

Causal Inference with the “Napkin Graph”

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Abstract

Unmeasured confounding can render identification strategies based on adjustment functionals invalid. We study the “Napkin graph,” a causal structure that encapsulates patterns of M-bias, instrumental variables, and the classical back-door and front-door models within a single graphical framework, yet requires a nonstandard identification strategy: the average treatment effect is expressed as a ratio of two g-formulas. We develop novel estimators for this functional, including doubly robust one-step and targeted minimum loss-based estimators that remain asymptotically linear when nuisance functions are estimated at slower-than-parametric rates using machine learning. We also show how a generalized independence restriction encoded by the Napkin graph, known as a Verma constraint, can be exploited to improve efficiency, illustrating more generally how such constraints in hidden variable DAGs can inform semiparametric inference. The proposed methods are validated through simulations and applied to the Finnish Life Course study to estimate the effect of educational attainment on income. An accompanying R package, [napkincausal](#), implements all proposed procedures.

Keywords: Causal inference; unmeasured confounding; doubly robust estimation; semiparametric inference; generalized independence restrictions; Verma constraints.

1 Introduction

Pearl’s *do-calculus* (Pearl 1995, Tian & Pearl 2002) provides a graphical framework for determining whether and how causal effects such as the average treatment effect (ATE) can be identified from observational data, by leveraging assumptions about both observed and unobserved variables encoded in a hidden variable directed acyclic graph (DAG). Subsequent work has established the *completeness* of the do-calculus (Shpitser & Pearl 2006, Huang & Valtorta 2006), showing that any identifiable causal effect can, in principle, be derived using its rules. Variations of a sound and complete identification algorithm have been proposed by Richardson et al. (2023) and Bhattacharya et al. (2022).

While do-calculus provides a complete identification theory, several subclasses of hidden variable DAGs admit simpler graphical criteria. The *back-door* criterion identifies the ATE by adjusting for covariates that block all non-causal paths between treatment and outcome (Robins 1986b, Pearl 2009). The *front-door* criterion applies when mediators are not subject to unmeasured confounding of either the treatment–mediator or mediator–outcome relations, and fully mediate the effect of treatment on the outcome (Pearl 2009). The more general *primal fixability* criterion requires that the treatment and its children lie in distinct latent components (c-component or district) (Tian & Pearl 2002, Richardson 2003, Bhattacharya et al. 2022). These criteria are easy to verify and lend themselves to practical estimation strategies as recent work has developed estimators with favorable asymptotic properties even under machine learning nuisance estimation (Fulcher et al. 2019, Bhattacharya et al. 2022, Jung et al. 2021, 2024, Guo et al. 2023, Guo & Nabi 2024).

Despite these advances, some causal graphs fall outside these convenient classes. A prominent example is the *Napkin graph* (Pearl & Mackenzie 2018) shown in Figure 1(a) with X as treatment, Y as outcome, unmeasured confounders U_1, U_2 , and observed pre-treatment variables W, Z . Several features illustrate why standard identification criteria fail. First,

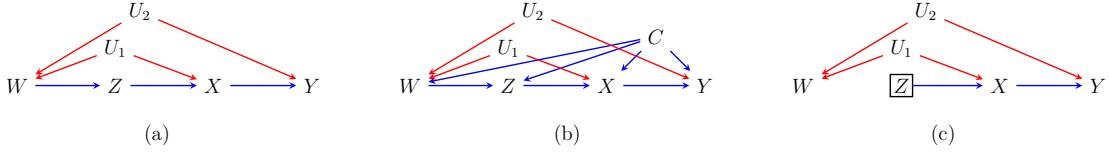


Figure 1: (a) The Napkin DAG; (b) A generalization with measured confounders C ; (c) The post-intervention graph under intervention on Z .

the path $X \leftarrow U_1 \rightarrow W \leftarrow U_2 \rightarrow Y$ forms a collider at W , a hallmark of M-bias (Pearl 2009, Ding & Miratrix 2015); conditioning on W (or on the downstream Z) opens this path, invalidating the back-door criterion. Second, no observed mediators lie between X and Y , ruling out the use of the front-door criterion. Third, X and Y belong to the same latent component, so primal fixability fails, implying that $P(Y^x, Z, W)$ is not identified according to Tian & Pearl (2002). Here we adopt the potential outcome notation Y^x to denote the outcome Y had X been set to x .

The variable Z , termed a *trapdoor* variable (Helske et al. 2021), may appear to serve as a generalized instrumental variable (IV), suggesting IV methods to identify the local average treatment effect (LATE) under additional assumptions such as monotonicity (Angrist et al. 1996, Baiocchi et al. 2014, Wang & Tchetgen Tchetgen 2018). The crucial insight, however, is that the marginal distribution $P(Y^x)$ is in fact nonparametrically identifiable in this graph. By do-calculus, the counterfactual mean $\mathbb{E}(Y^x)$ can be expressed as a ratio of two g-formulas: the numerator capturing the effect of Z on (X, Y) jointly, and the denominator capturing its effect on X alone. This ratio-based representation makes the Napkin graph a canonical example of how causal effects can be identified in hidden variable DAGs beyond standard back-door, front-door, and primal fixability criteria.

Aside from its graphical features, the Napkin graph is distinctive in terms of the statistical model it encodes: the observed data distribution $P(W, Z, X, Y)$ is not subject to any ordinary independence restrictions, but it does encode a generalized independence restriction, known as a Verma constraint (Verma & Pearl 1990, Robins 1986a). While semiparametric

efficiency theory is well established for models defined by ordinary conditional independences (Van der Vaart 2000, Tsiatis 2007), analogous results under Verma constraints remain largely undeveloped, and the efficiency gains they may offer are still poorly understood.

We consider nonparametric and semiparametric estimators of causal effects under the Napkin graph and develop novel influence-function–based estimators, including one-step and targeted minimum loss–based estimators. These remain asymptotically linear when nuisance functions are estimated at slower-than-parametric rates, accommodating flexible machine learning, and remain consistent even when some nuisances are inconsistently estimated, offering robustness beyond fully parametric plug-in approaches (e.g., Helske et al. (2021)).

We further show that exploiting Verma constraints in the semiparametric model improves efficiency, yielding more precise estimators than those under a fully nonparametric model. In simulations, these gains lead to substantial variance reductions (up to threefold under simple data-generating processes), highlighting the practical value of leveraging Verma constraints.

The rest of the paper is organized as follows. Section 2 presents the ATE identification assumptions and functional. Section 3 introduces novel ATE estimators under a fully nonparametric model and establishes their asymptotic properties for binary and continuous Z . Section 4 examines a semiparametric Napkin graph model, showing how an equality restriction can improve estimation efficiency. Section 5 reports simulation results, and Section 6 applies the estimators to the Finnish Life Course study on the causal effect of education on income. Section 7 concludes, and all proofs appear in the appendix.

2 Target parameter and identification

Let $O = \{W, Z, X, Y\}$ denote the observed variables and $U = \{U_1, U_2\}$ the unobserved ones. We assume $P(O, U)$ factorizes according to the Napkin graph in Figure 1(a). The

observed data distribution $P(O)$ is obtained by marginalizing $P(O, U)$ over the unobserved variables. We denote the support of each variable using calligraphic notation, e.g., \mathcal{Z} for Z . We write P for distributions and p for densities, assuming continuous variables admit Lebesgue densities (though this is not required).

For a binary treatment, the ATE is defined as $\mathbb{E}(Y^1 - Y^0)$. Since the identification and estimation of $\mathbb{E}(Y^1)$ and $\mathbb{E}(Y^0)$ are analogous, we consider $\mathbb{E}(Y^{x_0})$ for $x_0 \in \{0, 1\}$ as our target parameter. Identifying $\mathbb{E}(Y^{x_0})$ as a functional of $P(O)$ requires: (i) *Consistency*: if $Z = z$, then $Y^z = Y$ and $X^z = X$; (ii) *Conditional ignorability*: $Y^z, X^z \perp Z \mid W$; and (iii) *Positivity*: $p(X = 1, Z = z \mid W = w) > 0$ for all z and w where $p(W = w) > 0$.

Lemma 1. *Under assumptions (i)-(iii) and for any $z^* \in \mathcal{Z}$, $\mathbb{E}(Y^{x_0})$ is identified via the following functional, denoted by $\psi_{x_0}(P; z^*)$:*

$$\psi_{x_0}(P; z^*) = \kappa_{x_0,1}(P; z^*) / \kappa_{x_0,2}(P; z^*) , \quad (1)$$

where $\kappa_{x_0,1}(P; z) = \int y p(y|x_0, z, w) p(x_0|z, w) p(w) dw$ and $\kappa_{x_0,2}(P; z) = \int p(x_0|z, w) p(w) dw$.

Given a pre-specified weight function $z \mapsto \tilde{p}(z)$ such that $\int \tilde{p}(z) dz = 1$, $\mathbb{E}(Y^{x_0})$ can also be identified via:

$$\psi_{x_0}(P; \tilde{p}_z) = \int \{\kappa_{x_0,1}(P; z) / \kappa_{x_0,2}(P; z)\} \tilde{p}(z) dz . \quad (2)$$

See a proof in Appendix B.1.

According to (1), $\mathbb{E}(Y^{x_0})$ is identifiable as the ratio of two g-formulas: $\kappa_{x_0,1}(P; z^*)$ identifies the mean of the composite outcome $Y\mathbb{I}(X = x_0)$ and $\kappa_{x_0,2}(P; z^*)$ the mean of $\mathbb{I}(X = x_0)$, both under the intervention $Z = z^*$ (see Appendix (B.1)). The invariance of $\psi_{x_0}(P; z^*)$ to z^* follows from a Verma constraint encoded in the Napkin graph. The variable Z , which helps identify the causal effect of interest while remaining independent of the identification functional, is referred to as a trapdoor variable (Helske et al. 2021). Although identification does not depend on the choice of z^* , efficiency of estimators may, as discussed in Section 4.

The invariance of the identifying functional for $\mathbb{E}(Y^{x_0})$ under the Napkin graph allows for a reformulation that remains pathwise differentiable when Z is continuous, as in (2). This representation provides a valid basis for influence-function–based estimation in the case of a continuous-valued trapdoor variable. The weighting density $\tilde{p}(z)$ acts as an auxiliary distribution over the support of Z ; it need not coincide with the true marginal law of Z , but must assign positive probability to relevant regions to ensure the functional is well defined.

We note that the Napkin graph can be generalized to incorporate measured confounders, as shown in Figure 1(b), though Pearl’s original formulation did not explicitly consider this extension. For clarity, we focus in the main text on the case without measured confounders, with Appendix C describing how the identification results and estimation procedures extend to the more general setting. We now turn to estimation and inference for the identifying functional $\mathbb{E}(Y^{x_0})$ in a fully nonparametric model. Since the case where Z is continuous highlights the main technical challenges, we present our estimators in that setting first. When Z is discrete, the same estimators apply with simpler forms, and in some instances admit stronger robustness properties. We therefore treat the continuous case as primary, and provide remarks throughout on how the discrete case arises as a simplification.

3 Estimation and inference

We consider n i.i.d. copies of $O = (Y, X, Z, W)$ drawn from a distribution P that is Markov relative to the Napkin graph in Figure 1(a). Estimation of $\psi_{x_0}(P; \tilde{p}_z)$ requires several nuisance functions. We define the outcome regression $\mu(x, z, w) = \mathbb{E}(Y|X = x, Z = z, W = w)$, the propensity score $\pi(x|z, w) = P(X = x|Z = z, W = w)$, the conditional density $f_Z(z|w) = p(Z = z|W = w)$, and the marginal distribution $p_W(w) = p(W = w)$. These nuisances are collected in $Q = \{\mu, \pi, f_Z, p_W\}$. The functional $\psi_{x_0}(P; \tilde{p}_z)$ and its components $\kappa_{x_0,1}(P; z)$ and $\kappa_{x_0,2}(P; z)$ depend on P only through Q . To emphasize this, we write

$\psi_{x_0}(Q; \tilde{p}_z)$, $\kappa_{x_0,1}(Q; z)$, and $\kappa_{x_0,2}(Q; z)$ throughout the remainder of the paper.

In practice, the nuisance functions can be estimated parametrically or using flexible methods. For instance, μ may be estimated by regressing Y on (X, Z, W) , π by regressing X on (Z, W) , and f_Z using either a parametric model for the conditional density of Z given W or non/semiparametric kernel density methods (Hayfield & Racine 2008, Benkeser & Van Der Laan 2016); when Z is discrete, f_Z reduces to a regression of Z on W . The marginal distribution p_W can be estimated empirically. Throughout, we allow these regressions to be fit using machine learning methods, with cross-fitting employed when needed to ensure valid asymptotics. We denote the resulting estimates by $\hat{Q} = \{\hat{\mu}, \hat{\pi}, \hat{f}_Z, \hat{p}_W\}$.

A natural starting point is the plug-in estimator, denoted as $\psi_{x_0}^{\text{pi}}(\hat{Q}; \tilde{p}_z)$ and obtained by substituting the estimated nuisances \hat{Q} into the identification functional (2):

$$\psi_{x_0}^{\text{pi}}(\hat{Q}; \tilde{p}_z) = \int \left\{ \kappa_{x_0,1}^{\text{pi}}(\hat{Q}; z) / \kappa_{x_0,2}^{\text{pi}}(\hat{Q}; z) \right\} \tilde{p}(z) dz , \quad (3)$$

where $\kappa_{x_0,1}^{\text{pi}}(\hat{Q}; z) = n^{-1} \sum_{i=1}^n \hat{\mu}(x_0, z, W_i) \hat{\pi}(x_0|z, W_i)$ and $\kappa_{x_0,2}^{\text{pi}}(\hat{Q}; z) = n^{-1} \sum_{i=1}^n \hat{\pi}(x_0|z, W_i)$ are plug-in estimators of $\kappa_{x_0,1}(Q; z)$ and $\kappa_{x_0,2}(Q; z)$, respectively, and the integral with respect to $\tilde{p}(Z)$ is evaluated using Monte Carlo or other numerical integration methods.

Remark 2. When Z is discrete, $\tilde{p}(Z)$ may be specified as a probability mass function, in which case the integral in (3) reduces to a finite sum over the support of Z . Alternatively, one can work directly with a fixed level $z^* \in \mathcal{Z}$, where the probability mass function assigns all mass to this value, i.e., $\tilde{p}(z^*) = 1$, and construct the plug-in estimator of (1):

$$\psi_{x_0}^{pi}(\hat{Q}; z^*) = \kappa_{x_0,1}^{pi}(\hat{Q}; z^*) / \kappa_{x_0,2}^{pi}(\hat{Q}; z^*) . \quad (4)$$

Both approaches yield consistent estimators, with the latter highlighting the connection to the ratio form of the identification functional.

While the plug-in estimator is straightforward, it is limited in practice. A von Mises expan-

sion shows that $\psi_{x_0}^{\text{pi}}(\hat{Q}; \tilde{p}_z) - \psi_{x_0}(Q; \tilde{p}_z) = -P\Phi_{x_0}(\hat{Q}; \tilde{p}_z) + R_2(\hat{Q}, Q; \tilde{p}_z)$, where $\Phi_{x_0}(\hat{Q}; \tilde{p}_z)$ denotes a canonical gradient (a.k.a., influence function) for $\psi_{x_0}(Q; \tilde{p}_z)$ evaluated at \hat{Q} , and $R_2(\hat{Q}, Q; \tilde{p}_z)$ is a second-order remainder (Van der Vaart 2000, Tsiatis 2007). The leading error term, $-P\Phi_{x_0}(\hat{Q}; \tilde{p}_z)$, corresponds to the first-order bias and depends directly on the quality of the nuisance estimates in \hat{Q} . Achieving asymptotic linearity therefore requires all nuisance estimators to converge to the truth at a sufficiently fast rate of $o_P(n^{-1/2})$, which limits the use of flexible machine learning methods. To address this limitation, we develop estimators that control the first-order bias, attain asymptotic linearity under weaker conditions, and offer robustness properties not shared by the plug-in approach.

3.1 Influence-function-based estimators

We first present an influence function for $\psi_{x_0}(Q; \tilde{p}_z)$, which is uniquely defined under a fully nonparametric model but may not be unique within a semiparametric model.

Lemma 3. *For an observation $O_i = (Y_i, X_i, Z_i, W_i)$, a canonical gradient for the functional in (2), denoted as $\Phi_{x_0}(Q; \tilde{p}_z)(O_i)$, is given by*

$$\begin{aligned} \Phi_{x_0}(Q; \tilde{p}_z)(O_i) &= \underbrace{\frac{\mathbb{I}(X_i = x_0)}{\kappa_{x_0,2}(Q; Z_i)} \frac{\tilde{p}(Z_i)}{f_Z(Z_i | W_i)} \left\{ Y_i - \mu(x_0, Z_i, W_i) \right\}}_{\Phi_{Y,x_0}(Q; \tilde{p}_z)(O_i)} \\ &+ \underbrace{\frac{1}{\kappa_{x_0,2}(Q; Z_i)} \frac{\tilde{p}(Z_i)}{f_Z(Z_i | W_i)} \left\{ \mu(x_0, Z_i, W_i) - \psi_{x_0}(Q; Z_i) \right\} \left\{ \mathbb{I}(X_i = x_0) - \pi(x_0 | Z_i, W_i) \right\}}_{\Phi_{X,x_0}(Q; \tilde{p}_z)(O_i)} \\ &+ \underbrace{\int \frac{\pi(x_0 | z, W_i)}{\kappa_{x_0,2}(Q; z)} \left\{ \mu(x_0, z, W_i) - \psi_{x_0}(Q; z) \right\} \tilde{p}(z) dz}_{\Phi_{W,x_0}(Q; \tilde{p}_z)(O_i)} . \end{aligned} \quad (5)$$

See a proof in Appendix B.2.

This influence function admits a natural decomposition into components corresponding to variationally independent nuisance functionals, with each component lying in a tangent space spanned by the corresponding score function from the observed data distribution

factorization $p(o) = p(y|x, z, w)p(x|z, w)p(z|w)p(w)$. This yields contributions associated with the outcome regression, the propensity score, and the distribution of baseline covariates, denoted $\Phi_{Y,x_0}(Q; \tilde{p}_z)(O_i)$, $\Phi_{X,x_0}(Q; \tilde{p}_z)(O_i)$, and $\Phi_{W,x_0}(Q; \tilde{p}_z)(O_i)$, respectively. Importantly, the projection onto the tangent space for $p(z|w)$ is identically zero, so knowledge of f_Z provides no efficiency gain relative to estimating it from the observed data.

Remark 4. When Z is discrete, a simplification arises by focusing on a fixed level $z^* \in \mathcal{Z}$. In this case, $\tilde{p}(Z)$ can be represented as the indicator $\mathbb{I}(Z = z^*)$, and the EIF simplifies accordingly. Specifically, Φ_{Y,x_0} and Φ_{X,x_0} remain unchanged, while Φ_{W,x_0} reduces to $\Phi_{W,x_0}(Q; z^*)(O_i) = \frac{\pi(x_0|z^*, W_i)}{\kappa_{x_0,2}(Q; z^*)} \{\mu(x_0, z^*, W_i) - \psi_{x_0}(Q; z^*)\}$. More generally, when $\tilde{p}(Z)$ is specified as a probability mass function assigning nonzero probability across the support of Z , the EIF retains the same form, with the integration in Φ_{W,x_0} reducing to a finite sum.

There are several strategies for addressing the first-order bias term $-P\Phi_{x_0}(\hat{Q}; \tilde{p}_z)$, with $\Phi_{x_0}(Q; \tilde{p}_z)$ defined in (5). We next describe three estimators that implement these strategies.

3.1.1 Estimating equation

The first approach is to solve the estimating equation $P_n\Phi_{x_0}(\hat{Q}; \tilde{p}_z) = 0$, thereby enforcing that the empirical mean of $\Phi_{x_0}(\hat{Q}; \tilde{p}_z)$ vanishes and eliminating the first-order bias by construction; here $P_n f := \frac{1}{n} \sum_{i=1}^n f(O_i)$. The resulting estimator of $\psi_{x_0}(Q; \tilde{p}_z)$ in (2), denoted $\psi_{x_0}^{\text{ee}}(\hat{Q}; \tilde{p}_z)$, is given by

$$\psi_{x_0}^{\text{ee}}(\hat{Q}; \tilde{p}_z) = \psi_{x_0,1}^{\text{ee}}(\hat{Q}; \tilde{p}_z) / \psi_{x_0,2}^{\text{ee}}(\hat{Q}; \tilde{p}_z) , \quad (6)$$

where

$$\begin{aligned} \psi_{x_0,1}^{\text{ee}}(\hat{Q}; \tilde{p}_z) &= \frac{1}{n} \sum_{i=1}^n \left\{ \frac{1}{\kappa_{x_0,2}^{\text{pi}}(\hat{Q}; Z_i)} \frac{\tilde{p}(Z_i)}{\hat{f}_Z(Z_i | W_i)} \{ \mathbb{I}(X_i = x_0) Y_i \right. \\ &\quad \left. - \hat{\mu}(x_0, Z_i, W_i) \hat{\pi}(x_0 | Z_i, W_i) \} \right\} + \psi_{x_0}^{\text{pi}}(\hat{Q}; \tilde{p}_z) , \\ \psi_{x_0,2}^{\text{ee}}(\hat{Q}; \tilde{p}_z) &= \frac{1}{n} \sum_{i=1}^n \left\{ \frac{1}{\kappa_{x_0,2}^{\text{pi}}(\hat{Q}; Z_i)} \frac{\tilde{p}(Z_i)}{\hat{f}_Z(Z_i | W_i)} \{ \mathbb{I}(X_i = x_0) - \hat{\pi}(x_0 | Z_i, W_i) \} \right\} + 1 . \end{aligned}$$

Remark 5. When Z is discrete, solving the estimating equation $P_n \Phi_{x_0}(\hat{Q}; z^*) = 0$, for a fixed level $z^* \in \mathcal{Z}$, yields the following estimator for $\psi_{x_0}(Q; z^*)$ in (1):

$$\psi_{x_0}^{ee}(\hat{Q}; z^*) = \kappa_{x_0,1}^{\text{aipw}}(\hat{Q}; z^*) / \kappa_{x_0,2}^{\text{aipw}}(\hat{Q}; z^*) , \quad (7)$$

where the numerator and denominator coincide with the augmented inverse probability weighting (AIPW) estimators for $\kappa_{x_0,1}(Q; z^*)$ and $\kappa_{x_0,2}(Q; z^*)$, respectively. That is,

$$\begin{aligned} \kappa_{x_0,1}^{\text{aipw}}(\hat{Q}; z^*) &= \frac{1}{n} \sum_{i=1}^n \frac{\mathbb{I}(Z_i = z^*)}{\hat{f}_Z(z^* | W_i)} \{ \mathbb{I}(X_i = x_0) Y_i - \hat{\mu}(x_0, z^*, W_i) \hat{\pi}(x_0 | z^*, W_i) \} + \kappa_{x_0,1}^{\text{pi}}(\hat{Q}; z^*) , \\ \kappa_{x_0,2}^{\text{aipw}}(\hat{Q}; z^*) &= \frac{1}{n} \sum_{i=1}^n \frac{\mathbb{I}(Z_i = z^*)}{\hat{f}_Z(z^* | W_i)} \{ \mathbb{I}(X_i = x_0) - \hat{\pi}(x_0 | z^*, W_i) \} + \hat{\pi}(x_0 | z^*, W_i) . \end{aligned}$$

Detailed derivations are provided in Appendices B.2.3 and B.2.4.

3.1.2 One-step corrected plug-in estimator

An alternative strategy is to correct the plug-in estimator in (3) by adding an empirical estimate of its first-order bias. This yields the one-step estimator $\psi_{x_0}^+(\hat{Q}; \tilde{p}_z) = \psi_{x_0}^{\text{pi}}(\hat{Q}; \tilde{p}_z) + P_n \Phi_{x_0}(\hat{Q}; \tilde{p}_z)$. In many causal models, such as those identified by back-door adjustment, front-door adjustment, or primal fixability, the one-step and estimating equation estimators coincide. Under the Napkin model, however, they differ. The explicit form of the one-step estimator for $\psi_{x_0}(Q; \tilde{p}_z)$ in (2) is given by

$$\begin{aligned} \psi_{x_0}^+(\hat{Q}; \tilde{p}_z) &= \sum_{i=1}^n \left\{ \frac{\mathbb{I}(X_i = x_0)}{\kappa_{x_0,2}^{\text{pi}}(\hat{Q}; Z_i)} \frac{\tilde{p}(Z_i)}{\hat{f}_Z(Z_i | W_i)} \{ Y_i - \hat{\mu}(x_0, Z_i, W_i) \} \right. \\ &\quad + \frac{1}{\kappa_{x_0,2}^{\text{pi}}(\hat{Q}; Z_i)} \frac{\tilde{p}(Z_i)}{\hat{f}_Z(Z_i | W_i)} \{ \hat{\mu}(x_0, Z_i, W_i) - \psi_{x_0}^{\text{pi}}(\hat{Q}; Z_i) \} \{ \mathbb{I}(X_i = x_0) - \hat{\pi}(x_0 | Z_i, W_i) \} \quad (8) \\ &\quad \left. + \int \frac{\hat{\pi}(x_0 | z, W_i)}{\kappa_{x_0,2}^{\text{pi}}(\hat{Q}; z)} \{ \hat{\mu}(x_0, z^*, W_i) - \psi_{x_0}^{\text{pi}}(\hat{Q}; z) \} \tilde{p}(z) dz \right\} + \psi_{x_0}^{\text{pi}}(\hat{Q}; \tilde{p}_z) . \end{aligned}$$

In the estimator above, the plug-in version of $\kappa_{x_0,2}$ is used since the AIPW estimator, defined for discrete Z , becomes irregular when Z is continuous. This substitution affects the robustness properties of the one-step estimator, as discussed in Section 3.2.1.

Constructing $\psi_{x_0}^+(\hat{Q}; \tilde{p}_z)$ involves evaluating the plug-in estimator at each observed Z_i in the second line, and over all z in the support of $\tilde{p}(Z)$ in the third, integrating with respect to $\tilde{p}(Z)$. Thus, $\tilde{p}(Z)$ must be chosen such that for every z in its support, the nuisances $\mu(x_0, z, W_i)$ and $\pi(x_0|z, W_i)$ in $\psi_{x_0}^{\text{pi}}(\hat{Q}; z^*)$ are well defined and can be reliably estimated from the observed data. To guarantee this, we require $f_Z(z|w) > 0$ for all z in the support of $\tilde{p}(Z)$ and all w with $p_W(w) > 0$. This overlap condition ensures that $\tilde{p}(Z)$ aligns sufficiently with the observed data and is motivated by both identification and estimation considerations. For example, $\pi(x_0|z, W_i)$ is not well defined when $f_Z(z|W_i) = 0$, as the data contain no information about such (z, W_i) pairs. Thus, estimators would necessarily involve extrapolation, which may be unreliable.

Remark 6. Under discrete Z , the one-step estimator for $\psi_{x_0}(Q; z^*)$ in (1) is given by:

$$\begin{aligned}\psi_{x_0}^+(\hat{Q}; z^*) &= \frac{1}{n} \sum_{i=1}^n \left\{ \frac{\mathbb{I}(X_i = x_0)}{\kappa_{x_0,2}^{\text{aipw}}(\hat{Q}; z^*)} \frac{\mathbb{I}(Z_i = z^*)}{\hat{f}_Z(z^* | W_i)} \left\{ Y_i - \hat{\mu}(x_0, z^*, W_i) \right\} \right. \\ &\quad + \frac{1}{\kappa_{x_0,2}^{\text{aipw}}(\hat{Q}; z^*)} \frac{\mathbb{I}(Z_i = z^*)}{\hat{f}_Z(z^* | W_i)} \left\{ \hat{\mu}(x_0, z^*, W_i) - \psi_{x_0}^{\text{pi}}(\hat{Q}; z^*) \right\} \left\{ \mathbb{I}(X_i = x_0) - \hat{\pi}(x_0 | z^*, W_i) \right\} \quad (9) \\ &\quad \left. + \frac{\hat{\pi}(x_0 | z^*, W_i)}{\kappa_{x_0,2}^{\text{aipw}}(\hat{Q}; z^*)} \left\{ \hat{\mu}(x_0, z^*, W_i) - \psi_{x_0}^{\text{pi}}(\hat{Q}; z^*) \right\} \right\} + \psi_{x_0}^{\text{pi}}(\hat{Q}; z^*).\end{aligned}$$

In constructing this one-step estimator, $\kappa_{x_0,2}$ is estimated using the AIPW estimator from (7). The AIPW estimator is preferred over the plug-in or IPW alternatives because it ensures double robustness, a property discussed in detail in Section 3.2.2.

3.1.3 TMLE

We propose a targeted minimum loss-based estimator (TMLE) as our third estimator, which updates the initial nuisance estimates \hat{Q} through a *targeting* step so that the empirical mean of the influence function (i.e., the first-order bias) is asymptotically negligible under the updated nuisance estimates, denoted by \hat{Q}^* ; that is, $P_n \Phi_{x_0}(\hat{Q}^*; \tilde{p}_z) = o_P(n^{-1/2})$ (van

der Laan et al. 2011, van der Laan & Gruber 2016).

