Abstract

In contemporary statistical learning, covariate shift correction plays an important role when distribution of the testing data is shifted from the training data. In this scenario, importance weighting ([Huang et al., 2007]) is naturally used to adjust for covariate shift. However, this simple strategy is not robust to model misspecification or excessive estimation error. To handle this problem, we propose a doubly robust covariate shift regression method by introducing an imputation model for conditional mean of the response to augment the importance weighted estimating equation. With a novel semi-nonparametric construction on the nuisance importance weight and imputation model, our method is more robust to excessive fitting error compared to the existing nonparametric or machine learning approaches and less likely to suffer from model misspecification than the parametric approach. To remove the overfitting bias of the nonparametric components under potential model misspecification, we construct specific calibrated moment estimating equations for the semi-nonparametric models. Theoretical properties of our estimator are studied. We show that our estimator attains the parametric rate when at least one nuisance model is correctly specified, estimation for the parametric part of the nuisance models achieves parametric rate and the nonparametric components satisfy the rate double robustness property ([Chernozhukov et al., 2018]). Simulation studies demonstrate that our method is more robust and efficient than parametric and fully nonparametric (machine learning) estimators under various configurations. We also examine the utility of our method through a real example about transfer learning of phenotyping algorithm for bipolar disorder. Finally, we discuss on possible ways to improve the (intrinsic) efficiency of our estimator and the potentiality of incorporating other nonparametric, high dimensional and machine learning models with our proposed framework.

Keywords: Covariate shift correction, model misspecification, model double robustness, rate double robustness, semi-nonparametric model.
1 Introduction

1.1 Background

Covariate shift, i.e. shift in the probability distribution of the predictors $X$, is one of the main reasons for poor transportability and generalizability of a supervised learning model from one data set to another. An example that arises frequently in modern biomedical research is the between-hospital transportability of prediction algorithms trained from electronic health records (EHR) data (Weng et al., 2020). Frequently encountered heterogeneity between hospital systems include the underlying patient population and how the EHR system encodes the data. For example, the prevalence of rheumatoid arthritis (RA) among patients with at least one billing code of RA differ greatly among hospitals (Carroll et al., 2012).

On the other hand, the conditional distribution of the disease outcome given all important EHR features may remain stable and unchanged for different cohorts, covariate shift in these features still has a large potential impact on the performance of some common phenotyping algorithms trained in one source cohort on another target cohort (Rasmy et al., 2018). Thus, correcting for the covariate shift is crucial to the transfer learning across multiple heterogeneous studying cohorts.

Robustness of covariate shift correction is an important topic and has been widely studied in existing literature of statistical learning. A branch of work including Wen et al. (2014); Chen et al. (2016); Reddi et al. (2015); Liu and Ziebart (2017) focused on the covariate shift correction methods that are robust to the extreme importance weight incurred by the high dimensionality. Main concern of their work is the robustness of a learning model’s prediction performance on the target data to the poor behaviour of the true importance weight. However, no existing work in this field elaborates on improving the validity and efficiency of statistical inference under covariate shift, in terms of the robustness to misspecification or poor estimation of the importance weight model.

1.2 Problem Statement

Consider $n$ labelled samples with observed response $Y$ and covariates $X = (X_1, \ldots, X_d)$ and $N$ unlabelled samples only observed on $X$. We use $S = 1$ to indicate that the sample is labelled and $S = 0$ for the unlabelled data. Suppose the labelled observations $\{(s_i, y_i, x_i, s_i) : i = 1, 2, \ldots, n\}$ are generated from the source population $\mathcal{S}$ with $s_i = 1$ and $(Y, X) \sim p_{\mathcal{S}}(x)q(y|x)$, while the unlabelled data $\{(s_i, y_i, x_i, s_i) : i = n + 1, \ldots, N + n\}$ with $s_i = 0$ are drawn from the target population $\mathcal{T}$ with $(Y, X) \sim p_{\mathcal{T}}(x)q(y|x)$. Here $p_{\mathcal{S}}$ and $p_{\mathcal{T}}$ represent the probability density measure of the source and target population respectively and $q(y|x)$ is the conditional density of $Y$ given $X$, which is the same across the two populations. Our target is to estimate $\beta_0$, the outcome model parameter of the target population $\mathcal{T}$, defined as the solution to $E_{\mathcal{T}}X(Y - g(X^{T}\beta)) = 0$, where $E_{\mathcal{T}}$ is the expectation operator on the target population $\mathcal{T}$ and $g(\cdot)$ is a link function, e.g. $g(\theta) = \theta$ represents linear regression and $g(\theta) = 1/(1 + e^{-\theta})$ for logistics regression. Since $g(X^{T}\beta)$ is potentially misspecified for $E[Y|X]$, directly using the source data to solve for $\beta$ will end up with inconsistent estimator due to the covariate shift between $\mathcal{T}$ and $\mathcal{S}$.

