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Multiply robust estimation of causal effects under principal ignorability

Zhichao Jiang[1] | **Shu Yang[2]** | **Peng Ding[3]**

[1]Department of Biostatistics and Epidemiology, University of Massachusetts, Amherst, Massachusetts, USA

[2]Department of Statistics, North Carolina State University, Raleigh, North Carolina, USA

[3]University of California, Berkeley, Berkeley, California, USA

Correspondence
Peng Ding, University of California, Berkeley, CA 94720, USA.
Email: pengdingpku@berkeley.edu

Abstract

Causal inference concerns not only the average effect of the treatment on the outcome but also the underlying mechanism through an intermediate variable of interest. Principal stratification characterizes such a mechanism by targeting subgroup causal effects within principal strata, which are defined by the joint potential values of an intermediate variable. Due to the fundamental problem of causal inference, principal strata are inherently latent, rendering it challenging to identify and estimate subgroup effects within them. A line of research leverages the principal ignorability assumption that the latent principal strata are mean independent of the potential outcomes conditioning on the observed covariates. Under principal ignorability, we derive various nonparametric identification formulas for causal effects within principal strata in observational studies, which motivate estimators relying on the correct specifications of different parts of the observed-data distribution. Appropriately combining these estimators yields triply robust estimators for the causal effects within principal strata. These triply robust estimators are consistent if two of the treatment, intermediate variable and outcome models are correctly specified, and moreover, they are locally efficient if all three models are correctly specified. We show that these estimators arise naturally from either the efficient influence functions in the semiparametric theory or the model-assisted estimators in the

survey sampling theory. We evaluate different estimators based on their finite-sample performance through simulation and apply them to two observational studies.

KEYWORDS

noncompliance, principal stratification, sensitivity analysis, surrogate endpoint, truncation by death

1 | INTRODUCTION

Researchers are often interested in understanding the underlying causal mechanism from the treatment to the outcome when an intermediate variable is present between them. This requires proper adjustment for the intermediate variable—naively conditioning on its observed value does not have a valid causal interpretation unless it is essentially randomized conditional on the treatment and covariates (Rosenbaum, 1984). Frangakis and Rubin (2002) propose to estimate causal effects within principal strata, which are defined by the joint potential values of the intermediate variable under both treatment and control. Principal strata act as pretreatment covariates, so the causal effects within them, often referred to as principal causal effects (PCEs), are conceptually the same as the standard subgroup causal effects. PCEs are widely used in applied statistics to deal with noncompliance (Angrist et al., 1996; Frumento et al., 2012; Mealli & Pacini, 2013), truncation by death (Ding et al., 2011; Rubin, 2006; Wang et al., 2017), missing data (Frangakis & Rubin, 1999; Mattei et al., 2014), mediation (Elliott et al., 2010; Gallop et al., 2009; Mattei & Mealli, 2011; Rubin, 2004) and surrogate evaluation (Frangakis & Rubin, 2002; Gilbert & Hudgens, 2008; Huang & Gilbert, 2011; Jiang et al., 2016; Li et al., 2010).

Due to the fundamental problem of causal inference, the two potential values of the intermediate variable are not simultaneously observable, rendering it challenging to identify and estimate PCEs without additional assumptions. Angrist et al. (1996) establish the nonparametric identification of one PCE, often called the complier average causal effect or the local average treatment effect, under the monotonicity and the exclusion restriction (ER). The monotonicity assumes that the treatment changes the intermediate variable only in one direction for any unit, and the ER assumes that the treatment affects the outcome only through the intermediate variable. The identification result of Angrist et al. (1996) has motivated various estimation methods and efficiency theories (Abadie, 2003; Frölich, 2007; Ogburn et al., 2015; Tan, 2006). Although the ER is a standard assumption, it is not plausible when the treatment affects the outcome through pathways other than the intermediate variable. Hirano et al. (2000) give an example of the violation of the ER in a randomized experiment with noncompliance. Moreover, in mediation, truncation by death, and principal surrogate evaluation problems, testing the ER is a scientific question of interest. Thus, we cannot invoke ER *a priori*. Without the ER, Zhang et al. (2008) and Imai (2008) derive the large sample bounds on the PCEs, and Li et al. (2010), Zigler and Belin (2012), and Schwartz et al. (2011) perform model-based Bayesian analyses. Unfortunately, the bounds might be too wide to be informative, whereas the Bayesian analyses could be sensitive to models and priors. Assuming Normal linear outcome models within principal strata, Zhang et al. (2009) and Frumento et al. (2012) estimate the PCEs using the likelihood approach, but these analyses can be sensitive to the modelling assumptions and can be unstable even if the models are correctly

specified due to the mixture distributions of the observed data (Feller et al., 2022). Auxiliary covariates or secondary outcomes satisfying additional conditional independence assumptions can help to improve identification and estimation of the PCEs (e.g. Ding et al., 2011; Jiang & Ding, 2021; Jiang et al., 2016; Mattei & Mealli, 2011; Mattei et al., 2013; Mealli & Pacini, 2013; Yang & Small, 2016), but those additional assumptions may be hard to justify without prior knowledge.

We focus on an alternative nonparametric identification strategy under principal ignorability, an assumption in parallel with ignorability for estimating the average causal effect in observational studies (Rosenbaum & Rubin, 1983). Principal ignorability assumes that the observed covariates are adequate for controlling for confounding between the principal strata and outcome. This identification strategy has been popular in applied statistics (Egleston et al., 2009; Feller et al., 2017; Follmann, 2000; Hayden et al., 2005; Hill et al., 2002; Jo & Stuart, 2009; Jo et al., 2011; Stuart & Jo, 2015).

We develop a statistical methodology for estimating the PCEs in both randomized experiments and observational studies under principal ignorability. We first establish three identification formulas for each PCE. These formulas motivate three estimators for each PCE, which rely on correct specifications of two of the following three models:

1. the model of the treatment conditional on the covariates, called the *treatment probability*;
2. the model of the intermediate variable conditional on the treatment and covariates, called the *principal score* with a little abuse of terminology;
3. the model of the mean of the outcome conditional on the treatment, intermediate variable and covariates, called the *outcome mean*.

The existence of multiple estimators for the same parameter hints at the possibility of a combined estimator for each PCE. To guide the construction of principled estimators, we derive the efficient influence functions (EIFs; Bickel et al., 1993) for the PCEs under the nonparametric model. These EIFs motivate novel estimators for PCEs based on the treatment probability, principal score and outcome mean. Interestingly, the novel estimators are triply robust in that they are consistent and asymptotically Normal if any two of the three models in (a)–(c) are correctly specified, and locally efficient if all three models are correctly specified. These results extend the classic doubly robust estimators for the average causal effect in observational studies (Bang & Robins, 2005) and are similar in spirit to the triply robust estimators in other contexts of causal inference (Shi et al., 2020; Tchetgen Tchetgen & Shpitser, 2012; Wang & Tchetgen Tchetgen, 2018). The new triply robust estimators offer additional protection against model misspecification compared to other non-robust estimators. Finally, we establish an equivalence relationship between the triply robust estimation and the model-assisted estimation, extending the existing results on the average causal effect in observational studies (Kang & Schafer, 2007; Little & An, 2004; Lumley et al., 2011; Robins & Rotnitzky, 1998).

Previously, Ding and Lu (2017) establish some preliminary results for estimating the PCEs in randomized experiments including an identification formula based on weighting and the corresponding estimators for each PCE with and without adjusting for covariates. Their model-assisted estimator adjusts for covariates but is neither doubly robust nor semiparametrically efficient. So even in randomized experiments, the theory for estimating the PCEs is incomplete. We discuss a broader class of treatment assignments in both randomized experiments and unconfounded observational studies, providing two additional identification formulas for each PCE and proposing more principled estimators based on the EIFs. Our new estimators outperform those in Ding and Lu (2017) and we recommend using them in data analyses.

The rest of this paper proceeds as follows. Section 2 introduces notation and assumptions for identification. Section 3 presents three different identification formulas and the corresponding estimators of the PCEs. Section 4 derives the EIFs, proposes novel estimators and shows the triple robustness of the estimators. Section 5 uses simulation to evaluate the finite-sample properties of the estimators, and Section 6 applies the novel estimators to two observational studies. Section 7 concludes. The supplementary material contains the technical details including some extensions and the proofs.

2 | NOTATION AND ASSUMPTIONS FOR PRINCIPAL STRATIFICATION

Let $Z_i \in \{0, 1\}$ be the binary treatment, $S_i \in \{0, 1\}$ the binary intermediate variable, Y_i the outcome and X_i a vector of pretreatment covariates for unit $i = 1, \ldots, n$. We adopt the potential outcomes framework under the Stable Unit Treatment Value Assumption, and let S_{iz} and Y_{iz} be the potential values of the intermediate variable and outcome if unit i were to receive treatment condition z ($z = 0, 1$). The observed intermediate variable and outcome are thus $S_i = Z_i S_{i1} + (1 - Z_i) S_{i0}$ and $Y_i = Z_i Y_{i1} + (1 - Z_i) Y_{i0}$. Assume $\{Z_i, S_{i1}, S_{i0}, Y_{i1}, Y_{i0}, X_i : i = 1, \ldots, n\}$ are independent and identically distributed. Thus, the observed $\{Z_i, S_i, Y_i, X_i : i = 1, \ldots, n\}$ are also independent and identically distributed. For simplicity, we drop the subscript i when no confusion arises.