Let Q_j denote a nuisance parameter in Q , and Q_{-j} the collection of all other nuisances; with the corresponding estimates denoted by \hat{Q}_j and \hat{Q}_{-j} . Let \mathcal{M}_{Q_j} denote the model space of Q_j . To target \hat{Q}_j , we define a loss function $L(\tilde{Q}_j; \hat{Q}_{-j})$, for $\tilde{Q}_j \in \mathcal{M}_{Q_j}$, and a parametric submodel $\hat{Q}_j(\varepsilon_j; \hat{Q}_{-j})$, indexed by a univariate real-valued parameter ε_j . We include \hat{Q}_{-j} in the argument to point out that the loss function and submodel may rely on other nuisance estimates apart from \hat{Q}_j . A valid parametric submodel and loss function pair needs to satisfy the following three conditions: (C1) The submodel passes through the initial estimate at $\varepsilon_j = 0$: $\hat{Q}_j(0; \hat{Q}_{-j}) = \hat{Q}_j$; (C2) The true nuisance minimizes the expected loss: $Q_j = \arg \min_{\tilde{Q}_j \in \mathcal{M}_{Q_j}} \int L(\tilde{Q}_j; Q_{-j})(o) p(o) do$; and (C3) The derivative of the loss function at $\varepsilon_j = 0$ is proportional to the corresponding component of the influence function, denoted by Φ_j : $\left. \frac{\partial}{\partial \varepsilon_j} L(\hat{Q}_j(\varepsilon_j; \hat{Q}_{-j}); \hat{Q}_{-j}) \right|_{\varepsilon_j=0} \propto \Phi_j(\hat{Q})$.

The empirical first-order bias, $P_n \Phi_{x_0}(\hat{Q}; \tilde{p}_z)$, decomposes as $P_n \Phi_{Y,x_0}(\hat{Q}; \tilde{p}_z) + P_n \Phi_{X,x_0}(\hat{Q}; \tilde{p}_z) + P_n \Phi_{W,x_0}(\hat{Q}; \tilde{p}_z)$; see (5) for the definitions of Φ_{Y,x_0} , Φ_{X,x_0} , Φ_{W,x_0} . To ensure $P_n \Phi_{x_0}(\hat{Q}; \tilde{p}_z)$ is negligible, it suffices to ensure each component is $o_P(n^{-1/2})$. Given that \hat{p}_W is empirically estimated, $P_n \Phi_{W,x_0}(\hat{Q}; \tilde{p}_z) = o_P(n^{-1/2})$ once the remaining nuisances are successfully targeted. Updating \hat{f}_Z is also unnecessary, as the influence function projects to zero onto its tangent space. Consequently, the targeting reduces to updating $\hat{\mu}$ and $\hat{\pi}$. With $\hat{Q}^* = \{\hat{\mu}^*, \hat{\pi}^*, \hat{f}_Z, \hat{p}_W\}$, the TMLE, denoted by $\psi_{x_0}(\hat{Q}^*, \tilde{p}_z)$, is a plug-in estimator evaluated at \hat{Q}^* :

$$\psi_{x_0}(\hat{Q}^*; \tilde{p}_z) = \int \left\{ \sum_{i=1}^n \hat{\mu}^*(x_0, z, W_i) \hat{\pi}^*(x_0 | z, W_i) / \sum_{i=1}^n \hat{\pi}^*(x_0 | z, W_i) \right\} \tilde{p}(z) dz . \quad (10)$$

We next outline the targeting of $\hat{\mu}$ and $\hat{\pi}$ with their associated loss functions and submodels:

$$L_Y(\tilde{\mu}; \hat{\pi}, \hat{f}_Z) = \hat{H}_Y(X, Z, W; \tilde{p}_z) \{Y_i - \tilde{\mu}(x_0, Z, W)\}^2 ,$$

$$\hat{\mu}(\varepsilon_Y) = \hat{\mu}(x_0, Z, W) + \varepsilon_Y ,$$

with $\hat{H}_Y(X, Z, W; \tilde{p}_z) = \{\mathbb{I}(X = x_0) \tilde{p}(Z)\} / \{\kappa_{x_0, 2}^{\text{pi}}(\hat{Q}; Z) \hat{f}_Z(Z | W)\}$, and

$$L_X(\tilde{\pi}; \hat{f}_Z) = -\{\tilde{p}(Z)/\hat{f}_Z(Z | W)\} \log \tilde{\pi}(X | Z, W) ,$$

$$\hat{\pi}(\varepsilon_X; \hat{\mu}, \hat{\pi}, \hat{f}_Z) = \text{expit}\{\text{logit } \hat{\pi}(x_0 | Z, W) + \varepsilon_X \hat{H}_X(Z, W; \tilde{p}_z)\} ,$$

with $\hat{H}_X(Z, W; \tilde{p}_z) = \{\hat{\mu}(x_0, Z, W) - \psi_{x_0}^{\text{pi}}(\hat{Q}; Z)\}/\kappa_{x_0, 2}^{\text{pi}}(\hat{Q}; Z)$. See Appendix D.1 for a proof of validity of these submodel–loss function pairs under (C1)–(C3). These pairs only apply when the outcome Y is continuous; extensions for binary Y are discussed in Appendix D.2.

The loss function for $\hat{\mu}$ depends on $\hat{\pi}$ and the submodel for $\hat{\pi}$ depends on $\hat{\mu}$. These dependencies necessitate two types of iterative targeting. Within-nuisance targeting is required given that the submodel for $\hat{\pi}$ depends on itself. As the estimate is updated, its submodel must also be updated, requiring re-targeting within $\hat{\pi}$. Across-nuisance targeting is also needed as updating one nuisance parameter affects the loss function or submodel for the other nuisance parameter. This dependency requires returning to the first nuisance and re-targeting it using the updated information from the second.

We begin by targeting $\hat{\pi}$ through within-nuisance iterative updates. Once convergence is reached according to a pre-specified stopping criterion $C_{n,\text{stop}} = o_P(n^{-1/2})$, we target $\hat{\mu}$ in one step, then re-target $\hat{\pi}$ with the updated $\hat{\mu}$. This process is iterated until the nuisance estimates render the empirical first-order bias below $C_{n,\text{stop}}$.

Let $\hat{Q}^{(t,0)} = \{\hat{\mu}^{(t)}, \hat{\pi}^{(t,0)}, \hat{f}_Z, \hat{p}_W\}$ denote the nuisance estimates after completing the t -th across-nuisance targeting iteration. We initialize the process by setting $\hat{\mu}^{(0)} = \hat{\mu}$ and $\hat{\pi}^{(0,0)} = \hat{\pi}$, so $\hat{Q}^{(0,0)} = \hat{Q}$. The second index in the superscript of $\hat{\pi}$ and \hat{Q} is reserved to track the within-nuisance targeting updates for the estimate of π . Specifically, $\hat{\pi}^{(t,t')}$ denotes the estimate of π obtained after the t' -th within-nuisance targeting step, which initialized at $\hat{\pi}^{(t,0)}$. Correspondingly, $\hat{Q}^{(t,t')}$ denotes the collection of nuisance estimates that incorporates

$\hat{\pi}^{(t,t')}$ as the estimate of π .

At across-nuisance iteration t , with the current nuisance estimates as $\hat{Q}^{(t,0)}$, we follow targeting steps (T1-2) to arrive at $\hat{Q}^{(t+1,0)}$.

(T1): *Iterative risk minimization for π* . Given $\hat{\pi}^{(t,0)}$ as a starting point, the within-nuisance targeting is iteratively performed to update $\hat{\pi}^{(t,t')}$ to $\hat{\pi}^{(t,t'+1)}$.

We aim to find $\hat{\varepsilon}_X^{(t,t'+1)}$ that minimizes the loss function L_X . The optimization problem can be solved via a weighted logistic regression without intercept: $\mathbb{I}(X = x_0) \sim \text{offset}(\hat{\pi}^{(t,t')}(x_0|Z, W)) + \hat{H}_X^{(t,t')}(Z, W)$, with weight $\tilde{p}(Z)/\hat{f}_Z(Z|W)$, where $\hat{H}_X^{(t,t')}(Z, W)$ denotes the auxiliary variable evaluated using $\hat{Q}^{(t,t')}$. The auxiliary variable's coefficient is $\hat{\varepsilon}_X^{(t,t'+1)}$ which solves $\arg \min_{\varepsilon_X \in \mathbb{R}} P_n \Phi_{X,x_0}(\hat{Q}^{(t,t')}; \tilde{p}_z)$. Following update is then made:

$$\hat{\pi}^{(t,t'+1)}(\hat{\varepsilon}_X^{(t,t'+1)}; \hat{\mu}^{(t)}, \hat{f}_Z) = \text{expit}\left\{\text{logit}\hat{\pi}^{(t,t')}(x_0 | z^*, W) + \hat{\varepsilon}_X^{(t,t'+1)} \hat{H}_X^{(t,t')}(Z, W)\right\}.$$

This step is repeated until the pre-specified stopping criterion $C_{n,\text{stop}}$ is satisfied at some iteration t_X^* , where we have: $P_n \Phi_{X,x_0}(\hat{Q}^{(t,t_X^*)}; \tilde{p}(Z)) \leq C_{n,\text{stop}}$. This concludes (T1), with the latest update as $\hat{\pi}^{(t,t_X^*)}$. Given the nuisance estimates collection $\hat{Q}^{(t,t_X^*)} = \{\hat{\mu}^{(t)}, \hat{\pi}^{(t,t_X^*)}, \hat{f}_Z, \hat{p}_W\}$, we then proceed to step (T2) for updating $\hat{\mu}^{(t)}$.

(T2): *One-step risk minimization for μ* . $\hat{\mu}^{(t)}$ is updated by finding $\hat{\varepsilon}_Y^{(t+1)}$ that minimizes the loss function L_Y . The optimization problem can be solved via a weighted regression: $Y \sim \text{offset}(\hat{\mu}^{(t)}(x_0, Z, W))$, with weight $\hat{H}_Y^{(t,t_X^*)}(Z, W; \tilde{p}_z) = \{\mathbb{I}(X = x_0) \tilde{p}(Z)\}/\{\kappa_{x_0,2}^{\text{pi}}(\hat{Q}^{(t,t_X^*)}; Z) \hat{f}_Z(Z|W)\}$, where $\hat{H}_Y^{(t,t_X^*)}$ denotes the weight variable evaluated using $\hat{Q}^{(t,t_X^*)}$. The intercept coefficient gives $\hat{\varepsilon}_Y^{(t+1)}$, satisfying:

$$\hat{\varepsilon}_Y^{(t+1)} = \arg \min_{\varepsilon_Y \in \mathbb{R}} P_n \Phi_{Y,x_0}(\hat{Q}^{(t,t_X^*)}; \tilde{p}_z).$$

The following updates are then made: $\hat{\mu}^{(t+1)}(x_0, Z, W) = \hat{\mu}^{(t)}(x_0, Z, W) + \hat{\varepsilon}_Y^{(t+1)}$ and $\hat{Q}^{(t+1,0)} = \{\hat{\mu}^{(t+1)}, \hat{\pi}^{(t+1,0)}, \hat{f}_Z, \hat{p}_W\}$, where, for notational convenience, $\hat{\pi}^{(t+1,0)} := \hat{\pi}^{(t,t_X^*)}$.

The procedure repeats steps (T1) and (T2) until reaching a final across-nuisance iteration t^* , defined as the first iteration for which both $P_n \Phi_{Y,x_0}(\hat{Q}^{(t^*,0)}; \tilde{p}_z) \leq C_{n,\text{stop}}$ and $P_n \Phi_{X,x_0}(\hat{Q}^{(t^*,0)}; \tilde{p}_z) \leq C_{n,\text{stop}}$. We let $\hat{Q}^* = \hat{Q}^{(t^*,0)}$.

Although the combination of within-nuisance and across-nuisance targeting may appear complex, in practice convergence is typically achieved within about five iterations in both our simulation studies and the real data application.

A full presentation of the TMLE procedure is provided in Algorithm 2 in Appendix D.3.

The estimators developed here are equally applicable when Z is discrete under some modifications. First, in constructing these estimators, $\kappa_{x_0,2}^{\text{pi}}$ should be replaced by the corresponding AIPW estimator $\kappa_{x_0,2}^{\text{aipw}}$, since this substitution is feasible when Z is discrete and enhances the robustness properties of the resulting TMLE. Second, $\tilde{p}(Z)$ should be specified as a probability mass function, assigning nonnegative point mass $\tilde{p}(z^*)$ to each observed level z^* of Z . A special case arises when focusing on a fixed level z^* with $\tilde{p}(z^*) = 1$, in which the TMLE procedure simplifies as described below.

When Z is fixed at z^* under discrete setting, the targeting procedure reduces to only within-nuisance iterations. This distinction arises from differences in the corresponding influence functions. In particular, across-nuisance iterative targeting for $\hat{\mu}$ is no longer required, since the term $1/\kappa_{x_0,2}(Q; z^*)$ in the loss function for Y is constant and can be omitted when defining the loss function and submodel, thereby removing its dependence on the estimate of π , while still satisfying the requirement that the derivative of the loss function at ε_Y is proportional to the corresponding component of the IF. In comparison, when Z is continuous, $1/\kappa_{x_0,2}(Q; Z_i)$ is a function of Z , dependent on π , that varies across observations, and thus must be retained. As a result, the estimate of μ must be re-targeted whenever the estimate of π is updated. We now outline the simplified TMLE procedure.

We start by targeting $\hat{\mu}$ to obtain $\hat{\mu}^*$, then update $\hat{\pi}$ to obtain $\hat{\pi}^*$, while keeping \hat{f}_Z and \hat{p}_W unchanged. The submodels and loss functions for $\hat{\mu}$ and $\hat{\pi}$ are given as:

$$L_Y(\tilde{\mu}; \hat{f}_Z) = \{\mathbb{I}(X = x_0, Z = z^*) / \hat{f}_Z(z^* | W)\} \{Y - \tilde{\mu}(x_0, z^*, W)\}^2 ,$$

$$\hat{\mu}(\varepsilon_Y) = \hat{\mu}(x_0, z^*, W) + \varepsilon_Y ,$$

$$L_X(\tilde{\pi}) = -\{\mathbb{I}(Z = z^*) / \hat{f}_Z(z^* | W)\} \log \tilde{\pi}(X | Z, W) ,$$

$$\hat{\pi}(\varepsilon_X; \hat{f}_Z, \hat{\mu}, \hat{\pi}) = \text{expit}\{\text{logit}\hat{\pi}(x_0 | z^*, W) + \varepsilon_X \hat{H}_X(z^*, W)\} ,$$

where $\hat{H}_X(z^*, W) = \hat{\mu}^*(x_0, z^*, W) - \psi_{x_0}^{\text{pi}}(\hat{Q}; z^*)$.

These choices are suitable when Y is continuous. For binary outcomes, we provide alternative specifications in Appendix D.2.

These two nuisance estimates are updated through a risk minimization process to find $\hat{\varepsilon}_Y$ and $\hat{\varepsilon}_X$ which minimize their respective loss functions.

(T1): *Risk minimization for μ .* The optimization problem for finding $\hat{\varepsilon}_Y$ can be achieved via a weighted regression: $Y \sim \text{offset}(\hat{\mu}(x_0, z^*, W)) + 1$, with weight $\mathbb{I}(X = x_0, Z = z^*) / \hat{f}_Z(z^* | W)$. The intercept coefficient gives $\hat{\varepsilon}_Y$, satisfying: $\hat{\varepsilon}_Y = \arg \min_{\varepsilon_Y \in \mathbb{R}} P_n \Phi_{Y, x_0}(\hat{Q}; z^*)$. We then update $\hat{\mu}^* = \hat{\mu}(x_0, z^*, W) + \hat{\varepsilon}_Y$ and set $\hat{Q} = \{\hat{\mu}^*, \hat{\pi}, \hat{f}_Z, \hat{p}_W\}$.

(T2): *Iterative risk minimization for π .* Updating $\hat{\pi}$ requires an iterative procedure because changes to $\hat{\pi}$ affect the auxiliary variable $\hat{H}_X(z^*, W)$ through $\psi_{x_0}(\hat{Q}; z^*)$. Thus, each update to $\hat{\pi}$ necessitates recomputing $\hat{H}_X(z^*, W)$ and re-solving the risk minimization problem. Let $\hat{\pi}^{(t)}$ and $\hat{H}_X^{(t)}(z^*, W)$ denote the estimate and auxiliary variable at the t -th iteration, where $t = 0$ corresponds to the initial estimates. Let $\hat{\varepsilon}_X^{(t)}$ denote the optimizer at the t -th iteration, for $t \geq 1$. Let $\hat{Q}^{(t)} = \{\hat{\mu}^*, \hat{\pi}^{(t)}, \hat{f}_Z, \hat{p}_W\}$.

With estimates from the t -th iteration, $\hat{\varepsilon}_X^{(t+1)}$ is obtained via a weighted logistic regression without an intercept: $\mathbb{I}(X = x_0) \sim \text{offset}(\hat{\pi}^{(t)}(x_0 | z^*, W)) + \hat{H}_X^{(t)}(z^*, W)$, with weight $\mathbb{I}(Z = z^*) / \hat{f}(z^* | W)$. The auxiliary variable's coefficient solves: $\hat{\varepsilon}_X^{(t+1)} = \arg \min_{\varepsilon_X \in \mathbb{R}} P_n \Phi_{X, x_0}(\hat{Q}^{(t)}; z^*)$.

Updates are then applied as: $\hat{\pi}^{(t+1)}(\hat{\varepsilon}_X^{(t+1)}; \hat{f}_Z, \hat{\mu}^*, \hat{\pi}^{(t)}) = \text{expit}\{\log\hat{\pi}^{(t)}(x_0|z^*, W) + \hat{\varepsilon}_X^{(t+1)}\hat{H}_x^{(t)}(z^*, W)\}$ and $\hat{Q}^{(t+1)} = \{\hat{\mu}^*, \hat{\pi}^{(t+1)}, \hat{f}_Z, \hat{p}_W\}$.

The iteration in step (T2) is terminated once at some iteration t^* , $P_n\Phi_{X,x_0}(\hat{Q}^{(t^*)}; z^*) \leq C_{n,\text{stop}}$ for $C_{n,\text{stop}} = o_P(n^{-1/2})$. Let $\hat{\pi}^* = \hat{\pi}^{(t^*)}$ and $\hat{Q}^* = \{\hat{\mu}^*, \hat{\pi}^*, \hat{f}_Z, \hat{p}_W\}$.

The TMLE under discrete Z , denoted by $\psi_{x_0}(\hat{Q}^*; z^*)$, is a plug-in estimator:

$$\psi_{x_0}(\hat{Q}^*; z^*) = \frac{1}{n} \sum_{i=1}^n \hat{\mu}^*(x_0, z^*, W_i) \hat{\pi}^*(x_0 | z^*, W_i) / \left(\frac{1}{n} \sum_{i=1}^n \hat{\pi}^*(x_0 | z^*, W_i) \right), \quad (11)$$

A full presentation of the TMLE procedure is provided in Algorithm 1 in Appendix D.3.

Remark 7. *The iterative update for π can be avoided by using the IPW estimator, rather than the plug-in estimator, for $\psi_{x_0}(Q; z^*)$ when defining $\hat{H}_X(z^*, W)$. This is because the plug-in estimator for $\psi_{x_0}(Q; z^*)$ depends directly on $\hat{\pi}$, whereas the IPW estimator depends only on the nuisance estimate \hat{f}_Z . Consequently, updating π does not require re-estimating the auxiliary variable $\hat{H}_X(z^*, W)$, and iterations can be avoided. Nevertheless, we adopt the plug-in estimator for $\psi_{x_0}(Q; z^*)$ in constructing TMLEs to ensure a consistent and parallel presentation of the TMLE algorithm for both discrete and continuous Z . In the latter case, a regular IPW estimator that does not involve an estimate of π is not available, making the plug-in estimator the more favorable choice.*

3.2 Asymptotic linearity

We now examine the asymptotic behaviors of our proposed estimators in Section 3.1. Given an influence-function based estimator $\psi_{x_0}(\hat{Q})$ of the parameter $\psi_{x_0}(Q)$, we can write the von Mises expansion as:

$$\psi_{x_0}(\hat{Q}) - \psi_{x_0}(Q) = P_n\Phi_{x_0}(Q) + (P_n - P)\{\Phi_{x_0}(\hat{Q}) - \Phi_{x_0}(Q)\} + R_2(\hat{Q}, Q). \quad (12)$$

The first term in the expansion is the sample average of $\Phi_{x_0}(Q)$ which is mean zero, and thus enjoys $o_P(n^{-1/2})$ asymptotic behavior according to the central limit theorem.

The second term is an empirical process term, and enjoys $o_P(n^{-1/2})$ asymptotic behavior if $P\{\Phi_{x_0}(\hat{Q}) - \Phi_{x_0}(Q)\}^2 = o_P(1)$ and $\Phi_{x_0}(\hat{Q}) - \Phi_{x_0}(Q)$ falls in a P-Donsker class with probability tending to 1, where P-Donsker condition limits the complexity of the nuisance models. This condition can be avoided if sample splitting or cross-fitting is adopted for nuisance estimation (Zheng & Van Der Laan 2010, Chernozhukov et al. 2018). Consequently, the asymptotic linearity of $\psi_{x_0}(\hat{Q})$ is achieved if the third term enjoys $o_P(n^{-1/2})$ asymptotic behavior, which would then entail rate conditions on nuisance estimates in \hat{Q} . Below, we derive the form of the R_2 term for our estimators, and determine rate conditions on the nuisance estimates to ensure $R_2 = o_P(n^{-1/2})$.

3.2.1 Inference under continuous Z

We first examine the asymptotic linearity of the three proposed estimators for $\psi_{x_0}(Q; \tilde{p}_z)$ in (2): the estimating-equation estimator $\psi_{x_0}^{\text{ee}}(\hat{Q}; \tilde{p}_z)$ defined in Section 3.1.1 and (6); the one-step estimator $\psi_{x_0}^+(\hat{Q}; \tilde{p}_z)$ defined in Section 3.1.2 and (8); and the TMLE $\psi_{x_0}(\hat{Q}^*; \tilde{p}_z)$ defined in Section 3.1.3 and (10). We use the one-step estimator as the representative case to present the results, which apply analogously to the other two estimators.

Let $\|f\| = (Pf^2)^{1/2}$ denote the $L^2(P)$ -norm of the function f . Under the regularity conditions detailed in Appendix B.3.4, $R_2(\hat{Q}, Q)$ can be bounded above by a product of $L^2(P)$ norms, for some finite positive constant C :

$$R_2(\hat{Q}, Q) \leq C \left\{ \|\hat{f}_Z - f_Z\| \|\hat{\mu} - \mu\| + \|\hat{f}_Z - f_Z\| \|\hat{\pi} - \pi\| + \|\hat{\pi} - \pi\|^2 + \|\hat{\pi} - \pi\| \|\hat{\mu} - \mu\| \right\}. \quad (13)$$

See a proof in Appendix B.3.3.

We have the following theorem establishing asymptotic linearity of the one-step estimator $\psi_{x_0}^+(\hat{Q}; \tilde{p}_z)$ (and equivalently the other two estimators).

Theorem 8. *Assume the $L^2(P)$ convergence of nuisance estimates in \hat{Q} are as follows:*

$\|\hat{\pi} - \pi\| = o_P(n^{-\frac{1}{k}})$, $\|\hat{f}_Z - f_Z\| = o_P(n^{-\frac{1}{b}})$, $\|\hat{\mu} - \mu\| = o_P(n^{-\frac{1}{q}})$. Under the regularity conditions discussed in Appendix B.3.4, if $\frac{1}{b} + \frac{1}{q} \geq \frac{1}{2}$, $\frac{1}{k} + \frac{1}{b} \geq \frac{1}{2}$, $\frac{1}{k} \geq \frac{1}{4}$, and $\frac{1}{k} + \frac{1}{q} \geq \frac{1}{2}$ jointly hold, then the one-step estimator $\psi_{x_0}^+(\hat{Q}; \tilde{p}_z)$ is asymptotically linear, that is:

$$\psi_{x_0}^+(\hat{Q}; \tilde{p}_z) - \psi_{x_0}(Q; \tilde{p}_z) = P_n \Phi_{x_0}(Q; \tilde{p}_z) + o_P(n^{-1/2})$$

where $\Phi_{x_0}(Q; \tilde{p}_z)$ is given in Lemma 3.

This theorem requires $\hat{\pi}$ to converge at least at rate $o_P(n^{-1/4})$ for the estimators to be asymptotically linear. The condition arises because the plug-in estimator of $\kappa_{x_0,2}$ depends on $\hat{\pi}$. The robustness property of our estimators is formalized in the following corollary.

Corollary 9. $\psi_{x_0}^+(\hat{Q}; \tilde{p}_z)$ is consistent for $\psi_{x_0}(Q; \tilde{p}_z)$ if $\|\hat{\pi} - \pi\| = o_P(1)$ and further either (i) $\|\hat{\mu} - \mu\| = o_P(1)$, or (ii) $\|\hat{f}_Z - f_Z\| = o_P(1)$, or both (i) and (ii) hold.

3.2.2 Inference under discrete Z

We now examine the asymptotic linearity of our proposed estimators for $\psi_{x_0}(Q; z^*)$ in (1). We use the one-step estimator $\psi_{x_0}^+(\hat{Q}; z^*)$, defined in Section 3.1.2 and (9), as the representative case to present the results, which apply analogously to the other two estimators: the estimating-equation estimator $\psi_{x_0}^{\text{ee}}(\hat{Q}; z^*)$ defined in Section 3.1.1 and (7); and the TMLE $\psi_{x_0}(\hat{Q}^*; z^*)$ defined in Section 3.1.3 and (11).

Under the regularity conditions discussed in Appendix B.3.2, $R_2(\hat{Q}, Q)$ can be bounded above by a product of $L^2(P)$ norms, for some finite positive constant C :

$$R_2(\hat{Q}, Q) \leq C \left\{ \|\hat{f}_Z - f_Z\| \times \|\hat{\mu} - \mu\| + \|\hat{f}_Z - f_Z\| \times \|\hat{\pi} - \pi\| \right\}. \quad (14)$$

See a proof in Appendix B.3.1.

Building on this formulation, the theorem below specifies rate conditions under which the R_2 term is $o_P(n^{-1/2})$, thereby ensuring the asymptotic linearity of our proposed estimators.

Theorem 10. Assume the $L^2(P)$ convergence rates of nuisance estimates in \hat{Q} are as follows: $\|\hat{\pi} - \pi\| = o_P(n^{-\frac{1}{k}})$, $\|\hat{f}_Z - f_Z\| = o_P(n^{-\frac{1}{b}})$, $\|\hat{\mu} - \mu\| = o_P(n^{-\frac{1}{q}})$. Under the

regularity conditions discussed in Appendix B.3.2, if $\frac{1}{b} + \frac{1}{q} \geq \frac{1}{2}$ and $\frac{1}{k} + \frac{1}{b} \geq \frac{1}{2}$, then the one-step estimator $\psi_{x_0}^+(\hat{Q}; z^*)$ is asymptotically linear, that is: $\psi_{x_0}^+(\hat{Q}; z^*) - \psi_{x_0}(Q; z^*) = P_n \Phi_{x_0}(Q; z^*) + o_P(n^{-1/2})$ where $\Phi_{x_0}(Q; z^*)$ is the influence function described in Remark 4.

The above results suggest that the relevant nuisance parameters can be estimated at rates slower than $o_P(n^{-1/2})$, thereby broadening the applicability of flexible machine learning and statistical models for nuisance estimation. An immediate corollary of Theorem 10 is that our estimators are doubly robust, as formalized below.

Corollary 11. $\psi_{x_0}^+(\hat{Q}; z^*)$ is consistent for $\psi_{x_0}(Q; z^*)$ if either (i) $\|\hat{\pi} - \pi\| = o_P(1)$ and $\|\hat{\mu} - \mu\| = o_P(1)$, or (ii) $\|\hat{f}_Z - f_Z\| = o_P(1)$, or both (i) and (ii) hold.