Let the density ratio $\omega_{0}(x) = p_{\mathcal{T}}(x)/p_{\mathcal{S}}(x)$ and $\tilde{\omega}(x)$ be an estimation for $\omega_{0}(x)$. To correct for the covariate shift bias, it is simple and natural to use importance weighting that solves the estimator $\hat{\beta}_{IW}$ from:

$$
\frac{1}{n} \sum_{i=1}^{n} \tilde{\omega}(x_i)x_i\{y_i - g(x_i^{T}\hat{\beta})\} = 0.
$$

(1)
Note that consistency of $\hat{\beta}_{IV}$ heavily relies on the performance of $\hat{\omega}(x_i)$ and can be impacted when $\hat{\omega}(x_i)$ is misspecified or poorly estimated.

1.3 Our contribution

In this paper, we propose an augmented regression method utilizing the unlabelled target samples to enhance the robustness of the outcome estimator to model misspecification. Our method introduces an imputation model $m(x)$ more complex than the outcome $g(x^T\beta)$, to impute the missing $y$ for the unlabelled data and augments \( \Pi \) with the imputed data. It is doubly robust in the sense that the estimator approaches the target $\beta_0$ when either the importance weight model $\omega(x)$ or the imputation model $m(x)$ is correctly specified.

As reviewed in Section 1.4, there are generally two existing strategies of constructing the importance weight and imputation models including low dimensional parametric models such as ordinary linear and logistic regression and fully nonparametric or machine learning methods, both of which have their advantage and limitation concerning model complexity. With relatively low complexity, the parametric strategy has desirable convergence rates in estimating the nuisance models but is more prone to model misspecification. In contrast, the fully nonparametric estimator is unlikely to be misspecified but its convergence rate can be impacted due to the curse of dimensionality of the nonparametric approaches like kernel smoothing or the possibly inflated model complexity of the machine learning models.

Instead of sticking to either one of these two strategies, we propose to combine them through a novel semi-nonparametric strategy that uses semi-nonparametric (generalized partial linear) nuisance models and achieves better trade-off on model complexity. It is more robust to excessive fitting error compared to the fully nonparametric or machine learning approach and less fragile to model misspecification than the parametric approach. Our proposed method is not a trivial extension of the two existing strategies as one needs to construct the moment equations more elaborately when estimating the nuisance models, to remove the over-fitting bias. We take semi-nonparametric models with kernel smoothing or the sieve (series) estimator \( \text{Beder, 1987} \) as a specific example for realizing this strategy.

Theoretical analysis shows that our proposed estimator is consistent and asymptotically normal (at the parametric rate) when at least one of the two nuisance models is correctly specified, the parametric components in the two models are $\sqrt{n}$-consistent and both nonparametric components are consistent and production of their convergence rates is $o_p(n^{-1/2})$, known as the rate double robustness property \( \text{Chernozhukov et al. (2018); Smucler et al. (2019)} \). This property, as well as our numerical studies demonstrate that our work can enrich the tool-kits in semiparametric inference by providing a more flexible and powerful approach for nuisance model construction.

1.4 Related literature

As a crucial area in casual inference and missing data problem, doubly robust estimator has been extensively studied for a long time \[ \text{Bang and Robins, 2005; Qin et al., 2008; Cao et al., 2009; van der Laan and Gruber, 2010; Tan, 2010; Vermeulen and Vansteelandt, 2015}. \] Among existing literature, estimation of average treatment effect on the treated can be viewed as analog to our covariate shift problem. To improve the doubly robust estimation for average treatment effect on the treated, \[ \text{Graham et al. (2016)} \] proposed a auxiliary-to-study tilting method and studied its efficiency, \[ \text{Zhao and Percival (2017)} \] proposed an entropy balancing approach that achieves double robustness without augmentation and \[ \text{Shu and Tan (2018)} \] proposed a doubly robust estimator attaining local efficiency and intrinsic efficiency. Besides, existing work like \[ \text{Rotnitzky et al. (2012)} \]
and Han (2016) are similar to us in the sense that their parameters of interests are multidimensional regression coefficients. Properties including intrinsic efficiency and multiple robustness has been studied in their work.

Recently, Rothe and Firpo (2015) proposed to use a fully nonparametric local polynomial approach in estimating the nuisance functions and study its theoretical guarantee. Fan et al. (2016) considered a semiparametric or nonparametric construction for the covariates balancing approach and studied its rate double robustness. Although they considered semiparametric modelling like additive model, their analysis was restricted to the rate double robustness property under the assumption that both nuisance models are correctly specified, which is substantially different from us. Chernozhukov et al. (2018) extended such classic nonparametric constructions to the machine learning setting inspired by Neyman orthogonality and realized with cross-fitting. Their proposed double machine learning framework facilitates the use of machine learning methods in robust and efficient casual inference. As a follow up, a number of recent work (Semenova and Chernozhukov, 2020; Liu et al., 2020, e.g.) explored this general framework in different specific settings. Our proposed semi-nonparametric construction can be viewed as a mitigation of the parametric and nonparametric (machine learning) models. As shown in this paper, this combination is novel and challenging.