Frangakis and Rubin (2002) use the joint potential values of the intermediate variable to define the principal stratification variable, $U = (S_1, S_0)$. For a binary intermediate variable, U can be $(0, 0), (1, 0), (0, 1)$, and $(1, 1)$. For the ease of exposition, we will simplify (S_1, S_0) as $S_1 S_0$ throughout the paper. Define the PCE as the average causal effect within a principal stratum:

$$\tau_{s_1 s_0} = \mathbb{E}(Y_1 - Y_0 | U = s_1 s_0), \quad (s_1 s_0 = 00, 10, 11, 01).$$

The scientific meanings of the PCEs vary with the contexts. We review four canonical examples below.

Example 1 (Noncompliance). In noncompliance problems, Z is the treatment assigned, S is the treatment received and Y is the outcome. The principal strata $U = (0, 0), (1, 0), (0, 1), (1, 1)$ are referred to as never-takers, compliers, always-takers and defiers respectively. Angrist and Imbens (1994) and Angrist et al. (1996) propose to estimate τ_{10}, the complier average causal effect, which is also called the local average treatment effect.

Example 2 (Truncation by death). In truncation-by-death problems, Z is the treatment, S is the survival status, and Y is often a measure of the quality of life. Rubin (2006) points out that the only well-defined causal effect is τ_{11}, which characterizes the treatment effect for patients who would survive regardless of the treatment. Other PCEs are not well defined because the quality of life is defined only for survived patients.

Example 3 (Mediation). In mediation analysis, S is the mediator that lies on the causal pathway from the treatment Z to the outcome Y. The subgroup effects τ_{11} and τ_{00} can assess the direct effect of the treatment on the outcome because the treatment does not change the mediator in these two strata (Gallop et al., 2009; Mattei & Mealli, 2011; Rubin, 2004). In contrast, the subgroup effects τ_{10} and τ_{01} are less interpretable because they consist of both direct and indirect effects (VanderWeele, 2011).

Example 4 (Surrogate evaluation). In surrogate evaluation problems, S is the surrogate candidate for the effect of the treatment Z on the outcome Y. Frangakis and Rubin (2002) propose the principal surrogate criterion based on 'causal necessity'. It requires that Z affects Y only if Z affects S, that is, $\tau_{11} = \tau_{00} = 0$. Gilbert and Hudgens (2008) argue that a valid surrogate should also satisfy 'causal sufficiency'. It requires that if the treatment effect on the surrogate is non-zero, then the treatment effect on the outcome is also non-zero, that is, $\tau_{10} \neq 0$ and $\tau_{01} \neq 0$. See Jiang et al. (2016) for a related discussion.

We will focus on the setting with treatment ignorability for both the intermediate variable and outcome, extending the classic treatment ignorability in observational studies.

Assumption 1 (Treatment ignorability). $Z \perp\!\!\!\perp (S_0, S_1, Y_0, Y_1)|X$.

Assumption 1 rules out latent confounding between the treatment and intermediate variable and that between the treatment and outcome. It holds by the design of a randomized experiment, where the treatment is independent of all the potential values and covariates, that is, $Z \perp\!\!\!\perp (S_0, S_1, Y_0, Y_1, X)$; Ding and Lu (2017) focus on this special case. It also holds by the design of a stratified experiment based on a discrete X, where the treatment is independent of all the potential values within each stratum of X. In observational studies, its plausibility relies on whether or not the observed covariates include all the confounders that affect the treatment as well as the outcome and intermediate variable.

Since we do not observe S_1 and S_0 simultaneously, U is not directly observable. As a result, the PCEs are not identifiable without additional assumptions. We impose the standard monotonicity assumption throughout the paper, which helps to identify the distribution of U, even though the individual U_i's are not observed for all units.

Assumption 2 (Monotonicity). $S_1 \geq S_0$.

Assumption 2 requires that the treatment has a non-negative impact on the intermediate variable for all units, which rules out stratum $U = 01$. It holds automatically when $S_0 = 0$, for example, in one-sided noncompliance problems (Sommer & Zeger, 1991) and vaccine trials without immune response under control (Follmann, 2006).

Under Assumptions 1 and 2, two nonparametric identification strategies exist for the PCEs, relying on different additional assumptions. We review them below.

2.1 | Strategy one based on exclusion restriction

The first strategy assumes the ER:

$$\tau_{11} = \tau_{00} = 0. \tag{1}$$

A stronger version of the ER is $Y_1 = Y_0$ for $U = 11$ or 00. Under Assumptions 1, 2, and Equation (1), Angrist and Imbens (1994) and Angrist et al. (1996) establish the nonparametric identification of the complier average causal effect

$$\tau_{10} = \frac{\mathbb{E}(Y|Z=1) - \mathbb{E}(Y|Z=0)}{\mathbb{E}(S|Z=1) - \mathbb{E}(S|Z=0)}.$$

By definition, the PCE τ_{10} represents the effect of the treatment assigned for compliers. Moreover, for compliers with $U = 10$, the treatment assigned is identical to the treatment received, so τ_{10} also measures the effect of the treatment received. This formulation of the noncompliance problem is due to Frangakis and Rubin (2002) where the potential outcome Y_z corresponds to the treatment assigned. It corresponds to the intervention Z in the actual experiment without assuming that S is another hypothetical intervention. However, it might cause notational incoherence with Angrist and Imbens (1994) and Angrist et al. (1996). Angrist and Imbens (1994) index the potential outcome Y_s by the treatment received, and thus enforce the ER assumption automatically; Angrist et al. (1996) index the potential outcome Y_{zs} by both the treatment assigned and received, and reduce it to Y_s under the ER assumption. These different formulations do not cause fundamental differences. An advantage of Frangakis and Rubin (2002)'s formulation is its generality to deal with other problems with intermediate variables. In Example 1 with noncompliance, it allows us to assess the plausibility of the ER by estimating τ_{11} and τ_{00}; see Section 6.1 for more details.

The ER requires that the treatment has no direct effect on the outcome, which is sometimes implausible in open-label randomized experiments. More importantly, it cannot be invoked in problems where τ_{00} and τ_{11} are the quantities of interest, such as truncation by death in Example 2, mediation in Example 3, and surrogate evaluation in Example 4.

Without the ER, the PCEs are not identifiable. Under weak assumptions, the large-sample bounds on the PCEs are often not informative (Imai, 2008; Zhang et al., 2008). In contrast, Bayesian methods often require specifying strong mixture model assumptions and prior distributions (Li et al., 2010; Schwartz et al., 2011; Zigler & Belin, 2012). They are not easy to implement and can be numerically unstable in practice (Feller et al., 2022). Due to these limitations, we focus on another approach assuming principal ignorability.

2.2 | Strategy two based on principal ignorability

The principal ignorability can be viewed as the analogue of the treatment ignorability assumption in unconfounded observational studies.

Assumption 3 (Principal ignorability). $\mathbb{E}(Y_1|U = 11, X) = \mathbb{E}(Y_1|U = 10, X)$ and $\mathbb{E}(Y_0|U = 00, X) = E(Y_0|U = 10, X)$.

Assumption 3 requires that the expectations of the potential outcomes do not vary across principal strata conditional on the covariates. It is widely used in applied statistics (Follmann, 2000; Hill et al., 2002; Jo & Stuart, 2009; Jo et al., 2011; Stuart & Jo, 2015). Under Assumptions 1–2, Assumption 3 is equivalent to

$$\mathbb{E}(Y_1|U = 11, Z = 1, S = 1, X) = \mathbb{E}(Y_1|U = 10, Z = 1, S = 1, X), \tag{2}$$

$$\mathbb{E}(Y_0|U = 00, Z = 0, S = 0, X) = \mathbb{E}(Y_0|U = 10, Z = 0, S = 0, X). \tag{3}$$

The observed stratum ($Z = 1$, $S = 1$) is a mixture of two principal strata $U = 11, 10$. Therefore, Equation (2) means that within the observed stratum ($Z = 1$, $S = 1$), the expectation of the potential outcome Y_1 does not vary across the two principal strata conditional on the covariates. So the conditional expectations in Equation (2) simplify to the observable

conditional expectation $\mathbb{E}(Y|Z = 1, S = 1, X)$. Similarly, Equation (3) means that within the observed stratum ($Z = 0, S = 0$), the two principal strata $U = 00, 10$ are ignorable for the expectation of the potential outcome Y_0 conditional on the covariates. So the conditional expectations in Equation (3) simplify to the observable conditional expectation $\mathbb{E}(Y|Z = 0, S = 0, X)$. Intuitively, principal ignorability simplifies a latent mixture problem to an observed mixture problem. With this assumption, we can treat the subpopulation ($Z = z$, $S = s$) as a mixture of strata defined by the observed covariates, which is easier to deal with than a mixture of latent principal strata.

We start with Assumptions 2 and 3 because they allow for deriving simple identification formulas and easy-to-implement estimators. These estimators are numerically stable and statistically robust. They can be benchmark estimators in data analyses. Nevertheless, their plausibility cannot be validated by the observed data, so they should be made with caution. To supplement the theory under Assumptions 2 and 3, we also propose corresponding sensitivity analysis techniques for the potential violations of these assumptions. Due to the space limit, we include the theoretical results and numerical examples in the supplementary material.

2.3 | Principal ignorability and sequential ignorability in mediation analysis

Before giving the nonparametric identification formulas of the PCEs based on principal ignorability, we comment on its relationship with a commonly used assumption in mediation analysis. We also make a brief comparison of principal stratification and mediation analysis.