The double robustness property of $\psi_{x_0}^+(\hat{Q}; z^*)$ follows from the double robustness of the influence-function-based estimators for $\kappa_{x_0,1}(Q; z^*)$ and $\kappa_{x_0,2}(Q; z^*)$. This is most easily seen in the estimator $\psi_{x_0}^{\text{ee}}(\hat{Q}; z^*)$, defined as the ratio of two AIPW estimators, $\kappa_{x_0,1}^{\text{aipw}}(\hat{Q}; z^*)$ and $\kappa_{x_0,2}^{\text{aipw}}(\hat{Q}; z^*)$. Existing theory for AIPW estimators in back-door models (Robins et al. 1994) implies that $\kappa_{x_0,1}^{\text{aipw}}(\hat{Q}; z^*)$ is a consistent estimator of $\kappa_{x_0,1}(Q; z^*)$ if either \hat{f}_Z is consistent, or both $\hat{\mu}$ and $\hat{\pi}$ are consistent. Similarly, $\kappa_{x_0,2}^{\text{aipw}}(\hat{Q}; z^*)$ is consistent for $\kappa_{x_0,2}(Q; z^*)$ if either \hat{f}_Z or $\hat{\pi}$ is consistent. Consequently, the estimator $\psi_{x_0}^{\text{ee}}(\hat{Q}; z^*)$ inherits double robustness as long as conditions are met to ensure the consistency of both $\kappa_{x_0,1}^{\text{aipw}}(\hat{Q}; z^*)$ and $\kappa_{x_0,2}^{\text{aipw}}(\hat{Q}; z^*)$. The same intuition applies to the other two influence function-based estimators.

4 Efficiency gains in a semiparametric Napkin model

4.1 Model constraint

The statistical model for the observed variables in a latent DAG model is defined by *equality restrictions* of two types: (i) ordinary independences, implied by the d-separation rules (Pearl 2009), and (ii) generalized independences or Verma constraints, which correspond

to independences in post-intervention distributions where certain variables are fixed by intervention (Verma & Pearl 1990, Spirtes et al. 2001). When no such restrictions are present, the model is nonparametrically saturated (Bhattacharya et al. 2022).

The Napkin model is not saturated. The missing edge between Z and Y does not encode an ordinary conditional independence but rather a Verma constraint; a generalized independence that arises in the post-intervention distribution where Z is fixed, as depicted by the conditional DAG in Figure 1(c). An intervention on a variable removes all incoming edges to that variable and fixes it at a specified level. Using the d-separation rules on the conditional DAG, one can read the implied independence $Z \perp Y \mid X$.

This graphical restriction translates into a probabilistic form through the corresponding post-intervention Markov kernel (Richardson et al. 2023), denoted $q(Y, X, W \mid Z)$, defined as

$$q(Y, X, W \mid Z) = p(Y \mid X, Z, W) p(X \mid Z, W) p(W) .$$

The Verma constraint suggests that $q(Y \mid X, Z)$ is invariant to Z , where $q(Y \mid X, Z)$ denotes the conditional kernel of Y given X , when Z is intervened on, and derived as:

$$q(Y \mid X, Z) = \frac{\int q(Y, X, w \mid Z) dw}{\int q(y, X, w \mid Z) dy dw} = \frac{\int p(Y \mid X, Z, w) p(X \mid Z, w) p(w) dw}{\int p(X \mid Z, w) p(w) dw} , \quad (15)$$

where y and w are values in the respective domains of Y and W . The semiparametric model for the Napkin graph is defined as the set of observed-data distributions $p(Y, X, Z, W)$ that satisfy this equality constraint. The next subsection outlines heuristics for constructing more efficient estimators that leverage this constraint.

The Verma constraint, namely the expression in (15) being invariant to Z , closely aligns with the identification functional in (1), revealing a fundamental connection between the two. Specifically, the identification functional corresponds to a mean-level version of (15), reflecting that $\mathbb{E}_q(Y \mid X = x_0, Z = z^*)$ is invariant to z^* , where \mathbb{E}_q denotes expectation taken

with respect to the Markov kernel $q(Y, X, W|Z)$.

4.2 Deriving more efficient estimators

The identification functional in (1) can be viewed as a mapping from the distribution P and a value $z^* \in \mathcal{Z}$ to the real line. The Verma constraint ensures that for a fixed P this mapping yields the same value for all $z^* \in \mathcal{Z}$. However, the gradient of the identification functional may differ across values of z^* , which affects the relative efficiency of the corresponding estimators. Thus, while the estimand itself is invariant, certain choices of z^* may result in more efficient estimators than others.

Consider the case where Z is discrete, and assume for simplicity that it is binary. The extension to discrete Z with more than two levels is provided in Appendix B.4. With the influence functions $\Phi_{x_0}(Q; z^* = 1)$ and $\Phi_{x_0}(Q; z^* = 0)$, a class of influence functions can be constructed as a weighted average of the two: $\alpha \times \Phi_{x_0}(Q; z^* = 1) + (1 - \alpha) \times \Phi_{x_0}(Q; z^* = 0)$, where $\alpha \in \mathbb{R}$. The optimal choice of α , denoted as α^{opt} , can be found by minimizing the variance of the weighted influence functions, with the proof given in Appendix B.4:

$$\begin{aligned} \alpha^{\text{opt}} &= \underset{\alpha \in \mathbb{R}}{\operatorname{argmin}} \operatorname{Var}\{\alpha \times \Phi_{x_0}(Q; z^* = 1) + (1 - \alpha) \times \Phi_{x_0}(Q; z^* = 0)\} \\ &= \frac{\mathbb{E}[\Phi_{x_0}(Q; z^* = 0) (\Phi_{x_0}(Q; z^* = 0) - \Phi_{x_0}(Q; z^* = 1))]}{\mathbb{E}[(\Phi_{x_0}(Q; z^* = 0) - \Phi_{x_0}(Q; z^* = 1))^2]}. \end{aligned} \quad (16)$$

A unique solution for α^{opt} exists, given that the optimization problem is quadratic and convex. The optimal weight is estimated using \hat{Q} and empirically evaluating the expectations in (16). Let $\hat{\alpha}^{\text{opt}}$ denote the estimate. For illustration, the resulting optimal one-step estimator, denoted by $\psi_{x_0}^{+, \text{opt}}(\hat{Q}; z^*)$, is given by:

$$\psi_{x_0}^{+, \text{opt}}(\hat{Q}; z^*) = \hat{\alpha}^{\text{opt}} \times \psi_{x_0}^+(\hat{Q}; z^* = 1) + (1 - \hat{\alpha}^{\text{opt}}) \times \psi_{x_0}^+(\hat{Q}; z^* = 0).$$

The optimal estimating equation estimator and TMLE are defined analogously and denoted

by $\psi_{x_0}^{\text{ee},\text{opt}}(\hat{Q}; z^*)$, and $\psi_{x_0}^{\text{opt}}(\hat{Q}^*; z^*)$, respectively.

When Z is continuous, a class of influence functions can be defined, indexed by the weighting function $\tilde{p}(Z)$. Identifying an optimal choice of $\tilde{p}(Z)$ is challenging, since infinitely many choices exist. We therefore recommend exploring several candidates and selecting the one that yields the most efficient estimator through numerical comparisons.

5 Simulations

We conducted five sets of simulation studies to assess the statistical properties of the proposed estimators and to evaluate their performance under various challenging scenarios: (1–2) On *theoretical properties*, examining the asymptotic behavior and robustness of the estimators under the proposed conditions; (3) On *weak overlap*, evaluating estimators' performances when the positivity assumption is nearly violated; (4) On *model misspecification*, comparing performances when nuisance parameters are estimated using misspecified parametric models versus flexible machine learning methods; and (5) On *cross-fitting*, investigating the impact of applying versus omitting cross-fitting when flexible machine learning methods are used for nuisance estimation. Across all simulations, we focused on the ATE and denoted the corresponding ATE estimators by omitting the subscript x_0 .

The [napkincausal](#) package in R, developed to implement the proposed estimators, is available at [annaguo-bios/napkincausal](#). The simulation code, which depends on this package, is provided separately at [annaguo-bios/Napkin-paper](#).

Simulation 1: Asymptotic linearity. We evaluated the asymptotic bias and variance of the proposed estimators under the conditions specified in Theorem 10 for binary Z and Theorem 8 for continuous Z . The corresponding data-generating processes (DGPs) are described in Appendix E.1. For binary Z , we assessed the three proposed estimators

at $z^* = 1$ and $z^* = 0$, along with the estimators constructed using the optimal weights described in Section 4.2. For continuous Z , we examined the three estimators under two specifications of \tilde{p}_z , a Normal and a Uniform distribution, each with valid support on Z .

All estimators exhibited the expected convergence behavior, with notable efficiency gains achieved through the use of the Verma constraint. Specifically, with binary Z , estimators that incorporate the optimal weight attained variances that were approximately three times smaller than those using $z^* = 1$ and about 1.5 times smaller than those using $z^* = 0$. A similar pattern was observed under continuous Z , where specifying \tilde{p}_z as a Uniform distribution resulted in variances about 1.7 times smaller than when specifying it as a Normal distribution. For brevity, the detailed implementation procedures and results are provided in Appendix E.6, where Figure 3 presents the results under binary Z , and Figure 4 presents the results under continuous Z .

Simulation 2: Double robustness. We further evaluated the robustness of our estimators, as established in Corollaries 9 and 11. For continuous Z , \tilde{p}_z was set to a Uniform distribution with a valid support on Z , using the same DGP as in Simulation 1.

We assessed performance of these estimators at sample sizes 500, 1000, and 2000, with 1000 simulation replicates for each sample size. Nuisance parameters were estimated under three specifications: two implied by the corollaries, which are expected to yield consistent estimators, and one additional specification in which all nuisance models were misspecified. Details on model specifications for each scenario are provided in Appendix E.2. For all specifications, the estimators were evaluated based on five metrics: the average bias, standard deviation (SD), mean squared error (MSE), 95% confidence interval (CI) coverage, and average CI width. The same estimators, sample sizes, and evaluation metrics are used throughout the remaining simulations.

Across all scenarios, the estimators demonstrated the expected robustness property. Specifi-

Table 1: Simulation results validating the robustness property of the proposed estimators when Z is continuous, with pre-specified $\tilde{p}(Z) = \text{Uniform}(0.1, 0.25)$.

	TMLEs			One-step estimators			Estimating equations			
	<i>Correct model(s)</i>	f_Z, π	μ, π	<i>None</i>	f_Z, π	μ, π	<i>None</i>	f_Z, π	μ, π	<i>None</i>
n=500	Bias	0.003	0.003	-0.169	0.003	0.001	-1.574	0.003	0.006	-1.595
	SD	0.123	0.144	0.125	0.123	0.199	0.28	0.123	0.202	0.233
	MSE	0.015	0.021	0.044	0.015	0.04	2.557	0.015	0.041	2.598
	CI coverage	93.3%	100%	100%	93.4%	99.4%	79.6%	93.5%	98.9%	82%
	CI width	0.463	1.179	3.633	0.464	1.187	3.603	0.464	1.187	3.603
n=1000	Bias	0.003	0.006	-0.171	0.003	0.005	-1.583	0.003	0.008	-1.599
	SD	0.083	0.096	0.084	0.083	0.135	0.198	0.083	0.136	0.159
	MSE	0.007	0.009	0.036	0.007	0.018	2.545	0.007	0.019	2.583
	CI coverage	94.2%	100%	100%	94.3%	99.6%	6.4%	94.3%	99.6%	1.7%
	CI width	0.328	0.831	2.573	0.329	0.834	2.552	0.329	0.834	2.552
n=2000	Bias	0	0	-0.175	0	0.001	-1.586	0	0.002	-1.6
	SD	0.059	0.07	0.059	0.059	0.1	0.136	0.059	0.101	0.108
	MSE	0.003	0.005	0.034	0.003	0.01	2.533	0.003	0.01	2.57
	CI coverage	95.7%	100%	100%	95.6%	99.4%	0%	95.7%	99.4%	0%
	CI width	0.232	0.589	1.821	0.233	0.59	1.805	0.233	0.59	1.805

cally, under the two specifications implied by the corollaries, the average bias approached zero as the sample size increased. In contrast, when all models were misspecified, a persistent nonzero bias remained even at large sample sizes. Results for the continuous Z are shown in Table 1, and those for binary Z appear in Appendix Table 7.

Simulation 3: Weak overlap. We compared the performance of the proposed estimators under weak overlap (or near-positivity violation), a setting in which TMLEs have previously been shown to have better performance than others (Porter et al. 2011). Our analysis focused on the case with binary Z , as weak overlap in the Napkin model arises through f_Z , extreme values of which is more commonly observed when Z is binary. Specifically, we set $f_Z(1|W) = \text{expit}(-\frac{5}{6} + \frac{5}{3}W)$, which ranges from about 0.007 to 0.993 for $W \sim \text{Unif}(-2.5, 3.5)$, creating a weak-overlap scenario. The detailed DGP is provided in Appendix E.3.

Table 2: Comparison between TMLEs, onestep estimators, estimating equation estimators under weak overlapping when Z is binary. Results from the estimating equation estimator coincide with those of the one-step estimator up to three decimal places and are therefore omitted.

	$\psi(\hat{Q}^*; z^* = 0)$	$\psi^+(\hat{Q}; z^* = 0)$	$\psi(\hat{Q}^*; z^* = 1)$	$\psi^+(\hat{Q}; z^* = 1)$	$\psi^{\text{opt}}(\hat{Q}^*; z^*)$	$\psi^{+,\text{opt}}(\hat{Q}; z^*)$	
n=500	Bias	-0.025	-0.023	0	0.009	0	-0.121
	SD	0.235	0.839	0.159	0.336	0.13	0.276
	MSE	0.056	0.703	0.025	0.113	0.017	0.091
	CI coverage	97.1%	83.3%	97.5%	98.3%	96.7%	88.1%
n=1000	CI width	1.302	3.03	1.024	1.532	0.609	1.019
	Bias	-0.001	0.007	0	-0.007	0.003	-0.063
	SD	0.162	0.544	0.103	0.231	0.085	0.199
	MSE	0.026	0.296	0.011	0.053	0.007	0.043
n=2000	CI coverage	98.5%	88.4%	99.3%	98%	98.6%	90.4%
	CI width	0.938	2.289	0.791	1.131	0.487	0.831
	Bias	-0.001	-0.016	0	-0.002	0.003	-0.04
	SD	0.118	0.369	0.076	0.169	0.068	0.149
	MSE	0.014	0.136	0.006	0.029	0.005	0.024
	CI coverage	98.9%	91.8%	99.3%	98.6%	98.9%	94.8%
	CI width	0.713	1.679	0.613	0.898	0.39	0.672

Results are summarized in Table 2. Across all sample sizes and fixed levels of z^* , the TMLEs consistently outperform the other two estimators, exhibiting smaller bias, standard deviation, MSE, and CI coverage closer to the nominal 95% level.

Simulation 4: Misspecified models vs. flexible estimation. This simulation is motivated by the practical challenge that the true specifications of nuisance models are typically unknown, making model misspecification a common concern. We evaluated the performance of the proposed estimators under model misspecification and assessed whether incorporating more flexible machine learning methods can mitigate this issue, leveraging the fact that our estimators allow for such flexibility in nuisance estimation.

We compared three approaches for fitting nuisance models: linear models, Super Learner, and Super Learner with 10-fold cross-fitting. The linear models are misspecified by omitting key main effects, using incorrect link functions for logistic regression, or specifying an incorrect

Table 3: Comparative analysis of TMLEs, one-step, and estimating equation estimators under model misspecifications when Z is continuous, with pre-specified $\tilde{p}(Z) = \text{Uniform}(0.1, 0.25)$. Linear refers to generalized linear regressions, SL refers to Super Learner, and CF denotes Super Learner with cross fitting using 10 folds.

	TMLEs			One-step estimators			Estimating equations			
	Linear	SL	CF	Linear	SL	CF	Linear	SL	CF	
n=500	Bias	-0.167	0.026	0.028	-0.291	0.093	0.102	-0.291	-0.063	-0.063
	SD	0.177	0.144	0.146	0.204	0.2	0.204	0.204	0.096	0.096
	MSE	0.059	0.021	0.022	0.126	0.049	0.052	0.126	0.013	0.013
	CI coverage	97.4%	100%	100%	86%	97.9%	97.7%	85.9%	91.1%	91.1%
	CI width	1.026	1.16	1.198	1.022	1.153	1.19	1.022	0.375	0.375
n=1000	Bias	-0.172	0.022	0.023	-0.298	0.068	0.073	-0.298	-0.062	-0.062
	SD	0.113	0.094	0.095	0.131	0.132	0.133	0.131	0.069	0.069
	MSE	0.042	0.009	0.01	0.106	0.022	0.023	0.106	0.009	0.009
	CI coverage	95.2%	100%	100%	69.1%	99.2%	99.4%	68.9%	83.6%	83.6%
	CI width	0.727	0.825	0.84	0.724	0.819	0.834	0.724	0.265	0.265
n=2000	Bias	-0.173	0.012	0.013	-0.298	0.043	0.046	-0.297	-0.059	-0.059
	SD	0.083	0.068	0.068	0.097	0.095	0.095	0.097	0.049	0.049
	MSE	0.037	0.005	0.005	0.098	0.011	0.011	0.098	0.006	0.006
	CI coverage	84.8%	100%	100%	32.7%	99.6%	99.5%	33%	75.8%	75.8%
	CI width	0.514	0.588	0.594	0.512	0.584	0.591	0.512	0.187	0.187

parametric family for the conditional density f_Z . Details on DGPs, model specifications, and library of algorithms used in Super Learner are provided in Appendix E.4.

The results under continuous Z are shown in Table 3, and those for binary Z appear in Appendix Table 8. The results indicate that relying solely on main-term linear models led to persistent bias across all sample sizes. In contrast, employing the Super Learner for nuisance estimation reduced both bias and MSE as the sample size increased. Incorporating cross-fitting alongside the Super Learner produced comparable improvements.

Simulation 5: Impact of cross-fitting. We further examined the impact of cross-fitting by focusing on random forests, which prior work suggests perform less effectively when

Table 4: Comparative analysis for the impact of cross-fitting on TMLEs and one-step estimators in conjunction with the use of random forests under the first DGP, presented in Appendix E.1. RF refers to random forest with 500 trees and a minimum node size of 5 for a continuous variable and 1 for binary, and CF denotes random forest with cross fitting using 5 folds. $\tilde{p}(Z)$ is chosen as $\hat{p}(Z)$.

		n=500					n=1000					n=2000				
		Bias	SD	MSE	Coverage	CI width	Bias	SD	MSE	Coverage	CI width	Bias	SD	MSE	Coverage	CI width
TMLE	RF	-0.461	0.09	0.221	0.3%	0.08	-0.366	0.076	0.14	0.3%	0.06	-0.284	0.059	0.084	0.3%	0.047
	CF	-0.061	0.112	0.016	80.7%	0.338	-0.075	0.082	0.012	68.9%	0.246	-0.072	0.068	0.01	60.4%	0.195
One-step	RF	-0.659	0.09	0.442	0.7%	0.101	-0.514	0.061	0.268	0.2%	0.068	-0.396	0.07	0.162	0.5%	0.06
	CF	-0.134	0.169	0.047	66.8%	0.461	-0.143	0.09	0.029	43.5%	0.294	-0.124	0.072	0.02	34.9%	0.221

cross-fitting is not applied ([Chernozhukov et al. 2018](#), [Biau 2012](#)).

We analyzed DGPs of varying complexity. For binary Z , the DGP matched that in Simulation 4, exhibiting moderate complexity. For continuous Z , the DGP incorporated ten confounders with complex interactions and higher-order terms to create a more challenging scenario. Detailed specifications are provided in Appendix E.5.

Results for the continuous Z are reported in Table 4, and those for binary Z appear in Appendix Table 9. Cross-fitting reduced average bias and MSE and improved 95% CI coverage, with more pronounced improvements under the DGP with continuous Z . In both settings, it also increased SD and widened CIs, reflecting the bias–variance trade-off. Overall, these results indicate the benefit of cross-fitting for bias reduction when machine learning is used for nuisance estimation in complex high-dimensional settings.

6 Data application

We applied our proposed estimation framework to the Life Course 1971–2002 dataset from Finnish Social Science Data Archive ([Jorma 2018](#)). This longitudinal study follows 634 Finnish children born in 1964–1968 in Jyvaskyla, Finland, and collects detailed information on cognitive ability, family background, and educational outcomes to understand their

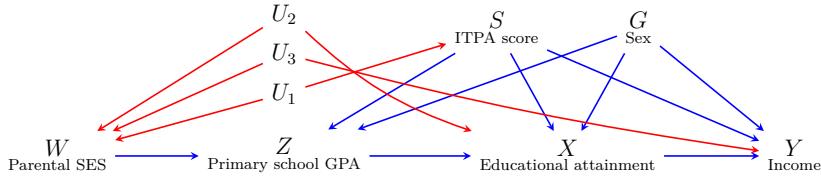


Figure 2: An illustration of the causal relationships among variables in the real data application.

impact on a person’s life course. In the early 1970s, when the children were aged between 3 and 9, the Illinois Test of Psycholinguistic Abilities (ITPA) was used to test their verbal intelligence. Information on participants’ major life events and socioeconomic outcomes were collected in 1984, 1991, and 2002.

Using our proposed estimation methods, we evaluate the causal effect of educational attainment on income, under the assumptions represented by the DAG in Figure 2, as introduced and justified by [Helske et al. \(2021\)](#). The graph aligns with the extended Napkin graph that includes measured confounders, with details on identification, estimation, and inference provided in Appendix C. Here, X denotes educational attainment, categorized into three levels: secondary or less, lower tertiary, and higher tertiary, and Y is yearly income (in euros) measured in 2000. Covariates include parental socioeconomic status (W ; low, middle, high), primary school GPA (Z), ITPA score (S), and sex (G ; male, female). Compared to the extended Napkin graph, this version assumes unmeasured confounding between W and measured confounder S rather than a direct effect from S to W . Despite this change, the identification functional remains valid under the proof provided in Appendix B.1.

We evaluated the causal effects in two ways: the pooled analysis using the entire population to understand the overall impact of educational attainment on income, and the subgroup analyses which use a categorized subsample based on sex and whether the ITPA score is below or above the sample average to explore effects within each subpopulation. Estimations are conducted using our three proposed estimators for continuous Z . Nuisances were estimated via semiparametric kernel methods and machine learning, detailed in Appendix F.

Table 5: ATEs of educational attainment on income comparing lower tertiary vs secondary or less, and higher vs lower tertiary: pooled and subgroup analyses by sex and ITPA scores. Estimates are shown with 95% confidence intervals in parentheses. In the pooled analysis, the estimating equation estimator coincides with the one-step estimator and is therefore omitted.

Sex ITPA (n)	Female		Male		Pooled
	Below avg (137)	Above avg (133)	Below avg (126)	Above avg (113)	Pooled (137)
Lower tertiary vs secondary or less					
TMLE	2523 (115,4930)	2945 (-1151,7041)	-464 (-4994,4065)	2214 (-2213,6642)	977 (-1559,3513)
One-step	2483 (67,4900)	2541 (-1702,6785)	-400 (-4933,4133)	2190 (-2230,6611)	1064 (-1466,3595)
Est Eq	2686 (270,5103)	2745 (-1499,6988)	501 (-4032,5034)	3181 (-1240,7601)	
Higher vs lower tertiary					
TMLE	4373 (713,8033)	6789 (736,12842)	-2006 (-8016,4004)	6346 (286,12407)	5575 (2685,8464)
One-step	4506 (740,8272)	6795 (76,13514)	-1937 (-8008,4134)	5630 (-383,11643)	5139 (2238,8039)
Est Eq	5097 (1332,8863)	6937 (218,13656)	-525 (-6596,5546)	6039 (26,12052)	

A detailed summary of the analysis results is presented in Table 5. Overall, our analysis demonstrates a positive causal effect of higher educational attainment on future income. The increase in average income is more substantial when comparing higher versus lower tertiary education than when comparing lower tertiary to secondary or lower education. This finding is consistent with the original analysis by [Helske et al. \(2021\)](#), which employed a plug-in estimator and reported average incomes (with 95% CI) under three educational interventions (from lowest to highest) as €19500 (19484, 19515), €21600 (21576, 21623), and €26600 (26558, 26641). Similar patterns are observed across subgroups defined by sex and ITPA score, except for males with below-average ITPA scores, where higher educational attainment is associated with a small, non-significant decrease in income.

7 Discussion

In this work, we proposed a flexible estimation framework for the average treatment effect under the Napkin graph. We developed three influence function-based estimators, namely the one-step estimator, the estimating equation estimator, and TMLE, and established their robustness properties along with the nuisance rate conditions required for achieving

asymptotic linearity. These theoretical results were complemented by simulation studies, addressing the gap in the literature where estimation of the ATE under the Napkin graph has been largely underexplored. A further contribution of this work is to highlight the role of the Verma constraint in the semiparametric Napkin model, resulting in large efficiency gains under simple data generating processes. Beyond the specific setting of the Napkin graph, our proposals contribute to the broader semiparametric efficiency literature, since Verma constraints arise in a wide class of causal latent DAG models. All proposed estimators are implemented in the [napkincausal](#) R package, enabling practitioners to readily apply our methods in practice.

This work also opens several avenues for future research. First, while we constructed efficient estimators by considering linear combinations of influence functions at each level of variable Z in the discrete case, and demonstrated constructing more efficient estimators via empirical evaluation when Z is continuous, an important next step is to theoretically derive the semiparametric efficient influence function for the Napkin graph. Such a result would inform the construction of a universally most efficient estimator regardless of whether Z is discrete or continuous. More generally, a systematic theory for deriving efficient influence functions in the presence of Verma constraints would extend the semiparametric efficiency theory, which is presently limited to ordinary equality constraints. Second, our framework assumes that the Napkin graph correctly represents the underlying data-generating process. In practice, developing statistical tests to assess the validity of this assumption would complement expert knowledge in causal model selection; see ([Bhattacharya & Nabi 2022](#)) and ([Guo et al. 2023](#)) for related tests in the front-door settings. Finally, incorporating the Napkin graph and other graphical models for which identification cannot be achieved through a single g-computation into general semiparametric estimation frameworks ([Bhattacharya et al. 2022](#), [Jung et al. 2024](#), [Guo & Nabi 2024](#)) would further expand the applicability of

causal inference methods in diverse applied settings.

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Appendix

The appendix is structured as follows. Appendix A offers a summary of the notations used throughout the manuscript to aid in understanding and reference. Appendix B provides proofs for the identification results, efficient influence function derivations, and all claims related to inference and robustness. Appendix C extends the main results to include measured confounders that affect all observed variables in the Napkin graph. It details how the identification, estimation, inference, and robustness results generalize to this broader setting. Appendix D provides additional details on the TMLE procedures and their extensions to binary outcomes. Appendices E and F present additional details for the simulation studies and the real data application, respectively.