Technically, our calibrated estimating equation for the nuisance models is in a similar spirit with the doubly robust average treatment effect estimator constructed using high dimensional sparse nuisance models (Smucler et al., 2019; Tan, 2020; Ning et al., 2020; Dukes and Vansteelandt, 2020; Ghosh and Tan, 2020; Liu et al., 2020). Similar to them, we impose certain moment conditions when constructing the nuisance models, to remove their first order (over-fitting) bias. The main difference between our work and theirs is that we treat the parametric and the nonparametric parts in our construction differently while they fit regularized high dimensional models on all covariates. This provides us more flexibility on model specification, as will be discussed in Section 6.3. Also, we mainly considers using the kernel or sieve to estimate our nonparametric components while they fits high dimensional parametric models. In addition, we consider a more complicated regression model case than the single average treatment effect in Tan (2020), which brings about additional challenges to handle, like irregular weights.

A similar idea of constructing semi-nonparametric nuisance models has been considered by Chakrabortty and Cai (2018) using this to improve the efficiency of linear regression under a semi-supervised setting with no covariate shift between the labelled and unlabelled data. They proposed a refitting procedure to adjust for the bias incurred by the nonparametric components in the imputation model while our method can be viewed as an extension of their approach that leverages the importance weight and imputation models to correct for the bias of each other, which is substantially novel and more challenging. As another main difference, we use semi-nonparametric model to estimate the parametric parts of the nuisance models that ensures their correctness and $\sqrt{n}$-consistency. While Chakrabortty and Cai (2018) did not actually elaborate on this point and only used parametric regression to estimate the parametric part, which does not guarantee the model double robustness property achieved by our method.

1.5 Outline of the paper

Remaining of the paper will be organized as follow. In Section 2 we introduce the general doubly robust estimating equation, our semi-nonparametric framework and specific procedures to estimate the parametric and nonparametric components of nuisance models. In Section 3 we present the large sample properties of our proposed method, i.e. its double robustness concerning model specification and estimation. In Section 4 we study the finite sample performance of our method and compare it with existing methods under various simulation settings. In Section 5, we apply our
method on transferring a phenotyping algorithm for bipolar disorder across two cohorts. Finally, we propose and comment on some potential ways to improve and extend our method in Section 6.

2 Method

2.1 General form of the doubly robust estimating equation

Let \( m_0(x) = E(Y|X = x) \) and specify an imputation model \( m(x) \) for \( m_0(x) \). First fitting the labelled source data to obtain its estimation \( \hat{m}(x) \), we then augment the estimating equation (1) with the term

\[
\frac{1}{N} \sum_{i=n+1}^{N+n} x_i \{ \hat{m}(x_i) - g(x_i^T \beta) \} - \frac{1}{n} \sum_{i=1}^{n} \hat{\omega}(x_i) x_i \{ \hat{m}(x_i) - g(x_i^T \beta) \},
\]

and construct the augmented estimating equation:

\[
\frac{1}{n} \sum_{i=1}^{n} \hat{\omega}(x_i) x_i \{ y_i - \hat{m}(x_i) \} + \frac{1}{N} \sum_{i=n+1}^{N+n} x_i \{ \hat{m}(x_i) - g(x_i^T \beta) \} = 0.
\]

We denote its solution as \( \hat{\beta}_{DR} \). When the density ratio model is correctly specified and consistently estimated, terms in (2) converge to 0 and the estimating equation (1) gives consistent estimation for \( \beta \). When the imputation model is correct, the term \( n^{-1} \sum_{i=1}^{n} \hat{\omega}(x_i) x_i \{ y_i - \hat{m}(x_i) \} \) in (3) converges to 0 and the estimating equation \( N^{-1} \sum_{i=n+1}^{N+n} x_i \{ \hat{m}(x_i) - g(x_i^T \beta) \} = 0 \) can give consistent estimator for \( \beta \). Thus, our construction (3) is doubly robust to the specification of the two nuisance models.

2.2 Semi-nonparametric nuisance models

Now we introduce our semi-nonparametric construction for the nuisance models in (3). Let \( z \in \mathbb{R}^{p_z} \), \( \psi \in \mathbb{R}^{p_{\phi}} \) and \( \phi \in \mathbb{R}^{p_{\beta}} \) be some functional bases of \( x \) and consider the nuisance models specified as

\[
\omega(x) = \exp\{ \psi^T \alpha + h(z) \} \quad \text{and} \quad m(x) = g(\phi^T \gamma + r(z)),
\]

where \( \psi^T \alpha \) and \( \phi^T \gamma \) represent some parametric components and \( h(z) \) and \( r(z) \) are unknown functions of \( z \) representing the nonparametric components. Correspondingly, we denote their estimation used in (3) as \( \hat{\omega}(x) = \exp\{ \psi^T \hat{\alpha} + \hat{h}(z) \} \) and \( \hat{m}(x) = g(\phi^T \hat{\gamma} + \hat{r}(z)) \).

Unlike \( \hat{\alpha} \) and \( \hat{\gamma} \), estimation errors of \( \hat{h}(z) \) and \( \hat{r}(z) \) are excessively larger than the desirable parametric rate \( n^{-1/2} \) since they are estimated using non-parametric approaches like kernel smoothing. To remove the bias incurred by their fitting error, we now fix the goal as estimating \( c^T \beta_0 \), an arbitrary linear functional of \( \beta_0 \), for simplicity and consider the asymptotic expansion for \( c^T \beta_{DR} \) that solves (3). In order not to let our math distract attention here, we leave the details of expansion in the theoretical part and directly present the key terms, i.e. the first order (over-fitting) bias incurred by \( \hat{h}(z) \) and \( \hat{r}(z) \).

