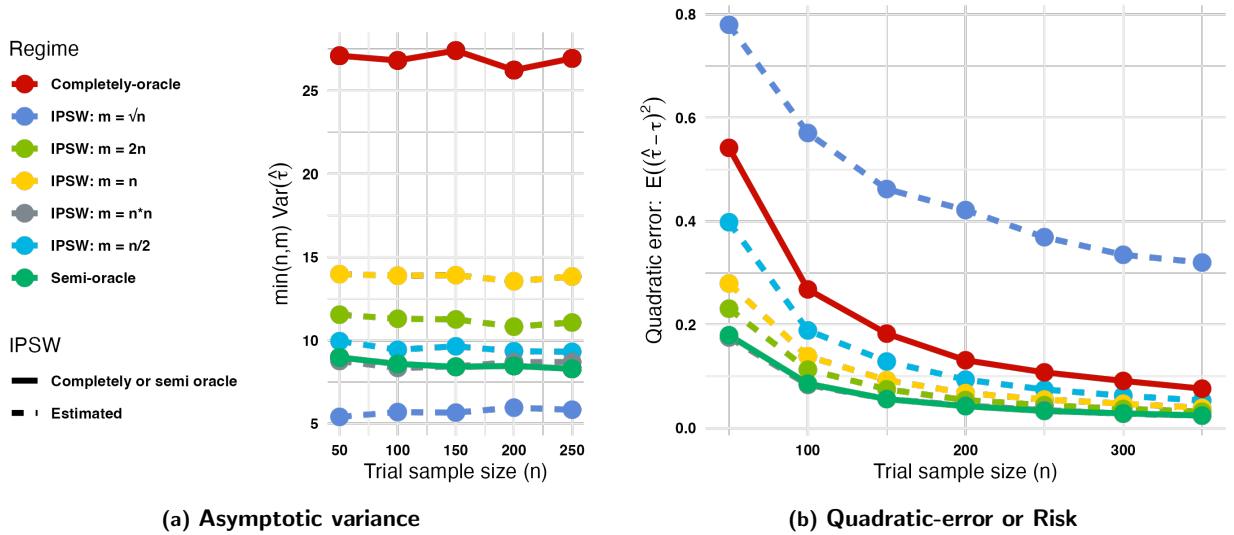


Figure 6: Risks and different asymptotic regimes: Based on the toy example simulation (see Section 2 and data-generative process from Figure 3a) where empirical variance from either the completely oracle (Definition 3), the semi-oracle (Definition 5) or the completely estimated IPSW (Definition 6) are estimated repeating 6,000 times each simulation for each trial sample size (x -axis). Simulations cover different regimes of size n and m . On the y -axis the empirical variance $\min(n,m) \text{Var}[\hat{\tau}_{n,m}]$ is plotted (with the exception of $\min(n,m) = n$ for completely- and semi- oracle variants, represented in plain lines). Each color represents one specific estimator and regime.

2. An observational cohort, called Traumabase, comprising 23 French Trauma centers, collects detailed clinical data from the scene of the accident to the release from the hospital. The resulting database, called the Traumabase, comprises 23,000 trauma admissions to date, and is continually updated, representing a fair, almost-exhaustive data base about actual individuals taken in charge in France and suffering from trauma.

These two data sources are turned into two source populations representing a real-world situation with six covariates so that the distribution structure and, in particular, the distributional shift mimics a real-world situation. The six covariates kept in common are: GCS (categorical), gender (categorical), pupil reactivity (categorical), age (continuous), systolic blood pressure (continuous), and time-to-treatment (TTT) (continuous). The continuous covariates are then turned into categories. Additional details about data preparation are available in Appendix (see Section C). In this semi-synthetic simulation, only the outcome model is completely synthetic, and follows

$$Y := f(\text{GCS}, \text{Gender}) + A\tau(\text{TTT}, \text{Blood Pressure}) + \epsilon_{\text{TTT}}, \quad (15)$$

where f and τ are two functions of the covariates, and ϵ_{TTT} is a gaussian noise such that $E[\epsilon_{\text{TTT}} | X] = 0$, but where heteroscedasticity is observed along the covariate TTT. The higher the time-to-treatment, the more variable the outcome Y (see Section C for the detailed generated function). This outcome model is such that only time-to-treatment (TTT), age, and gender are so-called treatment effect modifiers, while other covariates only affects the baseline value or have no impact. Each time a simulation is conducted observations are sampled from the two populations with replacement, and the outcome is created following equation (15). The trial is such that $\pi = 0.5$.

5.2.2 Results

Simulations illustrate the re-weighting procedure, and in particular the fact that estimating π (Definition 9) or not (Definition 6) changes the variance, as shown on Figure 7 (1,000 repetitions). Note that the variance of the IPSW - with estimation of π or not - has a similar variance as the estimates coming from the RCT only (Horvitz-Thomson or difference-in-means). This is due to the presence of heteroscedasticity or not in the generative model (see equation (15)). The fact that the model is such that individuals treated lately have more uncertainty in the response (encoded in ϵ_{TTT} , whose variance depends on the covariate TTT) can lead to an IPSW variance that is smaller than the treatment effect estimator on the trial. This is what can also be observed on Figure 7.

5.2.3 Additional takeaway

Finally, we would like to emphasize that re-weighting the trial does not necessarily lead to wider confidence intervals, as illustrated on Figure 7. A common and intuitive idea stating that a re-weighted trial always has a

Figure 7: IPSW estimating π or not: Simulations with $n = 500$, $m = 10000$ where the IPSW estimator from Definitions 6 and 9 are compared to the estimates of the non-reweighted trials (Definitions 1 and 2) showing that the IPSW allow to recover the true ATE on the target population represented by the red dashed line (illustrating consistency from Theorem 3). Estimating π leads to a lower variance as expected (Conjecture 1).

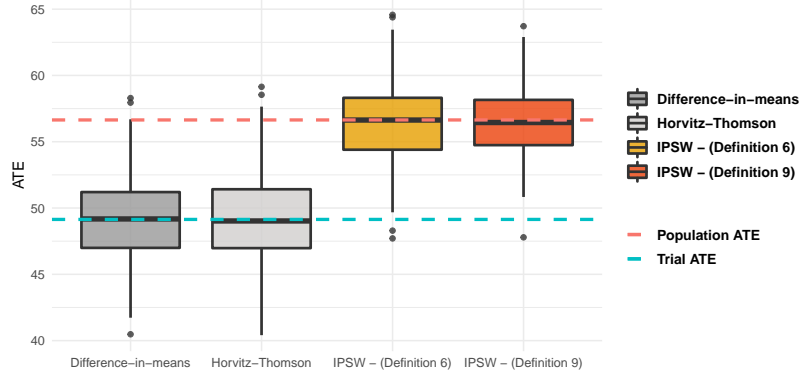
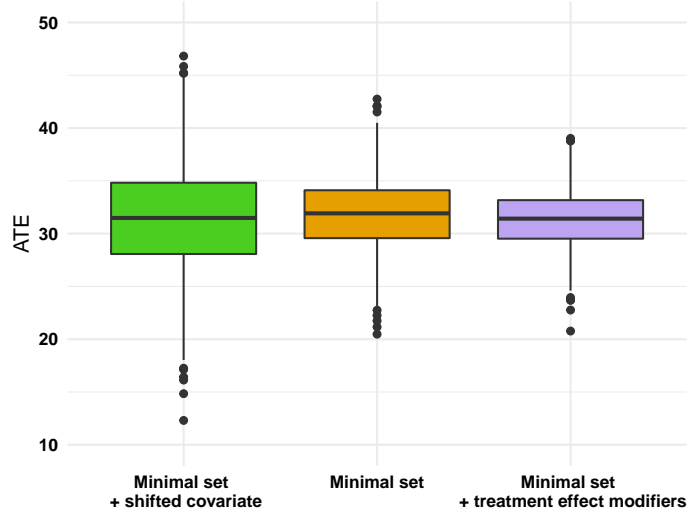


Figure 8: Effect of non-necessary covariates on the variance: IPSW (Definition 9) with $n = 3000$ and $m = 10000$ showing that the addition of the covariate GCS (shifted covariate not being a treatment effect modifier) increases the variance of the IPSW, while the addition of a non-shifted treatment effect modifier (here simulated as no covariates from the actual data base where not shifted) leads to an improvement in variance, compared to the minimal set. Simulations are repeated 1,000 times.



larger variance than the trial itself (Gatsonis and Sally, 2017; Ling et al., 2022) can be found in the literature. Indeed, this is due to the multiplication of weights that can take large values (in particular if, for some x , $p_R(x) \ll p_T(x)$). For example, the asymptotic variance of the semi-oracle IPSW from Corollary 1 highlights that this intuitive and reasonable idea is not necessarily true, as soon as there is heteroscedascity, which occurs if some categories for which potential outcomes have higher uncertainty (bigger noise) are more represented on the trial than in the target population.

$$V_{so} = \sum_{x \in \mathcal{X}} \underbrace{\frac{p_T^2(x)}{p_R(x)}}_{\text{Weights}} \left(\frac{\text{Var}[Y^{(1)}|X=x]}{\pi} + \frac{\text{Var}[Y^{(0)}|X=x]}{1-\pi} \right)$$

Can be small for some x with high weights $\frac{p_T^2(x)}{p_R(x)}$

In the semi-simulation strata, high TTT are more represented on the trial than on the target population, and admit responses with higher noise as detailed in the outcome model (15). Therefore in Figure 7, the re-weighted trials have a lower variance.

6 Conclusion and future work

In this work, we establish finite-sample and asymptotic results on different versions of the so-called *Inverse Propensity Sampling Weights* estimator, when the adjustment set is constituted of categorical covariates. The explicit expressions of the biases and variances are computed for all estimates, together with their quadratic risk. Our detailed analysis allows us to compare this different estimate in different finite-sample regimes. Indeed, to the best of our knowledge, our work is the first to study the impact of finite trial and observational data sets on IPSW performance in the context of generalization, by providing rate of convergence for several IPSW estimates. By doing so, we link these results with former results in epidemiology where one data source was considered infinite, and also explain how certain observations can be seen through the eyes of seminal work in causal inference (efficient estimation with IPW). This work also emphasizes that great care should be taken when selecting the covariates to generalize. From applied literature, we have noticed that practitioners usually

select almost all available covariates to build the weights, which is encouraged by the serious fear of missing one important shifted treatment effect modifier. We show that inclusion of many covariates is at the risk of adjusting on shifted covariates that are not treatment effect modifiers, which can drastically damage the precision. On the contrary, even though adding some non-shifted covariates may sound counter intuitive, we show that such practice improves asymptotic precision, as soon as the non-shifted additional covariate set modulates treatment effect. Still, adding too many covariates endangers overlap and therefore can lead to finite sample bias. In light of these theoretical results, we believe that physicians and epidemiologists have an important role to play in selecting a limited number of covariates when generalizing trial’s findings.

Future work While studying only categorical covariates might sound restrictive, this remark is balanced by the fact that within the medical field, clinical indicators and covariates are often scores and categories. For example Berkowitz et al. (2018) apply the IPSW to generalize the effect of blood pressure control relying on many categorical covariates such as health insurance status (insured, uninsured), tobacco smoking status (never, current, former), and so on. Even when facing an hybrid set of covariates - continuous and categorical - the user can still create bins for continuous covariates. Indeed, doing so leads to within-stratum confounding, that is a residual confounding due to rough bins, and therefore to an asymptotic bias due to factors that are poorly controlled on. To avoid within-stratum residual confounding, it is desirable to carve the data into more strata, but stratifying too finely may lead to (i) a variance inflation and (ii) the support inclusion assumption’s invalidity. Therefore, when facing continuous covariates in practice, the solution would be found at the crossroads between identification bias (due to imprecise bins) and variance inflation or finite sample bias (due to numerous bins). Quantifying such a tradeoff in specific setting would definitely help the practitioners by providing clear guidelines.

Future works will focus on extending our theoretical results to more general settings, including, for example, continuous covariates. As the IPSW is known for its high variance, future works should extend theoretical results in finite sample and different asymptotic regimes for other estimators of the target population ATE, such as G-formula or Augmented-IPSW.

Acknowledgment

Part of this work was written during a visiting scholar period in the Stanford’s Statistics Department. Therefore, we would like to thank the department for their welcoming and all the helpful and inspiring discussions, in particular with Prof. Trevor HASTIE.

References

- Arnould, L., C. Boyer, and E. Scornet (2021, 18–24 Jul). Analyzing the tree-layer structure of deep forests. In M. Meila and T. Zhang (Eds.), *Proceedings of the 38th International Conference on Machine Learning*, Volume 139 of *Proceedings of Machine Learning Research*, pp. 342–350. PMLR.
- Athey, S., R. Chetty, and G. Imbens (2020). Combining experimental and observational data to estimate treatment effects on long term outcomes. *arXiv preprint arXiv:2006.09676*.
- Bareinboim, E. and J. Pearl (2012a). Controlling selection bias in causal inference. In N. D. Lawrence and M. Girolami (Eds.), *Proceedings of the Fifteenth International Conference on Artificial Intelligence and Statistics*, Volume 22 of *Proceedings of Machine Learning Research*, La Palma, Canary Islands, pp. 100–108. PMLR.
- Bareinboim, E. and J. Pearl (2012b). Transportability of causal effects: Completeness results. In *Proceedings of the Twenty-Sixth AAAI Conference on Artificial Intelligence*, AAAI’12, pp. 698–704. AAAI Press.
- Berkowitz, S. A., J. B. Sussman, D. E. Jonas, and S. Basu (2018). Generalizing intensive blood pressure treatment to adults with diabetes mellitus. *Journal of the American College of Cardiology* 72(11), 1214–1223. SPECIAL FOCUS ISSUE: BLOOD PRESSURE.
- Biau, G. (2012). Analysis of a random forests model. *Journal of Machine Learning Research* 13(38), 1063–1095.
- Brookhart, M. A., S. Schneeweiss, K. J. Rothman, R. J. Glynn, J. Avorn, and T. Stürmer (2006). Variable selection for propensity score models. *American journal of epidemiology* 163(12), 1149–1156.
- Buchanan, A. L., M. G. Hudgens, S. R. Cole, K. R. Mollan, P. E. Sax, E. S. Daar, A. A. Adimora, J. J. Eron, and M. J. Mugavero (2018). Generalizing evidence from randomized trials using inverse probability of sampling weights. *Journal of the Royal Statistical Society: Series A (Statistics in Society)* 181, 1193–1209.