A Glossary of terms and notations

Table 6: Glossary of terms and notations

Symbol	Definition	Symbol	Definition
X, x_0	Treatment, fixed assignment	$\pi(X Z, W)$	propensity score
Y, Y^{x_0}	Outcome, potential outcome	$\mu(X, Z, W)$	Outcome regression
W, Z	Observed covariates	$f_Z(Z W)$	Conditional density of Z
U	Unmeasured variables	p_W	Marginal density of W
O, P	Observed data, its distribution	Q	Collection of nuisances
$\psi_{x_0}(P; \tilde{p}_z)$	Target parameter with $\tilde{p}(Z)$	$\psi(P; z^*)$	Target parameter at z^*
$\kappa_{x_0,1}(P; z)$	Notations below focus on \tilde{p}_z		Similar rules apply for z^*
$\int y p(y x_0, z, w) p(x_0 z, w) p(w) dw$			$\int p(x_0 z, w) p(w) dw$
\mathcal{M}	Model space	$\kappa_{x_0,2}(P; z)$	Support of Z
$\psi^{\text{pi}}(\hat{Q}; \tilde{p}_z)$	Plug-in estimator of ψ_{x_0}	$\Phi_{x_0}(\hat{Q}; \tilde{p}_z)$	Influence function of ψ_{x_0}
$\kappa_{x_0,1}^{\text{pi}}(\hat{Q}; z)$	Plug-in estimator of $\kappa_{x_0,1}$	$\kappa_{x_0,2}^{\text{pi}}(\hat{Q}; z)$	Plug-in estimator of $\kappa_{x_0,2}$
$\kappa_{x_0,1}^{\text{aipw}}(\hat{Q}; z)$	AIPW estimator of $\kappa_{x_0,1}$	$\kappa_{x_0,2}^{\text{aipw}}(\hat{Q}; z)$	AIPW estimator of $\kappa_{x_0,2}$
$\psi_{x_0}^{\text{ee}}(\hat{Q}; \tilde{p}_z)$	Est equation (ee) estimator	$\psi_{x_0}^+(\hat{Q}; \tilde{p}_z)$	One-step estimator
$\psi_{x_0}(\hat{Q}^*, \tilde{p}_z)$	TMLE	$R_2(\hat{Q}, Q; \tilde{p}_z)$	Second-order remainder
\hat{Q}^*	Nuisance estimates in TMLE	$L_Y, \hat{\mu}(\varepsilon_Y)$	Loss function, submodel for μ
$L_X, \hat{\pi}(\varepsilon_X; \cdot)$	Loss function, submodel for π	$C_{n,\text{stop}}$	Stopping criterion in TMLE
$\ f\ $	$(Pf^2)^{1/2}$	$q(Y, X, W Z)$	Post-intervention Markov kernel
\mathbb{E}_q	Expectation wrt $q(Y, X, W Z)$	$\alpha, \alpha^{\text{opt}}$	Weight, optimal weight
$\psi_{x_0}^{\text{ee, opt}}(\hat{Q}; z^*)$	Optimal ee estimator	$\psi_{x_0}^{+, \text{opt}}(\hat{Q}; z^*)$	Optimal one-step estimator
$\psi_{x_0}^{\text{opt}}(\hat{Q}^*; z^*)$	Optimal TMLE		

B Proofs

B.1 Identification

The identification functional for $\mathbb{E}(Y^{x_0})$, equivalently $\mathbb{E}(Y | \text{do}(x_0))$, can be derived using Pearl's do-calculus rules (Pearl 2009). Let z^* be a value in \mathcal{Z} . Following the probability and do-calculus rules, the identification proceeds as follows:

$$\begin{aligned} p(y | \text{do}(x_0)) &= p(y | \text{do}(x_0), \text{do}(z^*)) && \text{(3rd rule of do-calculus)} \\ &= p(y | x_0, \text{do}(z^*)) && \text{(2nd rule of do-calculus)} \\ &= \frac{p(y, x_0 | \text{do}(z^*))}{p(x_0 | \text{do}(z^*))} && \text{(Bayes rule)} \\ &= \frac{\int p(y, x_0 | z^*, w) p(w) dw}{\int p(x_0 | z^*, w) p(w) dw}. && \text{(back-door rule)} \end{aligned}$$

Thus, given our nuisance notations, our parameter of interest is identified as:

$$\mathbb{E}(Y^{x_0}) = \frac{\int \mu(x_0, z^*, w) \pi(x_0 | z^*, w) p(w) dw}{\int \pi(x_0 | z^*, w) p(w) dw}.$$

The above functionals can also be derived using the identification algorithms of Richardson et al. (2023) and Bhattacharya et al. (2022). Specifically, Algorithm 2 in Bhattacharya et al. (2022) yields the following equivalent functional, known as the *nested-IPW*:

$$\mathbb{E}(Y^{x_0}) = \int \frac{\int \mu(x_0, z, w) \pi(x_0 | z, w) p(w) dw}{\int \pi(x_0 | z, w) p(w) dw} \tilde{p}(z) dz.$$

B.2 Estimation

B.2.1 Nonparametric efficient influence function for $\psi_{x_0}(Q; z^*)$

Let $\Phi_{x_0,1}(Q; z^*)$ and $\Phi_{x_0,2}(Q; z^*)$ denote the corresponding nonparametric efficient influence function (np-EIF) for $\kappa_{x_0,1}(Q; z^*)$ and $\kappa_{x_0,2}(Q; z^*)$, respectively. Following standard derivations in the literature, we have:

$$\begin{aligned}\Phi_{x_0,1}(Q; z^*)(O_i) &= \frac{\mathbb{I}(Z_i = z^*)}{f_Z(z^* | W_i)} \left(\mathbb{I}(X_i = x_0) Y_i - \mu(x_0, z^*, W_i) \pi(x_0 | z^*, W_i) \right) \\ &\quad + \mu(x_0, z^*, W_i) \pi(x_0 | z^*, W_i) - \kappa_{x_0,1}(Q; z^*) , \\ \Phi_{x_0,2}(Q; z^*)(O_i) &= \frac{\mathbb{I}(Z_i = z^*)}{f_Z(z^* | W_i)} \left(\mathbb{I}(X_i = x_0) - \pi(x_0 | z^*, W_i) \right) + \pi(x_0 | z^*, W_i) - \kappa_{x_0,2}(Q; z^*) .\end{aligned}$$

Using the delta method, the np-EIF for $\psi_{x_0}(Q; z^*)$, denoted by $\Phi_{x_0}(Q; z^*)$, is expressed as:

$$\Phi_{x_0}(Q; z^*)(O_i) = \frac{1}{\kappa_{x_0,2}(Q; z^*)} \Phi_{x_0,1}(Q; z^*)(O_i) - \frac{\kappa_{x_0,1}(Q; z^*)}{\kappa_{x_0,2}^2(Q; z^*)} \Phi_{x_0,2}(Q; z^*)(O_i) .$$

Substituting $\kappa_{x_0,1}$, $\kappa_{x_0,2}$, $\Phi_{x_0,1}$, and $\Phi_{x_0,2}$ with their explicit forms concludes the result.

B.2.2 Nonparametric efficient influence function for $\psi_{x_0}(Q; \tilde{p}_z)$

In the following, let $\tilde{P}(Z)$ denote the cumulative distribution function corresponding to $\tilde{p}(Z)$, and $o = \{y, x, z, w\}$ denote the realizations of the random variables $O = \{Y, X, Z, W\}$.

$$\begin{aligned}\frac{\partial}{\partial \varepsilon} \psi_{x_0}(P_\varepsilon; \tilde{p}_z) \Big|_{\varepsilon=0} &= \frac{\partial}{\partial \varepsilon} \int y \, dP_\varepsilon(y | x_0, z, w) \frac{dP_\varepsilon(x_0 | z, w)}{\int dP_\varepsilon(x_0 | z, w) \, dP_\varepsilon(w)} \, dP_\varepsilon(w) \, d\tilde{P}(z) \Big|_{\varepsilon=0} \\ &= \int y \, S(y | x_0, z, w) \, dP(y | x_0, z, w) \frac{dP(x_0 | z, w)}{\int dP(x_0 | z, w) \, dP(w)} \, dP(w) \, d\tilde{P}(z) \quad (17)\end{aligned}$$

$$+ \int y \, dP(y | x_0, z, w) \, \frac{\partial}{\partial \varepsilon} \left(\frac{dP_\varepsilon(x_0 | z, w)}{\int dP_\varepsilon(x_0 | z, w) \, dP_\varepsilon(w)} \right) \Big|_{\varepsilon=0} \, dP(w) \, d\tilde{P}(z) \quad (18)$$

$$+ \int y \, S(w) \, dP(y | x_0, z, w) \frac{dP(x_0 | z, w)}{\int dP(x_0 | z, w) \, dP(w)} \, dP(w) \, d\tilde{P}(z) . \quad (19)$$

Line 17 simplifies to

$$17 = \int \frac{\mathbb{I}(x = x_0)}{\kappa_{x_0,2}(Q; z)} \frac{\tilde{p}(z)}{f_Z(z | w)} \left(y - \mu(x_0, z, w) \right) S(o) \, dP(o) . \quad (20)$$

Line 18 simplifies to

$$18 = \int \mu(x_0, z, w) \left\{ \frac{S(x_0 | z, w) dP(x_0 | z, w)}{\kappa_{x_0,2}(Q; z)} - \frac{dP(x_0 | z, w) \int (S(x_0 | z, w) + S(w)) dP(x_0 | z, w) dP(w)}{\kappa_{x_0,2}^2(Q; z)} \right\} dP(w) d\tilde{P}(z) \\ = \int \mu(x_0, z, w) \frac{S(x_0 | z, w) dP(x_0 | z, w)}{\kappa_{x_0,2}(Q; z)} dP(w) d\tilde{P}(z) \quad (21)$$

$$- \int \mu(x_0, z, w) \frac{dP(x_0 | z, w) \int S(x_0 | z, w) dP(x_0 | z, w) dP(w)}{\kappa_{x_0,2}^2(Q; z)} dP(w, c) d\tilde{P}(z) \quad (22)$$

$$- \int \mu(x_0, z, w) \frac{dP(x_0 | z, w) \int S(w) dP(x_0 | z, w) dP(w)}{\kappa_{x_0,2}^2(Q; z)} dP(w) d\tilde{P}(z), \quad (23)$$

where 21, 22, and 23 can be further simplified as follows

$$21 = \int \frac{1}{\kappa_{x_0,2}(Q; z)} \frac{\tilde{p}(z)}{f_Z(z | w)} \mu(x_0, z, w) (\mathbb{I}(x = x_0) - \pi(x_0 | z, w)) S(o) dP(o). \quad (24)$$

$$22 = - \int \frac{\psi_{x_0}(Q; z)}{\kappa_{x_0,2}(Q; z)} S(x_0 | z, w) dP(x_0 | z, w) dP(w) d\tilde{P}(z) \\ = - \int \frac{\psi_{x_0}(Q; z)}{\kappa_{x_0,2}(Q; z)} \frac{\tilde{p}(z)}{f_Z(z | w)} (\mathbb{I}(x = x_0) - \pi(x_0 | z, w)) S(o) dP(o). \quad (25)$$

$$23 = - \int \frac{\psi_{x_0}(Q; z)}{\kappa_{x_0,2}(Q; z)} S(w) dP(x_0 | z, w) dP(w) d\tilde{P}(z) \\ = - \int \left\{ \int \left(\frac{\psi_{x_0}(Q; z)}{\kappa_{x_0,2}(Q; z)} \pi(x_0 | z, w) - \psi_{x_0}(Q; z) \right) \tilde{p}(z) dz \right\} S(w) dP(w). \quad (26)$$

Line 19 simplifies to

$$19 = \int \left\{ \int \left(\frac{\mu(x_0, z, w) \pi(x_0 | z, w)}{\kappa_{x_0,2}(Q, z)} - \psi_{x_0}(Q; z) \right) \tilde{p}(z) dz \right\} S(w) dP(w). \quad (27)$$

Combining terms 20, 24, 25, 26, and 27 yields the EIF as follows. Equation 20 corresponds to the first line, 24 and 25 form the second line, and 26 together with 27 form the third line:

$$\phi_{x_0}(Q; \tilde{p}(Z))(O_i) = \underbrace{\frac{\mathbb{I}(X_i = x)}{\kappa_{x_0,2}(Q; Z_i)} \frac{\tilde{p}(Z_i)}{f_Z(Z_i | W_i)} \left\{ Y_i - \mu(x_0, Z_i, W_i) \right\}}_{\phi_{Y,x_0}(Q; \tilde{p}(Z))(O_i)}$$

$$\begin{aligned}
& + \underbrace{\frac{1}{\kappa_{x_0,2}(Q; Z_i)} \frac{\tilde{p}(Z_i)}{f_Z(Z_i | W_i)} \left\{ \mu(x_0, Z_i, W_i) - \psi_{x_0}(Q; Z_i) \right\} \left\{ \mathbb{I}(X_i = x_0) - \pi(x_0 | Z_i, W_i) \right\}}_{\phi_{X,x_0}(Q; \tilde{p}(Z))(O_i)} \\
& + \underbrace{\int \frac{\pi(x_0 | z, W_i)}{\kappa_{x_0,2}(Q; z)} \left\{ \mu(x_0, z, W_i) - \psi_{x_0}(Q; z) \right\} \tilde{p}(z) dz}_{\phi_{W,x_0}(Q; \tilde{p}(Z))(O_i)} .
\end{aligned}$$

B.2.3 Construction of the estimating equation estimator under discrete Z

The estimating equation estimator aims to solve $P_n \Phi_{x_0}(\hat{Q}; z^*) = 0$. That is,

$$\begin{aligned}
& \frac{1}{n} \sum_{i=1}^n \left[\frac{1}{\kappa_{x_0,2}(\hat{Q}; z^*)} \Phi_{x_0,1}(\hat{Q}; z^*)(O_i) - \frac{\kappa_{x_0,1}(\hat{Q}; z^*)}{\kappa_{x_0,2}^2(\hat{Q}; z^*)} \Phi_{x_0,2}(\hat{Q}; z^*)(O_i) \right] \\
& = \frac{1}{\kappa_{x_0,2}(\hat{Q}; z^*)} \frac{1}{n} \sum_{i=1}^n \left[\Phi_{x_0,1}(\hat{Q}; z^*)(O_i) - \psi_{x_0}^{\text{ee}}(\hat{Q}; z^*) \Phi_{x_0,2}(\hat{Q}; z^*)(O_i) \right] = 0 .
\end{aligned}$$

The above implies $\psi_{x_0}^{\text{ee}}(\hat{Q}; z^*) = P_n \Phi_{x_0,1}(\hat{Q}; z^*) / P_n \Phi_{x_0,2}(\hat{Q}; z^*)$. Substitute $\Phi_{x_0,1}$, and $\Phi_{x_0,2}$ with their explicit forms yields the expression in (7).

B.2.4 Construction of the estimating equation estimator under continuous Z

The estimating equation estimator aims to solve $P_n \Phi_{x_0}(\hat{Q}; \tilde{p}_z) = 0$. That is,

$$\begin{aligned}
& \frac{1}{n} \sum_{i=1}^n \left[\frac{\mathbb{I}(X_i = x_0)}{\kappa_{x_0,2}^{\text{pi}}(\hat{Q}; Z_i)} \frac{\tilde{p}(Z_i)}{\hat{f}_Z(Z_i | W_i)} \left\{ Y_i - \hat{\mu}(x_0, Z_i, W_i) \right\} \right. \\
& + \frac{1}{\kappa_{x_0,2}^{\text{plug-in}}(\hat{Q}; Z_i)} \frac{\tilde{p}(Z_i)}{\hat{f}_Z(Z_i | W_i)} \left\{ \hat{\mu}(x_0, Z_i, W_i) - \psi_{x_0}^{\text{ee}}(\hat{Q}; \tilde{p}(Z)) \right\} \left\{ \mathbb{I}(X_i = x_0) - \hat{\pi}(x_0 | Z_i, W_i) \right\} \\
& \left. + \int \frac{\hat{\pi}(x_0 | z, W_i)}{\kappa_{x_0,2}^{\text{pi}}(\hat{Q}; z)} \left\{ \hat{\mu}(x_0, z, W_i) - \psi_{x_0}^{\text{ee}}(\hat{Q}; \tilde{p}(Z)) \right\} \tilde{p}(z) dz \right] = 0 .
\end{aligned}$$

The above implies

$$\begin{aligned}
& \sum_{i=1}^n \left\{ \frac{\mathbb{I}(X_i = x_0)}{\kappa_{x_0,2}^{\text{pi}}(\hat{Q}; Z_i)} \frac{\tilde{p}(Z_i)}{\hat{f}_Z(Z_i | W_i)} \left\{ Y_i - \hat{\mu}(x_0, Z_i, W_i) \right\} \right. \\
& + \left. \frac{1}{\kappa_{x_0,2}^{\text{pi}}(\hat{Q}; Z_i)} \frac{\tilde{p}(Z_i)}{\hat{f}_Z(Z_i | W_i)} \hat{\mu}(x_0, Z_i, W_i) \left\{ \mathbb{I}(X_i = x_0) - \hat{\pi}(x_0 | Z_i, W_i) \right\} \right\}
\end{aligned}$$

$$\begin{aligned}
& + \int \frac{\hat{\pi}(x_0 \mid z, W_i)}{\kappa_{x_0,2}^{\text{pi}}(\hat{Q}; z)} \hat{\mu}(x_0, z, W_i) \tilde{p}(z) dz \Big\} \\
= & \psi_{x_0}^{\text{ee}}(\hat{Q}; \tilde{p}_z) \sum_{i=1}^n \left\{ \frac{1}{\kappa_{x_0,2}^{\text{pi}}(\hat{Q}; Z_i)} \frac{\tilde{p}(Z_i)}{\hat{f}_Z(Z_i \mid W_i)} \left\{ \mathbb{I}(X_i = x_0) - \hat{\pi}(x_0 \mid Z_i, W_i) \right\} \right. \\
& \quad \left. + \int \frac{\hat{\pi}(x_0 \mid z, W_i)}{\kappa_{x_0,2}^{\text{pi}}(\hat{Q}; z)} \tilde{p}(z) dz \right\}.
\end{aligned}$$

Therefore, $\psi_{x_0}^{\text{ee}}(\hat{Q}; \tilde{p}_z)$ is given by:

$$\begin{aligned}
& \psi_{x_0}^{\text{ee}}(\hat{Q}; \tilde{p}_z) \\
= & \frac{\frac{1}{n} \sum_{i=1}^n \left\{ \frac{1}{\kappa_{x_0,2}^{\text{pi}}(\hat{Q}; Z_i)} \frac{\tilde{p}(Z_i)}{\hat{f}_Z(Z_i \mid W_i)} \left\{ \mathbb{I}(X_i = x_0) Y_i - \hat{\mu}(x_0, Z_i, W_i) \hat{\pi}(x_0 \mid Z_i, W_i) \right\} \right\} + \int \psi_{x_0}^{\text{pi}}(\hat{Q}; z) \tilde{p}(z) dz}{\frac{1}{n} \sum_{i=1}^n \left\{ \frac{1}{\kappa_{x_0,2}^{\text{pi}}(\hat{Q}; Z_i)} \frac{\tilde{p}(Z_i)}{\hat{f}_Z(Z_i \mid W_i)} \left\{ \mathbb{I}(X_i = x_0) - \hat{\pi}(x_0 \mid Z_i, W_i) \right\} \right\} + 1}.
\end{aligned}$$

B.3 Inference

B.3.1 Second-order remainder term for $\psi_{x_0}^+(\hat{Q}; z^*)$

$$\begin{aligned}
R_2(\hat{Q}, Q; z^*) &= \psi_{x_0}^{\text{pi}}(\hat{Q}; z^*) - \psi_{x_0}(Q; z^*) + \int \Phi_{x_0}(\hat{Q}; z^*)(o) dP(o) \\
&= \psi_{x_0}^{\text{pi}}(\hat{Q}; z^*) - \psi_{x_0}(Q; z^*) \\
&+ \int \frac{\mathbb{I}(x = x_0)}{\kappa_{x_0,2}^{\text{aipw}}(\hat{Q}; z^*)} \frac{\mathbb{I}(z = z^*)}{\hat{f}_Z(z^* \mid w)} \left\{ y - \hat{\mu}(x_0, z^*, w) \right\} dP(o) \tag{28}
\end{aligned}$$

$$\begin{aligned}
&+ \int \frac{1}{\kappa_{x_0,2}^{\text{aipw}}(\hat{Q}; z^*)} \frac{\mathbb{I}(z = z^*)}{\hat{f}_Z(z^* \mid w)} \left\{ \hat{\mu}(x_0, z^*, w) - \psi_{x_0}^{\text{pi}}(\hat{Q}; z^*) \right\} \left\{ \mathbb{I}(x = x_0) - \hat{\pi}(x_0 \mid z^*, w) \right\} dP(o) \tag{29}
\end{aligned}$$

$$+ \int \frac{\hat{\pi}(x_0 \mid z^*, w)}{\kappa_{x_0,2}^{\text{aipw}}(\hat{Q}; z^*)} \left\{ \hat{\mu}(x_0, z^*, w) - \psi_{x_0}^{\text{pi}}(\hat{Q}; z^*) \right\} dP(o). \tag{30}$$

Line (28) can be reformulated as

$$\begin{aligned}
(28) &= \int \frac{\pi(x_0 \mid z^*, w)}{\kappa_{x_0,2}^{\text{aipw}}(\hat{Q}; z^*)} \frac{1}{\hat{f}_Z(z^* \mid w)} \left\{ f_Z(z^* \mid w) - \hat{f}_Z(z^* \mid w) \right\} \left\{ \mu(x_0, z^*, w) - \hat{\mu}(x_0, z^*, w) \right\} dP(w) \\
&\quad (31)
\end{aligned}$$

$$+ \int \frac{\pi(x_0 \mid z^*, w)}{\kappa_{x_0,2}^{\text{aipw}}(\hat{Q}; z^*)} \left\{ \mu(x_0, z^*, w) - \hat{\mu}(x_0, z^*, w) \right\} dP(w). \tag{32}$$

Line (29) can be reformulated as

$$(29) = \int \frac{\hat{\mu}(x_0, z^*, w) - \psi_{x_0}^{\text{pi}}(\hat{Q}; z^*)}{\kappa_{x_0,2}^{\text{aipw}}(\hat{Q}; z^*) \hat{f}_Z(z^* | w)} \left\{ f_Z(z^* | w) - \hat{f}_Z(z^* | w) \right\} \left\{ \pi(x_0 | z^*, w) - \hat{\pi}(x_0 | z^*, w) \right\} dP(w) \quad (33)$$

$$+ \int \frac{\hat{\mu}(x_0, z^*, w)}{\kappa_{x_0,2}^{\text{aipw}}(\hat{Q}; z^*)} \left\{ \pi(x_0 | z^*, w) - \hat{\pi}(x_0 | z^*, w) \right\} dP(w) \quad (34)$$

$$- \int \frac{\psi_{x_0}^{\text{pi}}(\hat{Q}; z^*)}{\kappa_{x_0,2}^{\text{aipw}}(\hat{Q}; z^*)} \left\{ \pi(x_0 | z^*, w) - \hat{\pi}(x_0 | z^*, w) \right\} dP(w). \quad (35)$$

Line (30) can be reformulated as

$$(30) = \int \frac{\hat{\pi}(x_0 | z^*, w, c)}{\kappa_{x_0,2}^{\text{aipw}}(\hat{Q}; z^*)} \hat{\mu}(x_0, z^*, w) dP(o) \quad (36)$$

$$- \int \frac{\hat{\pi}(x_0 | z^*, w)}{\kappa_{x_0,2}^{\text{aipw}}(\hat{Q}; z^*)} \psi_{x_0}^{\text{pi}}(\hat{Q}; z^*) dP(o). \quad (37)$$

Combining lines (32), (34), (36), and term $-\psi_{x_0}(Q; z^*)$ results in

$$\begin{aligned} & \left(\frac{1}{\kappa_{x_0,2}^{\text{aipw}}(\hat{Q}; z^*)} - \frac{1}{\kappa_{x_0,2}(Q; z^*)} \right) \int \pi(x_0 | z^*, w) \mu(x_0, z^*, w) dP(w) \\ &= \kappa_{x_0,1}(Q; z^*) \frac{\kappa_{x_0,2}(Q; z^*) - \kappa_{x_0,2}^{\text{aipw}}(\hat{Q}; z^*)}{\kappa_{x_0,2}^{\text{aipw}}(\hat{Q}; z^*) \kappa_{x_0,2}(Q; z^*)}. \end{aligned}$$

By performing a von Mises expansion around $\kappa_{x_0,2}^{\text{aipw}}(\hat{Q}; z^*)$ and assuming the Donsker condition holds, the difference between $\kappa_{x_0,2}$ and its AIPW estimator can be expressed as

$$\int \frac{f_Z(z^* | w) - \hat{f}_Z(z^* | w)}{\hat{f}_Z(z^* | w)} (\pi(x_0 | z^*, w) - \hat{\pi}(x_0 | z^*, w)) dP(w) + o_P(n^{-1/2}), \quad (38)$$

where $o_P(n^{-1/2})$ represents the negligible first-order bias, ensured by the construction of $\kappa_{x_0,2}^{\text{aipw}}(\hat{Q}; z^*)$ as an AIPW estimator for $\kappa_{x_0,2}(Q; z^*)$.

Combining lines (35), (37), and term $\psi_{x_0}^{\text{pi}}(\hat{Q}; z^*)$ results in

$$(35) + (37) + \psi_{x_0}^{\text{pi}}(\hat{Q}; z^*) = \frac{\psi_{x_0}^{\text{pi}}(\hat{Q}; z^*)}{\kappa_{x_0,2}^{\text{aipw}}(\hat{Q}; z^*)} \left(\kappa_{x_0,2}^{\text{aipw}}(\hat{Q}; z^*) - \kappa_{x_0,2}(Q; z^*) \right),$$

where the difference between $\kappa_{x_0,2}(Q; z^*)$ and its estimator can be expanded as in (38).

Combining all terms yields the expression for the second-order remainder term as follows:

$$\begin{aligned} R_2(\hat{Q}, Q; z^*) &= \int \frac{\pi(x_0 | z^*, w)}{\kappa_{x_0,2}^{\text{aipw}}(\hat{Q}; z^*)} \frac{f_Z(z^* | w) - \hat{f}_Z(z^* | w)}{\hat{f}_Z(z^* | w)} (\mu(x_0, z^*, w) - \hat{\mu}(x_0, z^*, w)) dP(w) \\ &+ \int \frac{\hat{\mu}(x_0, z^*, w) - \psi_{x_0}^{\text{pi}}(\hat{Q}; z^*)}{\kappa_{x_0,2}^{\text{aipw}}(\hat{Q}; z^*) \hat{f}_Z(z^* | w)} (f_Z(z^* | w) - \hat{f}_Z(z^* | w)) \{\pi(x_0 | z^*, w) - \hat{\pi}(x_0 | z^*, w)\} dP(w) \\ &+ \frac{\psi_{x_0}(Q; z^*) - \psi_{x_0}^{\text{pi}}(\hat{Q}; z^*)}{\kappa_{x_0,2}^{\text{aipw}}(\hat{Q}; z^*)} \int \frac{f_Z(z^* | w) - \hat{f}_Z(z^* | w)}{\hat{f}_Z(z^* | w)} (\pi(x_0 | z^*, w) - \hat{\pi}(x_0 | z^*, w)) dP(w) \\ &+ o_P(n^{-1/2}). \end{aligned} \tag{39}$$

B.3.2 Regularity conditions for $R_2(\hat{Q}, Q; z^*)$

Let \mathcal{W} denote the domain of W . Assume

$$\inf_{w \in \mathcal{W}, z^* \in \mathcal{Z}} \hat{f}_Z(z^* | w) > 0, \quad \inf_{x_0 \in \{0,1\}, z^* \in \mathcal{Z}} \kappa_{x_0,2}^{\text{aipw}}(\hat{Q}; z^*) > 0. \tag{40}$$

Given the boundedness conditions in (40), applying the Cauchy–Schwarz inequality to each term in (39) yields the following bound for some sufficiently large constant $C \in \mathbb{R}$:

$$R_2(\hat{Q}, Q) \leq C \left[\|\hat{f}_Z - f_Z\| \times \|\hat{\mu} - \mu\| + \|\hat{f}_Z - f_Z\| \times \|\hat{\pi} - \pi\| \right].$$

B.3.3 Second-order remainder term for $\psi_{x_0}^+(\hat{Q}; \tilde{p}_z)$

$$R_2(\hat{Q}, Q; \tilde{p}_z) = \psi_{x_0}^{\text{pi}}(\hat{Q}; \tilde{p}_z) - \psi_{x_0}(Q) + \int \Phi_{x_0}(\hat{Q}) dP(O)$$

$$= \psi_{x_0}^{\text{pi}}(\hat{Q}; \tilde{p}_z) - \psi_{x_0}(Q) + \int \frac{\mathbb{I}(x = x_0)}{\kappa_{x_0,2}^{\text{pi}}(\hat{Q}; z)} \frac{\tilde{p}(z)}{\hat{f}_Z(z | w)} (y - \hat{\mu}(x_0, z, w)) dP(o) \quad (41)$$

$$+ \int \frac{1}{\kappa_{x_0,2}^{\text{pi}}(\hat{Q}; z)} \frac{\tilde{p}(z)}{\hat{f}_Z(z | w)} (\hat{\mu}(x_0, z, w) - \psi_{x_0}^{\text{pi}}(\hat{Q}; z)) (\mathbb{I}(x = x_0) - \hat{\pi}(x_0 | z, w)) dP(o) \quad (42)$$

$$+ \int \left\{ \int \frac{\hat{\pi}(x_0 | z, w)}{\kappa_{x_0,2}^{\text{pi}}(\hat{Q}; z)} (\hat{\mu}(x_0, z, w) - \psi_{x_0}^{\text{pi}}(\hat{Q}; z)) \tilde{p}(z) dz \right\} dP(w). \quad (43)$$

Line (41) can be reformulated as

$$(41) = \int \frac{\pi(x_0 | z, w)}{\kappa_{x_0,2}^{\text{pi}}(\hat{Q}; z)} \frac{\tilde{p}(z)}{\hat{f}_Z(z | w)} \frac{(f_Z(z | w) - \hat{f}_Z(z | w))}{f_Z(z | w)} (\mu(x_0, z, w) - \hat{\mu}(x_0, z, w)) dP(z, w) \quad (44)$$

$$+ \int \frac{\pi(x_0 | z, w)}{\kappa_{x_0,2}^{\text{pi}}(\hat{Q}; z)} \frac{\tilde{p}(z)}{f_Z(z | w)} \mu(x_0, z, w) dP(z, w) \quad (45)$$

$$- \int \frac{\pi(x_0 | z, w)}{\kappa_{x_0,2}^{\text{pi}}(\hat{Q}; z)} \frac{\tilde{p}(z)}{f_Z(z | w)} \hat{\mu}(x_0, z, w) dP(z, w). \quad (46)$$

Line (42) can be reformulated as

$$\int \frac{\hat{\mu}(x_0, z, w) - \psi_{x_0}^{\text{pi}}(\hat{Q}; z)}{\kappa_{x_0,2}^{\text{pi}}(\hat{Q}; z)} \frac{\tilde{p}(z)}{\hat{f}_Z(z | w)} \frac{(f_Z(z | w) - \hat{f}_Z(z | w))}{f_Z(z | w)} (\pi(x_0 | z, w) - \hat{\pi}(x_0 | z, w)) dP(z, w) \quad (47)$$

$$- \int \frac{\hat{\mu}(x_0, z, w) - \psi_{x_0}^{\text{pi}}(\hat{Q}; z)}{\kappa_{x_0,2}^{\text{pi}}(\hat{Q}; z)} \frac{\tilde{p}(z)}{f_Z(z | w)} \hat{\pi}(x_0 | z, w) dP(z, w) \quad (48)$$

$$+ \int \frac{1}{\kappa_{x_0,2}^{\text{pi}}(\hat{Q}; z)} \frac{\tilde{p}(z)}{f_Z(z | w)} \hat{\mu}(x_0, z, w) \pi(x_0 | z, w) dP(z, w) \quad (49)$$

$$- \int \frac{1}{\kappa_{x_0,2}^{\text{pi}}(\hat{Q}; z)} \frac{\tilde{p}(z)}{f_Z(z | w)} \psi_{x_0}^{\text{pi}}(\hat{Q}; z) \pi(x_0 | z, w) dP(z, w). \quad (50)$$

Note that (48) cancels out (43), and (49) cancels out (46).