A stronger version of Assumption 3 is $Y_z \perp\!\!\!\perp S_{1-z}|(S_z, X)$ for $z = 0, 1$. It assumes that conditional on the covariates, the potential outcome depends only on the potential intermediate variable under the same treatment condition, but not the one under a different treatment condition. Importantly, principal ignorability is different from the *sequential ignorability* between the intermediate variable and the outcome, which is a common assumption in mediation analysis (Imai et al., 2010; Pearl, 2001; Tchetgen Tchetgen & Shpitser, 2012). In particular, the sequential ignorability assumes away the dependence between the potential outcome and the potential intermediate variable given the covariates, while principal ignorability allows for such dependence but rules out the dependence between the potential outcome and intermediate variable under different treatment conditions. Hence, the sequential ignorability and principal ignorability focus on different relationships between the potential outcome and the potential intermediate variable and thus do not imply each other. Forastiere et al. (2018) propose a generalized strong principal ignorability and show that under monotonicity, it is equivalent to the sequential ignorability. Their definition does not imply Assumption 3, and thus it is essentially different from the principal ignorability used in the literature.

In general, principal stratification and mediation analysis can be conceptually different. Principal stratification does not require that S is a well-defined intervention as in Examples 2 and 4. In contrast, traditional mediation analysis requires that S is a well-defined intervention on the causal pathway from the treatment to the outcome. VanderWeele (2011) points out this issue, whereas Robins et al. (2020) attempt to relax this assumption with an alternative approach to mediation analysis.

3 | NONPARAMETRIC IDENTIFICATION AND ESTIMATION

3.1 | Identification formulas

To simplify the exposition, define

$$\pi(X) = \mathbb{P}(Z = 1|X), \quad e_u(X) = \mathbb{P}(U = u|X), \quad \mu_{zs}(X) = \mathbb{E}(Y|Z = z, S = s, X)$$

for $u = 10, 00, 11$ and $z, s = 0, 1$. The $\pi(X)$ is the treatment probability given the covariates, also known as the propensity score. The $e_u(X)$ is the principal score which equals the proportion of principal stratum u given the covariates. The $\mu_{zs}(X)$ is the mean of the outcome within the observed group ($Z = z, S = s$) given the covariates. Let $\pi = \mathbb{E}\{\pi(X)\} = \mathbb{P}(Z = 1)$ and $e_u = \mathbb{E}\{e_u(X)\}$ denote the marginalized treatment probability and principal score over the distribution of the covariates respectively. Thus, π represents the proportion of treated units and e_u represents the proportion of units with $U = u$.

Under Assumption 2, Table 1 shows the relationship between the observed strata defined by (Z, S) and the principal strata. So under Assumptions 1 and 2, the principal scores are identified by

$$e_{10}(X) = p_1(X) - p_0(X), \quad e_{00}(X) = 1 - p_1(X), \quad e_{11}(X) = p_0(X),$$

where $p_z(X) = \mathbb{P}(S = 1|Z = z, X)$ is the probability of the intermediate variable conditional on the treatment and covariates. Analogously, the proportions of principal strata are identified by

$$e_{10} = p_1 - p_0, \quad e_{00} = 1 - p_1, \quad e_{11} = p_0,$$

where $p_z = \mathbb{E}\{p_z(X)\}$ is the marginalized probability of the intermediate variable over the distribution of the covariates. Due to the one-to-one mapping between $\{p_1(X), p_0(X)\}$ and $\{e_{11}(X), e_{00}(X), e_{10}(X)\}$, we call both sets the principal score, and the exact meaning should be clear from the context. The following theorem provides three identification formulas for each PCE.

Theorem 1 (Nonparametric identification). *Suppose that Assumptions 1–3 hold, $e_u > 0$ for $u = 10, 00, 11$, and $0 < \pi(x) < 1$ for all x in the support of X. The following identification formulas hold for the PCEs.*

(a) *Based on the treatment probability and principal score,*

$$\tau_{10} = \mathbb{E}\left\{ \frac{e_{10}(X)}{p_1 - p_0} \frac{S}{p_1(X)} \frac{Z}{\pi(X)} Y \right\} - \mathbb{E}\left\{ \frac{e_{10}(X)}{p_1 - p_0} \frac{1 - S}{1 - p_0(X)} \frac{1 - Z}{1 - \pi(X)} Y \right\},$$

TABLE 1 Principal strata in the observed strata defined by (Z, S) under monotonicity

	$S = 0$	$S = 1$
$Z = 0$	$U \in \{00, 10\}$	$U = 11$
$Z = 1$	$U = 00$	$U \in \{11, 10\}$

$$\tau_{00} = \mathbb{E}\left\{\frac{1-S}{1-p_1}\frac{Z}{\pi(X)}Y\right\} - \mathbb{E}\left\{\frac{e_{00}(X)}{1-p_1}\frac{1-S}{1-p_0(X)}\frac{1-Z}{1-\pi(X)}Y\right\},$$

$$\tau_{11} = \mathbb{E}\left\{\frac{e_{11}(X)}{p_0}\frac{S}{p_1(X)}\frac{Z}{\pi(X)}Y\right\} - \mathbb{E}\left\{\frac{S}{p_0}\frac{1-Z}{1-\pi(X)}Y\right\}.$$

(b) *Based on the treatment probability and outcome mean,*

$$\tau_{10} = \mathbb{E}\left[\frac{SZ/\pi(X) - S(1-Z)/\{1-\pi(X)\}}{p_1 - p_0}\{\mu_{11}(X) - \mu_{00}(X)\}\right],$$

$$\tau_{00} = \mathbb{E}\left[\frac{1 - SZ/\pi(X)}{1-p_1}\{\mu_{10}(X) - \mu_{00}(X)\}\right],$$

$$\tau_{11} = \mathbb{E}\left[\frac{S(1-Z)/\{1-\pi(X)\}}{p_0}\{\mu_{11}(X) - \mu_{01}(X)\}\right].$$

(c) *Based on the principal score and outcome mean,*

$$\tau_{10} = \mathbb{E}\left[\frac{p_1(X) - p_0(X)}{p_1 - p_0}\{\mu_{11}(X) - \mu_{00}(X)\}\right],$$

$$\tau_{00} = \mathbb{E}\left[\frac{1 - p_1(X)}{1-p_1}\{\mu_{10}(X) - \mu_{00}(X)\}\right],$$

$$\tau_{11} = \mathbb{E}\left[\frac{p_0(X)}{p_0}\{\mu_{11}(X) - \mu_{01}(X)\}\right].$$

Theorem 1 gives identification formulas for the PCEs based on three different combinations of the likelihood components. Theorem 1(a) is an extension of Ding and Lu (2017) with an additional weighting term based on the inverse of the treatment probability, which is also mentioned by Jiang and Ding (2021). Theorem 1(b) and (c) are two additional sets of identification formulas.

Below we give some intuition based on only τ_{10} since the discussion for the other two PCEs is similar. Theorem 1(a) expresses τ_{10} as the difference between weighted averages of the outcome under the treatment and control. The weights in the formula consist of two parts: $Z/\pi(X)$ and $(1-Z)/\{1-\pi(X)\}$ correspond to the treatment probability; $e_{10}(X)S/p_1(X)$ and $e_{10}(X)(1-S)/\{1-p_0(X)\}$ correspond to the principal score. Under Assumptions 1 and 2, the conditional expectations of the weights equal

$$\mathbb{E}\left\{\frac{e_{10}(X)}{p_1 - p_0}\frac{S}{p_1(X)}\frac{Z}{\pi(X)}|X\right\} = \mathbb{E}\left\{\frac{e_{10}(X)}{p_1 - p_0}\frac{1-S}{1-p_0(X)}\frac{1-Z}{1-\pi(X)}|X\right\} = \frac{e_{10}(X)}{e_{10}}, \quad (4)$$

that is, the conditional probability of principal stratum $U = 10$ divided by its unconditional probability.

Theorem 1(b) expresses τ_{10} in terms of the treatment probability and outcome mean. Under principal ignorability, the difference between the outcome means equals

$$\mu_{11}(X) - \mu_{00}(X) = \mathbb{E}(Y_1|U = 10, X) - \mathbb{E}(Y_0|U = 10, X) = \mathbb{E}(Y_1 - Y_0|U = 10, X),$$

which is the PCE for stratum $U = 10$ conditional on X. Under Assumptions 1 and 2, the conditional expectation of the unnormalized weight equals $\mathbb{E}[SZ/\pi(X) - S(1-Z)/\{1-\pi(X)\}|X] =$

$e_{10}(X)$. Dividing this by the normalizing constant, $p_1 - p_0 = e_{10}$, yields $e_{10}(X)/e_{10}$, which, by Bayes' Theorem, is the density ratio of X conditional and unconditional on $U = 10$. Therefore, the identification formula for τ_{10} in Theorem 1(b) averages the conditional PCE over the distribution of X given $U = 10$, which gives the PCE within stratum $U = 10$.

Theorem 1(c) expresses τ_{10} in terms of the principal score and outcome mean. Compared with Theorem 1(b), the treatment probability weighting is replaced with the principal score weighting $\{p_1(X) - p_0(X)\}/(p_1 - p_0)$. Under Assumptions 1 and 2, the weight again equals $e_{10}(X)/e_{10}$. Therefore, similar to the discussion of Theorem 1(b), Theorem 1(c) identifies τ_{10} by averaging the conditional PCE over the distribution of X given $U = 10$.