- Chattopadhyay, A., E. R. Cohn, and J. R. Zubizarreta (2022). One-step weighting to generalize and transport treatment effect estimates to a target population.
- Cinelli, C., A. Forney, and J. Pearl (2022). A crash course in good and bad controls. *Sociological Methods & Research*.
- Cole, S. R. and E. A. Stuart (2010). Generalizing evidence from randomized clinical trials to target populations: The actg 320 trial. *American Journal of Epidemiology* 172, 107–115.
- Colnet, B., I. Mayer, G. Chen, A. Dieng, R. Li, G. Varoquaux, J.-P. Vert, J. Josse, and S. Yang (2020). Causal inference methods for combining randomized trials and observational studies: a review.
- Colnet, B., I. Mayer, G. Chen, A. Dieng, R. Li, G. Varoquaux, J.-P. Vert, J. Josse, and S. Yang (2021). Causal inference methods for combining randomized trials and observational studies: a review.
- CRASH-3 (2019). Effects of tranexamic acid on death, disability, vascular occlusive events and other morbidities in patients with acute traumatic brain injury (CRASH-3): a randomised, placebo-controlled trial. *The Lancet* 394(10210), 1713–1723.
- Dahabreh, I. J., S. E. Robertson, J. A. Steingrimsson, E. A. Stuart, and M. A. Hernán (2020). Extending inferences from a randomized trial to a new target population. *Statistics in Medicine* 39(14), 1999–2014.
- Dahabreh, I. J., J. M. Robins, S. J. Haneuse, and M. A. Hernán (2019). Generalizing causal inferences from randomized trials: counterfactual and graphical identification. *arXiv preprint arXiv:1906.10792*.
- D’Amour, A., P. Ding, A. Feller, L. Lei, and J. Sekhon (2017, 11). Overlap in observational studies with high-dimensional covariates. *Journal of Econometrics* 221.
- Deaton, A. and N. Cartwright (2018). Understanding and misunderstanding randomized controlled trials. *Social Science & Medicine* 210, 2–21. Randomized Controlled Trials and Evidence-based Policy: A Multidisciplinary Dialogue.
- Degtiar, I. and S. Rose (2021). A review of generalizability and transportability.
- Dewan, Y., E. Komolafe, J. Mejía-Mantilla, P. Perel, I. Roberts, and H. Shakur-Still (2012, 06). CRASH-3: Tranexamic acid for the treatment of significant traumatic brain injury: study protocol for an international randomized, double-blind, placebo-controlled trial. *Trials* 13, 87.
- Efron, B. and D. V. Hinkley (1978). Assessing the accuracy of the maximum likelihood estimator: Observed versus expected fisher information. *Biometrika* 65(3), 457–482.
- Egami, N. and E. Hartman (2021, 08). Covariate selection for generalizing experimental results: Application to a large-scale development program in uganda*. *Journal of the Royal Statistical Society: Series A (Statistics in Society)* 184.
- Gatsonis, C. and M. C. Sally (2017). *Methods in Comparative Effectiveness Research*, pp. 177–199. Chapman & Hall.
- Hahn, J. (1998). On the role of the propensity score in efficient semiparametric estimation of average treatment effects. *Econometrica* 66(2), 315–332.
- Hahn, J. (2004, 02). Functional restriction and efficiency in causal inference. *The Review of Economics and Statistics* 86, 73–76.
- Hartman, E. (2021). *Generalizing Experimental Results*, pp. 385–410. Cambridge University Press.
- Hartman, E., R. Grieve, R. Ramsahai, and J. S. Sekhon (2015). From sample average treatment effect to population average treatment effect on the treated: combining experimental with observational studies to estimate population treatment effects. *Journal of the Royal Statistical Society: Series A (Statistics in Society)* 178(3), 757–778.
- Henckel, L., E. Perković, and M. H. Maathuis (2019). Graphical criteria for efficient total effect estimation via adjustment in causal linear models.
- Hernan, MA Robins, J. (2020). *Causal Inference: What If*.
- Hirano, K., G. Imbens, and G. Ridder (2003, 02). Efficient estimation of average treatment effects using the estimated propensity score. *Econometrica* 71, 1161–1189.

- Horvitz, D. G. and D. J. Thompson (1952). A generalization of sampling without replacement from a finite universe. *Journal of the American Statistical Association* 47(260), 663–685.
- Huitfeldt, A., S. Swanson, M. Stensrud, and E. Suzuki (2019, 12). Effect heterogeneity and variable selection for standardizing causal effects to a target population. *European Journal of Epidemiology* 34.
- Imbens, G. W. and D. B. Rubin (2015). *Causal Inference in Statistics, Social, and Biomedical Sciences*. Cambridge UK: Cambridge University Press.
- Josey, K. P., S. A. Berkowitz, D. Ghosh, and S. Raghavan (2021). Transporting experimental results with entropy balancing. *Statistics in Medicine* 40(19), 4310–4326.
- Kallus, N., A. M. Puli, and U. Shalit (2018). Removing hidden confounding by experimental grounding. In *Advances in neural information processing systems*, pp. 10888–10897.
- Kern, H. L., E. A. Stuart, J. Hill, and D. P. Green (2016). Assessing methods for generalizing experimental impact estimates to target populations. *Journal of research on educational effectiveness* 9(1), 103–127.
- Lee, D., S. Yang, L. Dong, X. Wang, D. Zeng, and J. Cai (2022). Improving trial generalizability using observational studies. *doi:10.1111/biom.13609*.
- Lefebvre, G., J. Delaney, and R. Platt (2008, 08). Impact of mis-specification of the treatment model on estimates from a marginal structural model. *Statistics in medicine* 27, 3629–42.
- Ling, A. Y., M. E. Montez-Rath, P. Carita, K. Chandross, L. Lucats, Z. Meng, B. Sebastien, K. Kappahn, and M. Desai (2022). A critical review of methods for real-world applications to generalize or transport clinical trial findings to target populations of interest.
- Liu, R., S. Rizzo, S. Whipple, N. Pal, A. Lopez Pineda, M. Lu, B. Arnieri, Y. Lu, W. Capra, R. Copping, and J. Zou (2021, 04). Evaluating eligibility criteria of oncology trials using real-world data and ai. *Nature* 592.
- Lunceford, J. K. and M. Davidian (2004). Stratification and weighting via the propensity score in estimation of causal treatment effects: A comparative study. In *Statistics in Medicine*, pp. 2937–2960.
- Nie, X., G. Imbens, and S. Wager (2021). Covariate balancing sensitivity analysis for extrapolating randomized trials across locations.
- O’Muircheartaigh, C. and L. Hedges (2013, 11). Generalizing from unrepresentative experiments: A stratified propensity score approach. *Journal of the Royal Statistical Society: Series C (Applied Statistics)* 63.
- Pearl, J. (2015). Generalizing experimental findings. *Journal of Causal Inference* 3(2), 259–266.
- Pearl, J. and E. Bareinboim (2011). Transportability of causal and statistical relations: A formal approach. In *Proceedings of the Twenty-Fifth AAAI Conference on Artificial Intelligence, AAAI’11*, pp. 247–254. AAAI Press.
- Rosenbaum, P. R. and D. B. Rubin (1983). The central role of the propensity score in observational studies for causal effects. *Biometrika* 70(1), 41–55.
- Rothman, K. J. (2011). *Epidemiology: an introduction* (2 ed.). Oxford University Press.
- Rothman, K. J. and S. Greenland (2000). *Modern Epidemiology* (2 ed.). Lippincott Williams and Wilkins.
- Rothwell, P. (2007, 01). External validity of randomised controlled trials: “to whom do the results of this trial apply?”. *Lancet* 365, 82–93.
- Rotnitzky, A. and E. Smucler (2020). Efficient adjustment sets for population average causal treatment effect estimation in graphical models. *Journal of Machine Learning Research* 21(188), 1–86.
- Schnitzer, M., J. Lok, and S. Gruber (2015, 07). Variable selection for confounder control, flexible modeling and collaborative targeted minimum loss-based estimation in causal inference. *The international journal of biostatistics* 12.
- Stefanski, L. A. and D. D. Boos (2002). The calculus of m-estimation. *The American Statistician* 56(1), 29–38.
- Stuart, E. A., S. R. Cole, C. P. Bradshaw, and P. J. Leaf (2011). The use of propensity scores to assess the generalizability of results from randomized trials. *Journal of the Royal Statistical Society: Series A (Statistics in Society)* 174, 369–386.

- Stuart, E. A. and A. Rhodes (2017). Generalizing treatment effect estimates from sample to population: A case study in the difficulties of finding sufficient data. *Evaluation Review* 41(4), 357–388. PMID: 27491758.
- Tipton, E. (2013). Improving generalizations from experiments using propensity score subclassification: Assumptions, properties, and contexts. *Journal of Educational and Behavioral Statistics* 38, 239–266.
- Tipton, E., K. Hallberg, L. Hedges, and W. Chan (2016, 07). Implications of small samples for generalization: Adjustments and rules of thumb. *Evaluation Review* 41.
- Velentgas, P., N. A. Dreyer, P. Nourjah, S. R. Smith, and M. Torchia (2013). Developing a protocol for observational comparative effectiveness research: A user’s guide.
- Wager, S. (2020). Stats 361: Causal inference.
- Westreich, D., J. Edwards, C. Lesko, E. Stuart, and S. Cole (2017, 05). Transportability of trial results using inverse odds of sampling weights. *American journal of epidemiology* 186.
- Witte, J. and V. Didelez (2018, 10). Covariate selection strategies for causal inference: Classification and comparison. *Biometrical Journal* 61.
- Wooldridge, J. (2016). Should instrumental variables be used as matching variables? *Research in Economics* 70(2), 232–237.

APPENDIX

A Main proofs

A.1 Proof of Theorem 1 - Completely oracle estimator $\hat{\tau}_{\pi, \mathbb{T}, \mathbb{R}, n}^*$

We first recall the expression of the completely oracle estimator introduced in Definition 3,

$$\hat{\tau}_{\pi, \mathbb{T}, \mathbb{R}, n}^* = \frac{1}{n} \sum_{i=1}^n \frac{p_{\mathbb{T}}(X_i)}{p_{\mathbb{R}}(X_i)} \left(\frac{Y_i A_i}{\pi} - \frac{Y_i(1 - A_i)}{1 - \pi} \right).$$

This estimator can be rewritten as,

$$\hat{\tau}_{\pi, \mathbb{T}, \mathbb{R}, n}^* = \sum_{x \in \mathbb{X}} \frac{p_{\mathbb{T}}(x)}{p_{\mathbb{R}}(x)} \left(\frac{1}{n} \sum_{i=1}^n \mathbb{1}_{X_i=x} \left(\frac{Y_i A_i}{\pi} - \frac{Y_i(1 - A_i)}{1 - \pi} \right) \right),$$

since X_i take values in a categorical set \mathbb{X} . This rewriting is extensively used in the proof.

Bias

Recall that, for all $x \in \mathbb{X}$, $p_{\mathbb{R}}(x)$ and $p_{\mathbb{T}}(x)$ are not random variables. We have

$$\begin{aligned} \mathbb{E} [\hat{\tau}_{\pi, \mathbb{T}, \mathbb{R}, n}^*] &= \mathbb{E} \left[\sum_{x \in \mathbb{X}} \frac{p_{\mathbb{T}}(x)}{p_{\mathbb{R}}(x)} \frac{1}{n} \sum_{i=1}^n \mathbb{1}_{X_i=x} \left(\frac{Y_i A_i}{\pi} - \frac{Y_i(1 - A_i)}{1 - \pi} \right) \right] && \text{By definition} \\ &= \sum_{x \in \mathbb{X}} \mathbb{E} \left[\frac{p_{\mathbb{T}}(x)}{p_{\mathbb{R}}(x)} \frac{1}{n} \sum_{i=1}^n \mathbb{1}_{X_i=x} \left(\frac{Y_i A_i}{\pi} - \frac{Y_i(1 - A_i)}{1 - \pi} \right) \right] && \text{Linearity of } \mathbb{E}[\cdot] \\ &= \sum_{x \in \mathbb{X}} \frac{p_{\mathbb{T}}(x)}{p_{\mathbb{R}}(x)} \mathbb{E} \left[\frac{1}{n} \sum_{i=1}^n \mathbb{1}_{X_i=x} \left(\frac{Y_i A_i}{\pi} - \frac{Y_i(1 - A_i)}{1 - \pi} \right) \right] && p_{\mathbb{R}}(x) \text{ and } p_{\mathbb{T}}(x) \text{ are not random} \\ &= \sum_{x \in \mathbb{X}} \frac{p_{\mathbb{T}}(x)}{p_{\mathbb{R}}(x)} \mathbb{E}_{\mathbb{R}} \left[\mathbb{1}_{X_i=x} \left(\frac{Y_i A_i}{\pi} - \frac{Y_i(1 - A_i)}{1 - \pi} \right) \right] && \text{Linearity \& iid trial} \\ &= \sum_{x \in \mathbb{X}} \frac{p_{\mathbb{T}}(x)}{p_{\mathbb{R}}(x)} \mathbb{E}_{\mathbb{R}} \left[\mathbb{1}_{X_i=x} \left(\frac{Y_i^{(1)} A_i}{\pi} - \frac{Y_i^{(0)}(1 - A_i)}{1 - \pi} \right) \right] && \text{SUTVA (see Assumption 2).} \end{aligned}$$

Noting that,

$$p_{\mathbb{R}}(x) = \mathbb{P}_{\mathbb{R}}[X = x] = \mathbb{P}_{\mathbb{R}}[X_i = x] = \mathbb{E}_{\mathbb{R}}[\mathbb{1}_{X_i=x}],$$

one can condition on the random variable X_i , yielding

$$\mathbb{E}_{\mathbb{R}} \left[\mathbb{1}_{X_i=x} \left(\frac{Y_i^{(1)} A_i}{\pi} - \frac{Y_i^{(0)}(1 - A_i)}{1 - \pi} \right) \right] = \mathbb{E}_{\mathbb{R}} \left[\frac{Y_i^{(1)} A_i}{\pi} - \frac{Y_i^{(0)}(1 - A_i)}{1 - \pi} \mid X_i = x \right] \underbrace{\mathbb{E}_{\mathbb{R}}[\mathbb{1}_{X_i=x}]}_{=p_{\mathbb{R}}(x)}.$$

Then,

$$\begin{aligned}
\mathbb{E} [\hat{\tau}_{\pi, \text{T}, \text{R}, n}^*] &= \sum_{x \in \mathbb{X}} p_{\text{T}}(x) \mathbb{E}_{\text{R}} \left[\frac{Y_i^{(1)} A_i}{\pi} - \frac{Y_i^{(0)} (1 - A_i)}{1 - \pi} \mid X_i = x \right] && \text{From previous derivations} \\
&= \sum_{x \in \mathbb{X}} p_{\text{T}}(x) \left(\frac{\mathbb{E}_{\text{R}} [Y_i^{(1)} A_i \mid X_i = x]}{\pi} - \frac{\mathbb{E}_{\text{R}} [Y_i^{(0)} (1 - A_i) \mid X_i = x]}{1 - \pi} \right) && \text{Linearity of } \mathbb{E}[\cdot] \text{ and } \pi \text{ is constant} \\
&= \sum_{x \in \mathbb{X}} p_{\text{T}}(x) \left(\frac{\mathbb{E}_{\text{R}} [Y_i^{(1)} \mid X_i = x] \mathbb{E}_{\text{R}} [A_i \mid X_i = x]}{\pi} \right. \\
&\quad \left. - \frac{\mathbb{E}_{\text{R}} [Y_i^{(0)} \mid X_i = x] \mathbb{E}_{\text{R}} [(1 - A_i) \mid X_i = x]}{1 - \pi} \right) && \text{Randomization (see Assumption 2)} \\
&= \sum_{x \in \mathbb{X}} p_{\text{T}}(x) \left(\mathbb{E}_{\text{R}} [Y_i^{(1)} \mid X_i = x] - \mathbb{E}_{\text{R}} [Y_i^{(0)} A_i \mid X_i = x] \right) && \mathbb{E}_{\text{R}} [(1 - A_i) \mid X_i = x] = \pi \\
&= \sum_{x \in \mathbb{X}} p_{\text{T}}(x) \mathbb{E}_{\text{R}} [Y_i^{(1)} - Y_i^{(0)} \mid X_i = x] && \text{Linearity of } \mathbb{E}[\cdot] \\
&= \sum_{x \in \mathbb{X}} p_{\text{T}}(x) \mathbb{E}_{\text{T}} [Y_i^{(1)} - Y_i^{(0)} \mid X_i = x] && \text{Transportability (see Assumption 3)} \\
&= \tau, && \text{Law of total probability}
\end{aligned}$$

which concludes the first part of the proof.