Combining (45) with term $-\psi_{x_0}(Q)$ results in

$$(45) - \psi_{x_0}(Q) = \int \left[\frac{\kappa_{x_0,2}(Q; z) - \kappa_{x_0,2}^{\text{pi}}(\hat{Q}; z)}{\kappa_{x_0,2}(Q; z) \kappa_{x_0,2}^{\text{pi}}(\hat{Q}; z)} \mu(x_0, z, w) \pi(x_0 | z, w) \tilde{p}(z) dz \right] dP(w)$$

$$= \int \frac{\kappa_{x_0,2}(Q; z) - \kappa_{x_0,2}^{\text{pi}}(\hat{Q}; z)}{\kappa_{x_0,2}^{\text{pi}}(\hat{Q}; z)} \psi_{x_0}(Q; z) \tilde{p}(z) dz. \quad (51)$$

Combining (50) with term $\psi_{x_0}^{\text{pi}}(\hat{Q})$ results in

$$\psi_{x_0}^{\text{pi}}(\hat{Q}) + (50) = \int \frac{\kappa_{x_0,2}^{\text{pi}}(\hat{Q}; z) - \kappa_{x_0,2}(Q; z)}{\kappa_{x_0,2}^{\text{pi}}(\hat{Q}; z)} \psi_{x_0}^{\text{pi}}(\hat{Q}; z) \tilde{p}(z) dz. \quad (52)$$

Therefore, combining (45) and (50) with $\psi_{x_0}^{\text{pi}}(\hat{Q}) - \psi_{x_0}(Q)$ results in

$$\int \frac{\kappa_{x_0,2}(Q; z) - \kappa_{x_0,2}^{\text{pi}}(\hat{Q}; z)}{\kappa_{x_0,2}^{\text{pi}}(\hat{Q}; z)} (\psi_{x_0}(Q; z) - \psi_{x_0}^{\text{pi}}(\hat{Q}; z)) \tilde{p}(z) dz. \quad (53)$$

Combining all terms yields the expression for the second-order remainder term as follows:

$$\begin{aligned} R_2(\hat{Q}, Q; \tilde{p}_z) &= \int \frac{\pi(x_0 | z, w) \tilde{p}(z)}{\kappa_{x_0,2}^{\text{pi}}(\hat{Q}; z)} \frac{(f_Z(z | w) - \hat{f}_Z(z | w))}{\hat{f}_Z(z | w) f_Z(z | w)} (\mu(x_0, z, w) - \hat{\mu}(x_0, z, w)) dP(O) \\ &+ \int \frac{\hat{\mu}(x_0, z, w) - \psi_{x_0}^{\text{pi}}(\hat{Q}; z) \tilde{p}(z)}{\kappa_{x_0,2}^{\text{pi}}(\hat{Q}; z)} \frac{(f_Z(z | w) - \hat{f}_Z(z | w))}{\hat{f}_Z(z | w) f_Z(z | w)} (\pi(x_0 | z, w) - \hat{\pi}(x_0 | z, w)) dP(z, w) \\ &+ \int \frac{\kappa_{x_0,2}(Q; z) - \kappa_{x_0,2}^{\text{pi}}(\hat{Q}; z)}{\kappa_{x_0,2}^{\text{pi}}(\hat{Q}; z)} (\psi_{x_0}(Q; z) - \psi_{x_0}^{\text{pi}}(\hat{Q}; z)) \tilde{p}(z) dz, \end{aligned} \quad (54)$$

where the last line of (54) can be expanded as

$$\begin{aligned} &\int \frac{\kappa_{x_0,2}(Q; z) - \kappa_{x_0,2}^{\text{pi}}(\hat{Q}; z)}{\kappa_{x_0,2}^{\text{pi}}(\hat{Q}; z)} \frac{\kappa_{x_0,1}(Q; z) \kappa_{x_0,2}^{\text{pi}}(\hat{Q}; z) - \kappa_{x_0,1}^{\text{pi}}(\hat{Q}; z) \kappa_{x_0,2}(Q; z)}{\kappa_{x_0,2}(Q; z) \kappa_{x_0,2}^{\text{pi}}(\hat{Q}; z)} \tilde{p}(z) dz \\ &= \int \frac{-\kappa_{x_0,1}(Q; z) (\kappa_{x_0,2}(Q; z) - \kappa_{x_0,2}^{\text{pi}}(\hat{Q}; z))^2}{\kappa_{x_0,2}(Q; z) \kappa_{x_0,2}^{\text{pi}}(\hat{Q}; z)} \tilde{p}(z) dz \\ &\quad + \int \frac{(\kappa_{x_0,2}(Q; z) - \kappa_{x_0,2}^{\text{pi}}(\hat{Q}; z)) (\kappa_{x_0,1}(Q; z) - \kappa_{x_0,1}^{\text{pi}}(\hat{Q}; z))}{\kappa_{x_0,2}^{\text{pi}}(\hat{Q}; z)} \tilde{p}(z) dz \\ &= \int \frac{-\kappa_{x_0,1}(Q; z) (\kappa_{x_0,2}(Q; z) - \kappa_{x_0,2}^{\text{pi}}(\hat{Q}; z))^2}{\kappa_{x_0,2}(Q; z) \kappa_2^{\text{pi}^2}(\hat{Q}; z)} \tilde{p}(z) dz \\ &\quad + \int \frac{\int (\pi(x_0 | z, w) - \hat{\pi}(x_0 | z, w)) dP(w)}{\kappa_{x_0,2}^{\text{pi}^2}(\hat{Q}; z)} \\ &\quad \times \int (\mu(x_0, z, w) \pi(x_0 | z, w) - \hat{\mu}(x_0, z, w) \hat{\pi}(x_0 | z, w)) dP(w) \tilde{p}(z) dz \end{aligned}$$

$$\begin{aligned}
&= \int \frac{-\kappa_{x_0,1}(Q; z) (\kappa_{x_0,2}(Q; z) - \kappa_{x_0,2}^{\text{pi}}(\hat{Q}; z))^2}{\kappa_{x_0,2}(Q; z) \kappa_{x_0,2}^{\text{pi}^2}(\hat{Q}; z)} \tilde{p}(z) dz \\
&+ \int \frac{\int (\pi(x_0 | z, w) - \hat{\pi}(x_0 | z, w)) dP(w)}{\kappa_{x_0,2}^{\text{pi}^2}(\hat{Q}; z)} \int \mu(x_0, z, w) (\pi(x_0 | z, w) - \hat{\pi}(x_0 | z, w)) dP(w) \tilde{p}(z) dz \\
&+ \int \frac{\int (\pi(x_0 | z, w) - \hat{\pi}(x_0 | z, w)) dP(w)}{\kappa_{x_0,2}^{\text{pi}^2}(\hat{Q}; z)} \int \hat{\pi}(x_0 | z, w) (\mu(x_0, z, w) - \hat{\mu}(x_0, z, w)) dP(w) \tilde{p}(z) dz,
\end{aligned}$$

where $\kappa_{x_0,2}^{\text{pi}^2}(\hat{Q}; z) := (\kappa_{x_0,2}^{\text{pi}}(\hat{Q}; z))^2$.

When $\kappa_{x_0,2}$ is estimated using the AIPW estimator, (54) is accordingly modified as follows:

$$\begin{aligned}
R_2(\hat{Q}, Q; \tilde{p}_z) &= \int \frac{\pi(x_0 | z, w)}{\kappa_{x_0,2}^{\text{aipw}}(\hat{Q}; z)} \frac{\tilde{p}(z)}{\hat{f}_Z(z | w) f_Z(z | w)} (f_Z(z | w) - \hat{f}_Z(z | w)) (\mu(x_0, z, w) - \hat{\mu}(x_0, z, w)) dP(O) \\
&+ \int \frac{\hat{\mu}(x_0, z, w) - \psi_{x_0}(\hat{Q}; z)}{\kappa_{x_0,2}^{\text{aipw}}(\hat{Q}; z)} \frac{\tilde{p}(z)}{\hat{f}_Z(z | w) f_Z(z | w)} (f_Z(z | w) - \hat{f}_Z(z | w)) (\pi(x_0 | z, w) - \hat{\pi}(x_0 | z, w)) dP(z, w) \\
&+ \int \frac{\kappa_{x_0,2}(Q; z) - \kappa_{x_0,2}^{\text{aipw}}(\hat{Q}; z)}{\kappa_{x_0,2}^{\text{aipw}}(\hat{Q}; z)} (\psi_{x_0}(Q; z) - \psi_{x_0}^{\text{pi}}(\hat{Q}; z)) \tilde{p}(z) dz.
\end{aligned} \tag{55}$$

B.3.4 Regularity conditions for $R_2(\hat{Q}, Q; \tilde{p}_z)$

Assume the following regularity conditions:

$$\inf_{z \in \mathcal{Z}, w \in \mathcal{W}} \hat{f}_Z(z | w) > 0, \quad \inf_{x_0 \in \{0,1\}, z \in \mathcal{Z}} \kappa_{x_0,2}^{\text{pi}}(\hat{Q}; z) > 0. \tag{56}$$

Given the boundedness conditions in (56), applying the Cauchy–Schwarz inequality to each term in (54) yields the following bound for some sufficiently large constant $C \in \mathbb{R}$:

$$\begin{aligned}
R_2(\hat{Q}, Q; \tilde{p}_z) &\leq C \left[\|\hat{f}_Z - f_Z\| \times \|\hat{\mu} - \mu\| + \|\hat{f}_Z - f_Z\| \times \|\hat{\pi} - \pi\| \right. \\
&\quad \left. + \left\| \kappa_{x_0,2}^{\text{pi}}(\hat{Q}; z) - \kappa_{x_0,2}(Q; z) \right\|^2 + \|\hat{\pi} - \pi\|^2 + \|\hat{\pi} - \pi\| \times \|\hat{\mu} - \mu\| \right],
\end{aligned}$$

where the L^2 norm of $\kappa_{x_0,2}(\hat{Q}; z)$ can be further expanded to establish its connection with

the L^2 norms of the nuisance estimators in \hat{Q} :

$$\begin{aligned} \left\| \kappa_{x_0,2}^{\text{pi}}(\hat{Q}; z) - \kappa_{x_0,2}(Q; z) \right\|^2 &= \mathbb{E} \left[\left(\int (\hat{\pi}(x_0 | z, w) - \pi(x_0 | z, w)) dP(w) \right)^2 \right] \\ &\leq \mathbb{E} \left[\int (\hat{\pi}(x_0 | z, w) - \pi(x_0 | z, w))^2 dP(w) \right] \\ &= \|\hat{\pi} - \pi\|^2. \end{aligned}$$

The inequality follows from the observation that, for any $z \in \mathcal{Z}$, $\left(\int (\hat{\pi}(x_0 | z, w) - \pi(x_0 | z, w)) dP(w) \right)^2 \leq \int (\hat{\pi}(x_0 | z, w) - \pi(x_0 | z, w))^2 dP(w)$, which is a direct application of the Cauchy–Schwarz inequality.

B.4 Efficacy gain under discrete Z

Assume Z has K categories $\{1, \dots, K\}$. Consider the following class of influence functions, defined as linear combinations of the fixed- z^* influence functions, with weights $\alpha := (\alpha_1, \dots, \alpha_{K-1})$:

$$\begin{aligned} (1 - \sum_{i=1}^{K-1} \alpha_i) \Phi_{x_0}(Q; z^* = K) + \sum_{i=1}^{K-1} \alpha_i \Phi_{x_0}(Q; z^* = i) \\ = \Phi_{x_0}(Q; z^* = K) + \sum_{i=1}^{K-1} \alpha_i \left(\Phi_{x_0}(Q; z^* = i) - \Phi_{x_0}(Q; z^* = K) \right). \end{aligned}$$

Let $f(\alpha)$ denote the variance of this linear combination:

$$\begin{aligned} f(\alpha) &= \text{Var} \left\{ \Phi_{x_0}(Q; z^* = K) + \sum_{i=1}^{K-1} \alpha_i \left(\Phi_{x_0}(Q; z^* = i) - \Phi_{x_0}(Q; z^* = K) \right) \right\} \\ &= \mathbb{E} \left[\left\{ \Phi_{x_0}(Q; z^* = K) + \sum_{i=1}^{K-1} \alpha_i \left(\Phi_{x_0}(Q; z^* = i) - \Phi_{x_0}(Q; z^* = K) \right) \right\}^2 \right]. \end{aligned}$$

We aim to obtain the weight vector α that minimizes $f(\alpha)$. To start, we establish the existence and uniqueness of a minimizer by examining the curvature of $f(\alpha)$ through its

Hessian. For any $\alpha_i, \alpha_j \in \alpha$:

$$\begin{aligned}\frac{\partial^2 f(\alpha_1, \dots, \alpha_{K-1})}{\partial \alpha_i^2} &= \mathbb{E} \left[(\Phi_{x_0}(Q; z^* = i) - \Phi_{x_0}(Q; z^* = K))^2 \right] \\ \frac{\partial^2 f(\alpha_1, \dots, \alpha_{K-1})}{\partial \alpha_i \partial \alpha_j} &= \mathbb{E} \left[(\Phi_{x_0}(Q; z^* = j) - \Phi_{x_0}(Q; z^* = K)) (\Phi_{x_0}(Q; z^* = i) - \Phi_{x_0}(Q; z^* = K)) \right].\end{aligned}$$

Let $v_i := \Phi_{x_0}(Q; z^* = i) - \Phi_{x_0}(Q; z^* = K)$, and $v = (v_1, \dots, v_{K-1})^T$. Then the Hessian matrix H of $f(\alpha)$ can be written as

$$H = \mathbb{E}(v v^T), \quad \text{where } H_{ij} = \frac{\partial^2 f}{\partial \alpha_i \partial \alpha_j} = \mathbb{E}(v_i v_j).$$

For any $a \in \mathbb{R}^{K-1}$, $a^T H a = \mathbb{E}((a^T v)^2) \geq 0$. Thus, H is positive semi-definite.

It follows that any solution α^{opt} to the first-order condition $\partial f(\alpha)/\partial \alpha = 0$ is a local minimizer of $f(\alpha)$. If, in addition, the K influence functions $\Phi_{x_0}(Q; z^* = 1), \dots, \Phi_{x_0}(Q; z^* = K)$, are linearly independent, then H is positive definite, which implies that $f(\alpha)$ is strictly convex and admits a unique global minimizer.

We now solve for α^{opt} by setting the gradient to zero. For each $i \in \{1, \dots, K-1\}$,

$$\frac{\partial f(\alpha)}{\partial \alpha_i} = 2\mathbb{E} \left(v_i \left\{ \Phi_{x_0}(Q; z^* = K) + \sum_{j=1}^{K-1} \alpha_j v_j \right\} \right) = 0, \quad \text{for } i \in \{1, \dots, K-1\}.$$

Equivalently,

$$H \alpha^{\text{opt}} = - \begin{pmatrix} \mathbb{E}(v_1 \Phi_{x_0}(Q; z^* = K)) \\ \vdots \\ \mathbb{E}(v_{K-1} \Phi_{x_0}(Q; z^* = K)) \end{pmatrix},$$

which implies that

$$\alpha^{\text{opt}} = -H^{-1} \begin{pmatrix} \mathbb{E}(v_1 \Phi_{x_0}(Q; z^* = K)) \\ \vdots \\ \mathbb{E}(v_{K-1} \Phi_{x_0}(Q; z^* = K)) \end{pmatrix}.$$

C On the inclusion of measured confounders

We extend the nuisance functions from the main manuscript to incorporate measured confounders C . Let $\mu(x, z, w, c) := \mathbb{E}(Y | X = x, Z = z, W = w, C = c)$, $\pi(x | z, w, c) := P(X = x | Z = z, W = w, C = c)$, $f_Z(z | w, c) := p(Z = z | W = w, C = c)$, $f_W(w | c) := p(W = w | C = c)$, and $p_C(c) := p(C = c)$.

C.1 Identification in the presence of confounders C

When measured confounders C are present, the identification functional can be modified accordingly as follows:

$$\begin{aligned} p(y | \text{do}(x_0)) &= \int p(y | \text{do}(x_0), c) p(c) dc \\ &= \int p(y | \text{do}(x_0), \text{do}(z^*), c) p(c) dc && \text{(3rd rule of do-calculus)} \\ &= \int p(y | x_0, \text{do}(z^*), c) p(c) dc && \text{(2nd rule of do-calculus)} \\ &= \int \frac{p(y, x_0, c | \text{do}(z^*))}{p(x_0, c | \text{do}(z^*))} p(c) dc && \text{(Bayes rule)} \\ &= \int \frac{\int p(y, x_0 | z^*, w, c) p(w | c) dw}{\int p(x_0 | z^*, w, c) p(w | c) dw} p(c) dc. && \text{(back-door rule)} \end{aligned}$$

Thus, given our nuisance notations, our parameter of interest is identified as:

$$\mathbb{E}(Y^{x_0}) = \int \frac{\int \mu(x_0, z^*, w, c) \pi(x_0 | z^*, w, c) p(w | c) dw}{\int \pi(x_0 | z^*, w, c) p(w | c) dw} p(c) dc. \quad (57)$$

Algorithm 2 in [Bhattacharya et al. \(2022\)](#) yields the following equivalent functional, known as the *nested-IPW*, more suitable for continuous-valued Z :

$$\mathbb{E}(Y^{x_0}) = \int \frac{\int \mu(x_0, z, w, c) \pi(x_0 | z, w, c) p(w | c) dw}{\int \pi(x_0 | z, w, c) p(w | c) dw} p(c) \tilde{p}(z) dc dz . \quad (58)$$

C.2 Plug-in estimation in the presence of confounders C

Let $Q := \{\mu, \pi, f_Z, f_W, p_C\}$ denote the collection of nuisance parameters, and let $\hat{Q} := \{\hat{\mu}, \hat{\pi}, \hat{f}_Z, \hat{f}_W, \hat{p}_C\}$ collect the nuisance estimates. When W is univariate discrete, \hat{f}_W can be obtained using regression-based methods, and when W is univariate continuous or multivariate of mixed variable types, it can be obtained by non/semi-parametric kernel-based methods ([Hayfield & Racine 2008](#), [Benkeser & Van Der Laan 2016](#)). We use the same notation as in the main manuscript for deriving estimators, unless otherwise specified.

Based on the identification functional presented in Appendix C.1, the plug-in estimators for $\mathbb{E}(Y^{x_0})$ under discrete and continuous Z are constructed as follows:

$$\begin{aligned} \psi_{x_0}^{\text{pi}}(\hat{Q}; z^*) &= \frac{1}{n} \sum_{i=1}^n \kappa_{x_0,1}^{\text{pi}}(C_i, \hat{Q}; z^*) / \kappa_{x_0,2}^{\text{pi}}(C_i, \hat{Q}; z^*), && (\text{discrete } Z) \\ \psi_{x_0}^{\text{pi}}(\hat{Q}; \tilde{p}_z) &= \int \left(\frac{1}{n} \sum_{i=1}^n \kappa_{x_0,1}^{\text{pi}}(C_i, \hat{Q}; z) / \kappa_{x_0,2}^{\text{pi}}(C_i, \hat{Q}; z) \right) \tilde{p}(z) dz, && (\text{continuous } Z) \end{aligned}$$

where, $\kappa_{x_0,1}^{\text{pi}}(c, \hat{Q}; z^*)$ and $\kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z^*)$ are estimates of

$$\begin{aligned} \kappa_{x_0,1}(c, Q; z^*) &= \int \mu(x_0, z^*, w, c) \pi(x_0 | z^*, w, c) f_W(w | c) dw, \\ \kappa_{x_0,2}(c, Q; z^*) &= \int \pi(x_0 | z^*, w, c) f_W(w | c) dw. \end{aligned}$$

Specifically, they are computed as follows when W is discrete:

$$\begin{aligned}\kappa_{x_0,1}^{\text{pi}}(c, \hat{Q}; z^*) &= \int \hat{\mu}(x_0, z^*, w, c) \hat{\pi}(x_0 | z^*, w, c) \hat{f}_W(w | c) dw, \\ \kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z^*) &= \int \hat{\pi}(x_0 | z^*, w, c) \hat{f}_W(w | c) dw.\end{aligned}$$

Although these quantities can, in principle, be computed in the same way when W is non-discrete, the estimation of the conditional density f_W and the associated numerical integration present considerable computational challenges. Therefore, we instead use regression-based methods as follows:

$$\begin{aligned}\kappa_{x_0,1}^{\text{pi}}(c, \hat{Q}; z^*) &= \hat{\mathbb{E}}\left(\hat{\mu}(x_0, z^*, W, C) \hat{\pi}(x_0 | z^*, W, C) | C = c\right), \\ \kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z^*) &= \hat{\mathbb{E}}\left(\hat{\pi}(x_0 | z^*, W, C) | C = c\right),\end{aligned}$$

where the first conditional expectation is estimated by regressing the pseudo-outcome $\hat{\mu}(x_0, z^*, W_i, C_i) \hat{\pi}(x_0 | z^*, W_i, C_i)$ on C_i and predicting at $C = c$. The second is obtained analogously by regressing $\hat{\pi}(x_0 | z^*, W_i, C_i)$ on C_i and predicting at $C = c$.

The estimator $\psi_{x_0}^{\text{pi}}(\hat{Q}; \tilde{p}_z)$ under continuous Z is also applicable when Z is discrete by specifying \tilde{p}_Z as the probability mass function of Z and simplifying the corresponding integration to a finite summation over the support of Z .

C.3 IF-based estimation in the presence of confounders C

C.3.1 Estimation under discrete Z

We begin by deriving the nonparametric efficient influence function for $\psi_{x_0}(Q; z^*)$ in (57):

$$\frac{\partial}{\partial \varepsilon} \psi_{x_0}(P_\varepsilon; z^*) = \int \frac{\partial}{\partial \varepsilon} \frac{\kappa_{x_0,1}(c, P_\varepsilon; z^*)}{\kappa_{x_0,2}(c, P_\varepsilon; z^*)} dP(c) + \int \frac{\kappa_{x_0,1}(c, P; z^*)}{\kappa_{x_0,2}(c, P; z^*)} \frac{\partial}{\partial \varepsilon} dP_\varepsilon(c)$$

$$\begin{aligned}
&= \int \left(\frac{\frac{\partial}{\partial \varepsilon} \kappa_{x_0,1}(c, P_\varepsilon; z^*)}{\kappa_{x_0,2}(c, P; z^*)} - \frac{\kappa_{x_0,1}(c, P; z^*) \frac{\partial}{\partial \varepsilon} \kappa_{x_0,2}(c, P_\varepsilon; z^*)}{\kappa_{x_0,2}^2(c, P; z^*)} \right) dP(c) \\
&\quad + \int \frac{\kappa_{x_0,1}(c, P; z^*)}{\kappa_{x_0,2}(c, P; z^*)} \frac{\partial}{\partial \varepsilon} dP_\varepsilon(c),
\end{aligned}$$

where

$$\begin{aligned}
\frac{\partial}{\partial \varepsilon} \kappa_{x_0,1}(c, P_\varepsilon; z^*) &= \int \frac{\mathbb{I}(x = x_0) \mathbb{I}(z = z^*)}{f_Z(z^* | w, c)} (y - \mu(x_0, z^*, w, c)) S(y, x, z, w, c) dP(y, x, z, w | c) \\
&\quad + \int \frac{\mathbb{I}(z = z^*)}{f_Z(z^* | w, c)} \mu(x_0, z^*, w, c) (\mathbb{I}(x = x_0) - \pi(x_0 | z^*, w, c)) S(x, z, w, c) dP(x, z, w | c) \\
&\quad + \int (\mu(x_0, z^*, w, c) \pi(x_0 | z^*, w, c) - \kappa_{x_0,1}(c, P; z^*)) S(w, c) dP(w | c), \\
\frac{\partial}{\partial \varepsilon} \kappa_{x_0,2}(c, P_\varepsilon; z^*) &= \int \frac{\mathbb{I}(z = z^*)}{f_Z(z^* | w, c)} (\mathbb{I}(x = x_0) - \pi(x_0 | z^*, w, c)) S(x, z, w, c) dP(x, z, w | c) \\
&\quad + \int (\pi(x_0 | z^*, w, c) - \kappa_{x_0,2}(c, P; z^*)) S(w, c) dP(w | c), \\
\int \frac{\kappa_{x_0,1}(c, P; z^*)}{\kappa_{x_0,2}(c, P; z^*)} \frac{\partial}{\partial \varepsilon} dP_\varepsilon(c) &= \int \left(\frac{\kappa_{x_0,1}(c, P; z^*)}{\kappa_{x_0,2}(c, P; z^*)} - \psi_{x_0}(P; z^*) \right) S(c) dP(c).
\end{aligned}$$

By substituting the derivatives with their explicit forms and simplifying the resulting expressions, the influence function for $\psi_{x_0}(Q; z^*)$ in (57) can be written as:

$$\begin{aligned}
\Phi_{x_0}(Q; z^*)(O_i) &= \underbrace{\frac{\mathbb{I}(X_i = x_0)}{\kappa_{x_0,2}(C_i, Q; z^*)} \frac{\mathbb{I}(Z_i = z^*)}{f_Z(z^* | W_i, C_i)} \left\{ Y_i - \mu(x_0, z^*, W_i, C_i) \right\}}_{\Phi_{Y,x_0}(Q; z^*)(O_i)} \\
&\quad + \underbrace{\frac{1}{\kappa_{x_0,2}(C_i, Q; z^*)} \frac{\mathbb{I}(Z_i = z^*)}{f_Z(z^* | W_i, C_i)} \left\{ \mu(x_0, z^*, W_i, C_i) - \frac{\kappa_{x_0,1}(C_i, Q; z^*)}{\kappa_{x_0,2}(C_i, Q; z^*)} \right\} \left\{ \mathbb{I}(X_i = x_0) - \pi(x_0 | z^*, W_i, C_i) \right\}}_{\Phi_{X,x_0}(Q; z^*)(O_i)} \\
&\quad + \underbrace{\frac{\pi(x_0 | z^*, W_i, C_i)}{\kappa_{x_0,2}(C_i, Q; z^*)} \left\{ \mu(x_0, z^*, W_i, C_i) - \frac{\kappa_{x_0,1}(C_i, Q; z^*)}{\kappa_{x_0,2}(C_i, Q; z^*)} \right\}}_{\Phi_{W,x_0}(Q; z^*)(O_i)} \\
&\quad + \underbrace{\frac{\kappa_{x_0,1}(C_i, Q; z^*)}{\kappa_{x_0,2}(C_i, Q; z^*)} - \psi_{x_0}(Q; z^*)}_{\Phi_{C,x_0}(Q; z^*)(O_i)}. \tag{59}
\end{aligned}$$

Construction of the one-step estimator:

The one-step estimator coincides with the estimating equation estimator and is given by:

$$\begin{aligned}
\psi^+(\hat{Q}; z^*) &= \frac{1}{n} \sum_{i=1}^n \left\{ \frac{\mathbb{I}(X_i = x_0)}{\kappa_{x_0,2}^{\text{pi}}(C_i, \hat{Q}; z^*)} \frac{\mathbb{I}(Z_i = z^*)}{\hat{f}_Z(z^* | W_i, C_i)} \{Y_i - \hat{\mu}(x_0, z^*, W_i, C_i)\} \right. \\
&\quad + \frac{1}{\kappa_{x_0,2}^{\text{pi}}(C_i, \hat{Q}; z^*)} \frac{\mathbb{I}(Z_i = z^*)}{\hat{f}_Z(z^* | W_i, C_i)} \left\{ \hat{\mu}(x_0, z^*, W_i, C_i) - \frac{\kappa_{x_0,1}^{\text{pi}}(C_i, \hat{Q}; z^*)}{\kappa_{x_0,2}^{\text{pi}}(C_i, \hat{Q}; z^*)} \right\} \\
&\quad \times \{\mathbb{I}(X_i = x_0) - \hat{\pi}(x_0 | z^*, W_i, C_i)\} \\
&\quad + \frac{\hat{\pi}(x_0 | z^*, W_i, C_i)}{\kappa_{x_0,2}^{\text{pi}}(C_i, \hat{Q}; z^*)} \left\{ \hat{\mu}(x_0, z^*, W_i, C_i) - \frac{\kappa_{x_0,1}^{\text{pi}}(C_i, \hat{Q}; z^*)}{\kappa_{x_0,2}^{\text{pi}}(C_i, \hat{Q}; z^*)} \right\} \\
&\quad \left. + \frac{\kappa_{x_0,1}^{\text{pi}}(C_i, \hat{Q}; z^*)}{\kappa_{x_0,2}^{\text{pi}}(C_i, \hat{Q}; z^*)} \right\}.
\end{aligned}$$

Construction of the TMLE:

Unlike the setting without measured confounders discussed in the main manuscript, where $\Phi_{W,x_0}(\hat{Q}; z^*)$ becomes negligible once the nuisance estimates $\hat{\mu}$ and $\hat{\pi}$ are successfully targeted (as $p_W(w)$ is empirically estimated), this term is not negligible in the current setting because $f_W(w|c)$ is not estimated empirically. Consequently, an additional targeting step is required to control this term, introducing extra complexity since cross-nuisance targeting now also involves updating $\kappa_{x_0,1}^{\text{pi}}(C_i, \hat{Q}; z^*)/\kappa_{x_0,2}^{\text{pi}}(C_i, \hat{Q}; z^*)$.