3.2 | Estimators based on the nonparametric identification formulas

For each PCE, the three identification formulas in Theorem 1 motivate three estimators, which require correct specifications of different parts of the observed-data distribution. For descriptive convenience, we introduce additional notation. Let $\mathbb{P}_n$ denote the empirical average, for example, $\mathbb{P}_n h(V) = n^{-1}\sum_{i=1}^n h(V_i)$ for any $h(V)$. Let $\hat{\pi} = \mathbb{P}_n Z$ be the moment estimator of π. Let $\pi(X; \alpha)$ be a working parametric model for the treatment probability $\pi(X)$, $p_z(X; \gamma)$ a working parametric model for the principal score $p_z(X)$ for $z = 0, 1$, and $\mu_{zs}(X; \beta)$ a working parametric model for the outcome mean $\mu_{zs}(X)$ for $z, s = 0, 1$. Because $e_u(X)$ has a one-to-one mapping to $p_z(X)$, we use $e(X; \gamma)$ to denote a working parametric model for $e_u(X)$. We focus on parametric models here and will consider more flexible estimation strategies later. Based on the maximum likelihood estimation or the method of moments, we obtain estimators $\hat{\alpha}$, $\hat{\gamma}$ and $\hat{\beta}$. Assume they have probability limits α^*, γ^* and β^* respectively. We use $\mathcal{M}$ with subscripts 'tp', 'ps' and 'om' to denote models with the correct specification of the treatment probability, principal score and outcome mean respectively. Therefore, under $\mathcal{M}_{tp}$, we have $\pi(X; \alpha^*) = \pi(X)$; under $\mathcal{M}_{ps}$, we have $p_z(X; \gamma^*) = p_z(X)$ and $e_u(X; \gamma^*) = e_u(X)$ for $z = 0, 1$ and $u = 10, 00, 11$; under $\mathcal{M}_{om}$, we have $\mu_{zs}(X; \beta^*) = \mu_{zs}(X)$ for z, $s = 0, 1$. In addition, we use '+' in the subscript to indicate that more than one model is correctly specified. For example, $\mathcal{M}_{ps+om}$ denotes the model with correctly specified $p_z(X; \gamma)$ and $\mu_{zs}(X; \beta)$. We also use the union notation from the standard set theory to denote the correct specification of at least one model, for example, $\mathcal{M}_{tp} \cup \mathcal{M}_{ps+om}$ denotes the model with correctly specified $\pi(X; \alpha)$ or $\{p_z(X; \gamma), \mu_{zs}(X; \beta)\}$.

To obtain the estimators based on Theorem 1, we need to replace the components in the identification formulas with their estimated counterparts, and the expectations with the empirical averages. We use $\{\pi(X; \hat{\alpha}), p_z(X; \hat{\gamma}), \mu_{zs}(X; \hat{\beta})\}$ to denote the estimated version of $\{\pi(X; \alpha), p_z(X; \gamma), \mu_{zs}(X; \beta)\}$. For p_1 and p_0, we can simply use $\mathbb{P}_n\{p_1(X; \hat{\gamma})\}$ and $\mathbb{P}_n\{p_0(X; \hat{\gamma})\}$ as the estimators, which are consistent under $\mathcal{M}_{ps}$. Moreover, the doubly robust estimators (Bang & Robins, 2005),

$$\hat{p}_1 = \mathbb{P}_n\left[\frac{Z\{S - p_1(X; \hat{\gamma})\}}{\pi(X; \hat{\alpha})} + p_1(X; \hat{\gamma})\right], \quad \hat{p}_0 = \mathbb{P}_n\left[\frac{(1 - Z)\{S - p_0(X; \hat{\gamma})\}}{1 - \pi(X; \hat{\alpha})} + p_0(X; \hat{\gamma})\right],$$

improve them, which are consistent for p_1 and p_0 under $\mathcal{M}_{tp} \cup \mathcal{M}_{ps}$.

The identification formulas in Theorem 1(a) motivate the following weighting estimators based on the treatment probability and principal score.

Example 5 The treatment probability–principal score (tp-ps) estimators are

$$\widehat{\tau}_{10,\text{tp-ps}} = \mathbb{P}_n \left\{ \frac{e_{10}(X;\widehat{\gamma})}{\widehat{p}_1 - \widehat{p}_0} \frac{S}{p_1(X;\widehat{\gamma})} \frac{Z}{\pi(X;\widehat{\alpha})} Y - \frac{e_{10}(X;\widehat{\gamma})}{\widehat{p}_1 - \widehat{p}_0} \frac{1-S}{1-p_0(X;\widehat{\gamma})} \frac{1-Z}{1-\pi(X;\widehat{\alpha})} Y \right\},$$

$$\widehat{\tau}_{00,\text{tp-ps}} = \mathbb{P}_n \left\{ \frac{1-S}{1-\widehat{p}_1} \frac{Z}{\pi(X;\widehat{\alpha})} Y - \frac{e_{00}(X;\widehat{\gamma})}{1-\widehat{p}_1} \frac{1-S}{1-p_0(X;\widehat{\gamma})} \frac{1-Z}{1-\pi(X;\widehat{\alpha})} Y \right\},$$

$$\widehat{\tau}_{11,\text{tp-ps}} = \mathbb{P}_n \left\{ \frac{e_{11}(X;\widehat{\gamma})}{\widehat{p}_0} \frac{S}{p_1(X;\widehat{\gamma})} \frac{Z}{\pi(X;\widehat{\alpha})} Y - \frac{S}{\widehat{p}_0} \frac{1-Z}{1-\pi(X;\widehat{\alpha})} Y \right\}.$$

The weighting estimators in Example 5 involve the inverse of the treatment probability. Thus, they may be unstable if some estimated treatment probabilities are close to zero or one. A strategy to mitigate this issue is to stabilize the estimators by normalizing the weights (Hernán et al., 2001). For example, the stabilized weighting estimator of τ_{11} is

$$\widehat{\tau}'_{11,\text{tp-ps}} = \mathbb{P}_n \left\{ e_{11}(X;\widehat{\gamma}) \frac{S}{p_1(X;\widehat{\gamma})} \frac{Z}{\pi(X;\widehat{\alpha})} Y \right\} \Big/ \mathbb{P}_n \left\{ e_{11}(X;\widehat{\gamma}) \frac{S}{p_1(X;\widehat{\gamma})} \frac{Z}{\pi(X;\widehat{\alpha})} \right\}$$

$$- \mathbb{P}_n \left\{ \frac{s(1-Z)}{1-\pi(X;\widehat{\alpha})} Y \right\} \Big/ \mathbb{P}_n \left\{ \frac{s(1-Z)}{1-\pi(X;\widehat{\alpha})} \right\}.$$

The stabilized weighting estimators for τ_{10} and τ_{00} have similar forms. The estimators $\widehat{\tau}_{u,\text{tp-ps}}$ are consistent under $\mathcal{M}_{\text{tp+ps}}$, that is, correct specifications of the treatment probability and principal score. However, if either model is incorrectly specified, they are inconsistent.

The identification formulas in Theorem 1(b) motivate the following estimators based on the treatment probability and the outcome mean.

Example 6 The treatment probability–outcome mean (tp-om) estimators are

$$\widehat{\tau}_{10,\text{tp-om}} = \mathbb{P}_n \left[\frac{ZS/\pi(X;\widehat{\alpha}) - (1-Z)S/\{1-\pi(X;\widehat{\alpha})\}}{\widehat{p}_1 - \widehat{p}_0} \left\{ \mu_{11}(X;\widehat{\beta}) - \mu_{00}(X;\widehat{\beta}) \right\} \right],$$

$$\widehat{\tau}_{00,\text{tp-om}} = \mathbb{P}_n \left[\frac{Z(1-S)/\pi(X;\widehat{\alpha})}{1-\widehat{p}_1} \left\{ \mu_{10}(X;\widehat{\beta}) - \mu_{00}(X;\widehat{\beta}) \right\} \right],$$

$$\widehat{\tau}_{11,\text{tp-om}} = \mathbb{P}_n \left[\frac{(1-Z)S/\{1-\pi(X;\widehat{\alpha})\}}{\widehat{p}_0} \left\{ \mu_{11}(X;\widehat{\beta}) - \mu_{01}(X;\widehat{\beta}) \right\} \right].$$

Similar to the estimators in Example 5, we can also obtain the stabilized weighting version of the estimators in Example 6. For example, the stabilized version of $\widehat{\tau}_{11,\text{tp-om}}$ is

$$\widehat{\tau}'_{11,\text{tp-om}} = \mathbb{P}_n \left[\frac{(1-Z)S}{1-\pi(X;\widehat{\alpha})} \left\{ \mu_{11}(X;\widehat{\beta}) - \mu_{01}(X;\widehat{\beta}) \right\} \right] \Big/ \mathbb{P}_n \left\{ \frac{(1-Z)S}{1-\pi(X;\widehat{\alpha})} \right\}.$$

The estimators $\widehat{\tau}_{u,\text{tp-om}}$ are consistent under $\mathcal{M}_{\text{tp+om}}$.

The identification formulas in Theorem 1(c) motivate the following estimators based on the principal score and outcome mean.