Assume that the link function \( g(\cdot) \) has positive derivative \( \hat{g}(\cdot) \) and let \( \hat{g}(a) = \hat{g}(g^{-1}(a)) \), the information matrix of \( \beta \) be \( \Sigma_\beta = E_T [\hat{g}(X^T \beta)XX^T] \) and \( \bar{\Sigma}_\beta = N^{-1} \sum_{i=n+1}^{n+N} \hat{g}(x_i^T \beta)x_i x_i^T \). Suppose \( \hat{\omega}(x) \) and \( \hat{m}(x) \) converge to \( \omega(x) = \exp\{ \psi^T \alpha + \hat{h}(z) \} \) and \( m(x) = g(\phi^T \hat{\gamma} + \hat{r}(z)) \) and \( \beta_{DR} \) converges to \( \beta \). These limiting models or values are not necessarily the true models or values due to the potential model misspecification. Then the overfitting bias of \( c^T \beta_{DR} \) can be asymptotically
expressed as

\[
\Delta_1 = \frac{1}{\sqrt{n}} \sum_{i=1}^{n} \bar{\omega}(x_i) c^T \Sigma^{-1}_{\beta_0} x_i [y_i - g(\Phi^T \gamma + \bar{r}(z))] \{\bar{h}(z_i) - \bar{h}(z_i)\};
\]

\[
\Delta_2 = \frac{1}{\sqrt{n}} \sum_{i=1}^{n} \bar{\omega}(x_i) c^T \Sigma^{-1}_{\beta_0} x_i \bar{g}\{\bar{m}(x_i)\}\{\bar{r}(z_i) - \bar{r}(z_i)\}
\]

(4)

- \frac{\sqrt{n}}{N} \sum_{i=n+1}^{N+n} c^T \Sigma^{-1}_{\beta_0} x_i \bar{g}\{\bar{m}(x_i)\}\{\bar{r}(z_i) - \bar{r}(z_i)\}.

Technically, for the fully nonparametric or machine learning nuisance models like those in Rothe and Firpo (2015) and Chernozhukov et al. (2018), removing terms like \(\Delta_1\) and \(\Delta_2\) is natural for cross-fitted nuisance models, as one can assume \(\bar{m}(x) = m_0(x)\) and \(\bar{\omega}(x) = \omega_0(x)\) for the fully nonparametric construction and thus utilize the orthogonality between the “residual” of \(S\) or \(Y\) on the covariates \(X\) and the functional space of \(X\). Additional challenge occurs in our setting because this orthogonality does not hold for the whole set of covariates \(X\), due to the potential misspecification of the nuisance models. To handle this problem and eliminate the impact of \(\Delta_1\) and \(\Delta_2\) asymptotically, we impose moment conditions on the nonparametric components \(\bar{r}(\cdot)\) and \(\bar{h}(\cdot)\) that: for any measurable function \(f(\cdot)\) of the covariates \(Z\),

\[
E_S [\omega_0(X)c^T \Sigma^{-1}_{\beta_0} X (Y - g(\Phi^T \gamma + \bar{r}(Z))) f(Z)] = 0;
\]

(5)

\[
E_S [\exp\{\Psi^T \alpha + \bar{h}(Z)\} c^T \Sigma^{-1}_{\beta_0} X \bar{g}\{m_0(X)\} f(Z)] = E_T \left[ c^T \Sigma^{-1}_{\beta_0} X \bar{g}\{m_0(X)\} f(Z) \right].
\]

(6)

When the imputation model or the density ratio model is correctly specified, solving (5) or (6) leads to the true parameters \(r_0(\cdot)\) or \(h_0(\cdot)\) respectively. While if the models are potentially wrong, \(\bar{r}(\cdot)\) satisfying (5) and \(\bar{h}(\cdot)\) satisfying (6) still exist under some low-level regularity conditions. In specific, for each \(z \in \mathbb{R}^p\), \(\bar{r}(z)\) can be obtained by solving:

\[
E_S [\omega_0(X)c^T \Sigma^{-1}_{\beta_0} X (Y - g(\Phi^T \gamma + \bar{r}(z))) \mid Z = z] = 0,
\]

and \(\bar{h}(z)\) is given by

\[
\exp\{\bar{h}(z)\} = \frac{p_T(z) \cdot E_T \left[ c^T \Sigma^{-1}_{\beta_0} X \bar{g}\{m_0(X)\} \mid Z = z \right]}{p_S(z) \cdot E_S \left[ \exp(\Psi^T \alpha) c^T \Sigma^{-1}_{\beta_0} X \bar{g}\{m_0(X)\} \mid Z = z \right]}.
\]