Variance

To shorten notation, we denote by $\mathbf{X}_n \in \mathbb{X}^n$ the vector composed of the n observations in the trial. We then use the law of total variance, conditioning on \mathbf{X}_n ,

$$\text{Var} [\hat{\tau}_{\pi, \text{T}, \text{R}, n}^*] = \text{Var} [\mathbb{E} [\hat{\tau}_{\pi, \text{T}, \text{R}, n}^* \mid \mathbf{X}_n]] + \mathbb{E} [\text{Var} [\hat{\tau}_{\pi, \text{T}, \text{R}, n}^* \mid \mathbf{X}_n]]. \quad (16)$$

Considering the first term in the right-hand side of (16),

$$\begin{aligned}
\mathbb{E} [\hat{\tau}_{\pi, \text{T}, \text{R}, n}^* \mid \mathbf{X}_n] &= \mathbb{E} \left[\sum_{x \in \mathbb{X}} \frac{p_{\text{T}}(x)}{p_{\text{R}}(x)} \frac{1}{n} \sum_{i=1}^n \mathbb{1}_{X_i=x} \left(\frac{Y_i^{(1)} A_i}{\pi} - \frac{Y_i^{(0)} (1 - A_i)}{1 - \pi} \right) \mid \mathbf{X}_n \right] && \text{By definition (and SUTVA)} \\
&= \sum_{x \in \mathbb{X}} \frac{p_{\text{T}}(x)}{p_{\text{R}}(x)} \frac{1}{n} \mathbb{E} \left[\sum_{i=1}^n \mathbb{1}_{X_i=x} \left(\frac{Y_i^{(1)} A_i}{\pi} - \frac{Y_i^{(0)} (1 - A_i)}{1 - \pi} \right) \mid \mathbf{X}_n \right]. && \text{Linearity of } \mathbb{E}[\cdot]
\end{aligned}$$

Note that this last derivation also uses the fact that neither $p_{\text{T}}(x)$ nor $p_{\text{R}}(x)$ are random variables.

$$\begin{aligned}
\mathbb{E} [\hat{\tau}_{\pi, \text{T}, \text{R}, n}^* \mid \mathbf{X}_n] &= \sum_{x \in \mathbb{X}} \frac{p_{\text{T}}(x)}{p_{\text{R}}(x)} \sum_{i=1}^n \frac{\mathbb{1}_{X_i=x}}{n} \mathbb{E} \left[\frac{Y_i^{(1)} A_i}{\pi} - \frac{Y_i^{(0)} (1 - A_i)}{1 - \pi} \mid X_i \right] && \text{iid individuals} \\
&= \sum_{x \in \mathbb{X}} \frac{p_{\text{T}}(x)}{p_{\text{R}}(x)} \sum_{i=1}^n \frac{\mathbb{1}_{X_i=x}}{n} \tau(X_i) \\
&= \frac{1}{n} \sum_{x \in \mathbb{X}} \frac{p_{\text{T}}(x)}{p_{\text{R}}(x)} \tau(x) \sum_{i=1}^n \mathbb{1}_{X_i=x} && \text{Transportability (see Assumption 3)}
\end{aligned}$$

Now, this last term can be written as a unique sum on $i \in \{1, \dots, n\}$, that is,

$$\frac{1}{n} \sum_{x \in \mathbb{X}} \frac{p_{\text{T}}(x)}{p_{\text{R}}(x)} \tau(x) \sum_{i=1}^n \mathbb{1}_{X_i=x} = \frac{1}{n} \sum_{i=1}^n \frac{p_{\text{T}}(X_i)}{p_{\text{R}}(X_i)} \tau(X_i).$$

Taking the variance of this term leads to,

$$\begin{aligned}
\text{Var} [\mathbb{E}_{\text{R}} [\hat{\tau}_{\pi, \text{T}, \text{R}, n}^* \mid \mathbf{X}_n]] &= \text{Var} \left[\frac{1}{n} \sum_{i=1}^n \frac{p_{\text{T}}(X_i)}{p_{\text{R}}(X_i)} \tau(X_i) \right] \\
&= \frac{1}{n} \text{Var}_{\text{R}} \left[\frac{p_{\text{T}}(X)}{p_{\text{R}}(X)} \tau(X) \right]. && \text{iid observations on trial (Assumption 2)} \quad (17)
\end{aligned}$$

Regarding the second term,

$$\begin{aligned}
\text{Var} [\hat{\tau}_{\pi, T, R, n}^* | \mathbf{X}_n] &= \text{Var}_{\mathbb{R}} \left[\frac{1}{n} \sum_{i=1}^n \frac{p_T(X_i)}{p_R(X_i)} \left(\frac{Y_i A_i}{\pi} - \frac{Y_i(1-A_i)}{1-\pi} \right) | \mathbf{X}_n \right] \\
&= \frac{1}{n^2} \sum_{i=1}^n \left(\frac{p_T(X_i)}{p_R(X_i)} \right)^2 \text{Var}_{\mathbb{R}} \left[\left(\frac{Y_i A_i}{\pi} - \frac{Y_i(1-A_i)}{1-\pi} \right) | \mathbf{X}_n \right] \\
&= \frac{1}{n^2} \sum_{i=1}^n \left(\frac{p_T(X_i)}{p_R(X_i)} \right)^2 \text{Var}_{\mathbb{R}} \left[\left(\frac{Y_i A_i}{\pi} - \frac{Y_i(1-A_i)}{1-\pi} \right) | X_i \right]. \tag{18}
\end{aligned}$$

Recall that the variance of the Horvitz-Thomson estimator (see Definition 1) conditioned on X_i is given by

$$\text{Var}_{\mathbb{R}} [\hat{\tau}_{\text{HT}, n} | X_i] = \frac{1}{n} \text{Var}_{\mathbb{R}} \left[\left(\frac{Y_i A_i}{\pi} - \frac{Y_i(1-A_i)}{1-\pi} \right) | X_i \right]. \tag{19}$$

Then, one can use Lemma 1 (see Section D) to have

$$n \text{Var} [\hat{\tau}_{\text{HT}, n} | X_i] = \mathbb{E}_{\mathbb{R}} \left[\frac{(Y^{(1)})^2}{\pi} | X_i \right] + \mathbb{E}_{\mathbb{R}} \left[\frac{(Y^{(0)})^2}{1-\pi} | X_i \right] - \tau(X_i)^2 := V_{\text{HT}}(x). \tag{20}$$

Then, coming back to (18),

$$\begin{aligned}
\mathbb{E}_{\mathbb{R}} [\text{Var} [\hat{\tau}_{\pi, T, R, n}^* | \mathbf{X}_n]] &= \mathbb{E}_{\mathbb{R}} \left[\frac{1}{n^2} \sum_{i=1}^n \left(\frac{p_T(X_i)}{p_R(X_i)} \right)^2 V_{\text{HT}}(X_i) \right] \\
&= \mathbb{E}_{\mathbb{R}} \left[\frac{1}{n^2} \sum_{i=1}^n \left(\sum_{x \in \mathbb{X}} \mathbb{1}_{X_i=x} \right) \left(\frac{p_T(X_i)}{p_R(X_i)} \right)^2 V_{\text{HT}}(X_i) \right] \\
&= \mathbb{E}_{\mathbb{R}} \left[\sum_{x \in \mathbb{X}} \frac{1}{n^2} \left(\frac{p_T(x)}{p_R(x)} \right)^2 V_{\text{HT}}(x) \sum_{i=1}^n \mathbb{1}_{X_i=x} \right] \\
&= \sum_{x \in \mathbb{X}} \frac{1}{n^2} \left(\frac{p_T(x)}{p_R(x)} \right)^2 V_{\text{HT}}(x) \mathbb{E}_{\mathbb{R}} \left[\sum_{i=1}^n \mathbb{1}_{X_i=x} \right] \\
&= \sum_{x \in \mathbb{X}} \frac{1}{n} \left(\frac{p_T(x)}{p_R(x)} \right)^2 V_{\text{HT}}(x) \mathbb{E}_{\mathbb{R}} \left[\frac{\sum_{i=1}^n \mathbb{1}_{X_i=x}}{n} \right] \\
&= \sum_{x \in \mathbb{X}} \frac{1}{n} \left(\frac{p_T(x)}{p_R(x)} \right)^2 V_{\text{HT}}(x) p_R(x) \tag{Assumption 1} \\
&= \sum_{x \in \mathbb{X}} \frac{1}{n} \frac{p_T^2(x)}{p_R(x)} V_{\text{HT}}(x) \\
&= \frac{1}{n} \sum_{x \in \mathbb{X}} \frac{p_T^2(x)}{p_R(x)} \left(\mathbb{E}_{\mathbb{R}} \left[\frac{(Y^{(1)})^2}{\pi} | X=x \right] + \mathbb{E}_{\mathbb{R}} \left[\frac{(Y^{(0)})^2}{1-\pi} | X=x \right] - \tau(x)^2 \right), \tag{21}
\end{aligned}$$

Combining (21) and (17) into (16) leads to, for all n ,

$$\text{Var} [\hat{\tau}_{\pi, T, R, n}^*] = \frac{V_o}{n}$$

where

$$V_o = \text{Var} \left[\frac{p_T(X_i)}{p_R(X_i)} \tau(X_i) \right] + \sum_{x \in \mathbb{X}} \frac{p_T^2(x)}{p_R(x)} V_{\text{HT}}(x).$$

Quadratic risk and consistency

For any estimate $\hat{\tau}$, we have

$$\mathbb{E} [(\hat{\tau} - \tau)^2] = (\mathbb{E} [\hat{\tau}] - \tau)^2 + \text{Var} [\hat{\tau}].$$

Therefore, the risk of the completely oracle IPSW estimate satisfies

$$\mathbb{E} [(\hat{\tau} - \tau)^2] = \frac{V_o}{n}.$$

The L^2 consistency holds by letting n tend to infinity.

A.2 Proofs for the semi-oracle IPSW $\hat{\tau}_{\pi, \tau, n}^*$

A.2.1 Proof of Proposition 1

Proof. We first recall the definition of the semi-oracle estimator introduced in Definition 5:

$$\hat{\tau}_{\pi, \tau, n}^* = \frac{1}{n} \sum_{i=1}^n \frac{p_{\mathbb{T}}(X_i)}{\hat{p}_{\mathbb{R}, n}(X_i)} \left(\frac{Y_i A_i}{\pi} - \frac{Y_i(1 - A_i)}{1 - \pi} \right),$$

where, for all $x \in \mathbb{X}$,

$$\hat{p}_{\mathbb{R}, n}(x) = \frac{\sum_{i=1}^n \mathbb{1}_{X_i=x}}{n}. \quad (22)$$

Similarly to the completely oracle estimator, the semi-oracle estimator can be written as,

$$\hat{\tau}_{\pi, \tau, n}^* = \sum_{x \in \mathbb{X}} \frac{p_{\mathbb{T}}(x)}{\hat{p}_{\mathbb{R}, n}(x)} \left(\frac{1}{n} \sum_{i=1}^n \mathbb{1}_{X_i=x} \left(\frac{Y_i A_i}{\pi} - \frac{Y_i(1 - A_i)}{1 - \pi} \right) \right),$$

since X_i take values in a categorical set \mathbb{X} .

Bias

To shorten notation, we denote the full vector of covariates $\mathbf{X}_n \in \mathbb{X}^n$, comprising the n observations $X_1, X_2, \dots, X_n \in \mathbb{X}$ in the trial. We have

$$\begin{aligned} \mathbb{E} [\hat{\tau}_{\pi, \tau, n}^*] &= \mathbb{E} \left[\sum_{x \in \mathbb{X}} \frac{p_{\mathbb{T}}(x)}{\hat{p}_{\mathbb{R}, n}(x)} \left(\frac{1}{n} \sum_{i=1}^n \mathbb{1}_{X_i=x} \left(\frac{Y_i A_i}{\pi} - \frac{Y_i(1 - A_i)}{1 - \pi} \right) \right) \right] && \text{By definition} \\ &= \sum_{x \in \mathbb{X}} \mathbb{E} \left[\frac{p_{\mathbb{T}}(x)}{\hat{p}_{\mathbb{R}, n}(x)} \left(\frac{1}{n} \sum_{i=1}^n \mathbb{1}_{X_i=x} \left(\frac{Y_i^{(1)} A_i}{\pi} - \frac{Y_i^{(0)}(1 - A_i)}{1 - \pi} \right) \right) \right] && \text{Linearity and SUTVA} \\ &= \sum_{x \in \mathbb{X}} \mathbb{E} \left[\mathbb{E} \left[\frac{p_{\mathbb{T}}(x)}{\hat{p}_{\mathbb{R}, n}(x)} \left(\frac{1}{n} \sum_{i=1}^n \mathbb{1}_{X_i=x} \left(\frac{Y_i^{(1)} A_i}{\pi} - \frac{Y_i^{(0)}(1 - A_i)}{1 - \pi} \right) \right) \mid \mathbf{X}_n \right] \right] && \text{Law of total expect.} \\ &= \sum_{x \in \mathbb{X}} \mathbb{E} \left[p_{\mathbb{T}}(x) \mathbb{E} \left[\frac{1}{\hat{p}_{\mathbb{R}, n}(x)} \left(\frac{1}{n} \sum_{i=1}^n \mathbb{1}_{X_i=x} \left(\frac{Y_i^{(1)} A_i}{\pi} - \frac{Y_i^{(0)}(1 - A_i)}{1 - \pi} \right) \right) \mid \mathbf{X}_n \right] \right] && p_{\mathbb{T}}(x) \text{ is deterministic} \\ &= \sum_{x \in \mathbb{X}} \mathbb{E} \left[\frac{p_{\mathbb{T}}(x)}{\hat{p}_{\mathbb{R}, n}(x)} \mathbb{E} \left[\left(\frac{1}{n} \sum_{i=1}^n \mathbb{1}_{X_i=x} \left(\frac{Y_i^{(1)} A_i}{\pi} - \frac{Y_i^{(0)}(1 - A_i)}{1 - \pi} \right) \right) \mid \mathbf{X}_n \right] \right] \\ &= \sum_{x \in \mathbb{X}} \mathbb{E} \left[\frac{p_{\mathbb{T}}(x)}{\hat{p}_{\mathbb{R}, n}(x)} \frac{1}{n} \sum_{i=1}^n \mathbb{1}_{X_i=x} \mathbb{E} \left[\frac{Y_i^{(1)} A_i}{\pi} - \frac{Y_i^{(0)}(1 - A_i)}{1 - \pi} \mid \mathbf{X}_n \right] \right] \end{aligned}$$

This last line uses the fact that $\frac{\sum_{i=1}^n \mathbb{1}_{X_i=x}}{n}$ is measurable with respect to \mathbf{X}_n . Then, we use similar derivations as that for the oracle estimator to obtain,

$$\begin{aligned} \mathbb{1}_{X_i=x} \mathbb{E} \left[\frac{Y_i^{(1)} A_i}{\pi} - \frac{Y_i^{(0)}(1 - A_i)}{1 - \pi} \mid \mathbf{X}_n \right] &= \mathbb{1}_{X_i=x} \mathbb{E} \left[\frac{Y_i^{(1)} A_i}{\pi} - \frac{Y_i^{(0)}(1 - A_i)}{1 - \pi} \mid X_i \right] && \text{iid observations} \\ &= \mathbb{1}_{X_i=x} \mathbb{E} \left[\frac{Y_i^{(1)} A_i}{\pi} - \frac{Y_i^{(0)}(1 - A_i)}{1 - \pi} \mid X = x \right] && \text{Indicator forcing } X = x. \\ &= \mathbb{1}_{X_i=x} \tau(x) && \text{Transportability.} \end{aligned}$$

Therefore,

$$\begin{aligned} \mathbb{E} [\hat{\tau}_{\pi, \tau, n}^*] &= \sum_{x \in \mathbb{X}} \mathbb{E} \left[\frac{p_{\mathbb{T}}(x)}{\hat{p}_{\mathbb{R}, n}(x)} \frac{\sum_{i=1}^n \mathbb{1}_{X_i=x} \tau(x)}{n} \right] \\ &= \sum_{x \in \mathbb{X}} \mathbb{E} \left[\frac{p_{\mathbb{T}}(x)}{\frac{\sum_{i=1}^n \mathbb{1}_{X_i=x}}{n}} \frac{\sum_{i=1}^n \mathbb{1}_{X_i=x} \tau(x)}{n} \right] && \text{Estimation procedure - Equation 22} \end{aligned}$$

Let $Z_n(x) = \sum_{i=1}^n \mathbb{1}_{X_i=x}$ distributed as $\mathfrak{B}(n, p_R(x))$. Note that, by convention, the term inside the expectation is null if $Z_n(x) = 0$.⁵ This leads to the following equality,

$$\begin{aligned} \mathbb{E} [\hat{\tau}_{\pi, \tau, n}^*] &= \sum_{x \in \mathbb{X}} \mathbb{E} [p_T(x) \tau(x) \mathbb{1}_{Z_n(x) > 0}] \\ &= \sum_{x \in \mathbb{X}} p_T(x) \tau(x) \mathbb{E} [\mathbb{1}_{Z_n(x) > 0}] \\ &= \sum_{x \in \mathbb{X}} p_T(x) \tau(x) (1 - (1 - p(x))^n). \end{aligned}$$

Upper bound of the bias.