Following the procedure outlined in the main manuscript, we begin by performing within-nuisance iterative targeting to update $\hat{\pi}$. Once convergence is achieved, $\hat{\mu}$ is updated in a single step. The updated estimates of $\hat{\mu}$ and $\hat{\pi}$ are then used to update the plug-in estimates of $\kappa_{x_0,1}(C_i, Q; z^*)$ and $\kappa_{x_0,2}(C_i, Q; z^*)$. To make $P_n \Phi_{W,x_0}(\hat{Q}; z^*)$ negligible, we further update the estimate of ratio $\kappa_{x_0,1}(C_i, Q; z^*)/\kappa_{x_0,2}(C_i, Q; z^*)$ by performing a weighted regression of the updated $\hat{\mu}$ on an intercept, with the offset set to the current estimate of $\kappa_{x_0,1}/\kappa_{x_0,2}$ and weights given by the current estimate of $\pi(x_0|z^*, W_i, C_i)/\kappa_{x_0,2}(C_i, Q; z^*)$. The estimate of $\kappa_{x_0,1}/\kappa_{x_0,2}$ is then updated by adding the intercept coefficient from this regression to its previous estimate. After this update, we return to update current estimate of π and

continue iterating among estimates of π , μ , and $\kappa_{x_0,1}/\kappa_{x_0,2}$ until convergence is achieved.

The final TMLE is obtained as the sample mean of the updated estimate of $\kappa_{x_0,1}/\kappa_{x_0,2}$.

C.3.2 Estimation under continuous Z

We begin by deriving the nonparametric influence function for $\psi_{x_0}(Q; \tilde{p}_z)$ in (58). According to the product rule of derivatives, we have

$$\frac{\partial}{\partial \varepsilon} \psi_{x_0}(P_\varepsilon; \tilde{p}_z) = \int \left(\frac{\partial}{\partial \varepsilon} \frac{\kappa_{x_0,1}(c, P_\varepsilon; z)}{\kappa_{x_0,2}(c, P_\varepsilon; z)} dP_\varepsilon(c) \right) \tilde{p}(z) dz .$$

Informed by the presentation of the influence under discrete Z , the correspond form when Z is continuous can be written as:

$$\begin{aligned} \Phi_{x_0}(Q; \tilde{p}_z)(O_i) &= \underbrace{\frac{\mathbb{I}(X_i = x_0)}{\kappa_{x_0,2}(C_i, Q; Z_i)} \frac{\tilde{p}(Z_i)}{f_Z(Z_i | W_i, C_i)} \{Y_i - \mu(x_0, Z_i, W_i, C_i)\}}_{\Phi_{Y,x_0}(Q; z^*)(O_i)} \\ &+ \underbrace{\frac{1}{\kappa_{x_0,2}(C_i, Q; Z_i)} \frac{\tilde{p}(Z_i)}{f_Z(Z_i | W_i, C_i)} \left\{ \mu(x_0, Z_i, W_i, C_i) - \frac{\kappa_{x_0,1}(C_i, Q; Z_i)}{\kappa_{x_0,2}(C_i, Q; Z_i)} \right\} \{ \mathbb{I}(X_i = x_0) - \pi(x_0 | Z_i, W_i, C_i) \}}_{\Phi_{X,x_0}(Q; Z_i)(O_i)} \\ &+ \underbrace{\int \frac{\pi(x_0 | z, W_i, C_i)}{\kappa_{x_0,2}(C_i, Q; z)} \left\{ \mu(x_0, z, W_i, C_i) - \frac{\kappa_{x_0,1}(C_i, Q; z)}{\kappa_{x_0,2}(C_i, Q; z)} \right\} \tilde{p}(z) dz}_{\Phi_{W,x_0}(Q; z^*)(O_i)} \\ &+ \underbrace{\int \frac{\kappa_{x_0,1}(C_i, Q; z)}{\kappa_{x_0,2}(C_i, Q; z)} \tilde{p}(z) dz - \psi_{x_0}(Q; \tilde{p}_z)}_{\Phi_{C,x_0}(Q; \tilde{p}_z)(O_i)} . \end{aligned}$$

Construction of the one-step estimator:

The one-step estimator coincides with the estimating equation estimator and is given by:

$$\begin{aligned} \psi_{x_0}^+(\hat{Q}; \tilde{p}_z) &= \frac{1}{n} \sum_{i=1}^n \left\{ \frac{\mathbb{I}(X_i = x_0)}{\kappa_{x_0,2}^{\text{pi}}(C_i, \hat{Q}; Z_i)} \frac{\tilde{p}(Z_i)}{\hat{f}_Z(Z_i | W_i, C_i)} \{Y_i - \hat{\mu}(x_0, Z_i, W_i, C_i)\} \right. \\ &\quad + \left. \frac{1}{\kappa_{x_0,2}^{\text{pi}}(C_i, \hat{Q}; Z_i)} \frac{\tilde{p}(Z_i)}{\hat{f}_Z(Z_i | W_i, C_i)} \left\{ \hat{\mu}(x_0, Z_i, W_i, C_i) - \frac{\kappa_{x_0,1}^{\text{pi}}(C_i, \hat{Q}; Z_i)}{\kappa_{x_0,2}^{\text{pi}}(C_i, \hat{Q}; Z_i)} \right\} \right. \\ &\quad \times \left. \{ \mathbb{I}(X_i = x_0) - \hat{\pi}(x_0 | Z_i, W_i, C_i) \} \right\} \end{aligned}$$

$$\begin{aligned}
& + \int \frac{\hat{\pi}(x_0 \mid z, W_i, C_i)}{\kappa_{x_0,2}^{\text{pi}}(C_i, \hat{Q}; z)} \left\{ \hat{\mu}(x_0, z, W_i, C_i) - \frac{\kappa_{x_0,1}^{\text{pi}}(C_i, \hat{Q}; z)}{\kappa_{x_0,2}^{\text{pi}}(C_i, \hat{Q}; z)} \right\} \tilde{p}(z) dz \\
& + \int \frac{\kappa_{x_0,1}^{\text{pi}}(C_i, \hat{Q}; z)}{\kappa_{x_0,2}^{\text{pi}}(C_i, \hat{Q}; z)} \tilde{p}(z) dz \}.
\end{aligned}$$

The nuisance estimate $\kappa_{x_0,1}(C_i, \hat{Q}; Z_i)$ may lead to some ambiguity, which we clarify here. For $i \in \{1, \dots, n\}$, the estimation of $\kappa_{x_0,1}(C_i, \hat{Q}; Z_i)$ proceeds by regressing the pseudo-outcomes $\hat{\mu}(x_0, Z_i, W_j, C_j)$ and $\hat{\pi}(x_0 \mid Z_i, W_j, C_j)$ on C_j , evaluated for $j = 1, \dots, n$, and then predicting at C_i . The index j represents the observations used in the regression, distinguishing it from i , which appears in the estimator's definition. Consequently, one regression is performed for each i , resulting in a total of n regressions. The same procedure is applied to estimate $\kappa_{x_0,2}(C_i, \hat{Q}; Z_i)$.

Construction of the TMLE:

The construction of the TMLE is largely analogous to that for discrete Z , as described in Appendix C.3.1. The main difference is that the estimate of $\kappa_{x_0,1}/\kappa_{x_0,2}$ is updated by numerically solving the score equation $P_n \Phi_{W,x_0}(\hat{Q}; \tilde{p}_z) = 0$. Specifically, a constant is determined such that, when added to the current estimate of $\kappa_{x_0,1}/\kappa_{x_0,2}$, the updated estimate solves the score equation.

C.4 Inference in the presence of confounders C

C.4.1 Second-order remainder term for $\psi_{x_0}^+(\hat{Q}; z^*)$

$\psi_{x_0}^+(\hat{Q}; z^*)$ is given in (57).

$$R_2(\hat{Q}, Q; z^*) = \psi_{x_0}^{\text{pi}}(\hat{Q}; z^*) - \psi_{x_0}(Q; z^*) + \int \Phi_{x_0}(\hat{Q}; z^*)(o) dP(o) \quad (60)$$

$$= \psi_{x_0}^{\text{pi}}(\hat{Q}; z^*) - \psi_{x_0}(Q; z^*) \quad (61)$$

$$+ \int \frac{\mathbb{I}(x = x_0)}{\kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z^*)} \frac{\mathbb{I}(z = z^*)}{\hat{f}_Z(z^* \mid w, c)} \{y - \hat{\mu}(x_0, z^*, w, c)\} dP(o) \quad (62)$$

$$+ \int \frac{1}{\kappa_{x_0,2}^{\text{pi}}(c, Q; z^*)} \frac{\mathbb{I}(z = z^*)}{\hat{f}_Z(z^* \mid w, c)} \{\hat{\mu}(x_0, z^*, w, c)$$

$$-\frac{\kappa_{x_0,1}^{\text{pi}}(c, \hat{Q}; z^*)}{\kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z^*)}\} \{\mathbb{I}(x = x_0) - \hat{\pi}(x_0 | z^*, w, c)\} dP(o) \quad (63)$$

$$+ \int \frac{\hat{\pi}(x_0 | z^*, w, c)}{\kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z^*)} \{\hat{\mu}(x_0, z^*, w, c) - \frac{\kappa_{x_0,1}^{\text{pi}}(c, \hat{Q}; z^*)}{\kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z^*)}\} dP(w, c) \quad (64)$$

$$+ \int \left\{ \frac{\kappa_{x_0,1}^{\text{pi}}(c, \hat{Q}; z^*)}{\kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z^*)} - \psi_{x_0}^{\text{pi}}(\hat{Q}; z^*) \right\} dP(c) . \quad (65)$$

Line (62) can be reformulated as:

$$\int \frac{\pi(x_0 | z^*, w, c)}{\kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z^*)} \frac{f_Z(z^*, w, c) - \hat{f}_Z(z^*, w, c)}{\hat{f}_Z(z^*, w, c)} \{\mu(x_0, z^*, w, c) - \hat{\mu}(x_0, z^*, w, c)\} dP(w, c) \quad (66)$$

$$+ \int \frac{\pi(x_0 | z^*, w, c)}{\kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z^*)} \{\mu(x_0, z^*, w, c) - \hat{\mu}(x_0, z^*, w, c)\} dP(w, c) . \quad (67)$$

Line (63) can be reformulated as:

$$(63) = \int \left\{ \frac{\hat{\mu}(x_0, z^*, w, c)}{\kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z^*)} - \frac{\kappa_{x_0,1}^{\text{pi}}(c, \hat{Q}; z^*)}{\kappa_{x_0,2}^{\text{pi}^2}(c, \hat{Q}; z^*)} \right\} \frac{1}{\hat{f}_Z(z^* | w, c)} \times (f_Z(z^* | w, c) - \hat{f}_Z(z^* | w, c)) \{\pi(x_0 | z^*, w, c) - \hat{\pi}(x_0 | z^*, w, c)\} dP(w, c) \quad (68)$$

$$+ \int \left\{ \frac{\hat{\mu}(x_0, z^*, w, c)}{\kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z^*)} - \frac{\kappa_{x_0,1}^{\text{pi}}(c, \hat{Q}; z^*)}{\kappa_{x_0,2}^{\text{pi}^2}(c, \hat{Q}; z^*)} \right\} \{\pi(x_0 | z^*, w, c) - \hat{\pi}(x_0 | z^*, w, c)\} dP(x, z, w, c) .$$

(69)

Lines (67), (69), (64), (65), and (61) can be combined and simplified as follows, where we use same number of * to denote the corresponding cancellation:

$$\begin{aligned} & \int \left(\frac{\pi(x_0 | z^*, w, c) \mu(x_0, z^*, w, c)}{\kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z^*)} - \frac{\pi(x_0 | z^*, w, c) \hat{\mu}(x_0, z^*, w, c)}{\kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z^*)} \right)^* dP(w, c) \\ & + \int \left(\frac{\hat{\mu}(x_0, z^*, w, c) \pi(x_0 | z^*, w, c)}{\kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z^*)} - \frac{\hat{\mu}(x_0, z^*, w, c) \hat{\pi}(x_0 | z^*, w, c)}{\kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z^*)} \right)^{**} \\ & \quad - \frac{\kappa_{x_0,1}^{\text{pi}}(c, \hat{Q}; z^*) \pi(x_0 | z^*, w, c)}{\kappa_{x_0,2}^{\text{pi}^2}(c, \hat{Q}; z^*)} + \frac{\kappa_{x_0,1}^{\text{pi}}(c, \hat{Q}; z^*) \hat{\pi}(x_0 | z^*, w, c)}{\kappa_{x_0,2}^{\text{pi}^2}(c, \hat{Q}; z^*)} \right)^{***} dP(x, z, w, c) \end{aligned}$$

$$\begin{aligned}
& + \int \frac{\hat{\pi}(x_0 | z^*, w, c) \hat{\mu}(x_0, z^*, w, c)}{\kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z^*)} - \frac{\hat{\pi}(x_0 | z^*, w, c) \kappa_{x_0,1}^{\text{pi}}(c, \hat{Q}; z^*)}{\kappa_{x_0,2}^{\text{pi}^2}(c, \hat{Q}; z^*)} dP(w, c) \\
& + \int \left(\frac{\kappa_{x_0,1}^{\text{pi}}(c, \hat{Q}; z^*)}{\kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z^*)} - \frac{\kappa_{x_0,1}(c, Q; z^*)}{\kappa_{x_0,2}(c, Q; z^*)} \right) dP(c) \\
& = \int \frac{1}{\kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z^*)} (\kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z^*) - \kappa_{x_0,2}(c, Q; z^*)) \left(\frac{\kappa_{x_0,1}^{\text{pi}}(c, \hat{Q}; z^*)}{\kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z^*)} - \frac{\kappa_{x_0,1}(c, Q; z^*)}{\kappa_{x_0,2}(c, Q; z^*)} \right) dP(c).
\end{aligned}$$

As a result, we have:

$$\begin{aligned}
& = \int \frac{\pi(x_0 | z^*, w, c)}{\kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z^*)} \frac{1}{\hat{f}_Z(z^*, w, c)} \\
& \quad \times (f_Z(z^*, w, c) - \hat{f}_Z(z^*, w, c)) \{ \mu(x_0, z^*, w, c) - \hat{\mu}(x_0, z^*, w, c) \} dP(w, c) \\
& + \int \left\{ \frac{\hat{\mu}(x_0, z^*, w, c)}{\kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z^*)} - \frac{\kappa_{x_0,1}^{\text{pi}}(c, \hat{Q}; z^*)}{\kappa_{x_0,2}^{\text{pi}^2}(c, \hat{Q}; z^*)} \right\} \frac{f_Z(z^* | w, c) - \hat{f}_Z(z^* | w, c)}{\hat{f}_Z(z^* | w, c)} \\
& \quad \times \{ \pi(x_0 | z^*, w, c) - \hat{\pi}(x_0 | z^*, w, c) \} dP(w, c) \\
& + \int \frac{\kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z^*) - \kappa_{x_0,2}(c, Q; z^*)}{\kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z^*)} \left(\frac{\kappa_{x_0,1}^{\text{pi}}(c, \hat{Q}; z^*)}{\kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z^*)} - \frac{\kappa_{x_0,1}(c, Q; z^*)}{\kappa_{x_0,2}(c, Q; z^*)} \right) dP(c), \tag{70}
\end{aligned}$$

where the last line can be expanded as follows:

$$\begin{aligned}
& \int \frac{1}{\kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z^*)} (\kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z^*) - \kappa_{x_0,2}(c, \hat{Q}; z^*) + \kappa_{x_0,2}(c, \hat{Q}; z^*) - \kappa_{x_0,2}(c, Q; z^*)) \\
& \times \left(\frac{\kappa_{x_0,1}^{\text{pi}}(c, \hat{Q}; z^*)}{\kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z^*)} - \frac{\kappa_{x_0,1}(c, \hat{Q}; z^*)}{\kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z^*)} + \frac{\kappa_{x_0,1}(c, \hat{Q}; z^*)}{\kappa_{x_0,2}^{\text{pi}^2}(c, \hat{Q}; z^*)} - \frac{\kappa_{x_0,1}(c, Q; z^*)}{\kappa_{x_0,2}^{\text{pi}^2}(c, \hat{Q}; z^*)} + \frac{\kappa_{x_0,1}(c, Q; z^*)}{\kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z^*)} - \frac{\kappa_{x_0,1}(c, Q; z^*)}{\kappa_{x_0,2}(c, Q; z^*)} \right) dP(c) \\
& = \int \frac{1}{\kappa_{x_0,2}^{\text{pi}^2}(c, \hat{Q}; z^*)} (\kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z^*) - \kappa_{x_0,2}(c, \hat{Q}; z^*)) (\kappa_{x_0,1}^{\text{pi}}(c, \hat{Q}; z^*) - \kappa_{x_0,1}(c, \hat{Q}; z^*)) dP(c) \\
& + \int \frac{1}{\kappa_{x_0,2}^{\text{pi}^2}(c, \hat{Q}; z^*)} (\kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z^*) - \kappa_{x_0,2}(c, \hat{Q}; z^*)) (\kappa_{x_0,1}(c, \hat{Q}; z^*) - \kappa_{x_0,1}(c, Q; z^*)) dP(c) \\
& + \int \frac{\kappa_{x_0,1}(c, Q; z^*)}{\kappa_{x_0,2}^{\text{pi}^2}(c, \hat{Q}; z^*) \kappa_{x_0,2}(c, Q; z^*)} (\kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z^*) - \kappa_{x_0,2}(c, \hat{Q}; z^*)) (\kappa_{x_0,2}(c, Q; z^*) - \kappa_{x_0,2}(c, \hat{Q}; z^*)) dP(c) \\
& + \int \frac{\kappa_{x_0,1}(c, Q; z^*)}{\kappa_{x_0,2}^{\text{pi}^2}(c, \hat{Q}; z^*) \kappa_{x_0,2}(c, Q; z^*)} (\kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z^*) - \kappa_{x_0,2}(c, \hat{Q}; z^*)) (\kappa_{x_0,2}(c, \hat{Q}; z^*) - \kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z^*)) dP(c) \\
& + \int \frac{1}{\kappa_{x_0,2}^{\text{pi}^2}(c, \hat{Q}; z^*)} (\kappa_{x_0,2}(c, \hat{Q}; z^*) - \kappa_{x_0,2}(c, Q; z^*)) (\kappa_{x_0,1}^{\text{pi}}(c, \hat{Q}; z^*) - \kappa_{x_0,1}(c, \hat{Q}; z^*)) dP(c) \\
& + \int \frac{1}{\kappa_{x_0,2}^{\text{pi}^2}(c, \hat{Q}; z^*)} (\kappa_{x_0,2}(c, \hat{Q}; z^*) - \kappa_{x_0,2}(c, Q; z^*)) (\kappa_{x_0,1}(c, \hat{Q}; z^*) - \kappa_{x_0,1}(c, Q; z^*)) dP(c) \\
& + \int \frac{\kappa_{x_0,1}(c, Q; z^*)}{\kappa_{x_0,2}^{\text{pi}^2}(c, \hat{Q}; z^*) \kappa_{x_0,2}(c, Q; z^*)} (\kappa_{x_0,2}(c, \hat{Q}; z^*) - \kappa_{x_0,2}(c, Q; z^*)) (\kappa_{x_0,2}(c, Q; z^*) - \kappa_{x_0,2}(c, \hat{Q}; z^*)) dP(c)
\end{aligned}$$

$$+ \int \frac{\kappa_{x_0,1}(c, Q; z^*)}{\kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z^*) \kappa_{x_0,2}(c, Q; z^*)} (\kappa_{x_0,2}(c, \hat{Q}; z^*) - \kappa_{x_0,2}(c, Q; z^*)) (\kappa_{x_0,2}(c, \hat{Q}; z^*) - \kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z^*)) dP(c) .$$

C.4.2 Asymptotic linearity of $\psi_{x_0}^+(\hat{Q}; z^*)$

$\psi_{x_0}^+(\hat{Q}; z^*)$ is given in (57). Let \mathcal{W} denote the domain of W . Assume

$$\inf_{z^* \in \mathcal{Z}, w \in \mathcal{W}, c \in \mathcal{C}} \hat{f}_Z(z^* | w, c) > 0, \quad \inf_{x_0 \in \{0,1\}, z^* \in \mathcal{Z}, c \in \mathcal{C}} \kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z^*) > 0. \quad (71)$$

Given the boundedness conditions in (71), applying the Cauchy–Schwarz inequality to each term in (70) yields the following bound for some sufficiently large constant $C \in \mathbb{R}$:

$$\begin{aligned} R_2(\hat{Q}, Q; z^*) &\leq C \left[\|\hat{f}_Z - f_Z\| \times \|\hat{\mu} - \mu\| + \|\hat{f}_Z - f_Z\| \times \|\hat{\pi} - \pi\| \right. \\ &\quad + \|\hat{\pi} - \pi\| \times \|\hat{\mu} - \mu\| + \|\hat{\pi} - \pi\|^2 \\ &\quad + \|\hat{\pi} - \pi\| \times \|\kappa_{x_0,1}^{\text{pi}}(c, \hat{Q}; z^*) - \kappa_{x_0,1}(c, \hat{Q}; z^*)\| \\ &\quad + \|\hat{\pi} - \pi\| \times \|\kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z^*) - \kappa_{x_0,2}(c, \hat{Q}; z^*)\| \\ &\quad + \|\hat{\mu} - \mu\| \times \|\kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z^*) - \kappa_{x_0,2}(c, \hat{Q}; z^*)\| \\ &\quad + \|\kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z^*) - \kappa_{x_0,2}(c, \hat{Q}; z^*)\|^2 \\ &\quad \left. + \|\kappa_{x_0,1}^{\text{pi}}(c, \hat{Q}; z^*) - \kappa_{x_0,1}(c, \hat{Q}; z^*)\| \times \|\kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z^*) - \kappa_{x_0,2}(c, \hat{Q}; z^*)\| \right]. \end{aligned}$$

Here, $\kappa_{x_0,1}(c, \hat{Q}; z^*)$ and $\kappa_{x_0,2}(c, \hat{Q}; z^*)$ are nuisances evaluated under estimates $\hat{\mu}$ and $\hat{\pi}$, and are defined as follows when W is discrete:

$$\begin{aligned} \kappa_{x_0,1}(c, \hat{Q}; z^*) &= \int \hat{\mu}(x_0, z^*, w, c) \hat{\pi}(x_0 | z^*, w, c) f_W(w | c) dw, \\ \kappa_{x_0,2}(c, \hat{Q}; z^*) &= \int \hat{\pi}(x_0 | z^*, w, c) f_W(w | c) dw. \end{aligned}$$

They are modified as follows when W is non-discrete:

$$\begin{aligned}\kappa_{x_0,1}(c, \hat{Q}; z^*) &= \mathbb{E}(\hat{\mu}(x_0, z^*, W, C), \hat{\pi}(x_0 | z^*, W, C) | C = c), \\ \kappa_{x_0,2}(c, \hat{Q}; z^*) &= \mathbb{E}(\hat{\pi}(x_0 | z^*, W, C) | C = c).\end{aligned}$$

When W is non-discrete, the $L^2(P)$ conditions associated with the nuisance estimates $\kappa_{x_0,1}^{\text{pi}}(c, \hat{Q}; z^*)$ and $\kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z^*)$ can be interpreted as conditions on the two regression estimators used in their construction. When W is discrete, these nuisance estimates are obtained through integration with respect to \hat{f}_W , and the corresponding conditions simplify to a single requirement on $\|\hat{f}_W - f_W\|$. For coherence in presentation, however, we continue to refer to the $L^2(P)$ conditions for these two nuisance estimates, rather than provide separate discussions for different types of W .

Based on the analysis of the second-order remainder term, we have the following theorem establishing asymptotic linearity of the one-step estimator $\psi_{x_0}^+(\hat{Q}; z^*)$ (and equivalently the other two estimators).

Theorem 12. *Assume the $L^2(P)$ convergence of nuisance estimates in \hat{Q} are as follows: $\|\hat{\pi} - \pi\| = o_P(n^{-\frac{1}{k}})$, $\|\hat{f}_Z - f_Z\| = o_P(n^{-\frac{1}{b}})$, $\|\hat{\mu} - \mu\| = o_P(n^{-\frac{1}{q}})$, $\|\kappa_{x_0,1}^{\text{pi}}(c, \hat{Q}; z^*) - \kappa_{x_0,1}(c, \hat{Q}; z^*)\| = o_P(n^{-\frac{1}{p_1}})$, and $\|\kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z^*) - \kappa_{x_0,2}(c, \hat{Q}; z^*)\| = o_P(n^{-\frac{1}{p_2}})$. Under the regularity conditions discussed in Appendix Equation (71), if $\frac{1}{b} + \frac{1}{q} \geq \frac{1}{2}$, $\frac{1}{k} + \frac{1}{b} \geq \frac{1}{2}$, $\frac{1}{q} + \frac{1}{k} \geq \frac{1}{2}$, $\frac{1}{k} \geq \frac{1}{4}$, $\frac{1}{k} + \frac{1}{p_1} \geq \frac{1}{2}$, $\frac{1}{q} + \frac{1}{p_2} \geq \frac{1}{2}$, $\frac{1}{p_2} \geq \frac{1}{4}$, and $\frac{1}{p_1} + \frac{1}{p_2} \geq \frac{1}{2}$ jointly hold, then the one-step estimator $\psi_{x_0}^+(\hat{Q}; z^*)$ is asymptotically linear, that is: $\psi_{x_0}^+(\hat{Q}; z^*) - \psi_{x_0}(Q; z^*) = P_n \Phi_{x_0}(Q; z^*) + o_P(n^{-1/2})$ where $\Phi_{x_0}(Q; z^*)$ is the influence function given in (59).*

This theorem requires both $\hat{\pi}$ and $\kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z^*)$ to converge at least at rate $o_P(n^{-1/4})$ in order for the estimators to be asymptotically linear. The robustness property of our estimators are formalized in the following corollary.

Corollary 13. $\psi_{x_0}^+(\hat{Q}; z^*)$ is consistent for $\psi_{x_0}(Q; z^*)$ if $\|\hat{\pi} - \pi\| = o_P(1)$ and $\|\kappa_{x_0,1}^{pi}(c, \hat{Q}; z^*) - \kappa_{x_0,1}(c, \hat{Q}; z^*)\| = o_P(1)$, and in addition, at least one of the following holds: (i) $\|\hat{\mu} - \mu\| = o_P(1)$, or (ii) $\|\hat{f}_Z - f_Z\| = o_P(1)$, or both (i) and (ii).