Example 7 The principal score–outcome mean (ps-om) estimators are

$$\widehat{\tau}_{10,\text{ps-om}} = \mathbb{P}_n \left[\frac{p_1(X;\widehat{\gamma}) - p_0(X;\widehat{\gamma})}{\widehat{p}_1 - \widehat{p}_0} \left\{ \mu_{11}(X;\widehat{\beta}) - \mu_{00}(X;\widehat{\beta}) \right\} \right],$$

$$\widehat{\tau}_{00,\text{ps-om}} = \mathbb{P}_n \left[\frac{1 - p_1(X;\widehat{\gamma})}{1 - \widehat{p}_1} \left\{ \mu_{10}(X;\widehat{\beta}) - \mu_{00}(X;\widehat{\beta}) \right\} \right],$$

$$\widehat{\tau}_{11,\mathrm{ps-om}} = \mathbb{P}_n \left[\frac{p_0(X; \widehat{\gamma})}{\widehat{p}_0} \left\{ \mu_{11}(X; \widehat{\beta}) - \mu_{01}(X; \widehat{\beta}) \right\} \right].$$

The estimators $\widehat{\tau}_{u,\mathrm{ps-om}}$ are consistent under $\mathcal{M}_{\mathrm{ps+om}}$.

4 | FROM THE EIFS TO TRIPLY ROBUST ESTIMATORS

Theorem 1 presents three identification formulas, which motivate infinitely many estimators for each PCE. This calls for the construction of more principled estimators. In this section, we derive the EIF for each PCE to motivate a new estimator. The EIFs below are derived under the nonparametric model of the observed-data distribution, which is a standard strategy in the literature. In particular, the derivation ignores the restrictions implied by the monotonicity assumption (cf. Frölich, 2007; Hong & Nekipelov, 2010). For simplicity, we use the terminology 'EIF' throughout.

4.1 | EIFs and the resulting estimators

Because the PCEs have a ratio form $\tau_u = \mathbb{E}\{(Y_1 - Y_0)\mathbf{1}(U = u)\}/\mathbb{P}(U = u)$, we will first define a general quantity to represent the EIFs of the numerators and denominators, and then combine them to have the EIFs for the PCEs.

Define the following quantity for any function $f(Y, S, X)$:

$$\psi_{f(Y_z, S_z, X)} = \frac{\mathbf{1}(Z = z)[f(Y, S, X) - \mathbb{E}\{f(Y, S, X)|X, Z = z\}]}{\mathbb{P}(Z = z|X)} + \mathbb{E}\{f(Y, S, X)|X, Z = z\}. \quad (5)$$

Under Assumption 1, we can show that $\mathbb{E}\{\psi_{f(Y_z, S_z, X)}\} = \mathbb{E}\{f(Y_z, S_z, X)\}$. In fact, $\psi_{f(Y_z, S_z, X)} - \mathbb{E}\{f(Y_z, S_z, X)\}$ is the EIF for $\mathbb{E}\{f(Y_z, S_z, X)\}$; see Lemma S5 in the supplementary material. With $f(Y, S, X) = S$, Equation (5) reduces to

$$\psi_{S_z} = \frac{\mathbf{1}(Z = z)\{S - p_z(X)\}}{\mathbb{P}(Z = z|X)} + p_z(X),$$

and $\psi_{S_z} - \mathbb{E}(S_z)$ is the EIF for $\mathbb{E}(S_z)$. This reduces to a standard result in observational studies (Hahn, 1998), which is the foundation for constructing the doubly robust estimator for $\mathbb{E}(S_z)$ (Bang & Robins, 2005). With $f(Y, S, X) = YS$ and $z = 0$, Equation (5) reduces to

$$\psi_{Y_0 S_0} = \frac{\mathbf{1}(Z = 0)\{YS - \mu_{01}(X)p_0(X)\}}{1 - \pi(X)} + \mu_{01}(X)p_0(X),$$

and $\psi_{Y_0 S_0} - \mathbb{E}(Y_0 S_0)$ is the EIF for $\mathbb{E}(Y_0 S_0)$, which equals $\mathbb{E}(Y_0|U = 11)\mathbb{P}(U = 11)$ because $S_0 = 1$ is equivalent to $U = 11$ under monotonicity. Based on the ψ notation in Equation (5), the following theorem gives the EIFs for the PCEs.

Theorem 2 (EIFs). *Suppose τ_u's are identified in Theorem 1. The EIF for τ_{10} is $\phi_{10} = \{\phi_{1,10} - \phi_{0,10} - \tau_{10}(\psi_{S_1} - \psi_{S_0})\}/(p_1 - p_0)$, where*

$$\phi_{1,10} = \frac{e_{10}(X)}{p_1(X)}\psi_{Y_1 S_1} - \mu_{11}(X)\left\{\psi_{S_0} - \frac{p_0(X)}{p_1(X)}\psi_{S_1}\right\},$$

$$\phi_{0,10} = \frac{e_{10}(X)}{1 - p_0(X)} \psi_{Y_0(1-S_0)} - \mu_{00}(X) \left\{ \psi_{1-S_1} - \frac{1 - p_1(X)}{1 - p_0(X)} \psi_{1-S_0} \right\}.$$

The EIF for τ_{00} is $\phi_{00} = \left(\phi_{1,00} - \phi_{0,00} - \tau_{00} \psi_{1-S_1} \right) / (1 - p_1)$, where

$$\phi_{1,00} = \psi_{Y_1(1-S_1)}, \quad \phi_{0,00} = \frac{e_{00}(X)}{1 - p_0(X)} \psi_{Y_0(1-S_0)} + \mu_{00}(X) \left\{ \psi_{1-S_1} - \frac{1 - p_1(X)}{1 - p_0(X)} \psi_{1-S_0} \right\}.$$

The EIF for τ_{11} is $\phi_{11} = \left(\phi_{1,11} - \phi_{0,11} - \tau_{11} \psi_{S_0} \right) / p_0$, where

$$\phi_{1,11} = \frac{e_{11}(X)}{p_1(X)} \psi_{Y_1 S_1} + \mu_{11}(X) \left\{ \psi_{S_0} - \frac{p_0(X)}{p_1(X)} \psi_{S_1} \right\}, \quad \phi_{0,11} = \psi_{Y_0 S_0}.$$

From Theorem 2, the semiparametric efficiency bounds for the PCEs are $\mathbb{E}(\phi_u^2)$ for $u = 10, 00, 11$ (Bickel et al., 1993). The EIFs have mean zero, so we can obtain another set of identification formulas by solving $\mathbb{E}(\phi_u) = 0$.

Corollary 1 *Under Assumptions 1–3,*

$$\tau_{10} = \frac{\mathbb{E}(\phi_{1,10} - \phi_{0,10})}{\mathbb{E}(\psi_{S_1} - \psi_{S_0})}, \quad \tau_{00} = \frac{\mathbb{E}(\phi_{1,00} - \phi_{0,00})}{\mathbb{E}(1 - \psi_{S_1})}, \quad \tau_{11} = \frac{\mathbb{E}(\phi_{1,11} - \phi_{0,11})}{\mathbb{E}(\psi_{S_0})}. \tag{6}$$

As a sanity check of Equation (6), we can verify that the denominator of τ_u in Equation (6) equals $\mathbb{P}(U = u)$, and the numerator equals $\mathbb{E}\{(Y_1 - Y_0)\mathbf{1}(U = u)\}$, for $u = 10, 00, 11$. Based on Corollary 1, we can improve the estimators in Examples 5–7. Denote the estimator for $\psi_{f(Y_z, S_z, X)}$ by

$$\widehat{\psi}_{f(Y_z, S_z, X)} = \frac{\mathbf{1}(Z = z)[f(Y, S, X) - \widehat{\mathbb{E}}\{f(Y, S, X)|X, Z = z\}]}{\pi^z(X; \widehat{\alpha})\{1 - \pi(X; \widehat{\alpha})\}^{1-z}} + \widehat{\mathbb{E}}\{f(Y, S, X)|X, Z = z\},$$

where $\widehat{\mathbb{E}}\{f(Y, S, X)|X, Z = z\}$ is the fitted conditional expectation of $f(Y, S, X)$ given X and $Z = z$. When $f(Y, S, X) = S$, we have $\widehat{\mathbb{E}}\{f(Y, S, X)|X, Z = z\} = p_z(X; \widehat{\gamma})$, which reduces to the estimated principal score and results in the estimator $\mathbb{P}_n(\widehat{\psi}_{S_z}) = \widehat{p}_z$. When $f(Y, S, X) = YS$, we have $\widehat{\mathbb{E}}\{f(Y, S, X)|X, Z = z\} = \mu_{z1}(X; \widehat{\beta})p_z(X; \widehat{\gamma})$, which relies on both the principal score and outcome mean.