If $p_R(x) = 0$, then $p_T(x) = 0$ (due to the support inclusion assumption, see Assumption 4). Therefore, for all $x \in \mathbb{X}$, $0 < p_R(x)$. Then, it is possible to bound the bias for any sample size n , noting that,

$$\begin{aligned} |\mathbb{E} [\hat{\tau}_{\pi, \tau, n}^*] - \tau| &= \left| \sum_{x \in \mathbb{X}} p_T(x) \tau(x) (1 - (1 - p(x))^n) - \tau \right| \\ &= \left| \sum_{x \in \mathbb{X}} p_T(x) \tau(x) (1 - (1 - p(x))^n) - \sum_{x \in \mathbb{X}} p_T(x) \tau(x) \right| \\ &= \left| \sum_{x \in \mathbb{X}} p_T(x) \tau(x) (1 - p(x))^n \right| \\ &\leq \left(1 - \min_x p(x)\right)^n \left| \sum_{x \in \mathbb{X}} p_T(x) \tau(x) \right| \\ &\leq \left(1 - \min_x p(x)\right)^n \tau. \end{aligned}$$

Variance

The proof follows the same track as that of the completely oracle IPSW, conditioning on \mathbf{X}_n , and using the law of total variance,

$$\text{Var} [\hat{\tau}_{\pi, \tau, n}^*] = \text{Var} [\mathbb{E} [\hat{\tau}_{\pi, \tau, n}^* | \mathbf{X}_n]] + \mathbb{E} [\text{Var} [\hat{\tau}_{\pi, \tau, n}^* | \mathbf{X}_n]]. \quad (23)$$

For the first inside term,

$$\begin{aligned} \mathbb{E} [\hat{\tau}_{\pi, \tau, n}^* | \mathbf{X}_n] &= \mathbb{E} \left[\sum_{x \in \mathbb{X}} \frac{p_T(x)}{\hat{p}_{R, n}(x)} \frac{1}{n} \sum_{i=1}^n \mathbb{1}_{X_i=x} \left(\frac{Y_i^{(1)} A_i}{\pi} - \frac{Y_i^{(0)} (1 - A_i)}{1 - \pi} \right) \middle| \mathbf{X}_n \right] && \text{By definition (and SUTVA)} \\ &= \sum_{x \in \mathbb{X}} \frac{p_T(x)}{\hat{p}_{R, n}(x)} \frac{1}{n} \sum_{i=1}^n \mathbb{1}_{X_i=x} \mathbb{E} \left[\left(\frac{Y_i^{(1)} A_i}{\pi} - \frac{Y_i^{(0)} (1 - A_i)}{1 - \pi} \right) \middle| \mathbf{X}_n \right] && \text{Linearity of } \mathbb{E}[\cdot] \\ &= \sum_{x \in \mathbb{X}} \frac{p_T(x)}{\hat{p}_{R, n}(x)} \frac{1}{n} \sum_{i=1}^n \mathbb{1}_{X_i=x} \tau(X_i) \\ &= \sum_{x \in \mathbb{X}} p_T(x) \tau(x) && \text{Equation 22} \\ &= \tau, \end{aligned}$$

which leads to

$$\text{Var} [\mathbb{E} [\hat{\tau}_{\pi, \tau, n}^* | \mathbf{X}_n]] = 0. \quad (24)$$

On the other hand,

⁵Note that to be clearer we could have introduced the multiplication by $\mathbb{1}_{Z_n(x) > 0}$ in the formula summing over the categories from the beginning. Indeed, this was implicit as it is the re-writing of a sum on the trial's observations. But this also leads to heavy notations.

$$\begin{aligned}
\text{Var} [\hat{\tau}_{\pi, \tau, n}^* \mid \mathbf{X}_n] &= \text{Var} \left[\frac{1}{n} \sum_{i=1}^n \frac{p_{\text{T}}(X_i)}{\hat{p}_{\text{R}, n}(X_i)} \left(\frac{Y_i A_i}{\pi} - \frac{Y_i(1-A_i)}{1-\pi} \right) \mid \mathbf{X}_n \right] \\
&= \frac{1}{n^2} \sum_{i=1}^n \left(\frac{p_{\text{T}}(X_i)}{\hat{p}_{\text{R}, n}(X_i)} \right)^2 \text{Var} \left[\left(\frac{Y_i A_i}{\pi} - \frac{Y_i(1-A_i)}{1-\pi} \right) \mid \mathbf{X}_n \right] \\
&= \frac{1}{n^2} \sum_{i=1}^n \left(\frac{p_{\text{T}}(X_i)}{\hat{p}_{\text{R}, n}(X_i)} \right)^2 \text{Var} \left[\left(\frac{Y_i A_i}{\pi} - \frac{Y_i(1-A_i)}{1-\pi} \right) \mid X_i \right] \\
&= \frac{1}{n^2} \sum_{i=1}^n \left(\frac{p_{\text{T}}(X_i)}{\hat{p}_{\text{R}, n}(X_i)} \right)^2 V_{\text{HT}}(X_i),
\end{aligned}$$

where the last row comes from intermediary results in the completely oracle proof (see equation (20)), with

$$V_{\text{HT}}(x) := \mathbb{E}_{\text{R}} \left[\frac{(Y^{(1)})^2}{\pi} \mid X_i \right] + \mathbb{E}_{\text{R}} \left[\frac{(Y^{(0)})^2}{1-\pi} \mid X_i \right] - \tau(X)^2.$$

Then,

$$\begin{aligned}
\mathbb{E} [\text{Var} [\hat{\tau}_{\pi, \tau, n}^* \mid \mathbf{X}_n]] &= \mathbb{E} \left[\frac{1}{n^2} \sum_{i=1}^n \left(\frac{p_{\text{T}}(X_i)}{\hat{p}_{\text{R}, n}(X_i)} \right)^2 V_{\text{HT}}(X_i) \right] && \text{From previous derivations} \\
&= \mathbb{E} \left[\sum_{x \in \mathbb{X}} \left(\frac{1}{n^2} \sum_{i=1}^n \mathbb{1}_{X_i=x} \left(\frac{p_{\text{T}}(X_i)}{\hat{p}_{\text{R}, n}(X_i)} \right)^2 V_{\text{HT}}(X_i) \right) \right] && \text{Categorical } X \\
&= \mathbb{E} \left[\sum_{x \in \mathbb{X}} \frac{1}{n^2} \left(\frac{p_{\text{T}}(x)}{\hat{p}_{\text{R}, n}(x)} \right)^2 V_{\text{HT}}(x) \left(\sum_{i=1}^n \mathbb{1}_{X_i=x} \right) \right] \\
&= \sum_{x \in \mathbb{X}} \frac{1}{n^2} p_{\text{T}}(x)^2 V_{\text{HT}}(x) \mathbb{E} \left[\left(\frac{1}{\hat{p}_{\text{R}, n}(x)} \right)^2 \left(\sum_{i=1}^n \mathbb{1}_{X_i=x} \right) \right].
\end{aligned}$$

Replacing $\hat{p}_{\text{R}, n}(x)$ by its explicit expression,

$$\mathbb{E} [\text{Var} [\hat{\tau}_{\pi, \tau, n}^* \mid \mathbf{X}_n]] = \sum_{x \in \mathbb{X}} \frac{1}{n} p_{\text{T}}(x)^2 V_{\text{HT}}(x) \mathbb{E} \left[\left(\frac{1}{\frac{1}{n} \sum_{i=1}^n \mathbb{1}_{X_i=x}} \right)^2 \left(\frac{1}{n} \sum_{i=1}^n \mathbb{1}_{X_i=x} \right) \right]. \quad (25)$$

As in the study of the bias, we introduce $Z_n(x) = \sum_{i=1}^n \mathbb{1}_{X_i=x}$, distributed as $\mathfrak{B}(n, p)$. One can then write,

$$\mathbb{E} [\text{Var} [\hat{\tau}_{\pi, \tau, n}^* \mid \mathbf{X}_n]] = \sum_{x \in \mathbb{X}} \frac{1}{n} p_{\text{T}}(x)^2 V_{\text{HT}}(x) \mathbb{E} \left[\frac{\mathbb{1}_{Z_n(x) > 0}}{\frac{1}{n} \sum_{i=1}^n \mathbb{1}_{X_i=x}} \right].$$

Recalling (23),

$$\text{Var} [\hat{\tau}_{\pi, \tau, n}^*] = \underbrace{\text{Var} [\mathbb{E} [\hat{\tau}_{\pi, \tau, n}^* \mid \mathbf{X}_n]]}_{= 0, \text{ as (24)}} + \mathbb{E} [\text{Var} [\hat{\tau}_{\pi, \tau, n}^* \mid \mathbf{X}_n]],$$

we have

$$n \text{Var} [\hat{\tau}_{\pi, \tau, n}^*] = \sum_{x \in \mathbb{X}} p_{\text{T}}(x)^2 V_{\text{HT}}(x) \mathbb{E} \left[\frac{\mathbb{1}_{Z_n(x) > 0}}{\frac{1}{n} \sum_{i=1}^n \mathbb{1}_{X_i=x}} \right]. \quad (26)$$

Upper bound on the variance

According to [Arnould et al. \(2021\)](#) (see page 27), since $Z_n(x)$ is distributed as $\mathfrak{B}(n, p_{\text{R}})$, we have

$$\forall x \in \mathbb{X}, \frac{1 - (1 - p_{\text{R}}(x))^n}{(n+1)p_{\text{R}}(x)} \leq \mathbb{E} \left[\frac{\mathbb{1}_{Z_n(x) \neq 0}}{Z_n(x)} \right] \leq \frac{2}{(n+1)p_{\text{R}}(x)}.$$

Combining these inequalities with equation 26 yields, for all n ,

$$\sum_{x \in \mathbb{X}} p_{\text{T}}(x)^2 \frac{1 - (1 - p_{\text{R}}(x))^n}{(n+1)p_{\text{R}}(x)} V_{\text{HT}}(x) \leq \text{Var} [\hat{\tau}_{\pi, \tau, n}^*] \leq \frac{2}{n+1} \sum_{x \in \mathbb{X}} \frac{p_{\text{T}}(x)^2}{p_{\text{R}}(x)} V_{\text{HT}}(x).$$

This expression can be further simplified in,

$$\frac{1}{n+1} \sum_{x \in \mathbb{X}} \frac{p_{\text{T}}(x)^2}{p_{\text{R}}(x)} V_{\text{HT}}(x) - \frac{1}{n+1} \sum_{x \in \mathbb{X}} \frac{p_{\text{T}}(x)^2}{p_{\text{R}}(x)} (1 - p_{\text{R}}(x))^n V_{\text{HT}}(x) \leq \text{Var} [\hat{\tau}_{\pi, \text{T}, n}^*] \leq \frac{2}{n+1} \sum_{x \in \mathbb{X}} \frac{p_{\text{T}}(x)^2}{p_{\text{R}}(x)} V_{\text{HT}}(x),$$

that is

$$\frac{V_{so}}{n+1} - \frac{1}{n+1} \sum_{x \in \mathbb{X}} \frac{p_{\text{T}}(x)^2}{p_{\text{R}}(x)} (1 - p_{\text{R}}(x))^n V_{\text{HT}}(x) \leq \text{Var} [\hat{\tau}_{\pi, \text{T}, n}^*] \leq \frac{2}{n+1} V_{so}.$$

$$1 - \varepsilon_n \leq \frac{\text{Var} [\hat{\tau}_{\pi, \text{T}, n}^*]}{V_{so}/(n+1)} \leq 2.$$

with

$$\varepsilon_n = \frac{1}{V_{so}} \sum_{x \in \mathbb{X}} \frac{p_{\text{T}}(x)^2}{p_{\text{R}}(x)} (1 - p_{\text{R}}(x))^n V_{\text{HT}}(x).$$

In particular, we present only the upper bound in the Proposition 1. □

A.2.2 Proof of Corollary 1

Proof. Asymptotically unbiased

Recall the expression of the semi-oracle IPSW bias from Proposition 1.

$$\mathbb{E} [\hat{\tau}_{\pi, \text{T}, n}^*] = \sum_{x \in \mathbb{X}} p_{\text{T}}(x) \tau(x) (1 - (1 - p_{\text{R}}(x))^n).$$

According to Assumption 4, we have $\forall x \in \mathbb{X}, 0 < p_{\text{R}}(x) < 1$. As a consequence,

$$\lim_{n \rightarrow \infty} (1 - (1 - p_{\text{R}}(x))^n) = 1,$$

which leads to

$$\lim_{n \rightarrow \infty} \mathbb{E} [\hat{\tau}_{\pi, \text{T}, n}^*] = \tau.$$

Asymptotic variance

Recall the expression of the variance of the semi-oracle IPSW from Proposition 1:

$$n \text{Var} [\hat{\tau}_{\pi, \text{T}, n}^*] = \sum_{x \in \mathbb{X}} p_{\text{T}}(x)^2 V_{\text{HT}}(x) \mathbb{E}_{\text{R}} \left[\frac{\mathbb{1}_{Z_n(x) > 0}}{\frac{1}{n} \sum_{i=1}^n \mathbb{1}_{X_i = x}} \right]. \quad (27)$$

The next part of the proof consists in characterizing how the term $\mathbb{E}_{\text{R}} \left[\frac{\mathbb{1}_{Z_n(x) > 0}}{Z_n(x)/n} \right]$ converges. Let $\varepsilon > 0$. Since, for all $x, p_{\text{R}}(x) > 0$, we have

$$\mathbb{E} \left[\frac{\mathbb{1}_{Z_n(x) > 0}}{Z_n(x)} \right] = \mathbb{E} \left[\frac{\mathbb{1}_{Z_n(x) > 0}}{Z_n(x)} \mathbb{1}_{|Z_n(x) - p_{\text{R}}(x)| \geq \varepsilon} \right] + \mathbb{E} \left[\frac{\mathbb{1}_{Z_n(x) > 0}}{Z_n(x)} \mathbb{1}_{|Z_n(x) - p_{\text{R}}(x)| < \varepsilon} \right]. \quad (28)$$

Regarding the first term in (28), we have

$$\mathbb{E} \left[\frac{\mathbb{1}_{Z_n(x) > 0}}{Z_n(x)} \mathbb{1}_{|Z_n(x) - p_{\text{R}}(x)| \geq \varepsilon} \right] \leq n \mathbb{P} \left[\left| \frac{Z_n(x)}{n} - p_{\text{R}}(x) \right| \geq \varepsilon \right],$$

since, on the event $Z_n(x) > 0, Z_n(x) \geq 1$. Now, by Chernoff's inequality,

$$\mathbb{P} \left[\left| \frac{Z_n(x)}{n} - p_{\text{R}}(x) \right| \geq \varepsilon \right] \leq 2 \exp(-2\varepsilon^2 n),$$

which yields

$$\mathbb{E} \left[\frac{\mathbb{1}_{Z_n(x) > 0}}{\frac{Z_n(x)}{n}} \mathbb{1}_{\left| \frac{Z_n(x)}{n} - p_R(x) \right| \geq \varepsilon} \right] \leq 2n \exp(-2\varepsilon^2 n). \quad (29)$$

Regarding the second term in equation (28), since

$$\frac{\mathbb{1}_{Z_n(x) > 0}}{\frac{Z_n(x)}{n}} \mathbb{1}_{\left| \frac{Z_n(x)}{n} - p_R(x) \right| < \varepsilon}$$

is bounded above, for $\varepsilon < p_R(x)/2$ and converges in probability to $1/p_R(x)$, we have

$$\mathbb{E} \left[\frac{\mathbb{1}_{Z_n(x) > 0}}{Z_n(x)/n} \mathbb{1}_{\left| Z_n(x)/n - p_R(x) \right| < \varepsilon} \right] \rightarrow \frac{1}{p_R(x)}, \quad \text{as } n \rightarrow \infty. \quad (30)$$

Combining (29) and (30), we have

$$\mathbb{E} \left[\frac{\mathbb{1}_{Z_n(x) > 0}}{Z_n(x)/n} \right] \rightarrow \frac{1}{p_R(x)}, \quad \text{as } n \rightarrow \infty.$$

Using the explicit expression of the semi-oracle IPSW variance (27),

$$\lim_{n \rightarrow \infty} n \text{Var} [\hat{\tau}_{\pi, \tau, n}^*] = \sum_{x \in \mathbb{X}} \frac{p_T(x)^2}{p_R(x)} V_{\text{HT}}(x) = \mathbb{E} \left[\left(\frac{p_T(X)}{p_R(X)} \right)^2 V_{\text{HT}}(X) \right] := V_{\text{so}}.$$

□

A.2.3 Proof of Theorem 2

Proof. For any estimate $\hat{\tau}$, we have

$$\mathbb{E} [(\hat{\tau} - \tau)^2] = (\mathbb{E}[\hat{\tau}] - \tau)^2 + \text{Var}[\hat{\tau}].$$

Therefore, the risk of the semi-oracle IPSW estimate can be bounded using results from Subsection A.2.1 (or Proposition 1), and in particular the bounds on the variance and the bias,

$$\mathbb{E} [(\hat{\tau} - \tau)^2] \leq (1 - \min_x p_R(x))^{2n} \tau^2 + 2 \frac{V_{\text{so}}}{n+1}.$$

The L^2 consistency holds by letting n tend to infinity.