One should find that compared with (4), we replace some limiting model with the corresponding true model in (5) and (6), to avoid the ill-definition that both conditions involve \(\bar{\omega}(\cdot)\) and \(\bar{m}(\cdot)\), which have not been defined yet and should be given by (5) and (6) themselves. However, this does not mean we need to specify both nuisance models correctly. We would like to explain on this point here. In our framework, the moment conditions are worth considering only when at least one nuisance model is correctly specified. When the importance weight model is correct, i.e. \(\bar{\omega}(\cdot) = \omega_0(\cdot)\), \(\omega_0(\cdot)\) and \(\beta_0\) in (5) can be estimated consistently so that one can solve for \(\bar{r}(Z)\) via (5). While \(m_0(\cdot)\) in (6) may not be correctly estimated since we may actually use the wrong model \(\bar{m}(\cdot) \neq m_0(\cdot)\) for imputation. However, \(\Delta_2\) can still be eliminated through the moment condition defined by replacing \(m_0(\cdot)\) with the wrong model \(\bar{m}(\cdot)\) in (6), which is satisfied because \(\exp\{\Psi^T \alpha + \bar{h}(Z)\}\) is correct. And similar logic applies for the case that the imputation model is correctly specified. This subtle point can be understood by inspecting our theoretical analysis in Section 3 and Appendix B.
2.3 Specific implementation

In this section, we introduce our proposal on realizing the moment conditions (5) and (6) under the model double robustness assumption with observed samples. For now, we mainly focus on classic local regression approaches like kernel smoothing and sieve that aim for low dimensional and smooth nonparametric components \( r(\cdot) \) and \( h(\cdot) \). While the high dimensional and machine learning strategies will be discussed in Section 6.3 and Appendix D.

Similar to Chernozhukov et al. (2018), we adopt cross-fitting on the source sample to eliminate the dependence between the estimators and the samples on which they are evaluated, which could help to remove the first order bias \( \Delta_1 \) and \( \Delta_2 \) through concentration. Randomly split the source samples into \( K \) disjoint sets \( \mathcal{I}_1, \ldots, \mathcal{I}_K \) of equal size \( n/K \). For each \( k \in \{1, 2, \ldots, K\} \), we denote the source samples leaving out \( \mathcal{I}_k \) as \( \mathcal{I}_k \) and introduce our construction procedures of the nuisance models with each \( \mathcal{I}_k \).

Note that besides their targets \( r(\cdot) \) and \( h(\cdot) \), (5) and (6) involve unknown parameters including \( \omega_0(\cdot) \), \( m_0(\cdot) \), \( \beta_0 \), \( \tilde{\gamma}_0 \), and \( \tilde{\alpha}_0 \) that needs to be specified and estimated beforehand. So we initially implement some standard semiparametric regression to obtain the estimators \( \tilde{\omega}^{[k]}(x) = \exp\{\psi^T \tilde{\alpha}^{[k]} + \tilde{h}^{[k]}(z)\} \) and \( \tilde{m}^{[k]}(x) = g(\phi^T \tilde{\gamma}^{[k]} + \tilde{\gamma}^{[k]}(z)) \) on \( \mathcal{I}_k \cup \{n + 1, \ldots, n + N\} \) where the nonparametric components are estimated with either sieve (Beder, 1987) or profile kernel/backfitting (Lin and Carroll, 2006). Let \( \tilde{\omega}^{[k]}(x) \) and \( \tilde{m}^{[k]}(x) \) approach some limiting models \( \omega^*(x) \) and \( m^*(x) \) satisfying \( \omega^*(x) = \omega_0(x) \) or \( m^*(x) = m_0(x) \) when the importance weight or imputation model is correctly specified. Then we solve

\[
\frac{K}{n(K - 1)} \sum_{i \in \mathcal{I}_k} \tilde{\omega}^{[k]}(x_i) x_i \{y_i - \tilde{m}^{[k]}(x_i)\} + \frac{1}{N} \sum_{i=n+1}^{N+n} x_i \{\tilde{m}^{[k]}(x_i) - g(x_i^T \beta)\} = 0,
\]

for \( \beta \) and denote the solution as \( \tilde{\beta}^{[k]} \), an initial estimator consistent for \( \beta_0 \) when at least one nuisance model is correct but typically not achieving the desirable parametric rate.

Then we introduce different strategies to obtain \( \tilde{\alpha}^{[k]} \) and \( \tilde{\gamma}^{[k]} \) used for constructing the final estimating equation for \( \beta \). Estimators \( \tilde{\alpha}^{[k]} \) and \( \tilde{\gamma}^{[k]} \) are supposed to be \( \sqrt{n} \)-consistent for their limiting parameters denoted as \( \bar{\alpha} \) and \( \bar{\gamma} \), no matter the nuisance models are correctly specified or not. It is known that under mild smoothness and regularity conditions, \( \tilde{\alpha}^{[k]} \) or \( \tilde{\gamma}^{[k]} \) are \( \sqrt{n} \)-consistent when the corresponding nuisance models are correctly specified (Severini and Staniswalis, 1994; Lin and Carroll, 2006). So it seems natural to set \( \tilde{\alpha}^{[k]} = \bar{\alpha}^{[k]} \) and \( \tilde{\gamma}^{[k]} = \bar{\gamma}^{[k]} \), referred as the “plug-in” estimators (Chernozhukov et al., 2016). However, \( \sqrt{n} \)-consistency of the plug-in estimators is not generally guaranteed under misspecified model in existing theory (Ai and Chen, 2007). So we propose and study two alternative approaches. First, similar to Chakrabortty and Cai (2018), we simply fit some parametric models of \( S_i \sim \psi_i \) and \( y_i \sim \phi_i \) to obtain \( \tilde{\alpha}^{[k]} \) and \( \tilde{\gamma}^{[k]} \). Second, motivated by Van de Geer et al. (2014) and Tan (2019); Liu et al. (2020), we propose in Appendix A bias correction procedures for the initial estimators \( \tilde{\alpha}^{[k]} \) and \( \tilde{\gamma}^{[k]} \) leveraging a debiasing model to remove their first order bias and obtain \( \sqrt{n} \)-consistent \( \tilde{\alpha}^{[k]} \) and \( \tilde{\gamma}^{[k]} \) under potential model misspecification. Numerical performance of all these three strategies, i.e. “Plug-in”, “Parametric” and “Debiased” estimators are studied in Sections 4 and 5. And we shall briefly comment on properties of the “Parametric” and “Debiased” estimators in Remark 1.