C.4.3 Second-order remainder term for $\psi_{x_0}^+(\hat{Q}; \tilde{p}_z)$

$\psi_{x_0}^+(\hat{Q}; \tilde{p}_z)$ is given in (58).

$$R_2(\hat{Q}, Q; \tilde{p}_z) = \psi_{x_0}^{pi}(\hat{Q}; \tilde{p}_z) - \psi_{x_0}(Q; \tilde{p}_z) + \int \Phi_{x_0}(\hat{Q}; \tilde{p}_z)(o) dP(o) \quad (72)$$

$$= \psi_{x_0}^{pi}(\hat{Q}; \tilde{p}_z) - \psi_{x_0}(Q; \tilde{p}_z) \quad (73)$$

$$+ \int \frac{\mathbb{I}(x = x_0)}{\kappa_{x_0,2}^{pi}(c, \hat{Q}; z)} \frac{\tilde{p}(z)}{\hat{f}_Z(z | w, c)} \left\{ y - \hat{\mu}(x_0, z, w, c) \right\} dP(o) \quad (74)$$

$$+ \int \frac{1}{\kappa_{x_0,2}^{pi}(c, Q; z)} \frac{\tilde{p}(z)}{\hat{f}_Z(z | w, c)} \left\{ \hat{\mu}(x_0, z, w, c) - \frac{\kappa_{x_0,1}^{pi}(c, \hat{Q}; z)}{\kappa_{x_0,2}^{pi}(c, \hat{Q}; z)} \right\} \times \left\{ \mathbb{I}(x = x_0) - \hat{\pi}(x_0 | z, w, c) \right\} dP(o) \quad (75)$$

$$+ \int \frac{\hat{\pi}(x_0 | z, w, c)}{\kappa_{x_0,2}^{pi}(c, \hat{Q}; z)} \left\{ \hat{\mu}(x_0, z, w, c) - \frac{\kappa_{x_0,1}^{pi}(c, \hat{Q}; z)}{\kappa_{x_0,2}^{pi}(c, \hat{Q}; z^*)} \right\} \tilde{p}(z) dz dP(w, c) \quad (76)$$

$$+ \int \frac{\kappa_{x_0,1}^{pi}(c, \hat{Q}; z)}{\kappa_{x_0,2}^{pi}(c, \hat{Q}; z)} \tilde{p}(z) p(c) dz dc - \psi_{x_0}^{pi}(\hat{Q}; \tilde{p}_z). \quad (77)$$

Line (74) can be reformulated as

$$(74) = \int \frac{\pi(x_0 | z, w, c)}{\kappa_{x_0,2}^{pi}(c, \hat{Q}; z)} \frac{\tilde{p}(z)}{\hat{f}_Z(z | w, c) f_Z(z | w, c)} \times \left\{ f_Z(z | w, c) - \hat{f}_Z(z | w, c) \right\} \left\{ \mu(x_0, z, w, c) - \hat{\mu}(x_0, z, w, c) \right\} dP(o) \quad (78)$$

$$+ \int \frac{\pi(x_0 | z, w, c)}{\kappa_{x_0,2}^{pi}(c, \hat{Q}; z)} \frac{\tilde{p}(z)}{f_Z(z | w, c)} \mu(x_0, z, w, c) dP(z, w, c) \quad (78)$$

$$- \int \frac{\pi(x_0 | z, w, c)}{\kappa_{x_0,2}^{pi}(c, \hat{Q}; z)} \frac{\tilde{p}(Z)}{f_Z(z | w, c)} \hat{\mu}(x_0, z, w, c) dP(z, w, c). \quad (79)$$

Line (75) can be reformulated as

$$(75) = \int \frac{\hat{\mu}(x_0, z, w, c) - \frac{\kappa_{x_0,1}^{\text{pi}}(c, \hat{Q}; z)}{\kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z)}}{\kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z)} \frac{\tilde{p}(z)}{\hat{f}_Z(z | w, c) f_Z(z | w, c)} \\ \times \{f_Z(z | w, c) - \hat{f}_Z(z | w, c)\} (\pi(x_0 | z, w, c) - \hat{\pi}(x_0 | z, w, c)) dP(z, w, c) \\ - \int \frac{\hat{\mu}(x_0, z, w, c) - \frac{\kappa_{x_0,1}^{\text{pi}}(c, \hat{Q}; z)}{\kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z)}}{\kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z)} \frac{\tilde{p}(z)}{f_Z(z | w, c)} \hat{\pi}(x_0 | z, w, c) dP(z, w, c) \quad (80)$$

$$+ \int \frac{1}{\kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z)} \frac{\tilde{p}(z)}{f_Z(z | w, c)} \hat{\mu}(x_0, z, w, c) \pi(x_0 | z, w, c) dP(z, w, c) \quad (81)$$

$$- \int \frac{1}{\kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z)} \frac{\tilde{p}(z)}{f_Z(z | w, c)} \frac{\kappa_{x_0,1}^{\text{pi}}(c, \hat{Q}; z)}{\kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z)} \pi(x_0 | z, w, c) dP(z, w, c). \quad (82)$$

Note that (80) cancels out (76), and (81) cancels out (79).

Combining lines (73), (77), (78), and (82) results in

$$\int \left(\frac{\kappa_{x_0,1}^{\text{pi}}(c, \hat{Q}; z)}{\kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z)} - \frac{\kappa_{x_0,1}(c, Q; z)}{\kappa_{x_0,2}(c, Q; z)} + \frac{\kappa_{x_0,1}(c, Q; z)}{\kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z)} - \frac{\kappa_{x_0,2}(c, Q; z)}{\kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z)} \frac{\kappa_{x_0,1}^{\text{pi}}(c, \hat{Q}; z)}{\kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z)} \right) \tilde{p}(z) p(c) d(z, c) \\ = \int \frac{1}{\kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z)} \left(\frac{\kappa_{x_0,1}^{\text{pi}}(c, \hat{Q}; z)}{\kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z)} - \frac{\kappa_{x_0,1}(c, Q; z)}{\kappa_{x_0,2}(c, Q; z)} \right) \left(\kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z) - \kappa_{x_0,2}(c, Q; z) \right) \tilde{p}(z) p(c) d(z, c).$$

Combining all terms results in the expression for the second-order remainder term as follows:

$$R_2(\hat{Q}, Q; \tilde{p}_z) = \int \frac{\pi(x_0 | z, w, c)}{\kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z)} \frac{\tilde{p}(z)}{\hat{f}_Z(z | w, c) f_Z(z | w, c)} \\ \times \{f_Z(z | w, c) - \hat{f}_Z(z | w, c)\} \{\mu(x_0, z, w, c) - \hat{\mu}(x_0, z, w, c)\} dP(o) \\ + \int \frac{\hat{\mu}(x_0, z, w, c) - \frac{\kappa_{x_0,1}^{\text{pi}}(c, \hat{Q}; z)}{\kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z)}}{\kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z)} \frac{\tilde{p}(z)}{\hat{f}_Z(z | w, c) f_Z(z | w, c)} \\ \times \{f_Z(z | w, c) - \hat{f}_Z(z | w, c)\} (\pi(x_0 | z, w, c) - \hat{\pi}(x_0 | z, w, c)) dP(z, w, c) \\ + \int \frac{1}{\kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z)} \left(\frac{\kappa_{x_0,1}^{\text{pi}}(c, \hat{Q}; z)}{\kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z)} - \frac{\kappa_{x_0,1}(c, Q; z)}{\kappa_{x_0,2}(c, Q; z)} \right) \left(\kappa_{x_0,2}^{\text{pi}}(c, \hat{Q}; z) - \kappa_{x_0,2}(c, Q; z) \right) \tilde{p}(z) p(c) d(z, c). \quad (83)$$

The last line can be further expanded in the same manner as for the R_2 term under discrete Z in (70). We therefore omit the expansion here to avoid redundancy.

The estimator $\psi_{x_0}^+(\hat{Q}; \tilde{p}_z)$ exhibits the same asymptotic behavior as $\psi_{x_0}^+(\hat{Q}; z^*)$, discussed in Appendix C.4.2. Specifically, they require the same conditions on convergence rates of nuisance estimates to achieve asymptotic linearity and consistency under same regularity conditions. Therefore, we omit the detailed discussion here to avoid redundancy.

D Details and extensions of the TMLE procedures

D.1 Validity of loss function and submodel combinations

We establish the validity of the loss function and submodel combinations used for targeting the estimates of μ and π with continuous Z outlined in Section 3.1.3 and detailed in Algorithm 2. The proof for settings with discrete Z follows an analogous argument and is therefore omitted; see the corresponding TMLE procedure in Section 3.1.3 and Algorithm 1.

Loss function and submodel combination for targeting estimate of μ

$$L_Y(\tilde{\mu}; \hat{\pi}, \hat{f}_Z) = \hat{H}_Y(X, Z, W; \tilde{p}_z) \{Y_i - \tilde{\mu}(x_0, Z, W)\}^2 ,$$

$$\hat{\mu}(\varepsilon_Y) = \hat{\mu}(x_0, Z, W) + \varepsilon_Y ,$$

with $\hat{H}_Y(X, Z, W; \tilde{p}_z) = \{\mathbb{I}(X = x_0) \tilde{p}(Z)\} / \{\kappa_{x_0, 2}^{\text{pi}}(\hat{Q}; Z) \hat{f}_Z(Z | W)\}$.

Proof of (C1): $\hat{\mu}(\varepsilon_Y = 0) = \hat{\mu}(x_0, Z, W)$.

Proof of (C2):

$$\begin{aligned} \mathbb{E}(L_Y(\tilde{\mu}; \hat{\pi}, \hat{f}_Z)) &= \mathbb{E}\left(\hat{H}_Y(X, Z, W; \tilde{p}_z) \{Y - \tilde{\mu}(x_0, Z, W)\}^2\right) \\ &= \mathbb{E}\left(\hat{H}_Y(X, Z, W; \tilde{p}_z) \{Y - \mu(x_0, Z, W) + \mu(x_0, Z, W) - \tilde{\mu}(x_0, Z, W)\}^2\right) \\ &= \mathbb{E}\left(\hat{H}_Y(X, Z, W; \tilde{p}_z) \{Y - \mu(x_0, Z, W)\}^2\right) \\ &\quad + \mathbb{E}\left(\hat{H}_Y(X, Z, W; \tilde{p}_z) \{\mu(x_0, Z, W) - \tilde{\mu}(x_0, Z, W)\}^2\right) \\ &\quad + \underbrace{\mathbb{E}\left(2\hat{H}_Y(X, Z, W; \tilde{p}_z) \{Y - \mu(x_0, Z, W)\} \{\mu(x_0, Z, W) - \tilde{\mu}(x_0, Z, W)\}\right)}_{= 0} . \end{aligned}$$

Therefore, $\mathbb{E}(L_Y(\tilde{\mu}; \hat{\pi}, \hat{f}_Z))$ is minimized when $\mu(x_0, Z, W) = \tilde{\mu}(x_0, Z, W)$, which makes the second term in the last equality above equal to zero.

Proof of (C3):

$$\frac{\partial}{\partial \varepsilon_Y} L_Y(\hat{\mu}(\varepsilon_Y); \hat{\pi}, \hat{f}_Z) \Big|_{\varepsilon_Y=0} = 2\hat{H}_Y(X, Z, W; \tilde{p}_z) \{Y_i - \hat{\mu}(x_0, Z, W)\} \propto \Phi_{Y, x_0}(\hat{Q}; \tilde{p}_z).$$

Loss function and submodel combination for targeting estimate of π

$$L_X(\tilde{\pi}; \hat{f}_Z) = -\{\tilde{p}(Z)/\hat{f}_Z(Z | W)\} \log \tilde{\pi}(X | Z, W)$$

$$\hat{\pi}(\varepsilon_X; \hat{\mu}, \hat{\pi}, \hat{f}_Z) = \text{expit}\left\{\text{logit } \hat{\pi}(x_0 | Z, W) + \varepsilon_X \hat{H}_X(Z, W; \tilde{p}_z)\right\},$$

with $\hat{H}_X(Z, W; \tilde{p}_z) = \{\hat{\mu}(x_0, Z, W) - \psi_{x_0}^{\text{pi}}(\hat{Q}; Z)\}/\kappa_{x_0, 2}^{\text{pi}}(\hat{Q}; Z)$.

Proof of (C1): $\hat{\pi}(\varepsilon_X = 0; \hat{\mu}, \hat{\pi}, \hat{f}_Z) = \text{expit}\{\text{logit } \hat{\pi}(x_0 | Z, W)\} = \hat{\pi}(x_0 | Z, W)$.

Proof of (C2):

$$\begin{aligned} \mathbb{E}(L_X(\tilde{\pi}; \hat{f}_Z)) &= - \int \frac{\tilde{p}(z)}{\hat{f}_Z(z | w)} \sum_{x \in \{0, 1\}} \pi(x | z, w) \log \tilde{\pi}(x | Z, W) dP(z, w) \\ &= - \int \frac{\tilde{p}(z)}{\hat{f}_Z(z | w)} \underbrace{\left\{ \sum_{x \in \{0, 1\}} \pi(x | Z, W) \log \frac{\tilde{\pi}(x | z, w)}{\pi(x | z, w)} \right.}_{\text{Kullback-Leibler (KL) divergence}} \\ &\quad \left. + \sum_{x \in \{0, 1\}} \pi(x | Z, W) \log \pi(x | z, w) \right\} dP(z, w), \end{aligned}$$

where for any $z \in \mathcal{Z}$, $w \in \mathcal{W}$, the KL divergence from $\pi(x | z, w)$ to $\tilde{\pi}(x | z, w)$ is minimized when $\pi(x | z, w) = \tilde{\pi}(x | z, w)$. Therefore, $\mathbb{E}(L_X(\tilde{\pi}; \hat{f}_Z))$ is minimized under the same condition.

Proof of (C3):

$$\begin{aligned} \frac{\partial}{\partial \varepsilon_X} L_X(\hat{\pi}(\varepsilon_X; \hat{\mu}, \hat{\pi}, \hat{f}_Z); \hat{f}_Z) \\ &= - \frac{\tilde{p}(Z)}{\hat{f}_Z(Z | W)} \frac{(\mathbb{I}(X = x_0) - \mathbb{I}(X = 1 - x_0)) \hat{\pi}(x_0 | Z, W)(1 - \hat{\pi}(x_0 | Z, W)) \hat{H}_X(Z, W; \tilde{p}_z)}{\hat{\pi}(X | Z, W)} \\ &= - \frac{\tilde{p}(Z)}{\hat{f}_Z(Z | W)} \hat{H}_X(Z, W; \tilde{p}_z) \{\mathbb{I}(X = x_0) - \hat{\pi}(x_0 | Z, W)\} \propto \Phi_{X, x_0}(\hat{Q}; \tilde{p}_z). \end{aligned}$$

D.2 Extensions to binary outcome

Under continuous Z , the loss function and submodel for targeting $\hat{\mu}$ are given by

$$L_Y(\tilde{\mu}) = -Y \log \tilde{\mu}(x_0, Z, W) - (1 - Y) \log (1 - \tilde{\mu}(x_0, Z, W)) ,$$

$$\hat{\mu}(\varepsilon_Y; \hat{\pi}, \hat{f}_Z) = \text{expit}\left\{\text{logit } \hat{\mu}(x_0, Z, W) + \varepsilon_Y \hat{H}_Y(Z, W; \tilde{p}_z)\right\} ,$$

where $\hat{H}_Y(X, Z, W; \tilde{p}_z) = \{\mathbb{I}(X = x_0) \tilde{p}(Z)\}/\{\kappa_{x_0, 2}^{\text{pi}}(\hat{Q}; Z) \hat{f}_Z(Z|W)\}$. The validity of this loss function and submodel follows the same reasoning as the proof for targeting $\hat{\pi}$ in Appendix D.1 and is therefore omitted for brevity.

Accordingly, step (T2) in Section 3.1.3 of the main manuscript is modified as follows:

(T2): *One step risk minimization for μ .* $\hat{\mu}^{(t)}$ is updated by finding $\hat{\varepsilon}_Y^{(t+1)}$ that minimizes the loss function L_Y . The optimization problem can be solved via a logistic regression without intercept: $Y \sim \text{offset}(\hat{\mu}^{(t)}(x_0, Z, W)) + \hat{H}_Y^{(t, t_X^*)}(Z, W; \tilde{p}_z)$. The coefficient of $\hat{H}_Y^{(t, t_X^*)}$ gives $\hat{\varepsilon}_Y^{(t+1)}$, satisfying: $\hat{\varepsilon}_Y^{(t+1)} = \arg \min_{\varepsilon_Y \in \mathbb{R}} P_n \Phi_{Y, x_0}(\hat{Q}^{(t, t_X^*)}; \tilde{p}_z)$.

The following updates are then made: $\hat{\mu}^{(t+1)}(x_0, Z, W) = \text{expit}\{\text{logit} \hat{\mu}^{(t)}(x_0, Z, W) + \hat{\varepsilon}_Y^{(t+1)} \hat{H}_Y^{(t, t_X^*)}(Z, W; \tilde{p}_z)\}$ and $\hat{Q}^{(t+1, 0)} = \{\hat{\mu}^{(t+1)}, \hat{\pi}^{(t+1, 0)}, \hat{f}_Z, \hat{p}_W\}$, where, for notational convenience, we define $\hat{\pi}^{(t+1, 0)} := \hat{\pi}^{(t, t_X^*)}$.

Under discrete Z , the loss function and submodel for targeting $\hat{\mu}$ are given by

$$L_Y(\tilde{\mu}) = -\hat{H}_Y(X, Z, W; z^*) \{Y \log \tilde{\mu}(X, Z, W) - (1 - Y) \log (1 - \tilde{\mu}(X, Z, W))\} ,$$

$$\hat{\mu}(\varepsilon_Y; \hat{\pi}, \hat{f}_Z) = \text{expit}\{\text{logit } \hat{\mu}(x_0, z^*, W) + \varepsilon_Y\} ,$$

where $\hat{H}_Y(X, Z, W; z^*) = \{\mathbb{I}(X = x_0, Z = z^*)\}/\{\hat{f}_Z(Z|W)\}$. The modification to step (T1) follows similarly and therefore omitted.

D.3 TMLE algorithms

Algorithm 1 TMLE UNDER DISCRETE Z AT A PRE-SPECIFIED z^* ($\psi_{x_0}(\hat{Q}^*; z^*)$)

- 1: **Obtain initial nuisance estimates:** $\hat{\mu}$, $\hat{\pi}^{(0)}$, \hat{f}_Z , and \hat{p}_W .
Estimate of π at the t^{th} iteration is denoted by $\hat{\pi}^{(t)}$, with $\hat{\pi}^{(0)} := \hat{\pi}$.
- 2: **Define loss functions & submodels** indexed by ε_Y , $\varepsilon_X \in \mathbb{R}$.

- Given $\hat{Q} = \{\hat{\mu}, \hat{\pi}, \hat{f}_Z, \hat{p}_W\}$, define the loss function & submodels for μ , indexed by $\varepsilon_Y \in \mathbb{R}$:

$$L_Y(\tilde{\mu}; \hat{f}_Z) = \frac{\mathbb{I}(X = x_0) \mathbb{I}(Z = z^*)}{\hat{f}_Z(z^* | W)} \{Y - \tilde{\mu}(x_0, z^*, W)\} ,$$

$$\hat{\mu}(\varepsilon_Y) = \hat{\mu} + \varepsilon_Y .$$

- Given $\hat{Q}^{(t)} = \{\hat{\mu}^*, \hat{\pi}^{(t)}, \hat{f}_Z, \hat{p}_W\}$ at iteration t , define the loss function & submodels for π , indexed by $\varepsilon_X \in \mathbb{R}$:

$$L_X(\tilde{\pi}) = -\frac{\mathbb{I}(Z = z^*)}{\hat{f}_Z(z^* | W)} \log \tilde{\pi}(x_0 | z^*, W) ,$$

$$\hat{\pi}(\varepsilon_X; \hat{f}_Z, \hat{\mu}, \hat{\pi}^{(t)}) = \text{expit}[\text{logit } \hat{\pi}^{(t)}(x_0 | z^*, W) + \varepsilon_X \hat{H}_X^{(t)}(z^*, W)] ,$$

where the auxiliary variable $\hat{H}_X^{(t)}(z^*, W) = \hat{\mu}^*(x_0, z^*, W) - \psi_{x_0}^{\text{pi}}(\hat{Q}^{(t)}; z^*)$.

- 3: **Update $\hat{\mu}$ in one step.**

- Given $\hat{Q} = \{\hat{\mu}, \hat{\pi}, \hat{f}_Z, \hat{p}_W\}$, fit the weighted following regression:

$$Y \sim \text{offset}(\hat{\mu}(x_0, z^*, W)) + 1, \text{with weight } = \{\mathbb{I}(X = x_0) \mathbb{I}(Z = z^*)\}/\hat{f}_Z(z^* | W) .$$

The intercept is the minimizer $\hat{\varepsilon}_Y$. Update $\hat{\mu}(x_0, z^*, W)$ as

$$\hat{\mu}^*(x_0, z^*, W) = \hat{\mu}(x_0, z^*, W) + \hat{\varepsilon}_Y .$$

- Let $\hat{Q}^{(0)} = \{\hat{\mu}^*, \hat{\pi}^{(0)}, \hat{f}_Z, \hat{p}_W\}$.

- 4: **Update $\hat{\pi}^{(0)}$ iteratively.** At the t^{th} iteration:

- Given $\hat{Q}^{(t)} = \{\hat{\mu}^*, \hat{\pi}^{(t)}, \hat{f}_Z, \hat{p}_W\}$, fit the weighted logistic regression without an intercept:

$$\mathbb{I}(X = x_0) \sim \text{offset}(\text{logit } \hat{\pi}^{(t)}(x_0 | z^*, W)) + \hat{H}_X^{(t)}(z^*, W) ,$$

with weight $\mathbb{I}(Z = z^*)/\hat{f}_Z(z^* | W)$.

The coefficient in front of $\hat{H}_X^{(t)}(z^*, W)$ is the minimizer $\hat{\varepsilon}_X^{(t)}$. Update $\hat{\pi}^{(t)}$ to $\hat{\pi}^{(t+1)}$ as

$$\hat{\pi}^{(t+1)}(x_0 | z^*, W) = \text{expit}[\text{logit } \hat{\pi}^{(t)}(x_0 | z^*, W) + \varepsilon_X^{(t)} \hat{H}_X^{(t)}(z^*, W)] .$$

- Let $\hat{Q}^{(t+1)} = \{\hat{\mu}^*, \hat{\pi}^{(t+1)}, \hat{f}_Z, \hat{p}_W\}$.

Iterate over this step while $|P_n \Phi_{X, x_0}(\hat{Q}^{(t+1)})| > C_{\text{stop}}$ for $C_{\text{stop}} = o_P(n^{-1/2})$.

Assume convergence is achieved at iteration $t = t^*$. Let $\hat{\pi}^* = \hat{\pi}^{(t^*)}$.

- 5: **Return** The TMLE $\psi_{x_0}(\hat{Q}^*)$ as

$$\psi_{x_0}(\hat{Q}^*; z^*) = \frac{1}{n} \sum_{i=1}^n \hat{\mu}^*(x_0, z^*, W_i) \hat{\pi}^*(x_0 | z^*, W_i) / \left(\frac{1}{n} \sum_{i=1}^n \hat{\pi}^*(x_0 | z^*, W_i) \right) .$$

Algorithm 2 TMLE UNDER CONTINUOUS Z AT A PRE-SPECIFIED $\tilde{p}(Z)$ ($\psi_{x_0}(\hat{Q}^*; \tilde{p}_z)$)

1: **Obtain initial nuisance estimates:** $\hat{\mu}^{(0)}$, $\hat{\pi}^{(0,0)}$, \hat{f}_Z , and \hat{p}_W .

Estimate of μ at the t -th across-nuisance iteration is denoted by $\hat{\mu}^{(t)}$, with $\hat{\mu}^{(0)} := \hat{\mu}$.

Estimate of π at the t' -th within-nuisance iteration under the t -th across-nuisance iteration is denoted by $\hat{\pi}^{(t,t')}$, with $\hat{\pi}^{(0,0)} := \hat{\pi}$.

2: **Define loss functions & submodels** indexed by $\varepsilon_Y, \varepsilon_X \in \mathbb{R}$.

- Given $\hat{Q} = \{\hat{\mu}, \hat{\pi}, \hat{f}_Z, \hat{p}_W\}$, define the loss function & submodels for μ , indexed by $\varepsilon_Y \in \mathbb{R}$:

$$L_Y(\tilde{\mu}; \hat{\pi}, \hat{f}_Z) = \hat{H}_Y(X, Z, W; \tilde{p}_z) \{Y_i - \tilde{\mu}(x_0, Z, W)\}^2, \\ \hat{\mu}(\varepsilon_Y) = \hat{\mu}(x_0, z^*, W) + \varepsilon_Y,$$

where $\hat{H}_Y(X, Z, W; \tilde{p}_z) = \{\mathbb{I}(X = x_0) \tilde{p}(Z) / \kappa_{x_0, 2}^{\text{pi}}(\hat{Q}; Z) \hat{f}_Z(Z | W)\}$.

- Define the loss function & submodels for π , indexed by $\varepsilon_X \in \mathbb{R}$ as follows:

$$L_X(\tilde{\pi}; \hat{f}_Z) = -\{\tilde{p}(Z) / \hat{f}_Z(Z | W)\} \log \tilde{\pi}(X | Z, W),$$

$$\hat{\pi}(\varepsilon_X; \hat{\mu}, \hat{\pi}, \hat{f}_Z) = \text{expit}\{\text{logit } \hat{\pi}(x_0 | Z, W) + \varepsilon_X \hat{H}_X(Z, W; \tilde{p}_z)\},$$

where $\hat{H}_X(Z, W; \tilde{p}_z) = \{\hat{\mu}(x_0, Z, W) - \psi_{x_0}^{\text{pi}}(\hat{Q}; Z)\} / \kappa_{x_0, 2}^{\text{pi}}(\hat{Q}; Z)$.

3: **Update estimates of μ and π iteratively.** At t -th across-nuisance iteration, with $\hat{Q}^{(t,0)} = \{\hat{\mu}^{(t)}, \hat{\pi}^{(t,0)}, \hat{f}_Z, \hat{p}_W\}$:

3a: Update $\hat{\pi}^{(t,0)}$ iteratively. At the t' -th iteration: $\hat{Q}^{(t,t')} = \{\hat{\mu}^{(t)}, \hat{\pi}^{(t,t')}, \hat{f}_Z, \hat{p}_W\}$

- Fit the weighted logistic regression without an intercept:

$$\mathbb{I}(X = x_0) \sim \text{offset}(\hat{\pi}^{(t,t')}(x_0 | Z, W)) + \hat{H}_X^{(t,t')}(Z, W), \text{ with weight} = \tilde{p}(Z) / \hat{f}_Z(Z | W).$$

The coefficient in front of $\hat{H}_X^{(t,t')}$ is the minimizer $\hat{\varepsilon}_X^{(t,t')}$. Update $\hat{\pi}^{(t,t')}$ to $\hat{\pi}^{(t,t'+1)}$:

$$\hat{\pi}^{(t,t'+1)}(\hat{\varepsilon}_X^{(t,t'+1)}; \hat{\mu}^{(t)}, \hat{f}_Z) = \text{expit}\{\text{logit} \hat{\pi}^{(t,t')}(x_0 | z^*, W) + \hat{\varepsilon}_X^{(t,t'+1)} \hat{H}_X^{(t,t')}(Z, W)\}.$$

- Let $\hat{Q}^{(t,t'+1)} = \{\hat{\mu}^{(t)}, \hat{\pi}^{(t,t'+1)}, \hat{f}_Z, \hat{p}_W\}$.

Iteratively update the current estimate of π until, for $t = t_X^*$, $|P_n \Phi_{X,x_0}(\hat{Q}^{(t,t_X^*)})| \leq C_{\text{stop}}$ for pre-specified $C_{\text{stop}} = o_P(n^{-1/2})$. Let $\hat{Q}^{(t,t_X^*)} = \{\hat{\mu}^{(t)}, \hat{\pi}^{(t,t_X^*)}, \hat{f}_Z, \hat{p}_W\}$.

3b: Update $\hat{\mu}^{(t)}$ in one step.

- Given $\hat{Q}^{(t,t_X^*)}$, fit the following weighted regression:

$$Y \sim \text{offset}(\hat{\mu}^{(t)}(x_0, Z, W)) + 1, \text{ with weight} = \hat{H}_Y^{(t,t_X^*)}(Z, W; \tilde{p}_z).$$

The intercept is the minimizer $\hat{\varepsilon}_Y^{(t+1)}$. Update: $\hat{\mu}^{(t+1)}(x_0, Z, W) = \hat{\mu}^{(t)}(x_0, Z, W) + \hat{\varepsilon}_Y^{(t+1)}$.

- Let $\hat{Q}^{(t+1,0)} = \{\hat{\mu}^{(t+1)}, \hat{\pi}^{(t+1,0)}, \hat{f}_Z, \hat{p}_W\}$, where $\hat{\pi}^{(t+1,0)} = \hat{\pi}^{(t,t_X^*)}$.

Repeat steps 3(a-b) until an across-nuisance iteration t^* satisfies $P_n \Phi_{Y,x_0}(\hat{Q}^{(t^*,0)}; \tilde{p}_z) \leq C_{\text{stop}}$ and $P_n \Phi_{X,x_0}(\hat{Q}^{(t^*,0)}; \tilde{p}_z) \leq C_{\text{stop}}$. Set $\hat{Q}^* = \hat{Q}^{(t^*,0)}$.

4: **Return** The TMLE $\psi_{x_0}(\hat{Q}^*; \tilde{p}_z)$ as

$$\psi_{x_0}(\hat{Q}^*; \tilde{p}(Z)) = \int \left\{ \sum_{i=1}^n \hat{\mu}^*(x_0, z, W_i) \hat{\pi}^*(x_0 | z, W_i) / \sum_{i=1}^n \hat{\pi}^*(x_0 | z, W_i) \right\} \tilde{p}(z) dz.$$

E Additional details on simulations

E.1 Details for Simulation 1

We considered sample sizes of 250, 500, 1000, 2000 and 4000. For each sample size, 1000 simulation replicates were conducted to empirically construct confidence intervals for the evaluation metrics, namely \sqrt{n} -Bias and n -Variance. The true parameter and its variance were obtained using the true nuisance functionals under a large sample of size 10^8 . This same procedure was adopted for computing the true parameter in all subsequent simulations.