□

A.3 Proofs for (completely estimated) IPSW $\hat{\tau}_{\pi, n, m}$

A.3.1 Proof of Proposition 2

Proof. We first recall the definition of a fully estimated estimator introduced in Definition 6.

$$\hat{\tau}_{\pi, n, m} = \frac{1}{n} \sum_{i=1}^n \frac{\hat{p}_{T, m}(X_i)}{\hat{p}_{R, n}(X_i)} \left(\frac{Y_i A_i}{\pi} - \frac{Y_i(1 - A_i)}{1 - \pi} \right),$$

where, for all $x \in \mathbb{X}$,

$$\hat{p}_{R, n}(x) = \frac{\sum_{i=1}^n \mathbb{1}_{X_i=x}}{n}, \quad \text{and} \quad \hat{p}_{T, m}(x) = \frac{\sum_{i=1}^m \mathbb{1}_{X_i=x}}{m}. \quad (31)$$

Similar to the completely oracle estimator, this completely estimated IPSW can be written as,

$$\hat{\tau}_{\pi, n, m} = \sum_{x \in \mathbb{X}} \frac{\hat{p}_{T, m}(x)}{\hat{p}_{R, n}(x)} \left(\frac{1}{n} \sum_{i=1}^n \mathbb{1}_{X_i=x} \left(\frac{Y_i A_i}{\pi} - \frac{Y_i(1 - A_i)}{1 - \pi} \right) \right).$$

Expression of the bias

One has

$$\begin{aligned}
\mathbb{E} [\hat{\tau}_{\pi,n,m}] &= \sum_{x \in \mathbb{X}} \mathbb{E} \left[\frac{\hat{p}_{\mathbb{T},m}(x)}{\hat{p}_{\mathbb{R},n}(x)} \frac{\sum_{i=1}^n \mathbb{1}_{X_i=x}}{n} \tau(x) \right] \\
&= \sum_{x \in \mathbb{X}} \mathbb{E} \left[\frac{\hat{p}_{\mathbb{T},m}(x)}{\frac{\sum_{i=1}^n \mathbb{1}_{X_i=x}}{n}} \frac{\sum_{i=1}^n \mathbb{1}_{X_i=x}}{n} \tau(x) \right] && \text{Estimation procedure - Equation 22} \\
&= \sum_{x \in \mathbb{X}} \mathbb{E} [\hat{p}_{\mathbb{T},m}(x) \tau(x) \mathbb{1}_{Z_n(x) \neq 0}].
\end{aligned}$$

Note that $Z_n(x)$ only depend on the trial sample \mathcal{R} and $\hat{p}_{\mathbb{T},m}(x)$ on the observational sample. In addition, $\tau(x)$ is deterministic, therefore

$$\mathbb{E} [\hat{\tau}_{\pi,n,m}] = \sum_{x \in \mathbb{X}} \tau(x) \mathbb{E} [\hat{p}_{\mathbb{T},m}(x)] \mathbb{E} [\mathbb{1}_{Z_n(x) \neq 0}].$$

Note that $\mathbb{E} [\hat{p}_{\mathbb{T},m}(x)] = p_{\mathbb{T}}(x)$. Besides, according to the proof of the semi-oracle IPSW,

$$\mathbb{E} [\mathbb{1}_{Z_n(x) \neq 0}] = (1 - (1 - p_{\mathbb{R}}(x))^n).$$

Therefore,

$$\mathbb{E} [\hat{\tau}_{\pi,n,m}] = \sum_{x \in \mathbb{X}} p_{\mathbb{T}}(x) \tau(x) (1 - (1 - p_{\mathbb{R}}(x))^n).$$

Upper bound on the bias

It is possible to bound the bias for any sample size n , using the exact same derivations than for the semi-oracle IPSW.

Expression of the variance

The proof follows a similar spirit as the proof for the completely oracle estimator, conditioning on all observations \mathbf{X}_{n+m} .

$$\text{Var} [\hat{\tau}_{\pi,n,m}] = \text{Var} [\mathbb{E} [\hat{\tau}_{\pi,n,m} \mid \mathbf{X}_{n+m}]] + \mathbb{E} [\text{Var} [\hat{\tau}_{\pi,n,m} \mid \mathbf{X}_{n+m}]]. \quad (32)$$

$$\begin{aligned}
\mathbb{E} [\hat{\tau}_{\pi,n,m} \mid \mathbf{X}_{n+m}] &= \mathbb{E} \left[\sum_{x \in \mathbb{X}} \frac{\hat{p}_{\mathbb{T},m}(x)}{\hat{p}_{\mathbb{R},n}(x)} \left(\frac{1}{n} \sum_{i=1}^n \mathbb{1}_{X_i=x} \left(\frac{Y_i A_i}{\pi} - \frac{Y_i(1-A_i)}{1-\pi} \right) \right) \mid \mathbf{X}_{n+m} \right] \\
&= \sum_{x \in \mathbb{X}} \mathbb{E} \left[\frac{\hat{p}_{\mathbb{T},m}(x)}{\hat{p}_{\mathbb{R},n}(x)} \left(\frac{1}{n} \sum_{i=1}^n \mathbb{1}_{X_i=x} \left(\frac{Y_i A_i}{\pi} - \frac{Y_i(1-A_i)}{1-\pi} \right) \right) \mid \mathbf{X}_{n+m} \right] && \text{Linearity of } \mathbb{E}[\cdot] \\
&= \sum_{x \in \mathbb{X}} \frac{\hat{p}_{\mathbb{T},m}(x)}{\hat{p}_{\mathbb{R},n}(x)} \mathbb{E} \left[\frac{1}{n} \sum_{i=1}^n \mathbb{1}_{X_i=x} \left(\frac{Y_i A_i}{\pi} - \frac{Y_i(1-A_i)}{1-\pi} \right) \mid \mathbf{X}_{n+m} \right].
\end{aligned}$$

Indeed, $\hat{p}_{\mathbb{R},n}(x)$ and $\hat{p}_{\mathbb{T},m}$ are measurable with respect to \mathbf{X}_{n+m} . Pursuing the computation, we have

$$\begin{aligned}
\mathbb{E} [\hat{\tau}_{\pi,n,m} \mid \mathbf{X}_{n+m}] &= \sum_{x \in \mathbb{X}} \frac{\hat{p}_{\mathbb{T},m}(x)}{\hat{p}_{\mathbb{R},n}(x)} \mathbb{E} \left[\frac{1}{n} \sum_{i=1}^n \mathbb{1}_{X_i=x} \left(\frac{Y_i A_i}{\pi} - \frac{Y_i(1-A_i)}{1-\pi} \right) \mid \mathbf{X}_{n+m} \right] \\
&= \sum_{x \in \mathbb{X}} \frac{\hat{p}_{\mathbb{T},m}(x)}{\hat{p}_{\mathbb{R},n}(x)} \frac{1}{n} \sum_{i=1}^n \mathbb{E} \left[\mathbb{1}_{X_i=x} \left(\frac{Y_i A_i}{\pi} - \frac{Y_i(1-A_i)}{1-\pi} \right) \mid \mathbf{X}_{n+m} \right] && \text{Linearity of } \mathbb{E}[\cdot] \\
&= \sum_{x \in \mathbb{X}} \frac{\hat{p}_{\mathbb{T},m}(x)}{\hat{p}_{\mathbb{R},n}(x)} \frac{1}{n} \sum_{i=1}^n \mathbb{1}_{X_i=x} \mathbb{E} \left[\left(\frac{Y_i A_i}{\pi} - \frac{Y_i(1-A_i)}{1-\pi} \right) \mid \mathbf{X}_{n+m} \right] && \text{Conditioning on } \mathbf{X}_n \\
&= \sum_{x \in \mathbb{X}} \frac{\hat{p}_{\mathbb{T},m}(x)}{\hat{p}_{\mathbb{R},n}(x)} \tau(x) \frac{1}{n} \sum_{i=1}^n \mathbb{1}_{X_i=x} && \text{Transportability} \\
&= \sum_{x \in \mathbb{X}} \hat{p}_{\mathbb{T},m}(x) \tau(x) \mathbb{1}_{Z_n(x) \neq 0},
\end{aligned}$$

where $Z_n(x) = \sum_{i=1}^n \mathbb{1}_{X_i=x}$. Then,

$$\begin{aligned}
\text{Var} [\mathbb{E} [\hat{\tau}_{\pi,n,m} \mid \mathbf{X}_{n+m}]] &= \text{Var} \left[\sum_{x \in \mathbf{X}} \hat{p}_{\tau,m}(x) \tau(x) \mathbb{1}_{Z_n(x) \neq 0} \right] \\
&= \text{Var} \left[\sum_{x \in \mathbf{X}} \frac{\sum_{i=n+1}^m \mathbb{1}_{X_i=x}}{m} \tau(x) \mathbb{1}_{Z_n(x) \neq 0} \right] \\
&= \text{Var} \left[\frac{1}{m} \sum_{i=n+1}^m \tau(X_i) \mathbb{1}_{Z_n(X_i) \neq 0} \right]
\end{aligned}$$

Note that, contrary to the semi-oracle IPSW, this term is non-null due to estimation of $\hat{p}_{\tau,m}$. By the law of total variance,

$$\begin{aligned}
\text{Var} \left[\frac{1}{m} \sum_{i=n+1}^m \tau(X_i) \mathbb{1}_{Z_n(X_i) \neq 0} \right] &= \mathbb{E} \left[\text{Var} \left[\frac{1}{m} \sum_{i=n+1}^m \tau(X_i) \mathbb{1}_{Z_n(X_i) \neq 0} \mid \mathbf{X}_n \right] \right] \\
&\quad + \text{Var} \left[\mathbb{E} \left[\frac{1}{m} \sum_{i=n+1}^m \tau(X_i) \mathbb{1}_{Z_n(X_i) \neq 0} \mid \mathbf{X}_n \right] \right] \\
&= \frac{1}{m} \mathbb{E} [\text{Var} [\tau(X) \mathbb{1}_{Z_n(X) \neq 0} \mid \mathbf{X}_n]] + \text{Var} [\mathbb{E} [\tau(X) \mathbb{1}_{Z_n(X) \neq 0} \mid \mathbf{X}_n]] \\
&= \frac{1}{m} \text{Var} [\tau(X) \mathbb{1}_{Z_n(X) \neq 0}] + \left(1 - \frac{1}{m}\right) \text{Var} [\mathbb{E} [\tau(X) \mathbb{1}_{Z_n(X) \neq 0} \mid \mathbf{X}_n]],
\end{aligned}$$

where the last line comes from the law of total variance applied to $\text{Var} [\tau(X) \mathbb{1}_{Z_n(X) \neq 0}]$. Since

$$\begin{aligned}
\text{Var} [\mathbb{E} [\tau(X) \mathbb{1}_{Z_n(X) \neq 0} \mid \mathbf{X}_n]] &= \text{Var} [\mathbb{E} [\tau(X)] - \mathbb{E} [\mathbb{1}_{Z_n(X)=0} \mid \mathbf{X}_n]] \\
&= \text{Var} [\tau - \mathbb{E} [\mathbb{1}_{Z_n(X)=0} \mid \mathbf{X}_n]] \\
&= \text{Var} [\mathbb{E} [\mathbb{1}_{Z_n(X)=0} \mid \mathbf{X}_n]],
\end{aligned}$$

as the only source of randomness comes from $\mathbb{E} [\mathbb{1}_{Z_n(X)=0} \mid \mathbf{X}_n]$, we have

$$\text{Var} [\mathbb{E} [\hat{\tau}_{\pi,n,m} \mid \mathbf{X}_n]] = \frac{1}{m} \text{Var} [\tau(X) \mathbb{1}_{Z_n(X) \neq 0}] + \left(1 - \frac{1}{m}\right) \text{Var} [\mathbb{E} [\mathbb{1}_{Z_n(X)=0} \mid \mathbf{X}_n]]. \quad (33)$$

For the other term,

$$\begin{aligned}
\text{Var} [\hat{\tau}_{\pi,n,m} \mid \mathbf{X}_{n+m}] &= \text{Var} \left[\frac{1}{n} \sum_{i=1}^n \frac{\hat{p}_{\tau,m}(X_i)}{\hat{p}_{\text{R},n}(X_i)} \left(\frac{Y_i A_i}{\pi} - \frac{Y_i(1-A_i)}{1-\pi} \right) \mid \mathbf{X}_{n+m} \right] \\
&= \frac{1}{n^2} \sum_{i=1}^n \left(\frac{\hat{p}_{\tau,m}(X_i)}{\hat{p}_{\text{R},n}(X_i)} \right)^2 V_{\text{HT}}(X_i).
\end{aligned}$$

Derivations is very similar to the semi-oracle estimator, using the fact that $\hat{p}_{\text{R},n}(x)$ and $\hat{p}_{\tau,m}$ are measurable with respect to \mathbf{X}_{n+m} . We have

$$\begin{aligned}
\mathbb{E} [\text{Var} [\hat{\tau}_{\pi,n,m} \mid \mathbf{X}_{n+m}]] &= \mathbb{E} \left[\frac{1}{n^2} \sum_{i=1}^n \left(\frac{\hat{p}_{\tau,m}(X_i)}{\hat{p}_{\text{R},n}(X_i)} \right)^2 V_{\text{HT}}(X_i) \right] && \text{From previous derivations} \\
&= \mathbb{E} \left[\sum_{x \in \mathbf{X}} \left(\frac{1}{n^2} \sum_{i=1}^n \mathbb{1}_{X_i=x} \left(\frac{\hat{p}_{\tau,m}(X_i)}{\hat{p}_{\text{R},n}(X_i)} \right)^2 V_{\text{HT}}(X_i) \right) \right] && \text{Categorical } X \\
&= \mathbb{E} \left[\sum_{x \in \mathbf{X}} \frac{1}{n^2} \left(\frac{\hat{p}_{\tau,m}(x)}{\hat{p}_{\text{R},n}(x)} \right)^2 V_{\text{HT}}(x) \left(\sum_{i=1}^n \mathbb{1}_{X_i=x} \right) \right] \\
&= \sum_{x \in \mathbf{X}} \frac{1}{n^2} V_{\text{HT}}(x) \mathbb{E} \left[\left(\frac{\hat{p}_{\tau,m}(x)}{\hat{p}_{\text{R},n}(x)} \right)^2 \left(\sum_{i=1}^n \mathbb{1}_{X_i=x} \right) \right] \\
&= \sum_{x \in \mathbf{X}} \frac{1}{n} V_{\text{HT}}(x) \mathbb{E}_{\text{R}} \left[\frac{(\hat{p}_{\tau,m}(x))^2}{\hat{p}_{\text{R},n}(x)} \mathbb{1}_{Z_n(x) \neq 0} \right].
\end{aligned}$$

In particular, the last term can be simplified in

$$\mathbb{E} [\text{Var} [\hat{\tau}_{\pi,n,m} \mid \mathbf{X}_{n+m}]] = \sum_{x \in \mathbf{X}} \frac{1}{n} g(x) \mathbb{E} [(\hat{p}_{\tau,m}(x))^2] \mathbb{E} \left[\frac{\mathbb{1}_{Z_n(x) \neq 0}}{\hat{p}_{\text{R},n}(x)} \right]. \quad (34)$$

This last derivation is possible because $\hat{p}_{\mathcal{T},m}(x)$, which depends on \mathcal{T} , and $\hat{p}_{\mathcal{R},n}(x)$, which depends on \mathcal{R} , are independent. The difference from the semi-oracle estimator comes from the term

$$\begin{aligned}
\mathbb{E} \left[(\hat{p}_{\mathcal{T},m}(x))^2 \right] &= \mathbb{E} \left[\left(\frac{\sum_{i=n+1}^m \mathbb{1}_{X_i=x}}{m} \right)^2 \right] \\
&= \frac{1}{m^2} \mathbb{E} \left[\left(\sum_{i=n+1}^m \mathbb{1}_{X_i=x} \right)^2 \right] \\
&= \frac{1}{m^2} (mp_{\mathcal{T}}(x)(1-p_{\mathcal{T}}(x)) + m^2 p_{\mathcal{T}}^2(x)) \\
&= \frac{p_{\mathcal{T}}(x)(1-p_{\mathcal{T}}(x))}{m} + p_{\mathcal{T}}^2(x). \tag{35}
\end{aligned}$$

Using equation (33) and (35) in equation (32), we have

$$\text{Var} [\hat{\tau}_{\pi,n,m}] = \text{Var} [\mathbb{E} [\hat{\tau}_{\pi,n,m} | \mathbf{X}_n]] + \mathbb{E} [\text{Var} [\hat{\tau}_{\pi,n,m} | \mathbf{X}_n]] \tag{36}$$

$$= \frac{1}{m} \text{Var}_{\mathcal{T}} [\tau(X) \mathbb{1}_{Z_n(X) \neq 0}] + \left(1 - \frac{1}{m}\right) \text{Var} [\mathbb{E} [\mathbb{1}_{Z_n(X)=0} | \mathbf{X}_n]] \tag{37}$$

$$+ \frac{1}{n} \sum_{x \in \mathbb{X}} V_{\text{HT}}(x) \frac{p_{\mathcal{T}}(x)(1-p_{\mathcal{T}}(x))}{m} \mathbb{E} \left[\frac{\mathbb{1}_{Z_n(x) \neq 0}}{\hat{p}_{\mathcal{R},n}(x)} \right] + \underbrace{\frac{1}{n} \sum_{x \in \mathbb{X}} V_{\text{HT}}(x) p_{\mathcal{T}}^2(x) \mathbb{E} \left[\frac{\mathbb{1}_{Z_n(x) \neq 0}}{\hat{p}_{\mathcal{R},n}(x)} \right]}_{=\text{Var} [\hat{\tau}_{\pi,\mathcal{T},n}^*]}. \tag{38}$$

Upper bound on the variance.