Remark 1. “Parametric”, i.e. estimators obtained by simply fitting parametric models without the nonparametric components tend to achieve the parametric rate under misspecified model but may not converge to the true parameters even when the nuisance models are correct since the nonparametric components are excluded. While this method is still more robust than the fully
parametric nuisance models since the nonparametric components are estimated and included at the following steps. Debiased (locally robust) semiparametric estimation is regarded to be more robust to the excessive fitting errors and misspecified model than the plug-in estimator and our bias correction procedure grants $\sqrt{n}$-consistency under smoothness and mild regularity conditions.

Then we construct the estimating equations for the nonparametric components. Let $K(z)$ represent some kernel function satisfying $\int K(z)dz = 1$ and define that $K_h(z) = K(z/h)$. Localizing the terms in (5) and (6) with $K_h(\cdot)$, we solve for $r(z)$ and $h(z)$ respectively from

\[
\frac{K}{n(K-1)h_p} \sum_{i \in I_{k}} K_h(z_i - z)c^T \hat{\Sigma}^{-1}_B x_i \left[ y_i - g \left\{ \phi_i^T \hat{\gamma}^{[k]} + r(z) \right\} \right] = 0;
\]

\[
\frac{K}{n(K-1)h_p} \sum_{i \in I_{k}} K_h(z_i - z)c^T \hat{\Sigma}^{-1}_B x_i \hat{\eta}(m^{[k]}(x_i)) \exp \{ \psi_i^T \hat{\alpha}^{[k]} + h(z) \} = \frac{1}{Nh_p} \sum_{i = n+1}^{n+N} K_h(z_i - z)c^T \hat{\Sigma}^{-1}_B x_i \hat{\eta}(m^{[k]}(x_i)).
\]

Equation (7) can be viewed as a calibration on the nonparametric components to ensure the orthogonality between the conditional residuals of $Y$ or $S$ and functions of $Z$ weighted by some nuisance functions of $X$. The parametric parts can include different (usually larger) sets of covariates compared to the nonparametric $Z$, and there is no need to calibrate on them as long as they achieve the parametric rate. This substantially distinguishes our framework from existing work utilizing similar idea of orthogonality under the fully nonparametric/machine learning/high dimensional settings (Fan et al., 2016; Chernozhukov et al., 2018; Tan, 2020).

As $c^T\hat{\Sigma}^{-1}_B x_i > 0$ (or $c^T\hat{\Sigma}^{-1}_B x_i < 0$) for all $i \in I_{k} \cup \{n+1, \ldots, n+N\}$, both equations in (7) have unique solution for each $z$, denoted by $\hat{r}^{[k]}(z)$ and $\hat{h}^{[k]}(z)$. Practically, one usually has $c^T\hat{\Sigma}^{-1}_B x_i$ not positive (or negative) definite but nearly half of these weights are positive and half are negative with centralized covariates. This makes (7) irregular and ill-posed, which could lead to inefficient and even inconsistent estimation. To fix this problem, we propose to divide the samples into two batches as $I^+ = \{i : c^T\hat{\Sigma}^{-1}_B x_i \geq 0\}$ and $I^- = \{i : c^T\hat{\Sigma}^{-1}_B x_i < 0\}$. Instead of solving (7), we solve

\[
\frac{1}{|I_{k} \cap I^+|} \sum_{i \in I_{k} \cap I^+} K_h(z_i - z)\hat{r}^{[k]}(z_i)c^T \hat{\Sigma}^{-1}_B x_i \left[ y_i - g \left\{ \phi_i^T \hat{\gamma}^{[k]} + r(z) \right\} \right] = 0;
\]

\[
\frac{1}{|I_{k} \cap I^-|} \sum_{i \in I_{k} \cap I^-} K_h(z_i - z)c^T \hat{\Sigma}^{-1}_B x_i \hat{\eta}(\hat{m}^{[k]}(x_i)) \exp \{ \psi_i^T \hat{\alpha}^{[k]} + h(z) \} = \frac{1}{|I^-|} \sum_{i \in \{n+1, \ldots, n+N\} \cap I^-} K_h(z_i - z)c^T \hat{\Sigma}^{-1}_B x_i \hat{\eta}(\hat{m}^{[k]}(x_i)),
\]

with $I^-$ taken as $I^+$ and $I^-$ in parallel. Denote the solutions to (8) as $\hat{r}^{[k]}_+(z)$, $\hat{r}^{[k]}_-(z)$ for $I^+ = I^+$ and $\hat{r}^{[k]}_+(z)$, $\hat{r}^{[k]}_-(z)$ for $I^+ = I^-$. Then we take