Corollary 1 motivates the following estimators:

$$\widehat{\tau}_{10} = \frac{\mathbb{P}_n(\widehat{\phi}_{1,10} - \widehat{\phi}_{0,10})}{\mathbb{P}_n(\widehat{\psi}_{S_1} - \widehat{\psi}_{S_0})}, \quad \widehat{\tau}_{00} = \frac{\mathbb{P}_n(\widehat{\phi}_{1,00} - \widehat{\phi}_{0,00})}{\mathbb{P}_n(1 - \widehat{\psi}_{S_1})}, \quad \widehat{\tau}_{11} = \frac{\mathbb{P}_n(\widehat{\phi}_{1,11} - \widehat{\phi}_{0,11})}{\mathbb{P}_n(\widehat{\psi}_{S_0})}, \tag{7}$$

where

$$\widehat{\phi}_{1,10} = \frac{e_{10}(X; \widehat{\gamma})}{p_1(X; \widehat{\gamma})} \widehat{\psi}_{Y_1 S_1} - \mu_{11}(X; \widehat{\beta}) \left\{ \widehat{\psi}_{S_0} - \frac{p_0(X; \widehat{\gamma})}{p_1(X; \widehat{\gamma})} \widehat{\psi}_{S_1} \right\},$$

$$\widehat{\phi}_{0,10} = \frac{e_{10}(X; \widehat{\gamma})}{1 - p_0(X; \widehat{\gamma})} \widehat{\psi}_{Y_0(1-S_0)} - \mu_{00}(X; \widehat{\beta}) \left\{ \widehat{\psi}_{1-S_1} - \frac{1 - p_1(X; \widehat{\gamma})}{1 - p_0(X; \widehat{\gamma})} \widehat{\psi}_{1-S_0} \right\},$$

$$\widehat{\phi}_{0,00} = \frac{e_{00}(X; \widehat{\gamma})}{1 - p_0(X; \widehat{\gamma})} \widehat{\psi}_{Y_0(1-S_0)} + \mu_{00}(X; \widehat{\beta}) \left\{ \widehat{\psi}_{1-S_1} - \frac{1 - p_1(X; \widehat{\gamma})}{1 - p_0(X; \widehat{\gamma})} \widehat{\psi}_{1-S_0} \right\},$$

$$\widehat{\phi}_{1,11} = \frac{e_{11}(X;\widehat{\gamma})}{p_1(X;\widehat{\gamma})} \widehat{\psi}_{Y_1 S_1} + \mu_{11}(X;\widehat{\beta}) \left\{ \widehat{\psi}_{S_0} - \frac{p_0(X;\widehat{\gamma})}{p_1(X;\widehat{\gamma})} \widehat{\psi}_{S_1} \right\},$$

$$\widehat{\phi}_{1,00} = \widehat{\psi}_{Y_1(1-S_1)},$$

$$\widehat{\phi}_{0,11} = \widehat{\psi}_{Y_0 S_0}.$$

These estimators for the PCEs are all in ratio forms, similar to the classic Wald estimator for the complier average causal effect under the monotonicity and ER (Angrist et al., 1996).

Motivating estimators based on EIFs is a standard approach in semiparametric statistics. This approach, however, involves advanced statistical theory. To add more intuition for the estimators above, we offer an alternative perspective in the supplementary material based on model-assisted estimation from the classic survey sampling theory. This extends the results on doubly robust and model-assisted estimation for the average causal effect in unconfounded observational studies (Kang & Schafer, 2007; Little & An, 2004; Lumley et al., 2011; Robins & Rotnitzky, 1998).

Interestingly, although the $\widehat{\tau}_u$'s involve models for the treatment probability, principal score, and outcome, their consistency does not require the correct specification of all three models. We will characterize this *triple robustness* property in the next subsection.

4.2 | Triple robustness

The following theorem shows the triple robustness and local efficiency of the estimators constructed based on the EIFs.

Theorem 3 (Triple robustness and local efficiency). *Suppose that Assumptions 1–3 hold, $\delta < \{\pi(x;\alpha^*), \pi(x;\widehat{\alpha})\} < 1 - \delta$, and $\{p_1(x;\gamma^*), p_1(x;\widehat{\gamma}), 1 - p_0(x;\gamma^*), 1 - p_0(x;\widehat{\gamma})\} > \delta$ for some $\delta \in (0, 1)$ and all x in the support of X. Each estimator $\widehat{\tau}_u$ in Equation (7) is triply robust in the sense that it is consistent for τ_u under $\mathcal{M}_{\text{tp+ps}} \cup \mathcal{M}_{\text{tp+om}} \cup \mathcal{M}_{\text{ps+om}}$. Moreover, $\widehat{\tau}_u$ has the influence function ϕ_u and therefore achieves the semiparametric efficiency bound under $\mathcal{M}_{\text{tp+ps+om}}$.*

The regularity condition in Theorem 3 is similar to the classic overlap condition (D'Amour et al., 2020; Rosenbaum & Rubin, 1983), which rules out small quantities in the denominators of the estimators. Theorem 3 states that $\widehat{\tau}_u$ is consistent if any two of the three models are correctly specified, and locally efficient if all three models are correctly specified. For the variance calculation of these estimators, we use the nonparametric bootstrap.

To gain more intuition, we then give the sketch of the proof for the triple robustness of $\widehat{\tau}_{10} = (\mathbb{P}_n \widehat{\phi}_{1,10} - \mathbb{P}_n \widehat{\phi}_{0,10})/(\mathbb{P}_n \widehat{\psi}_{S_1} - \mathbb{P}_n \widehat{\psi}_{S_0})$ and relegate additional technical details to the supplementary material. For simplicity in this paragraph, let $\mathcal{M}_{\text{triple}} = \mathcal{M}_{\text{tp+ps}} \cup \mathcal{M}_{\text{tp+om}} \cup \mathcal{M}_{\text{ps+om}}$ denote the set containing at least two correct models. The denominator is consistent for $\mathbb{E}(S_1 - S_0) = \mathbb{P}(U = 10)$ under $\mathcal{M}_{\text{tp}} \cup \mathcal{M}_{\text{ps}} \supseteq \mathcal{M}_{\text{triple}}$. For the terms in the numerator, we calculate their asymptotic biases in Section S7. In particular, $\mathbb{P}_n \widehat{\phi}_{1,10} - \mathbb{E}\{Y_1 \mathbf{1}(U = 10)\}$ has the probability limit $B_1 + B_2 - B_3$, where

$$B_1 = \mathbb{E}\left[\frac{\{\mu_{11}(X)p_1(X) - \mu_{11}(X;\beta^*)p_1(X;\beta^*)\}\{\pi(X) - \pi(X;\alpha^*)\}}{\pi(X;\alpha^*)} \right],$$

$$B_2 = \mathbb{E}\left[\frac{\{\pi(X)p_0(X;\gamma^*)p_1(X) - \pi(X;\alpha^*)p_0(X)p_1(X;\gamma^*)\}\{\mu_{11}(X) - \mu_{11}(X;\beta^*)\}}{\pi(X;\alpha^*)p_1(X;\gamma^*)} \right],$$

$$B_3 = \mathbb{E}\left[\frac{\{\pi(X) - \pi(X; \alpha^*)\}\{p_0(X) - p_0(X; \gamma^*)\}\mu_{11}(X; \beta^*)}{1 - \pi(X; \alpha^*)}\right].$$

The bias B_1 equals 0 under $\mathcal{M}_{ps+om} \cup \mathcal{M}_{tp}$; the bias B_2 equals 0 under $\mathcal{M}_{tp+ps} \cup \mathcal{M}_{om}$; the bias B_3 equals 0 under $\mathcal{M}_{tp} \cup \mathcal{M}_{ps}$. Each of these three sets contains $\mathcal{M}_{triple}$. As a result, $\mathbb{P}_n(\widehat{\phi}_{1,10})$ is consistent for $\mathbb{E}\{Y_1\mathbf{1}(U = 10)\}$ under $\mathcal{M}_{triple}$. Similarly, we can show $\mathbb{P}_n(\widehat{\phi}_{0,10})$ is consistent for $\mathbb{E}\{Y_0\mathbf{1}(U = 10)\}$ under $\mathcal{M}_{triple}$. So the triple robustness of $\widehat{\tau}_{10}$ holds.

The bias formulas above suggest that the proposed triply robust estimator would remain consistent and asymptotically Normal under some regularity conditions when using nonparametric or machine learning estimation for the nuisance functions $\pi(X)$, $p_z(X)$, and $\mu_{zs}(X)$, denoted by $\widehat{\pi}(X)$, $\widehat{p}_z(X)$, and $\widehat{\mu}_{zs}(X)$. This property would be similar to that of the doubly robust estimator for estimating the average causal effect in unconfounded observational studies (Chernozhukov et al., 2018). In other contexts involving intermediate variables, Zheng and van der Laan (2017) and Miles et al. (2020) have established similar results for multiply robust estimators. Theorem 4 formalizes the results for the proposed estimators using nonparametric or machine learning estimation.

Theorem 4 (Triple machine learning estimation). *Suppose that Assumptions 1–3 hold,*

(a) $\{\widehat{\pi}(x), \widehat{p}_z(x), \widehat{\mu}_{zs}(x)\} \rightarrow \{\pi(x), p_z(x), \mu_{zs}(x)\}$ *in probability for all x in the support of X,*

(b) $\{\widehat{\pi}(x), \widehat{p}_z(x), \widehat{\mu}_{zs}(x)\}$ *and* $\{\pi(x), p_z(x), \mu_{zs}(x)\}$ *are in a Donsker class,*

(c) $\delta < \{\pi(x), \widehat{\pi}(x)\} < 1 - \delta$, $\{p_1(x), \widehat{p}_1(x), 1 - p_0(x), 1 - \widehat{p}_0(x)\} > \delta$ *and* $\{|\widehat{\mu}_{zs}(x)|, |\mu_{zs}(x)|\} < C$ *for some $\delta \in (0, 1)$, $C > 0$, and all x in the support of X, and*

(d) $\|\widehat{g}(X) - g(X)\|_2 \times \|\widehat{h}(X) - h(X)\|_2 = o_\mathbb{P}(n^{-1/2})$, *for any $g \neq h \in (\pi, p_z, \mu_{zs})$, where $\|\cdot\|_2$ denotes the L_2-norm, that is, $\|f(X)\|_2^2 = \int f(x)^2 \mathrm{d}F_X(x)$.*

Then $\widehat{\tau}_u$ in Equation (5) is asymptotically Normal, has the influence function ϕ_u, and achieves the semiparametric efficiency bound.