We first bound (33), corresponding to

$$\text{Var} [\mathbb{E} [\hat{\tau}_{\pi,n,m} | \mathbf{X}_{n+m}]] = \frac{1}{m} \text{Var}_{\mathcal{T}} [\tau(X) \mathbb{1}_{Z_n(X) \neq 0}] + \left(1 - \frac{1}{m}\right) \text{Var} [\mathbb{E} [\mathbb{1}_{Z_n(X)=0} | \mathbf{X}_{n+m}]],$$

by

$$\begin{aligned}
\text{Var} [\mathbb{E} [\hat{\tau}_{\pi,n,m} | \mathbf{X}_{n+m}]] &\leq \frac{\text{Var}_{\mathcal{T}} [\tau(X)]}{m} + \mathbb{P} [Z_n(X) = 0] \\
&\leq \frac{\text{Var}_{\mathcal{T}} [\tau(X)]}{m} + \sum_{x \in \mathbb{X}} p_{\mathcal{T}}(x)(1-p_{\mathcal{R}}(x))^n. \tag{39}
\end{aligned}$$

Then, for the other term of the asymptotic variance, one can use the results from [Arnould et al. \(2021\)](#) (see page 27) to bound the variance, which leads to

$$\begin{aligned}
\mathbb{E} [\text{Var} [\hat{\tau}_{\pi,n,m} | \mathbf{X}_{n+m}]] &= \sum_{x \in \mathbb{X}} \frac{1}{n} g(x) \mathbb{E} \left[(\hat{p}_{\mathcal{T},m}(x))^2 \right] \mathbb{E} \left[\frac{\mathbb{1}_{Z_n(x) \neq 0}}{\frac{Z_n(x)}{n}} \right] \\
&\leq \sum_{x \in \mathbb{X}} g(x) \mathbb{E} \left[(\hat{p}_{\mathcal{T},m}(x))^2 \right] \frac{2}{(n+1)p_{\mathcal{R}}(x)} \tag{Arnould et al. (2021) (p.27)} \\
&= \sum_{x \in \mathbb{X}} g(x) \left(\frac{p_{\mathcal{T}}(x)(1-p_{\mathcal{T}}(x))}{m} + p_{\mathcal{T}}(x)^2 \right) \frac{2}{(n+1)p_{\mathcal{R}}(x)}
\end{aligned}$$

Finally, using (39), and (36),

$$\begin{aligned}
\text{Var} [\hat{\tau}_{\pi,n,m}] &\leq \frac{\text{Var}_{\mathcal{T}} [\tau(X)]}{m} + \sum_{x \in \mathbb{X}} p_{\mathcal{T}}(x)(1-p_{\mathcal{R}}(x))^n \\
&\quad + \frac{2}{n+1} \left(\mathbb{E}_{\mathcal{R}} \left[\left(\frac{p_{\mathcal{T}}(X)}{p_{\mathcal{R}}(X)} \right)^2 V_{\text{HT}}(X) \right] + \frac{1}{m} \mathbb{E}_{\mathcal{R}} \left[\frac{p_{\mathcal{T}}(X)(1-p_{\mathcal{T}}(X))}{p_{\mathcal{R}}(X)^2} V_{\text{HT}}(X) \right] \right).
\end{aligned}$$

□

A.3.2 Proof of Corollary 2

Asymptotic bias

The proof is exactly the same as for the semi-oracle IPSW, see Subsection A.2.2.

Asymptotic variance

We recall that the explicit expression of the variance is

$$\begin{aligned} \text{Var} [\hat{\tau}_{\pi,n,m}] &= \frac{1}{m} \text{Var}_{\mathbb{T}} [\tau(X) \mathbb{1}_{Z_n(X) \neq 0}] + \left(1 - \frac{1}{m}\right) \text{Var} [\mathbb{E} [\mathbb{1}_{Z_n(X)=0} | \mathbf{X}_n]] \\ &\quad + \frac{1}{n} \sum_{x \in \mathbb{X}} V_{\text{HT}}(x) \frac{p_{\mathbb{T}}(x)(1-p_{\mathbb{T}}(x))}{m} \mathbb{E} \left[\frac{\mathbb{1}_{Z_n(x) \neq 0}}{\hat{p}_{\mathbb{R},n}(x)} \right] + \text{Var} [\hat{\tau}_{\pi,\mathbb{T},n}^*]. \end{aligned}$$

Let's consider a slightly different quantity, multiplying by $\min(n, m)$,

$$\begin{aligned} \min(n, m) \text{Var} [\hat{\tau}_{\pi,n,m}] &= \frac{\min(n, m)}{m} \text{Var}_{\mathbb{T}} [\tau(X) \mathbb{1}_{Z_n(X) \neq 0}] + \min(n, m) \left(1 - \frac{1}{m}\right) \text{Var} [\mathbb{E} [\mathbb{1}_{Z_n(X)=0} | \mathbf{X}_n]] \\ &\quad + \frac{\min(n, m)}{nm} \sum_{x \in \mathbb{X}} V_{\text{HT}}(x) p_{\mathbb{T}}(x)(1-p_{\mathbb{T}}(x)) \mathbb{E} \left[\frac{\mathbb{1}_{Z_n(x) \neq 0}}{\hat{p}_{\mathbb{R},n}(x)} \right] + \min(n, m) \text{Var} [\hat{\tau}_{\pi,\mathbb{T},n}^*]. \end{aligned}$$

Now, we study an asymptotic regime where n and m can grow toward infinity but at different paces. Let

$$\lim_{n,m \rightarrow \infty} \frac{m}{n} = \lambda \in [0, \infty],$$

where λ characterizes the regime.

Case 1: If $\lambda \in [1, \infty]$, one can replace $\min(n, m)$ by n , so that

$$\begin{aligned} \lim_{n,m \rightarrow \infty} n \text{Var} [\hat{\tau}_{\pi,n,m}] &= \lim_{n,m \rightarrow \infty} \left(\underbrace{\frac{n}{m}}_{\frac{1}{\lambda}} \text{Var}_{\mathbb{T}} [\tau(X) \mathbb{1}_{Z_n(X) \neq 0}] + n \left(1 - \frac{1}{m}\right) \text{Var} [\mathbb{E} [\mathbb{1}_{Z_n(X)=0} | \mathbf{X}_n]] \right) \\ &\quad + \underbrace{\lim_{n,m \rightarrow \infty} \left(\frac{1}{m} \sum_{x \in \mathbb{X}} V_{\text{HT}}(x) p_{\mathbb{T}}(x)(1-p_{\mathbb{T}}(x)) \mathbb{E} \left[\frac{\mathbb{1}_{Z_n(x) \neq 0}}{\hat{p}_{\mathbb{R},n}(x)} \right] \right)}_{=0} \\ &\quad + \underbrace{\lim_{n,m \rightarrow \infty} (n \text{Var} [\hat{\tau}_{\pi,\mathbb{T},n}^*])}_{=V_{\text{so}}}, \end{aligned} \tag{Corollary 1}$$

where we also used from former proof, (29) and (30) stating that

$$\mathbb{E} \left[\frac{\mathbb{1}_{Z_n(x) > 0}}{Z_n(x)/n} \right] \rightarrow \frac{1}{p_{\mathbb{R}}(x)}, \quad \text{as } n \rightarrow \infty.$$

Recalling (39),

$$0 \leq \text{Var} [\mathbb{E} [\mathbb{1}_{Z_n(X)=0} | \mathbf{X}_n]] \leq \sum_{x \in \mathbb{X}} p_{\mathbb{T}}(x)(1-p_{\mathbb{R}}(x))^n,$$

due to the exponential convergence one has,

$$\lim_{n \rightarrow \infty} n \text{Var} [\mathbb{E} [\mathbb{1}_{Z_n(X)=0} | \mathbf{X}_n]] = 0,$$

and therefore,

$$\lim_{n,m \rightarrow \infty} n \left(1 - \frac{1}{m}\right) \text{Var} [\mathbb{E} [\mathbb{1}_{Z_n(X)=0} | \mathbf{X}_n]] = 0. \tag{40}$$

To summarize, if $\lambda \in [1, \infty]$, and using

$$\lim_{n \rightarrow \infty} \text{Var}_{\mathbb{T}} [\tau(X) \mathbb{1}_{Z_n(X) \neq 0}] = \text{Var}_{\mathbb{T}} [\tau(X)],$$

and

$$\lim_{n \rightarrow \infty} n \text{Var} [\mathbb{E} [\mathbb{1}_{Z_n(X)=0} | \mathbf{X}_n]] = 0,$$

as $\text{Var} [\mathbb{E} [\mathbb{1}_{Z_n(X)=0} | \mathbf{X}_n]]$ converges exponentially toward 0, one can conclude that

$$\lim_{n, m \rightarrow \infty} n \text{Var} [\hat{\tau}_{\pi, n, m}] = \frac{\text{Var} [\tau(X)]}{\lambda} + V_{so}. \quad (41)$$

Case 2: If $\lambda \in [0, 1]$, one can replace $\min(n, m)$ by m , so that

$$\begin{aligned} \lim_{n, m \rightarrow \infty} m \text{Var} [\hat{\tau}_{\pi, n, m}] &= \lim_{n, m \rightarrow \infty} \text{Var}_{\mathbb{T}} [\tau(X) \mathbb{1}_{Z_n(X) \neq 0}] + \lim_{n, m \rightarrow \infty} m \left(1 - \frac{1}{m}\right) \text{Var} [\mathbb{E} [\mathbb{1}_{Z_n(X)=0} | \mathbf{X}_n]] \\ &+ \lim_{n, m \rightarrow \infty} \frac{1}{n} \sum_{x \in \mathbb{X}} V_{\text{HT}}(x) p_{\mathbb{T}}(x) (1 - p_{\mathbb{T}}(x)) \mathbb{E} \left[\frac{\mathbb{1}_{Z_n(x) \neq 0}}{\hat{p}_{\mathbb{R}, n}(x)} \right] \\ &+ \lim_{n, m \rightarrow \infty} \lambda \sum_{x \in \mathbb{X}} V_{\text{HT}}(x) p_{\mathbb{T}}^2(x) \mathbb{E} \left[\frac{\mathbb{1}_{Z_n(x) \neq 0}}{\hat{p}_{\mathbb{R}, n}(x)} \right]. \end{aligned}$$

In particular,

$$\lim_{n, m \rightarrow \infty} \text{Var}_{\mathbb{T}} [\tau(X) \mathbb{1}_{Z_n(X) \neq 0}] = \text{Var}_{\mathbb{T}} [\tau(X)],$$

and

$$m \left(1 - \frac{1}{m}\right) \text{Var} [\mathbb{E} [\mathbb{1}_{Z_n(X)=0} | \mathbf{X}_n]] \leq n \left(1 - \frac{1}{m}\right) \text{Var} [\mathbb{E} [\mathbb{1}_{Z_n(X)=0} | \mathbf{X}_n]],$$

such that

$$\lim_{n, m \rightarrow \infty} m \left(1 - \frac{1}{m}\right) \text{Var} [\mathbb{E} [\mathbb{1}_{Z_n(X)=0} | \mathbf{X}_n]] = 0$$

due to (40). In addition, (29) and (30) ensure that

$$\lim_{n, m \rightarrow \infty} \lambda \sum_{x \in \mathbb{X}} V_{\text{HT}}(x) p_{\mathbb{T}}^2(x) \mathbb{E} \left[\frac{\mathbb{1}_{Z_n(x) \neq 0}}{\hat{p}_{\mathbb{R}, n}(x)} \right] = \lambda V_{so}.$$

As an intermediary conclusion, if $\lambda \in [0, 1]$,

$$\lim_{n, m \rightarrow \infty} \min(n, m) \text{Var} [\hat{\tau}_{\pi, n, m}] = \text{Var} [\tau(X)] + \lambda V_{so} \quad (42)$$

General conclusion: It is possible to express result from (41) and (42) in one single conclusion, factorizing the expression by $\min(1, \lambda)$. Therefore, letting $\lim_{n, m \rightarrow \infty} m/n = \lambda \in [0, \infty]$, the asymptotic variance of completely estimated IPSW satisfies

$$\lim_{n, m \rightarrow \infty} \min(n, m) \text{Var} [\hat{\tau}_{\pi, n, m}] = \min(1, \lambda) \left(\frac{\text{Var} [\tau(X)]}{\lambda} + V_{so} \right).$$

A.3.3 Proof of Theorem 3

Proof. For any estimate $\hat{\tau}$, we have

$$\mathbb{E} [(\hat{\tau} - \tau)^2] = (\mathbb{E} [\hat{\tau}] - \tau)^2 + \text{Var} [\hat{\tau}].$$

Therefore, the risk of the (completely estimated) IPSW estimate can be bounded using results from Subsection A.3.1 (or Proposition 2), and in particular the bounds on the variance and the bias,

$$\begin{aligned} \mathbb{E} [(\hat{\tau} - \tau)^2] &\leq (1 - \min_x p_R(x))^{2n} \tau^2 + \frac{\text{Var}_T[\tau(X)]}{m} + \sum_{x \in \mathbb{X}} p_T(x) (1 - p_R(x))^n \\ &\quad + \frac{2}{n+1} \left(\mathbb{E}_R \left[\left(\frac{p_T(X)}{p_R(X)} \right)^2 V_{HT}(X) \right] + \frac{1}{m} \mathbb{E}_R \left[\frac{p_T(X) (1 - p_T(X))}{p_R(X)^2} V_{HT}(X) \right] \right) \\ &\leq \left(1 - \min_x p_R(x) \right)^n (\tau^2 + 1) + \frac{\text{Var}_T[\tau(X)]}{m} \\ &\quad + \frac{2V_{so}}{n+1} + \frac{2}{m(n+1)} \mathbb{E}_R \left[\frac{p_T(X) (1 - p_T(X))}{p_R(X)^2} V_{HT}(X) \right], \end{aligned}$$

noting that,

$$(1 - \min_x p_R(x))^{2n} \tau^2 \leq (1 - \min_x p_R(x))^n \tau^2,$$

and

$$\sum_{x \in \mathbb{X}} p_T(x) (1 - p_R(x))^n \leq (1 - \min_x p_R(x))^n$$

The L^2 consistency holds by letting n and m tend to infinity. □

A.4 Completely estimated IPSW with estimated $\hat{\pi}$ - Proof of Corollary 3

Proof. We start by computing the bias of

$$\begin{aligned} \mathbb{E} [\hat{\tau}_{n,m}] &= \mathbb{E} \left[\frac{1}{n} \sum_{i=1}^n \frac{\hat{p}_{T,m}(X_i)}{\hat{p}_{R,n}(X_i)} Y_i \left(\frac{A_i}{\hat{\pi}_n(X_i)} - \frac{1 - A_i}{1 - \hat{\pi}_n(X_i)} \right) \right] \\ &= \frac{1}{n} \mathbb{E} \left[\sum_{x \in \mathbb{X}} \frac{p_T(x)}{\hat{p}_{R,n}(x)} \sum_{i=1}^n \mathbb{1}_{X_i=x} Y_i \left(\frac{A_i}{\hat{\pi}_n(x)} - \frac{1 - A_i}{1 - \hat{\pi}_n(x)} \right) \right] \\ &= \frac{1}{n} \mathbb{E} \left[\sum_{x \in \mathbb{X}} \frac{p_T(x)}{\hat{p}_{R,n}(x)} \sum_{i=1}^n \mathbb{1}_{X_i=x} Y_i \left(\frac{A_i}{\hat{\pi}_n(x)} - \frac{1 - A_i}{1 - \hat{\pi}_n(x)} \right) \right], \end{aligned}$$

where the last line is obtained by conditioning on all variables except X_{n+1}, \dots, X_{n+m} .