\[
\hat{r}^{[k]}_+(z_i) = I(i \in I^+)\hat{r}^{[k]}_+(z_i) + I(i \in I^-)\hat{r}^{[k]}_-(z_i) \quad \text{and} \quad \hat{r}^{[k]}_-(z_i) = I(i \in I^+)\hat{r}^{[k]}_+(z_i) + I(i \in I^-)\hat{r}^{[k]}_-(z_i),
\]

with a little abuse of notation as $I(i \in I^+)$ and $I(i \in I^-)$ are not deterministic on $z_i$. This modification still guarantees asymptotic removal of $\Delta_1$ and $\Delta_2$ since the divided two data sets are
disjoint with each other and one could trivially handle them separately and combine their derived convergence rates together.

After obtaining \( \hat{\gamma}^{[k]}(z_i) \) and \( \hat{\alpha}^{[k]}(z_i) \) for each \( k \in \{1, 2, \ldots, K\} \), we take \( \omega^{[k]}(x) = \exp\{\psi^T \hat{\alpha}^{[k]} + \hat{\gamma}(x)\} \), \( \tilde{m}^{[k]}(x) = g(\phi^T \hat{\alpha}^{[k]} + \hat{\gamma}(x)) \) and \( \hat{m}(x) = K^{-1}\sum_{k=1}^K \tilde{m}^{[k]}(x) \) and plug these estimated nuisance models into the cross-fitted version of the doubly robust estimating equation (3) written as:

\[
\frac{1}{n} \sum_{k=1}^K \sum_{i \in I_k} \omega^{[k]}(x_i) x_i \left\{ y_i - \tilde{m}^{[k]}(x_i) \right\} + \frac{1}{N} \sum_{i=n+1}^{N+n} x_i \{ \hat{m}(x_i) - g(x_i^T \beta) \} = 0. \tag{9}
\]

Let the solution of (9) be \( \hat{\beta}_{DR} \) and we take \( c^T \hat{\beta}_{DR} \) as the estimation for \( c^T \beta_0 \). For interval estimation of \( c^T \beta_0 \), we use bootstrap, which appears to have better numerical performance than using the asymptotic variance estimated directly by the moment estimator.

**Remark 2.** Different from the nonparametric components, we do not specify the estimating equation for the parametric estimators \( \hat{\alpha}^{[k]} \) and \( \hat{\gamma}^{[k]} \). In our framework, they could basically be estimated (and debiased) with any estimating equations that guarantee their \( \sqrt{n} \)-consistency for some limiting parameters equal to the true ones when the corresponding nuisance models are correct. This flexibility is particularly useful when the intrinsic efficiency \( \text{[Tan, 2010; Rotnitzky et al., 2013]} \) of our estimator is further desirable, i.e. \( c^T \hat{\beta}_{DR} \) is the most efficient among all the doubly robust estimators when \( \omega(\cdot) \) is correct and \( m(\cdot) \) has certain wrong specification. Interestingly, we find that one could elaborate an estimating procedure for \( \gamma(\cdot) \) to realize this property and shall leave relevant details in Section 6.2 and Appendix E.

### 3 Theoretical analysis

Assume \( \rho = n/N = O(1) \), \( K = O(1) \) and introduce three sets of assumptions as follows.

**Assumption 1** (Regularity condition). The link function \( g(\cdot) \) has continuous derivative \( \hat{g}(\cdot) \). Covariates \( X, Z, \Phi \) and \( \Psi \) belong to compact sets, response \( Y \) satisfies that \( E|Y|^2 < \infty \) and the information matrix \( \Sigma_{\beta_0} \) has its all eigenvalues bounded away from 0 and \( \infty \).

**Assumption 2** (Specification of the nuisance models). At least one of the following two conditions holds. (i) The importance weight model is correctly specified: \( \omega_0(x) = \exp\{\psi^T \alpha_0 + h_0(z)\} \) and \( \omega^*(x) = \tilde{\omega}(x) = \omega_0(x) \); \( \bar{r}(\cdot) \) solves the moment condition (4). (ii) The imputation model is correct: \( m_0(x) = g(\phi^T \gamma_0 + r_0(z)) \) and \( m^*(x) = \tilde{m}(x) = m_0(x) \); \( \bar{h}(\cdot) \) solves the moment condition (4).

**Assumption 3** (Estimation of the nuisance models). Let \( Z \) represent the domain of \( Z \). The estimation of the nuisance models satisfies that (i) \( \sqrt{n}(\hat{\alpha}^{[k]} - \alpha) \) and \( \sqrt{n}(\hat{\gamma}^{[k]} - \gamma) \) weakly converges to Gaussian distribution with mean 0 and variance of order 1; (ii) \( \sup_{z \in Z} |\hat{\gamma}^{[k]}(z) - \bar{\gamma}(z)| = o_p(1) \) and \( E_S\{\hat{\gamma}^{[k]}(Z) - \bar{\gamma}(Z)\}^2 = o_p(1/n) \). For each \( k \in \{1, 2, \ldots, K\} \).