We generated data from a DGP that ensures the identification functional for $\mathbb{E}(Y^{x_0})$ is invariant to the choice of z^* while maintaining a simple parametric form that allows theoretical computation of both the true ATE and the nonparametric EIF. The DGP satisfying these conditions is presented below, where “(binary)” refers to the setup with binary Z , and “(continuous)” refers to the setup with continuous Z .

$$W \sim \text{Binomial}(0.5)$$

$$(\text{binary}) \quad Z \sim \text{Binomial}(\text{expit}(-1 + W)), \quad (\text{continuous}) \quad Z \sim \text{Uniform}(0.1, 0.25(1 + W))$$

$$X \sim \text{Binomial}\left(\frac{1}{4}(2 - W + ZW)\right)$$

$$Y \sim 4 + X + \frac{1}{2}Z - \frac{1}{2}ZW - \frac{3}{2}W + (1 - W)(1 - X)(1 - Z) + \mathcal{N}(0, 0.1).$$

We prove the following expression is irrelevant of z .

$$\begin{aligned} & \frac{\sum_w \mu(x, z, w) \pi(x | z, w) p(w)}{\sum_w \pi(x | z, w) p(w)} \\ &= \mu(x, z, w = 1) + \frac{\mu(x, z, w = 0) - \mu(x, z, w = 1)}{\frac{\pi(x|z,w=1)}{\pi(x|z,w=0)} + 1} \\ &= \frac{1}{8} \left[4 + X - \frac{3}{2} \right] + \frac{1}{8}, \quad (\text{if } Y \text{ is binary}) \end{aligned}$$

$$= \left[4 + X - \frac{3}{2} \right] + 1, \quad (\text{if } Y \text{ is continuous}).$$

The key idea is to construct $\mu(x, z, w = 1, c)$ to be independent of z and to impose the condition $\mu(x, z, w = 0) - \mu(x, z, w = 1) = \alpha \left(\frac{\pi(x|z, w=1)}{\pi(x|z, w=0)} + 1 \right)$, for some constant α .

E.2 Details for Simulation 2

To induce model misspecification, we estimated the nuisance functionals using incorrect model specifications as follows:

Univariate binary Z setting

- *Misspecified models for μ and π :*
 - μ : $Y \sim 1 + X + Z + W$
 - π : $X \sim 1 + W + Z$ with a logit link
- *Misspecified model for f_Z :*
 - f_Z : $Z \sim 1$ with a logit link
- *All models misspecified:*
 - μ : $Y \sim 1 + X + Z + W$
 - π : $X \sim 1 + W + Z$ with a logit link
 - f_Z : $Z \sim 1$ with a logit link.

Univariate continuous Z setting

- *Misspecified models for μ :*
 - μ : $Y \sim 1 + X + Z + W$
- *Misspecified model for f_Z :*
 - f_Z : assume a conditional Normal distribution, with conditional mean estimated via a linear regression of the form $Z \sim 1 + W$
- *All models misspecified:*
 - μ : $Y \sim 1 + X + Z + W$
 - π : $X \sim 1 + W + Z$ with a logit link
 - f_Z : assume a conditional Normal distribution, with conditional mean estimated via a linear regression of the form $Z \sim 1$.

E.3 Details for Simulation 3

The DGP for Simulation 3 is given by:

$$W \sim \text{Uniform}(-2.5, 3.5), \quad (\text{binary}) \ Z \sim \text{Binomial}(\text{expit}\left(-\frac{5}{6} + \frac{5}{3} W\right)),$$

$$X \sim \text{Binomial}\left(\frac{1}{10}(5.5 + W - 2.75 Z - 0.5 ZW)\right), \quad Y \sim 1 + XZ + WX - XZW + \mathcal{N}(0, 1).$$

One can prove the following expression is irrelevant of z :

$$\frac{\int \mu(x, z, w) \pi(x | z, w) p(w) dw}{\int \pi(x | z, w) p(w) dw}$$

$$= \frac{\int (1 + xz) \pi(x | z, w) p(w) dw + x(1 - z) \int w \pi(x | z, w) p(w) dw}{\int \pi(x | z, w) p(w) dw}.$$

The key idea is to specify the distribution of W and the propensity score π such that when $x = 1$, we have $\int w \pi(x | z, w) p(w) dw = \int \pi(x | z, w) p(w) dw$. It is straightforward to show that this is true under the specified distributions:

When $x = 1$

$$\int w \pi(1 | z, w) p(w) dw = \int w \frac{1}{10}(5.5 + w - 2.75 z - 0.5 zw) p(w) dw$$

$$= \frac{1}{10}(5.5 * 0.5 + 3.25 - 2.75 * 0.5 z - 0.5 * 3.25 z)$$

$$\int \pi(1 | z, w) p(w) dw = \int \frac{1}{10}(5.5 + w - 2.75 z - 0.5 zw) p(w) dw$$

$$= \frac{1}{10}(5.5 + 0.5 - 2.75 z - 0.5 * 0.5 z).$$

E.4 Details for Simulation 4

Under continuous Z , the DGP is identical to that in Simulation 1. Under binary Z , the DGP parallels that of Simulation 3, except that the conditional distribution of $Z | W$ is

modified to include interaction and piecewise higher-order terms, specified as

$$(\text{binary}) \quad Z \sim \text{Binomial}(\text{expit}(-1 + 1 \cdot W + 0.4 \cdot \mathbb{I}(W < 0.3) \cdot W^2)).$$

When fitting the nuisance models using generalized linear regressions, key interaction and higher-order terms were intentionally omitted to induce model misspecification. Under continuous Z , the nuisance models were fitted following the same approach as in Simulation 2, where all models were misspecified. Under binary Z , the nuisance models were specified analogously, except that f_Z was estimated using a logistic regression of the form $Z \sim 1 + W$ with a logit link. The Super Learner incorporated a diverse library of algorithms, including generalized linear models (`SL.glm`), Bayesian generalized linear models (`SL.bayesglm`), generalized additive models (`SL.gam`), multivariate adaptive regression splines (`SL.earth`), random forests (`SL.ranger`), and the mean predictor (`SL.mean`).

E.5 Details for Simulation 5

The DGP under continuous Z is provided in display (84), where U_1 and U_2 denote two collections of unmeasured confounders, between W, X and W, Y respectively.

$$C_i \sim \text{Uniform}(0, 1), \quad i \in \{1, \dots, 10\}, \quad C = [C_1, \dots, C_{10}]$$

$$U_{1,i} \sim \mathcal{N}(0, 1), \quad i \in \{1, \dots, 10\}, \quad U_1 = [U_{2,1}, \dots, U_{2,10}]$$

$$U_{2,i} \sim \text{Uniform}(0, 1), \quad i \in \{1, \dots, 10\}, \quad U_2 = [U_{1,1}, \dots, U_{1,10}]$$

$$W \sim \mathcal{N}(C V_W^{1-10} + U_2 V_W^{11-20} + U_1 V_W^{21-30} + V_W^{31} \sum_{i=1}^{10} (C_i U_{2,i} + C_i U_{1,i} + U_{2,i} U_{1,i} + C_i U_{2,i} U_{1,i}), 0.5)$$

$$(\text{continuous}) Z \sim \mathcal{N}(V_Z^1 + V_Z^2 W + C V_Z^{3-12}, 0.5)$$

$$X \sim \text{Binomial}(\text{expit}(V_X^1 + V_X^2 Z + C V_X^{3-12} + U_1 V_X^{13-22} + V_X^{23} \sum_{i=1}^{10} (Z C_i + Z U_{1,i} + C_i U_{1,i})))$$

$$Y \sim \mathcal{N}(V_Y^1 + X V_Y^2 + C V_Y^{3-12} + U_2 V_Y^{13-22} + V_Y^{23} \sum_{i=1}^{10} (X C_i + X U_{2,i} + C_i U_{2,i}), 0.5), \text{ where}$$

$$\begin{aligned} V_M^T &= [0.5, -0.1, -0.4, -0.4, -0.3, 0.3, -0.2, 0.5, -0.3, 0.0, -0.3, -0.3, 0.3, -0.4, 0.0, -0.4, 0.1, -0.5, \\ &\quad 0.5, -0.2, 0.1, -0.2, 0.5, 0.4, 0.5, -0.4, 0.1, 0.0, 0.5, -0.1, 1.0] \end{aligned}$$

$$V_Z^T = [0.2, 0.5, 0.4, -0.5, -0.6, -0.6, -0.2, 0.7, 0.0, 0.6, 0.7, -0.1]$$

$$\begin{aligned} V_X^T &= [-0.2, 0.5, 0.3, -0.1, 0.3, -0.1, 0.4, -0.2, -0.4, 0.3, 0.4, 0.5, 0.1, 0.2, 0.3, 0.1, 0.2, -0.1, \\ &\quad -0.3, -0.3, -0.1, -0.2, 0.3] \end{aligned}$$

$$\begin{aligned} V_Y^T &= [0.1, 0.6, -0.3, 0.0, 0.3, 0.2, 0.0, 0.2, 0.0, 0.0, -0.2, -0.1, -0.2, 0.1, 0.3, \\ &\quad 0.1, -0.4, 0.1, -0.1, -0.1, 0.1, 0.4, 0.3]. \end{aligned} \tag{84}$$

Here, we use numeric superscripts to denote element selection. For example, V_Z^1 refers to the first element of the vector V_Z , while V_Z^{3-12} denotes the subvector consisting of the 3rd through 12th elements of V_Z , inclusive. We use superscript T to indicate the transpose operator, so that all the coefficient vectors, V_M , V_Z , V_X , and V_Y , are column vectors.

Calculating the true ATE via correct nuisance model specification is challenging under this DGP, as the closed-form expressions for the nuisance functionals are complex. Therefore, instead of relying on the identification functional defined by true nuisance functionals, we approximate the true ATE by intervening on X , setting it to 1 and 0, respectively, and computing the sample means of the resulting Y values to estimate $\mathbb{E}(Y^1)$ and $\mathbb{E}(Y^0)$. The difference between these two estimates defines the ATE.

E.6 Additional results on simulations

This subsection presents additional results from the simulation studies. Figures 3 and 4 illustrate the asymptotic convergence behavior of the TMLEs, one-step, and estimating equation estimators when all nuisance models are correctly specified, under univariate binary and continuous Z , respectively. Tables 7, 8, and 9 summarize the results for Simulations 2, 4, and 5, respectively, under the binary Z setting.

F Additional details on real data application

To model the relationships among variables flexibly, we estimated the conditional densities $p(Z | W)$ or $p(Z | W, S, G)$ via semiparametric kernel methods, implemented in the `np` R package (Hayfield & Racine 2008), and estimated other nuisance parameters using Super Learner with a library including generalized linear models (`SL.glm`), generalized additive models (`SL.gam`), multivariate adaptive regression splines (`SL.earth`), random forests (`SL.ranger`), and intercept-only models (`SL.mean`).

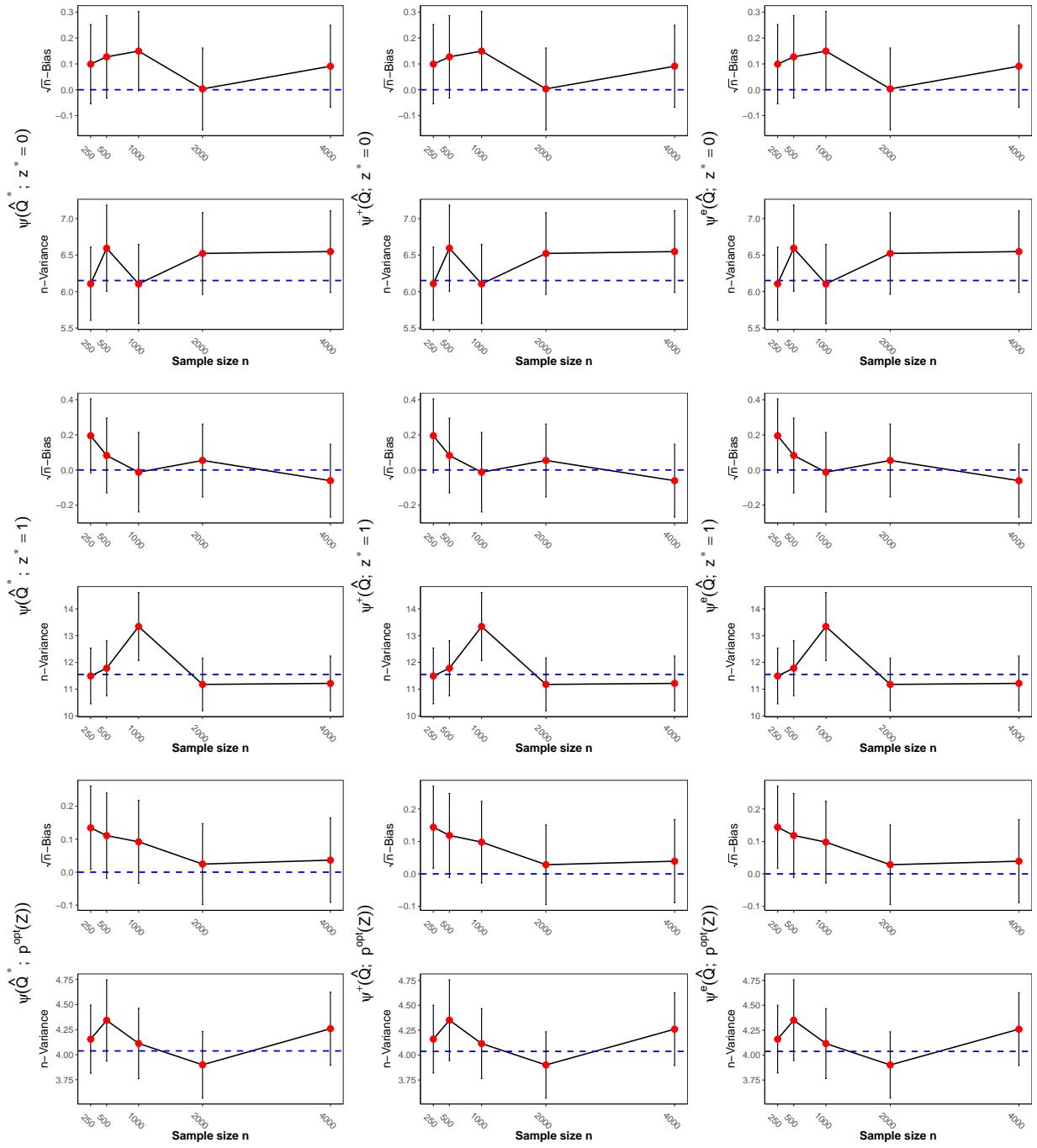


Figure 3: Simulation results demonstrating asymptotic linearity under univariate binary Z . The left column is for TMLE, the middle column is for the one-step estimators, and the right column is for the estimating equation estimators.

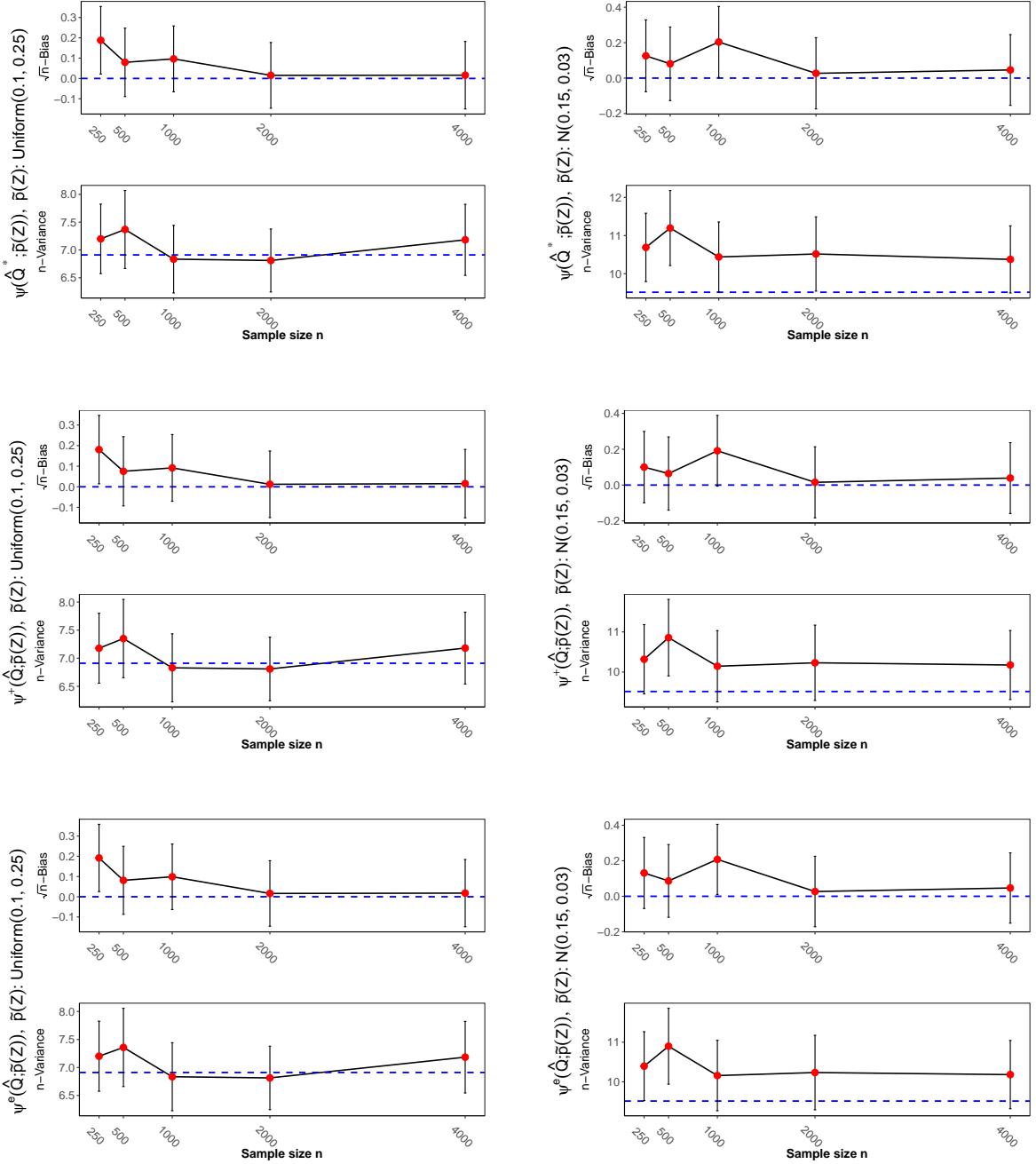


Figure 4: Simulation results demonstrating asymptotic linearity under univariate continuous Z . The first, second, and third rows correspond to TMLEs, one-step estimators, and estimating equation estimators, respectively. The first column reports results with $\tilde{p}(Z)$ specified as a Normal distribution $N(0.15, 0.03)$, and the second column reports results with $\tilde{p}(Z)$ specified as a Uniform distribution $\text{Uniform}(0.1, 0.25)$.

Table 7: Simulation results validating the double robustness property of the proposed estimators when Z is binary. Results from the estimating equation estimator coincide with those of the one-step estimator up to three decimal places and are therefore omitted.

		TMLEs						One-step estimators										
		f_Z			μ, π			f_Z			μ, π			<i>None</i>				
<i>Correct model(s)</i>		0	1	$p^{opt}(Z)$	0	1	$p^{opt}(Z)$	0	1	$p^{opt}(Z)$	0	1	$p^{opt}(Z)$	0	1	$p^{opt}(Z)$		
n=500	Bias	0.006	0.004	0.005	0.006	0.004	0.005	-0.079	0.004	-0.049	0.006	0.004	0.005	-0.095	0.036	-0.048		
	SD	0.115	0.154	0.093	0.115	0.153	0.094	0.119	0.154	0.095	0.115	0.154	0.093	0.117	0.134	0.092	0.115	0.147
	MSE	0.013	0.024	0.009	0.013	0.024	0.009	0.02	0.024	0.012	0.013	0.024	0.009	0.014	0.018	0.009	0.022	0.023
	CI coverage	93.7%	95.1%	93.2%	93.1%	93.9%	92.5%	88.2%	93.9%	88.1%	93.8%	95.3%	93.2%	92.4%	96.5%	92.9%	86.9%	94.1%
	CI width	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	88.7%	
	Bias	0.005	0	0.003	0.005	0	0.003	-0.08	0	-0.053	0.005	0	0.003	0.005	0.001	0.003	-0.096	0.032
n=1000	SD	0.078	0.116	0.064	0.078	0.115	0.065	0.081	0.116	0.066	0.078	0.116	0.064	0.08	0.1	0.063	0.079	0.11
	MSE	0.006	0.013	0.004	0.006	0.013	0.004	0.013	0.013	0.007	0.006	0.013	0.004	0.006	0.01	0.004	0.016	0.013
	CI coverage	95.1%	93.5%	94.8%	94.6%	92.1%	93.9%	83.3%	92.1%	84.9%	95.3%	93.7%	94.8%	93.6%	95.5%	94.8%	77.4%	91.5%
	CI width	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	85.6%	
	Bias	0	0.001	0.001	0	0.001	0.001	-0.085	0.001	-0.055	0	0.001	0.001	0	0.001	0	-0.101	0.033
	SD	0.057	0.075	0.044	0.057	0.075	0.044	0.059	0.075	0.045	0.057	0.075	0.044	0.058	0.065	0.044	0.058	0.071
n=2000	MSE	0.003	0.006	0.002	0.003	0.006	0.002	0.011	0.006	0.005	0.003	0.006	0.002	0.003	0.004	0.002	0.014	0.006
	CI coverage	94.6%	95.6%	95.1%	93.9%	93.9%	94%	65.7%	93.9%	75.2%	94.7%	95.6%	95.1%	93.4%	97.2%	94.9%	55%	93.5%
	CI width	0.22	0.298	0.177	0.214	0.284	0.17	0.217	0.285	0.172	0.221	0.299	0.177	0.214	0.284	0.17	0.218	0.286

Table 8: Comparative analysis of TMLEs, one-step, and estimating equation estimators under model misspecifications when Z is binary. Linear refers to generalized linear regression including only main effects, RF refers to random forest with 500 trees and a minimum node size of 5 for a continuous variable and 1 for binary, and CF denotes random forest with cross fitting using 10 folds. Results from the estimating equation estimator coincide with those of the one-step estimator up to three decimal places and are therefore omitted.

TMLEs $\psi(\hat{Q}^*; z^*)$												One-step estimators $\psi^+(\hat{Q}; z^*)$							
		Linear				SL				Linear				SL					
		$p^{opt}(Z)$		$p^{opt}(Z)$		$p^{opt}(Z)$		$p^{opt}(Z)$		$p^{opt}(Z)$		$p^{opt}(Z)$		$p^{opt}(Z)$		$p^{opt}(Z)$			
n=500	Bias	-0.199	-0.054	-0.102	-0.066	-0.017	-0.038	-0.005	0.017	0.006	-0.221	-0.079	-0.135	-0.098	-0.03	-0.06	-0.004	0.018	0.004
	SD	0.191	0.168	0.132	0.197	0.161	0.127	0.201	0.164	0.128	0.19	0.166	0.13	0.198	0.161	0.129	0.205	0.164	0.129
	MSE	0.076	0.031	0.028	0.043	0.026	0.017	0.04	0.027	0.017	0.085	0.034	0.035	0.049	0.027	0.02	0.042	0.027	0.017
	CI coverage	84.5%	93.4%	85%	91.7%	92.5%	91.7%	96.7%	95.2%	96.1%	84.1%	94%	83.1%	90.7%	93.7%	90.6%	97.7%	96.2%	96.9%
	- CI width	-0.791	-0.626	-0.482	-0.728	-0.588	-0.457	-0.842	-0.65	-0.508	-0.848	-0.677	-0.52	-0.793	-0.615	-0.487	-0.939	-0.677	-0.543
	Bias	-0.194	-0.052	-0.098	-0.041	-0.012	-0.025	-0.004	0.011	0.004	-0.217	-0.078	-0.131	-0.068	-0.022	-0.042	-0.008	0.011	0.001
n=1000	SD	0.141	0.12	0.091	0.152	0.117	0.092	0.15	0.116	0.089	0.139	0.119	0.09	0.155	0.118	0.097	0.151	0.116	0.089
	MSE	0.057	0.017	0.018	0.025	0.014	0.009	0.022	0.013	0.008	0.066	0.02	0.025	0.029	0.015	0.011	0.023	0.013	0.008
	CI coverage	70.2%	91.4%	79.5%	89.7%	92.6%	91%	94.6%	95.1%	95.7%	68.9%	90.2%	72.6%	88.7%	93.3%	88.1%	96.7%	95.6%	96.7%
	- CI width	-0.556	-0.449	-0.345	-0.521	-0.427	-0.332	-0.571	-0.457	-0.357	-0.595	-0.483	-0.372	-0.565	-0.443	-0.351	-0.628	-0.473	-0.379
	Bias	-0.196	-0.052	-0.099	-0.033	-0.008	-0.018	-0.007	0.006	0	-0.22	-0.079	-0.13	-0.053	-0.014	-0.03	-0.012	0.006	-0.002
	SD	0.095	0.082	0.065	0.101	0.079	0.064	0.098	0.079	0.063	0.094	0.081	0.064	0.104	0.08	0.066	0.099	0.079	0.063
n=2000	MSE	0.047	0.009	0.014	0.011	0.006	0.004	0.01	0.006	0.004	0.057	0.013	0.021	0.014	0.007	0.005	0.01	0.006	0.004
	CI coverage	51.2%	89.7%	63.7%	91.9%	95.2%	92.1%	95.7%	95.8%	96.1%	46%	86.8%	51.1%	90%	95.2%	90.1%	96.6%	96.8%	96.8%
	CI width	0.395	0.319	0.247	0.377	0.31	0.241	0.401	0.323	0.253	0.422	0.341	0.265	0.405	0.319	0.253	0.436	0.333	0.266

Table 9: Comparative analysis for the impact of cross-fitting on TMLEs, one-step, and estimating equation estimators in conjunction with the use of random forests. RF refers to random forest with 500 trees and a minimum node size of 5 for a continuous variable and 1 for binary, and CF denotes random forest with cross fitting using 10 folds. Results from the estimating equation estimator coincide with those of the one-step estimator up to three decimal places and are therefore omitted.

TMLEs $\psi(\hat{Q}^*; z^*)$												One-step estimators $\psi^+(\hat{Q}; z^*)$					
	RF			CF			RF			CF							
	z^*	0	1	$p^{opt}(Z)$	0	1	$p^{opt}(Z)$	0	1	$p^{opt}(Z)$	0	1	$p^{opt}(Z)$				
n=500	Bias	-0.571	-0.053	-0.277	-0.411	-0.042	-0.21	-0.596	-0.154	-0.336	-0.435	-0.03	-0.218				
	SD	0.174	0.143	0.119	0.185	0.156	0.125	0.159	0.13	0.11	0.182	0.16	0.124				
	MSE	0.356	0.023	0.091	0.203	0.026	0.06	0.381	0.04	0.125	0.223	0.026	0.063				
	CI coverage	3.5%	83.5%	18.2%	36.8%	94.2%	56.2%	1.9%	65.8%	6.2%	33.2%	94.5%	56.1%				
	CI width	0.509	0.424	0.325	0.698	0.623	0.462	0.512	0.42	0.328	0.712	0.642	0.476				
	Bias	-0.557	-0.051	-0.269	-0.404	-0.038	-0.206	-0.583	-0.147	-0.326	-0.428	-0.028	-0.211				
n=1000	SD	0.128	0.102	0.084	0.135	0.113	0.09	0.118	0.094	0.078	0.133	0.115	0.089				
	MSE	0.327	0.013	0.079	0.181	0.014	0.05	0.353	0.03	0.112	0.2	0.014	0.052				
	CI coverage	0.1%	79.6%	2.8%	13.3%	93.6%	31.9%	0.1%	49.7%	0.3%	10.5%	94.1%	31.3%				
	CI width	0.362	0.299	0.23	0.491	0.44	0.327	0.363	0.297	0.233	0.499	0.45	0.335				
	Bias	-0.558	-0.05	-0.269	-0.407	-0.035	-0.206	-0.584	-0.144	-0.325	-0.43	-0.026	-0.21				
	SD	0.088	0.071	0.06	0.092	0.077	0.063	0.082	0.065	0.056	0.091	0.079	0.063				
n=2000	MSE	0.32	0.007	0.076	0.174	0.007	0.046	0.347	0.025	0.109	0.193	0.007	0.048				
	CI coverage	0%	77.2%	0.1%	0.6%	93.5%	7.1%	0%	27.4%	0%	0.6%	94.3%	6.5%				
	CI width	0.256	0.211	0.163	0.346	0.311	0.231	0.256	0.21	0.164	0.351	0.316	0.236				