$$\begin{aligned} \mathbb{E} [\hat{\tau}_{n,m}] &= \frac{1}{n} \mathbb{E} \left[\sum_{x \in \mathbb{X}} \frac{p_T(x)}{\hat{p}_{R,n}(x)} \sum_{i=1}^n \mathbb{1}_{X_i=x} \left(\frac{Y_i^{(1)} A_i}{\hat{\pi}_n(x)} - \frac{Y_i^{(0)} (1 - A_i)}{1 - \hat{\pi}_n(x)} \right) \right] \\ &= \frac{1}{n} \mathbb{E} \left[\sum_{x \in \mathbb{X}} \frac{p_T(x)}{\hat{p}_{R,n}(x)} \sum_{i=1}^n \mathbb{1}_{X_i=x} \mathbb{E} \left[\left(\frac{Y_i^{(1)} A_i}{\hat{\pi}_n(x)} - \frac{Y_i^{(0)} (1 - A_i)}{1 - \hat{\pi}_n(x)} \right) \mid \mathbf{X}_n, \mathbf{Y}_n^{(1)}, \mathbf{Y}_n^{(0)} \right] \right] \end{aligned}$$

Let us consider, for any fixed $x \in \mathbb{X}$,

$$\mathbb{E} \left[\frac{Y_i^{(1)} A_i}{\hat{\pi}_n(x)} \mid \mathbf{X}_n, \mathbf{Y}_n^{(1)}, \mathbf{Y}_n^{(0)} \right] = Y_i^{(1)} \mathbb{E} \left[\frac{A_i}{\hat{\pi}_n(x)} \mid \mathbf{X}_n \right].$$

Up to reordering the X_i 's, we have

$$\begin{aligned} \mathbb{E} \left[\frac{A_i}{\hat{\pi}_n(x)} \mid \mathbf{X}_n \right] &= Z_n(x) \mathbb{E} \left[\frac{A_i}{\sum_{j=1}^{Z_n(x)} A_j} \mid \mathbf{X}_n \right] \\ &= \frac{Z_n(x)}{2} \mathbb{E} \left[\frac{1}{1 + \sum_{j=2}^{Z_n(x)} A_j} \mid \mathbf{X}_n \right]. \end{aligned}$$

According to Lemma 11, (i) in Biau (2012), for any $B_n \sim B(n, p)$, we have

$$\mathbb{E} \left[\frac{1}{1 + B_n} \right] = \frac{1}{(n+1)p} - \frac{(1-p)^{n+1}}{(n+1)p}.$$

Since, conditional on \mathbf{X}_n , $\sum_{j=2}^{Z_n(x)} A_j$ is distributed as $B(Z_n(x) - 1, 1/2)$, we have

$$\begin{aligned}\mathbb{E}\left[\frac{A_i}{\hat{\pi}_n(x)}|\mathbf{X}_n\right] &= \frac{Z_n(x)}{2}\left(\frac{2}{Z_n(x)} - 2\frac{(1/2)^{Z_n(x)}}{Z_n(x)}\right) \\ &= 1 - (1/2)^{Z_n(x)}.\end{aligned}$$

Similarly,

$$\mathbb{E}\left[\frac{(1 - A_i)}{1 - \hat{\pi}_n(x)}|\mathbf{X}_n\right] = 1 - (1/2)^{Z_n(x)}.$$

Consequently,

$$\mathbb{E}\left[\left(\frac{Y_i^{(1)}A_i}{\hat{\pi}_n(x)} - \frac{Y_i^{(0)}(1 - A_i)}{1 - \hat{\pi}_n(x)}\right)|\mathbf{X}_n, \mathbf{Y}_n^{(1)}, \mathbf{Y}_n^{(0)}\right] = \left(1 - (1/2)^{Z_n(x)}\right).$$

Hence,

$$\begin{aligned}\mathbb{E}[\hat{\tau}_{n,m}] &= \frac{1}{n}\mathbb{E}\left[\sum_{x \in \mathbb{X}} \frac{p_{\text{T}}(x)}{\hat{p}_{\text{R},n}(x)} \sum_{i=1}^n \mathbf{1}_{X_i=x} (Y_i^{(1)} - Y_i^{(0)}) \left(1 - (1/2)^{Z_n(x)}\right)\right] \\ &= \frac{1}{n}\mathbb{E}\left[\sum_{x \in \mathbb{X}} \frac{p_{\text{T}}(x)}{\hat{p}_{\text{R},n}(x)} \sum_{i=1}^n \mathbf{1}_{X_i=x} \tau(x) \left(1 - (1/2)^{Z_n(x)}\right)\right] \\ &= \frac{1}{n} \sum_{x \in \mathbb{X}} p_{\text{T}}(x) \tau(x) \mathbb{E}\left[\frac{1}{\hat{p}_{\text{R},n}(x)} Z_n(x) \left(1 - (1/2)^{Z_n(x)}\right)\right] \\ &= \tau - \sum_{x \in \mathbb{X}} p_{\text{T}}(x) \tau(x) \mathbb{E}\left[(1/2)^{Z_n(x)} \mathbf{1}_{Z_n(x) > 0}\right] \\ &= \tau - \sum_{x \in \mathbb{X}} p_{\text{T}}(x) \tau(x) \mathbb{E}\left[(1/2)^{Z_n(x)} (1 - \mathbf{1}_{Z_n(x)=0})\right] \\ &= \tau - \sum_{x \in \mathbb{X}} p_{\text{T}}(x) \tau(x) \mathbb{E}\left[(1/2)^{Z_n(x)}\right] - \sum_{x \in \mathbb{X}} p_{\text{T}}(x) \tau(x) \mathbb{E}\left[(1/2)^{Z_n(x)} \mathbf{1}_{Z_n(x)=0}\right] \\ &= \tau - \sum_{x \in \mathbb{X}} p_{\text{T}}(x) \tau(x) \mathbb{E}\left[(1/2)^{Z_n(x)}\right] - \sum_{x \in \mathbb{X}} p_{\text{T}}(x) \tau(x) \mathbb{P}[Z_n(x) = 0].\end{aligned}$$

Now, note that $\mathbb{P}[Z_n(x) = 0] = (1 - p_{\text{R}}(x))^n$ and

$$\begin{aligned}\mathbb{E}\left[(1/2)^{Z_n(x)}\right] &= \prod_{j=1}^n \mathbb{E}\left[(1/2)^{\mathbf{1}_{X_j=x}}\right] \\ &= \left(\frac{p_{\text{R}}(x)}{2} + 1 - p_{\text{R}}(x)\right)^n \\ &= \left(1 - \frac{p_{\text{R}}(x)}{2}\right)^n.\end{aligned}$$

Finally, the bias of the completely estimated IPSW with estimated treatment proportion is given by

$$\mathbb{E}[\hat{\tau}_{n,m}] - \tau = - \sum_{x \in \mathbb{X}} p_{\text{T}}(x) \tau(x) \left(1 - \frac{p_{\text{R}}(x)}{2}\right)^n - \sum_{x \in \mathbb{X}} p_{\text{T}}(x) \tau(x) (1 - p_{\text{R}}(x))^n. \quad (43)$$

□

B Extended adjustment set

B.1 Proof of Corollary 4

Proof. According to Corollary 1, we have

$$\lim_{n \rightarrow \infty} n \text{Var}[\hat{\tau}_{\text{T},n}^*(X)] = V_{\text{so}}, \quad (44)$$

where

$$V_{\text{so}} := \mathbb{E}_{\mathbb{R}} \left[\left(\frac{p_{\text{T}}(X)}{p_{\text{R}}(X)} \right)^2 V_{\text{HT}}(X) \right],$$

with

$$V_{\text{HT}}(x) = \mathbb{E}_{\mathbb{R}} \left[\frac{(Y^{(1)})^2}{\pi} \mid X = x \right] + \mathbb{E}_{\mathbb{R}} \left[\frac{(Y^{(0)})^2}{1 - \pi} \mid X = x \right] - \tau(x)^2.$$

Since, by assumption, V is composed of covariates that are not treatment effect modifiers, using Definition 10, we have, for all (x, v) ,

$$V_{\text{HT}}(x, v) = V_{\text{HT}}(x). \quad (45)$$

Now, considering the set (X, V) instead of X in the expression (44) leads to

$$\begin{aligned} \lim_{n \rightarrow \infty} n \text{Var}_{\mathbb{R}} [\hat{\tau}_{\text{T},n}^*(X, V)] &= \mathbb{E}_{\mathbb{R}} \left[\left(\frac{p_{\text{T}}(X, V)}{p_{\text{R}}(X, V)} \right)^2 V_{\text{HT}}(X, V) \right] \\ &= \sum_{x, v \in \mathcal{X}, \mathcal{V}} \frac{p_{\text{T}}^2(x, v)}{p_{\text{R}}(x, v)} V_{\text{HT}}(x, v) \\ &= \sum_{x, v \in \mathcal{X}, \mathcal{V}} \frac{p_{\text{T}}^2(x, v)}{p_{\text{R}}(x, v)} V_{\text{HT}}(x) && \text{Equation. (45)} \\ &= \sum_{x, v \in \mathcal{X}, \mathcal{V}} \frac{p_{\text{T}}^2(x) p_{\text{T}}^2(v)}{p_{\text{R}}(x) p_{\text{R}}(v)} V_{\text{HT}}(x) && V \perp\!\!\!\perp X \\ &= \left(\sum_{v \in \mathcal{V}} \frac{p_{\text{T}}(v)^2}{p_{\text{R}}(v)} \right) \sum_{x \in \mathcal{X}} \frac{p_{\text{T}}^2(x)}{p_{\text{R}}(x)} V_{\text{HT}}(x) \\ &= \left(\sum_{v \in \mathcal{V}} \frac{p_{\text{T}}(v)^2}{p_{\text{R}}(v)} \right) \lim_{n \rightarrow \infty} n \text{Var}_{\mathbb{R}} [\hat{\tau}_{\text{T},n}^*(X)], \end{aligned}$$

Now, note that

$$\begin{aligned} \sum_{v \in \mathcal{V}} \frac{p_{\text{T}}(v)^2}{p_{\text{R}}(v)} &= \mathbb{E}_{\mathbb{R}} \left[\frac{p_{\text{T}}(V)^2}{p_{\text{R}}(V)^2} \right] \\ &\geq \left(\mathbb{E}_{\mathbb{R}} \left[\frac{p_{\text{T}}(V)}{p_{\text{R}}(V)} \right] \right)^2 \\ &\geq \left(\sum_{v \in \mathcal{V}} p_{\text{T}}(v) \right)^2 \\ &\geq 1, \end{aligned}$$

where the first inequality results from Jensen's inequality. Consequently,

$$\lim_{n \rightarrow \infty} n \text{Var}_{\mathbb{R}} [\hat{\tau}_{\text{T},n}^*(X, V)] \geq \lim_{n \rightarrow \infty} n \text{Var}_{\mathbb{R}} [\hat{\tau}_{\text{T},n}^*(X)].$$

□

B.2 Proof of Corollary 5

Proof. By the law of total variance, we have, for all x ,

$$V_{\text{HT}}(x) = \mathbb{E} [V_{\text{HT}}(x, V)] + \text{Var} [\tau(x, V)]. \quad (46)$$

Indeed, according to the law of total variance, for all random variables Z, X_1, X_2 , we have, a.s.,

$$\text{Var} [Z \mid X_1] = \mathbb{E} [\text{Var} [Z \mid X_1, X_2] \mid X_1] + \text{Var} [\mathbb{E} [Z \mid X_1, X_2] \mid X_1].$$

Letting $X_1 = X$, $X_2 = V$ and $Z = (YA/\pi) - (Y(1 - A)/\pi)$ yields equation (46). Now, we can write

$$\begin{aligned}
\lim_{n \rightarrow \infty} n \text{Var}_{\mathbb{R}} [\hat{\tau}_{T,n}^*(X, V)] &= \mathbb{E}_{\mathbb{R}} \left[\left(\frac{p_T(X, V)}{p_R(X, V)} \right)^2 V_{\text{HT}}(X, V) \right] \\
&= \sum_{x, v \in \mathcal{X}, \mathcal{V}} \frac{p_T^2(x, v)}{p_R(x, v)} V_{\text{HT}}(x, v) \\
&= \sum_{x, v \in \mathcal{X}, \mathcal{V}} \frac{p_T^2(x) p_T^2(v)}{p_R(x) p_R(v)} V_{\text{HT}}(x, v) && V \perp\!\!\!\perp X \\
&= \sum_{x \in \mathcal{X}} \frac{p_T^2(x)}{p_R(x)} \sum_{v \in \mathcal{V}} \frac{p_T^2(v)}{p_R(v)} V_{\text{HT}}(x, v) \\
&= \sum_{x \in \mathcal{X}} \frac{p_T^2(x)}{p_R(x)} \sum_{v \in \mathcal{V}} p_T(v) V_{\text{HT}}(x, v) && \text{by Definition 11} \\
&= \sum_{x \in \mathcal{X}} \frac{p_T^2(x)}{p_R(x)} (V_{\text{HT}}(x) - \text{Var}[\tau(x, V)]) && \text{Equation (46)} \\
&= \lim_{n \rightarrow \infty} n \text{Var}_{\mathbb{R}} [\hat{\tau}_{T,n}^*(X)] - \mathbb{E}_{\mathbb{R}} \left[\frac{p_T(X)}{p_R(X)} \text{Var}[\tau(X, V) \mid X] \right],
\end{aligned}$$

which concludes the proof. \square

C Semi-synthetic simulation's data preparation

C.1 Context

The semi-synthetic simulation is made of real world data, a trial called CRASH-3 (Dewan et al., 2012; CRASH-3, 2019) and an observational data base called Traumabase. The covariates of both data sources are used to generate the true distribution from which the simulated data are generated. This part details the pre-treatment performed on the covariates, which is contained in the R notebook entitled `Prepare-semi-synthetic-simulation.Rmd`. As explained in the main document, in this semi-synthetic simulation we only consider six baseline covariates:

- Glasgow Coma Scale score⁶ (GCS) (categorical);
- Gender (categorical);
- Pupil reactivity (categorical);
- Age (continuous);
- Systolic blood pressure (continuous);
- Time-to-treatment (continuous), being the time between the trauma and the administration of the treatment.

As three covariates out of 6 are continuous, we categorize them to obtain a completely categorical data. The time-to-treatment is categorized in 4 levels, systolic blood pressure in 3 levels, and age in 3 levels. To further reduce the number of categories, and follow the CRASH-3 trial stratification, the Glasgow score is also gathered in 3 levels, from severe to moderately injured individuals, based on their Glasgow score.

CRASH-3 trial The CRASH-3 trial data contains information on 12,737 individuals. Over the six covariates of interest and the 12,737 individuals, 108 values are missing. We imputed them using the R package `missRanger`.

Traumabase observational data The complete Traumabase data contains 20,037 observations, but when keeping only the individuals suffering from Traumatic Brain Injury (TBI) as it is the case in the CRASH-3 trial, only 8,289 observations could be kept. Many data are missing, in particular 2,660 missing values for 8,289 individuals and along 5 baseline covariates considered. We impute them with the R package `missRanger`, using 35 other available baseline covariates. Because the time to treatment is not observed in the Traumabase this covariate is generated following a beta law, and considering a shifted distribution compared to the trial, in particular toward lower time-to-treatment values than in the trial.