Conditions (a)–(d) are analogous to those for double machine learning estimation of average causal effects (e.g. Bradic et al., 2019; Kennedy, 2016). The consistency in (a) and the rates of convergence in (d) are well studied for commonly used flexible models. Condition (b) restricts the complexity of the spaces of the nuisance functions and their estimators. The cross-fitting technique can be used to relax this condition (Chernozhukov et al., 2018). The conditions in (c) may not be necessary but enable bounding the error $|\widehat{\tau}_u - \mathbb{P}_n\phi_u|$ by the summation of the terms in the form of $\|\widehat{g}(X) - g(X)\|_2 \times \|\widehat{h}(X) - h(X)\|_2$ with $g \neq h \in (\pi, p_z, \mu_{zs})$. Thus, by Condition (d), the results in Theorem 4 follow.

Section S3 in the supplementary material extends the identification and estimation framework to two important scenarios under randomization, that is, $Z \perp\!\!\!\perp (S_1, S_0, Y_1, Y_0, X)$, and strong monotonicity, that is, $S_1 \geq S_0$ respectively. We also establish robustness properties of the corresponding estimators there.

5 | SIMULATION

We evaluate the finite-sample properties of various estimators at sample size $n = 500$. Generate covariate $X \in \mathbb{R}^5$ by $X_j \sim N(0.25, 1)$ for $j = 1, \ldots, 4$, and $X_5 \sim$ Bernoulli (0.5). We use linear predictors, $C_j = X_j - 0.25$, or quadratic predictors, $\widetilde{C}_j = (X_j^2 - 1)/\sqrt{2}$, for $j = 1, \ldots, 4$. Generate the

treatment by $Z|X \sim \text{Bernoulli}\{\pi(X)\}$, the intermediate variable by $S|(Z = z, X) \sim \text{Bernoulli}\{p_z(X)\}$, and the outcome by $Y|(Z = z, S = s, X) \sim N\{\mu_{zs}(X), 1\}$. To assess the robustness of the estimators to model misspecification, we consider two different choices for each of $\pi(X)$, $p_z(X)$ and $\mu_{zs}(X)$, summarized in Table 2. We indicate the models by the name of the dependent variable and whether or not the predictors are linear. For example, 'tp:no' is the model with $\pi(X) = 2\sum_{j=1}^{4}\tilde{C}_j/5$, and 'ps:yes' is the model with $p_z(X) = 2\{(2z - 1) - \sum_{j=1}^{4}C_j\}/5$.

We calculate the true value of τ_u based on the identification formulas in Theorem 1 and the true models. We then compare the following estimators for τ_u:

1. weighting estimators: $\hat{\tau}_{u,\text{tp-ps}}$ and $\hat{\tau}'_{u,\text{tp-ps}}$ given in Example 5;
2. regression estimators: $\hat{\tau}_{u,\text{tp-om}}$ given in Example 6 and $\hat{\tau}_{u,\text{ps-om}}$ given in Example 7;
3. triply robust estimators: $\hat{\tau}_u$ and $\hat{\tau}_{u,\text{ml}}$ with parametric models and with flexible generalized additive models for nuisance functions respectively.

We also consider the weighting estimator and the regression estimator in Ding and Lu (2017), which are proposed under randomized experiments. Under 'ps:yes' and 'ps:no', we estimate the principal score by logistic regressions with linear predictors X and (X_1, X_2) respectively; we estimate the outcome mean by linear regressions with the linear predictor X. Therefore, under generative models with the label 'yes', the fitting models are correctly specified, while under generative models with the label 'no', the fitting models are misspecified.

We compare the estimators in $2^3 = 8$ scenarios depending on whether the treatment probability, principal score or outcome model is correctly specified. Figure 1 presents the violin plots based on 1000 repeated sampling of the estimators. For all the three PCEs, the weighting estimators $\hat{\tau}_{u,\text{tp-ps}}$ and $\hat{\tau}'_{u,\text{tp-ps}}$ (indicated by 'w1' and 'w2' in the figures) are biased when the treatment probability or principal score model is misspecified. The bias with a misspecified treatment probability is larger than that with a misspecified principal score because the weights corresponding to the treatment probability are unbounded while the weights corresponding to the principal score are bounded within [0, 1]. The weighting estimator in Ding and Lu (2017) (indicated by 'w3' in the figures) performs similarly to $\hat{\tau}_{u,\text{tp-ps}}$ and $\hat{\tau}'_{u,\text{tp-ps}}$, because the treatment is randomized under 'tp:yes'. As our theory predicts, the regression estimator $\hat{\tau}_{u,\text{tp-om}}$ (indicated by 'r1' in the figures) is unbiased under $\mathcal{M}_{\text{tp+om}}$; the regression estimator $\hat{\tau}_{u,\text{ps-om}}$ (indicated by 'r2' in the figures) is unbiased under $\mathcal{M}_{\text{ps+om}}$. The regression estimator in Ding and Lu (2017) (indicated by 'r3' in the figures) performs similarly to $\hat{\tau}_{u,\text{tp-om}}$ in terms of bias. The triply robust estimator $\hat{\tau}_u$ (indicated by 'tr' in the figures) is unbiased under $\mathcal{M}_{\text{tp+ps}} \cup \mathcal{M}_{\text{tp+om}} \cup \mathcal{M}_{\text{ps+om}}$, verifying its triple robustness. With flexible models for the nuisance functions, $\hat{\tau}_{u,\text{ml}}$ is unbiased under $\mathcal{M}_{\text{tp+ps}} \cup \mathcal{M}_{\text{tp+om}} \cup \mathcal{M}_{\text{ps+om}}$ and is less biased than other estimators in most scenarios.

TABLE 2 Models for simulation with two specifications for each of logit$\{\pi(X)\}$, logit$\{p_z(X)\}$, and $\mu_{zs}(X)$, indicated by 'Yes' and 'No'

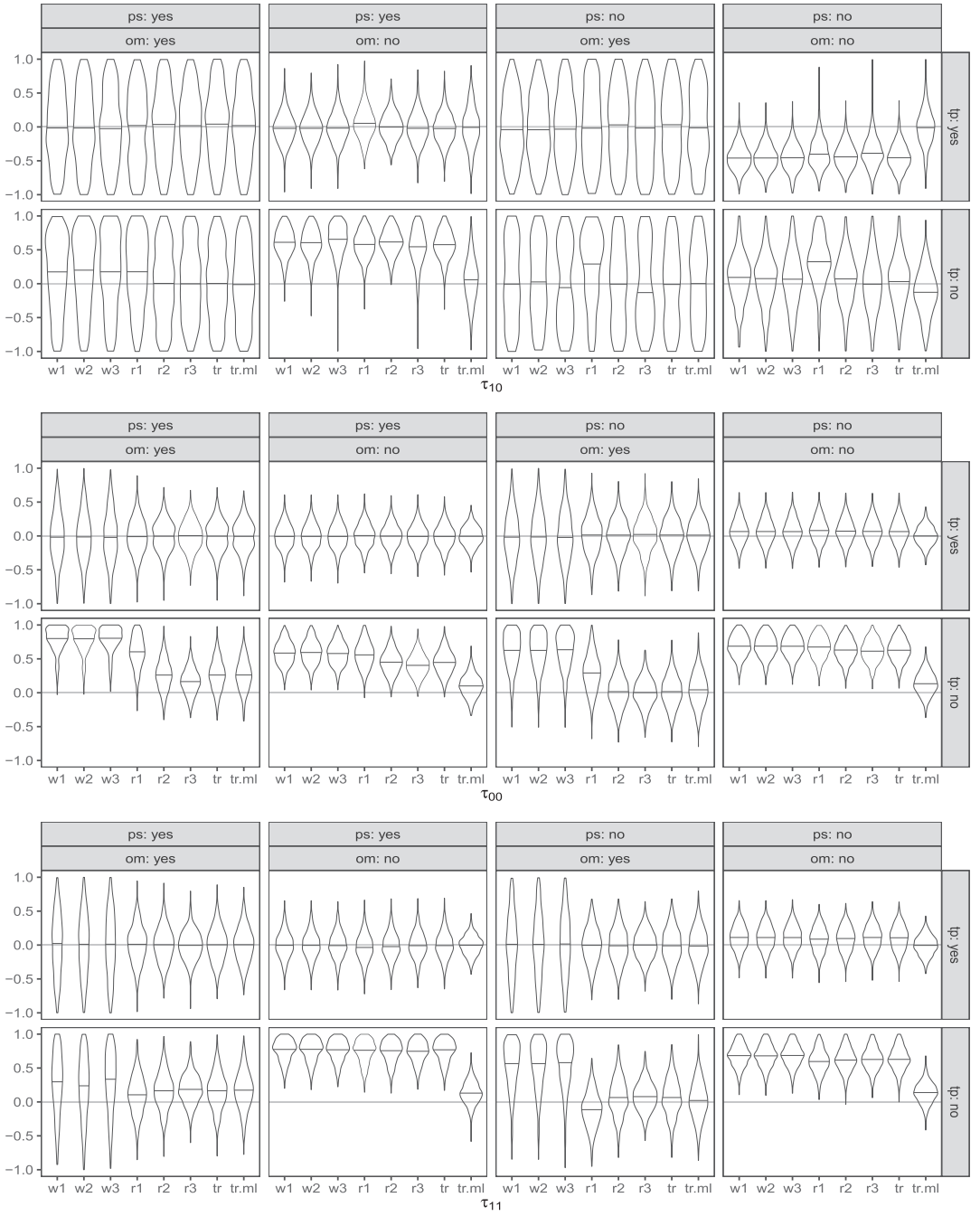|	logit$\{\pi(X)\}$	logit$\{p_z(X)\}$	$\mu_{zs}(X)$
Yes	0	$2\{(2z - 1) - \sum_{j=1}^{4}C_j\}/5$	$\sum_{j=1}^{5}C_j(1 + z + s)/4$
No	$2\sum_{j=1}^{4}\tilde{C}_j/5$	$2\{(2z - 1) - \sum_{j=1}^{4}\tilde{C}_j\}/5$	$\sum_{j=1}^{5}\tilde{C}_j(1 + z + s)/4$