⁶The GCS is a neurological scale which aims to assess a person's consciousness. The lower the score, the higher the severity of the trauma.

Ensuring overlap When binding the two data sets, we had to ensure that the support inclusion assumption (Assumption 4) was verified. Out of the 586 modalities present in the target data, only 192 are also present in the trial data. Therefore only these observations are kept, such that the observational sample finally contains 8,058 observations (8,289 at the beginning). All the observations in the trial are kept as there is no restriction for the trial to contain a larger support as presented in Assumption 4.

C.1.1 Covariate shift visualization

For each of the six baseline and categorical considered, visualization of the covariate shift between the two data source is represented on Figures 9, 10, 11, 12, 13, and 14.

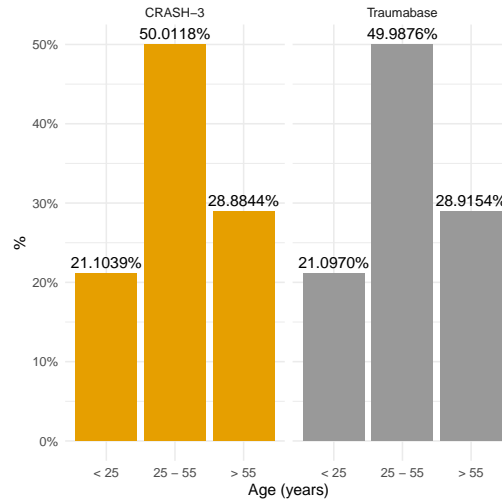


Figure 9: Bar plot of categorized age in the semi-synthetic simulation

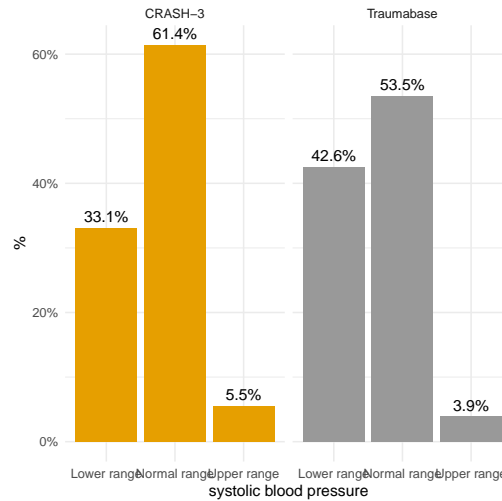


Figure 10: Bar plot of categorized systolic blood pressure in the semi-synthetic simulation

C.2 Synthetic outcome model

As detailed above, for now the covariate support reflects a true situation, where only the time-to-treatment covariate was created as it is missing in the target population sample (Colnet et al., 2021).

For the purpose of simulation, the outcome model is completely synthetic, and for each strata a number is affected, from 1 to the number of strata, starting to the lowest category (for example youngest strata, or lowest Glasgow score, or lower systolic blood pressure), to the highest one.

Doing so, the outcome model considered is such as,

$$Y = 10 - \text{Glasgow} + (\text{if Girl: } -5 \text{ else: } 0) + A(15(6 - \text{TTT}) + 3 * (\text{Systolic.blood.pressure} - 1)^2) + \varepsilon_{\text{TTT}},$$

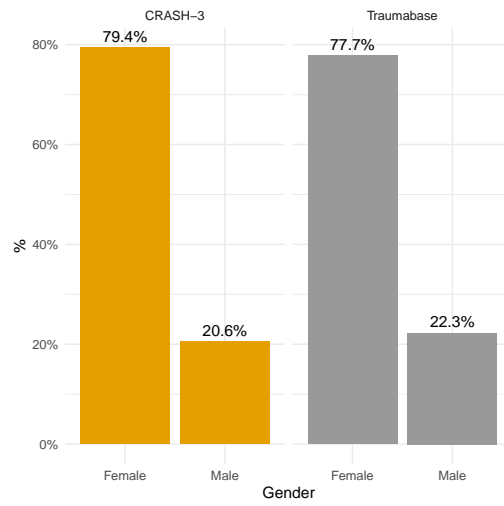


Figure 11: Bar plot of gender in the semi-synthetic simulation

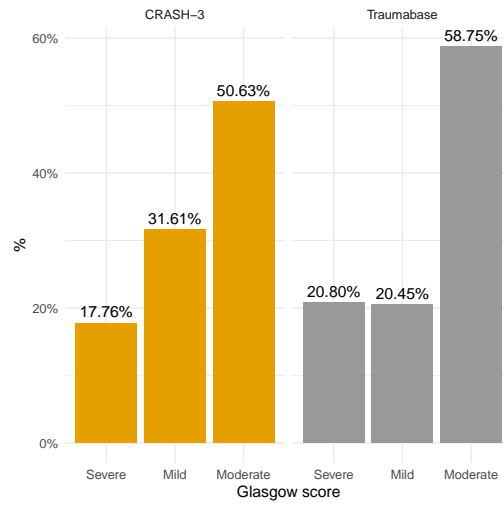


Figure 12: Bar plot of the glasgow score in the semi-synthetic simulation

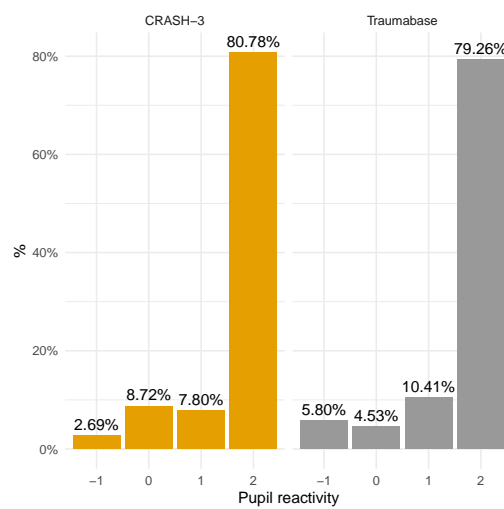


Figure 13: Bar plot of pupil reactivity (-1 encoding not able to measure) in the semi-synthetic simulation

where ε_{TTT} is a random Gaussian noise with a standard deviation depending on the value of the covariate TTT. In particular if the treatment is given later, then the noise is stronger.

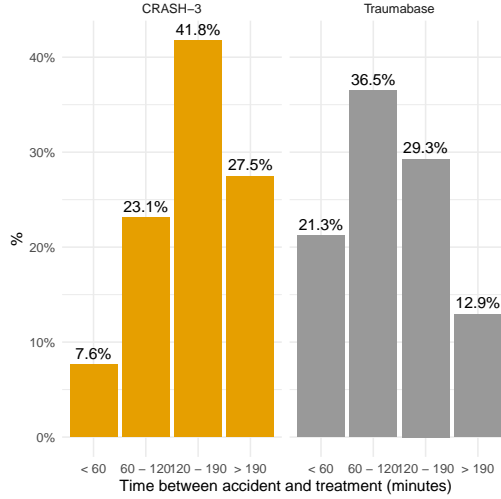


Figure 14: Bar plot of categorized time-to-treatment in the semi-synthetic simulation

D Useful results about RCTs

Here we recall one definition (Bernoulli trial) and results (variance expression of the Horvitz-Thomson and variance inequality) used in this work. Chapter 2 of [Imbens and Rubin \(2015\)](#) details the trial’s designs and many results about Randomized Controlled Trials, in particular consistency. We also recommend to read Lecture 1 of [Wager \(2020\)](#) for details about the difference-in-means estimator.

D.1 Bernoulli trial

A Bernoulli trial is a trial where the treatment assignment vector, being $\mathbf{A} = (A_1, \dots, A_n)$ follows a Bernoulli law with a constant probability. More formally,

Definition 12 (Assignment mechanism for a Bernoulli Trial). *If the assignment mechanism is a Bernoulli trial with a probability π , then*

$$\forall i, \mathbb{P}[A_i] = \pi,$$

and considering a sample for n units,

$$\mathbb{P}[\mathbf{A} \mid i \in \mathcal{R}] = \prod_{i=1}^n \left[\pi^{A_i} \cdot (1 - \pi)^{1-A_i} \right],$$

where \mathbf{A} denotes the vector of treatment allocation for the trial sample \mathcal{R} .

In this design the treatment allocation is independent of all other treatment allocations. A disadvantage of such design is the fact that there is always a small probability that all units receive the treatment or no treatment. This is why other designs are possible, where the treatment allocation depends on previous decision for other units. The interest is to ensure to get a balanced group of treated and controls, and avoid a possible pathological case of high unbalance between the number of treated and control individuals.

D.2 Horvitz-Thomson’s variance on subgroup

This lemma is used in the proofs of Section A.

Lemma 1. *Assuming model described in Subsection 3.1.1 and Assumption 2, then*

$$\forall x \in \mathbb{X}, \forall n, n \text{ Var} [\hat{\tau}_{HT,n} \mid X = x] = \mathbb{E} \left[\frac{(Y^{(1)})^2}{\pi} \mid X = x \right] + \mathbb{E} \left[\frac{(Y^{(0)})^2}{1 - \pi} \mid X = x \right] - \tau(x)^2.$$

Proof.

$$\begin{aligned}
\text{Var}_{\mathbb{R}} [\hat{\tau}_{\text{HT},n} | X] &= \text{Var}_{\mathbb{R}} \left[\frac{1}{n} \sum_{i=1}^n \frac{A_i Y_i}{\pi} - \frac{(1-A_i)Y_i}{1-\pi} \mid X \right] \\
&= \frac{1}{n^2} \text{Var}_{\mathbb{R}} \left[\sum_{i=1}^n \frac{A_i Y_i^{(1)}}{\pi} - \frac{(1-A_i)Y_i^{(0)}}{1-\pi} \mid X \right] && \text{Assumption 2} \\
&= \frac{1}{n} \text{Var}_{\mathbb{R}} \left[\frac{AY^{(1)}}{\pi} - \frac{(1-A)Y^{(0)}}{1-\pi} \mid X \right]. && iid
\end{aligned}$$

Then,

$$\text{Var} [\hat{\tau}_{\text{HT},n} | X_i] = \frac{1}{n} \left(\text{Var}_{\mathbb{R}} \left[\frac{AY^{(1)}}{\pi} \mid X_i \right] + \text{Var}_{\mathbb{R}} \left[\frac{(1-A)Y^{(0)}}{1-\pi} \mid X_i \right] - 2 \text{Cov}_{\mathbb{R}} \left[\frac{AY^{(1)}}{\pi}, \frac{(1-A)Y^{(0)}}{1-\pi} \mid X_i \right] \right). \quad (47)$$

The first two terms can be simplified, noting that

$$\begin{aligned}
\mathbb{E}_{\mathbb{R}} \left[\left(\frac{AY^{(1)}}{\pi} \right)^2 \mid X_i \right] &= \mathbb{E}_{\mathbb{R}} \left[\mathbb{1}_{\{A_i=1\}} \left(\frac{Y^{(1)}}{\pi} \right)^2 \mid X_i \right] && A \text{ is binary} \\
&= \mathbb{E}_{\mathbb{R}} \left[\frac{(Y^{(1)})^2}{\pi^2} \mid X_i \right] \mathbb{E}_{\mathbb{R}} [\mathbb{1}_{\{A_i=1\}} \mid X_i] && \text{Randomization of trial} \\
&= \mathbb{E}_{\mathbb{R}} \left[\frac{(Y^{(1)})^2}{\pi} \mid X_i \right] && \text{Definition of } \pi
\end{aligned}$$

Similarly,

$$\mathbb{E}_{\mathbb{R}} \left[\left(\frac{(1-A)Y^{(0)}}{1-\pi} \mid X_i \right)^2 \right] = \mathbb{E}_{\mathbb{R}} \left[\frac{(Y^{(0)})^2}{1-\pi} \mid X_i \right].$$

So,

$$\begin{aligned}
\text{Var}_{\mathbb{R}} \left[\frac{AY^{(1)}}{\pi} \mid X_i \right] &= \mathbb{E}_{\mathbb{R}} \left[\left(\frac{AY^{(1)}}{\pi} \right)^2 \mid X_i \right] - \mathbb{E} \left[\frac{AY^{(1)}}{\pi} \mid X_i \right]^2 \\
&= \mathbb{E}_{\mathbb{R}} \left[\frac{(Y^{(1)})^2}{\pi} \mid X_i \right] - \mathbb{E}_{\mathbb{R}} [Y^{(1)} \mid X_i]^2.
\end{aligned}$$

Similarly,

$$\text{Var}_{\mathbb{R}} \left[\frac{(1-A)Y^{(0)}}{1-\pi} \mid X_i \right] = \mathbb{E}_{\mathbb{R}} \left[\frac{(Y^{(0)})^2}{1-\pi} \mid X_i \right] - \mathbb{E}_{\mathbb{R}} [Y^{(0)} \mid X_i]^2.$$

The third term in equation (47) can also be decomposed, so that,

$$\begin{aligned}
\text{Cov}_{\mathbb{R}} \left[\frac{AY^{(1)}}{\pi}, \frac{(1-A)Y^{(0)}}{1-\pi} \mid X_i \right] &= \mathbb{E}_{\mathbb{R}} \left[\left(\frac{AY^{(1)}}{\pi} - \mathbb{E} [Y^{(1)} \mid X_i] \right) \left(\frac{(1-A)Y^{(0)}}{1-\pi} - \mathbb{E}_{\mathbb{R}} [Y^{(0)} \mid X_i] \right) \mid X_i \right] \\
&= \mathbb{E}_{\mathbb{R}} \left[\underbrace{\frac{AY^{(1)}(1-A)Y^{(0)}}{\pi(1-\pi)}}_{=0} \mid X_i \right] - \mathbb{E}_{\mathbb{R}} [Y^{(0)} \mid X_i] \mathbb{E}_{\mathbb{R}} [Y^{(1)} \mid X_i].
\end{aligned}$$

Finally,

$$n \text{Var} [\hat{\tau}_{\text{HT},n} | X_i] = \mathbb{E}_{\mathbb{R}} \left[\frac{(Y^{(1)})^2}{\pi} \mid X_i \right] + \mathbb{E}_{\mathbb{R}} \left[\frac{(Y^{(0)})^2}{1-\pi} \mid X_i \right] - \tau(X)^2 := V_{\text{HT}}(x).$$

□

D.3 Variance inequality

In this work we use the following inequality to compare the variance of the Horvitz-Thomson with the variance of the Difference-in-means,

$$V_{\text{DM}} = V_{\text{HT}} - \left(\sqrt{\frac{1-\pi}{\pi}} \mathbb{E}_{\text{R}}[Y^{(1)}] + \sqrt{\frac{\pi}{1-\pi}} \mathbb{E}_{\text{R}}[Y^{(0)}] \right)^2 \leq V_{\text{HT}}.$$

We detail the derivations used.

Proof. Recall that,

$$V_{\text{HT}} = \mathbb{E} \left[\frac{(Y^{(1)})^2}{\pi} \right] + \mathbb{E} \left[\frac{(Y^{(0)})^2}{1-\pi} \right] - \tau^2.$$

Noting that,

$$\tau^2 = \left(\mathbb{E} [Y^{(1)} - Y^{(0)}] \right)^2 = \mathbb{E} [Y^{(1)}]^2 + \mathbb{E} [Y^{(0)}]^2 - 2\mathbb{E} [Y^{(1)}] \mathbb{E} [Y^{(0)}],$$

and that for any $a \in \{0, 1\}$,

$$\text{Var} [Y^{(a)}] = \mathbb{E} \left[(Y^{(a)})^2 \right] - \mathbb{E} [Y^{(a)}]^2,$$

allows to obtain,

$$\begin{aligned} V_{\text{HT}} &= \frac{\text{Var} [Y^{(1)}]}{\pi} + \frac{\text{Var} [Y^{(0)}]}{1-\pi} - \left(1 - \frac{1}{\pi}\right) \mathbb{E} [Y^{(1)}]^2 - \left(1 - \frac{1}{1-\pi}\right) \mathbb{E} [Y^{(0)}]^2 + 2\mathbb{E} [Y^{(1)}] \mathbb{E} [Y^{(0)}] \\ &= V_{\text{DM}} + \left(\sqrt{\frac{1-\pi}{\pi}} \mathbb{E}_{\text{R}}[Y^{(1)}] + \sqrt{\frac{\pi}{1-\pi}} \mathbb{E}_{\text{R}}[Y^{(0)}] \right)^2. \end{aligned}$$

□