FIGURE 1 Violin plots of estimators in eight scenarios. Labels: 'w1' for $\hat{\tau}_{u,\text{tp-ps}}$, 'w2' for $\hat{\tau}'_{u,\text{tp-ps}}$, and 'w3' for the weighting estimator in Ding and Lu (2017); 'r1' for $\hat{\tau}_{u,\text{tp-om}}$; 'r2' for $\hat{\tau}_{u,\text{ps-om}}$; 'r3' for the regression estimator in Ding and Lu (2017); 'tr' for the triply robust estimator $\hat{\tau}_u$ and 'tr.ml' for the triply robust estimator $\hat{\tau}_{u,\text{ml}}$

6 | APPLICATIONS TO TWO OBSERVATIONAL STUDIES

6.1 | Return to schooling

The dataset from the U.S. National Longitudinal Survey of Young Men contains 3010 men with age between 14 and 24 in the year 1966. Card (1993) uses it to estimate the causal effect of education on earnings, utilizing the geographic variation in college proximity as an instrumental variable for education. Thus, the treatment Z is the indicator of growing up near a 4-year college; the intermediate variable S is the indicator of whether the individual receives education beyond high school; and the outcome Y is the log wage in the year 1976, ranging from 4.6 to 7.8. Monotonicity is plausible because living close to a college would make an individual more likely to receive higher education. To make principal ignorability plausible, we include the following covariates: race, age and squared age, a categorical variable indicating living with both parents, single mom, or both parents, and variables summarizing the living areas in the past. Unlike Card (1993), we do not invoke the ER that living near a college affected the earnings only through education. Rather, under principal ignorability, our analysis can assess the plausibility of the ER. Guo et al. (2014) and Yang et al. (2014) used similar strategies to test the ER.

We use a linear model for the outcome mean and logistic models for the treatment probability and principal score, and estimate the asymptotic variances by the nonparametric bootstrap. Table 3 presents the results for the estimated proportions of principal strata ($\widehat{e}_u$) and PCEs using the weighting estimators ($\widehat{\tau}_{u,\text{tp-ps}}$ and $\widehat{\tau}'_{u,\text{tp-ps}}$), regression estimators ($\widehat{\tau}_{u,\text{tp-om}}$ and $\widehat{\tau}_{u,\text{ps-om}}$), and the triply robust estimator ($\widehat{\tau}_u$). We omit $\widehat{\tau}_{u,\text{tr.ml}}$ because it produces similar results as $\widehat{\tau}_u$. All estimators are close, except for the unstabilized weighting estimator. This is due to the extreme fitted treatment probabilities. The estimators for τ_{00} and τ_{11} are not significant, suggesting no significant evidence of violating the ER. The estimated τ_{10} is positive and statistically significant, implying education has a positive effect on earnings. This finding corroborates with previous analyses.

6.2 | Causal effect of flooding on health

We re-analyse a dataset from Guo et al. (2018) with 774 households in Bangladesh to investigate the effect of flooding on children's diarrhoea. The treatment Z is the indicator of whether a household was severely affected by the flood; the intermediate variable S is the indicator of whether

TABLE 3 Analysis of the national longitudinal survey of young men (all significant effects are in bold)

	$u = 10$	$u = 00$	$u = 11$
$\widehat{e}_u$	7% (3%, 10%)	48% (46%, 50%)	45% (42%, 49%)
$\widehat{\tau}_{u,\text{tp-ps}}$	**−0.87 (−1.69, −0.05)**	0.10 (−0.25, 0.44)	0.50 (−0.06, 1.05)
$\widehat{\tau}'_{u,\text{tp-ps}}$	**0.15 (0.00, 0.30)**	0.01 (−0.04, 0.06)	0.02 (−0.04, 0.08)
$\widehat{\tau}_{u,\text{tp-om}}$	0.09 (−0.03, 0.21)	0.02 (−0.02, 0.07)	0.01 (−0.05, 0.08)
$\widehat{\tau}_{u,\text{ps-om}}$	**0.12 (0.03, 0.21)**	0.02 (−0.03, 0.07)	0.01 (−0.05, 0.07)
$\widehat{\tau}_u$	0.10 (−0.01, 0.23)	0.02 (−0.03, 0.07)	0.01 (−0.05, 0.07)

the per capita calorie consumption of the household was less than 2000 calories; and the outcome Y is the number of days a child had diarrhoea. Monotonicity is plausible because the calorie consumption would be negatively affected if the household was severely affected by the flood. To ensure principal ignorability, we include the following covariates: gender, age, the size of the household, mother's education, father's education, mother's age and father's age. As pointed out by Del Ninno (2001), the ER might be violated due to an alternative pathway through mother's health. We use our method to evaluate this assumption by estimating τ_{00} and τ_{11}.

Again we use a linear model for the outcome mean and logistic models for the treatment probability and principal score. Table 4 presents the results for the estimated proportions of principal strata and PCEs. The estimated τ_{00} and τ_{11} are both positive and the estimated τ_{00} is statistically significant, indicating that being affected by the flood tends to directly increase the number of days of diarrhoea. This also confirms the suspicion of the violation of the ER in Del Ninno (2001). Although the estimated τ_{10} is positive, it is imprecisely estimated and not statistically significant, due to the small proportion of stratum $U = 10$.

7 | DISCUSSION

PCEs characterize subgroup causal effects of important scientific meanings, providing insights into the underlying causal mechanism between the treatment and outcome. We develop an identification and estimation framework for PCEs under principal ignorability. The proposed estimators are analogous to those for the average causal effect in unconfounded observational studies. They are easy to implement which involve the model fitting of the treatment, intermediate variable and outcome conditional on baseline covariates. They are triply robust and locally efficient, naturally extending the classic doubly robust estimator for the average causal effect.

In mediation analysis, Tchetgen Tchetgen and Shpitser (2012) develop a general semiparametric framework for the direct and indirect effects. They focus on two scalar estimands, the natural direct and indirect effects, in the overall population. In contrast, we focus on the treatment effects within principal strata, resulting in more estimands in different subpopulations. Although the PCEs and the direct and indirect effects are related in certain scenarios (Forastiere et al., 2018; VanderWeele, 2008, 2011) there is no universal relationship between them, and the PCEs are applicable to a number of applications other than mediation analysis. Moreover, as discussed in Section 2, the identification assumptions in the two methods concern different aspects of the relationship between the potential outcome and the potential intermediate variable.

TABLE 4 Analysis of the flood data (all significant effects are in bold)

	$u = 10$	$u = 00$	$u = 11$
$\hat{e}_u$	9% (2%, 15%)	45% (41%, 50%)	46% (41%, 51%)
$\hat{\tau}_{u,\text{tp-ps}}$	0.74 (-3.60, 5.09)	**0.98 (0.19, 1.77)**	1.97 (-0.52, 2.47)
$\hat{\tau}'_{u,\text{tp-ps}}$	0.86 (-3.35, 5.07)	**0.92 (0.13, 1.71)**	1.11 (-0.36, 2.58)
$\hat{\tau}_{u,\text{tp-om}}$	1.74 (-3.55, 7.03)	**0.93 (0.10, 1.77)**	1.01 (-0.45, 2.47)
$\hat{\tau}_{u,\text{ps-om}}$	1.50 (-3.01, 6.01)	**0.92 (0.09, 1.75)**	1.10 (-0.33, 2.53)
$\hat{\tau}_u$	1.51 (-3.68, 6.71)	**0.88 (0.05, 1.71)**	1.10 (-0.33, 2.53)

We can generalize the theory to other causal estimands within principal strata by invoking a stronger version of principal ignorability: $Y_1 \perp\!\!\!\perp U|(Z = 1, S = 1, X)$ and $Y_0 \perp\!\!\!\perp U|(Z = 0, S = 0, X)$. Under this assumption, we can identify the effects on a transformation of the outcome: $\mathbb{E}\{h(Y_1, X)|U = u\} - \mathbb{E}\{h(Y_0, X)|U = u\}$ for any function $g(\cdot)$. This further ensures the identification of distributional or quantile causal effects within principal strata. Similar to the main paper, we can also derive EIFs and propose robust estimators for these causal estimands.

More generally, we can extend the results to deal with a continuous S, where the number of principal strata is infinity. The principal score becomes the conditional density of $U = (S_1, S_0)$ given covariates, which is not identifiable even under monotonicity. Therefore, the extension requires more sophisticated identification and estimation strategies. We leave the technical investigation to future research.

DATA AVAILABILITY STATEMENT
The data used in our paper are publicly available.

ORCID
Zhichao Jiang https://orcid.org/0000-0002-8571-0217
Shu Yang https://orcid.org/0000-0001-7703-707X
Peng Ding https://orcid.org/0000-0002-2704-2353

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