**Remark 3.** Assumption [7] is mild and commonly used for asymptotic analysis of \( M \)-estimators \( \text{[Van der Vaart, 2000]} \). It is possible to relax it to have unbounded covariates with certain orders of moment and less smooth \( g(\cdot) \) without essentially changing the other assumptions. Assumption [2] assumes that at least one nuisance model is correct while the limiting value of the parametric part in the wrong model can be arbitrarily specified, which is conceptually similar to the ordinary double robustness condition for the parametric nuisance models \( \text{[Bang and Robins, 2005; Qin et al., 2008]} \). In addition, it naturally assumes that the limiting models are identical with the true models under
correct model specification and existence of the nonparametric components solving (5) and (6) under wrong modelling as verified in Section 2.3.

Remark 4. As commented in Remark 2, the bias corrected version of \( \hat{\alpha}^{[k]} \) and \( \hat{\gamma}^{[k]} \) are the most satisfactory to our theoretical framework as they simultaneously preserve validity (correctness) and asymptotic normality in Assumption 3(i) under potential model misspecification. Assumption 3(ii) assumes that both the nonparametric components are consistently estimated and production of their mean squared errors (MSE) is below \( o_p(1/n) \), in a similar sense as the rate doubly robust assumption brought out by Chernozhukov et al. (2018). For one-dimensional \( Z \), under mild regularity conditions like Assumption 1 and that limits of the components estimated nonparametrically are Lipschitz continuous, Assumption 3(ii) holds for the classic sieve or kernel specification (Tsybakov, 2008).

We impose the rate double robustness assumption, i.e. Assumption 3(ii) directly on the calibrated estimators \( \hat{\alpha}^{[k]}(\cdot) \) and \( \hat{\gamma}^{[k]}(\cdot) \) instead of looking into their specific estimation procedures, to preserve the generality of our theoretical results. While theoretical justification of Assumption 3(ii) on our specific construction introduced in Section 2.3 (or other possible constructions discussed in Section 6.3) is not trivially the same as the fully nonparametric or machine model case in Chernozhukov et al. (2018). It is because the estimating equations (7) involve the nuisance initial estimators so the calibrated nonparametric components are impacted by their estimation errors. It is concluded that our framework typically requires one to be able to estimate both nonparametric components at \( o_p(1/\sqrt{n}) \), which is stronger than Assumption 3(ii) that only requires their production to be \( o_p(1/n) \). We shall leave more details to Appendix C. Similar issue occurs to the calibration method for doubly robust estimator with high dimensional nuisance models proposed by Tan (2020) that requires the high dimensional coefficients of both nuisance models to be ultra-sparse so that their MSEs are controlled at rate \( o_p(1/\sqrt{n}) \).

Finally, we present the main theoretical results about the consistency and asymptotic validity of our estimator \( c^\top \hat{\beta}_{DR} \) in Theorem 1 with its proof found in Appendix B.

**Theorem 1.** Under Assumptions 1 to 3 it holds that \( \| \hat{\beta}_{DR} - \beta_0 \|_2 = o_p(1) \) and \( \sqrt{n}(c^\top \hat{\beta}_{DR} - c^\top \beta_0) \) weakly converges to Gaussian distribution with mean 0 and variance of order 1.

### 4 Simulation studies

We conduct simulation studies to investigate the performance of our proposed method and compare it with existing doubly robust approaches. To generate the data, we sample \( \mathbf{W} = (W_1, \ldots, W_4)^\top \) from gaussian distribution with mean 0 and auto-regressive covariance structure of order 1 and correlation coefficient 0.2. Then each \( W_j \) is truncated by \((-2, 2)\) and standardized to have mean 0 and variance 1. And we generate \( \mathbf{X} = (1, X_1, \ldots, X_4)^\top \) where \( X_1, X_2, X_3 \) and \( X_4 \) are taken as the standardized \( \exp(0.5W_1), W_2/(1 + \exp(W_1)), W_3 \exp(-0.2W_1) \) and \( |W_4|^{\frac{5}{2}} \) respectively. Let \( \Phi(\cdot) \) represent the cumulative distribution function of standard normal distribution. We design four configurations introduced as follows to simulate different scenarios of model specification.

(i) Assign the source indicator \( S \) via \( P(S = 1 \mid \mathbf{W}) = g(-0.6W_1 - 0.4W_3 - 0.4W_4 + h(W_2)) \), where \( g(a) = e^a/(1 + e^a) \). And generate binary outcome \( Y \) with:

\[
P(Y = 1 \mid \mathbf{X}) = g(0.5X_1 - 0.5X_3 - 0.5X_4 + 0.15X_1X_2 + 0.25X_3X_4 + r(X_2)),
\]

where \( h(W_2) = 0.4\{3\Phi(W_2) - 1.5\}^3 \) and \( r(X_2) = 0.4\{2\Phi(X_2) - 1\}^2 + 2\{2\Phi(X_2) - 1\}^3 \).
For (i)–(iv), we set the goal is to estimate the logistic model on the target population \( X \). In configurations (i) and (ii), model of addition, we add a nonlinear function \( X \) with linear and interaction of machine learning estimators with different construction strategies that remain the same under all models. Similar logic applies to the configurations (iii) and (iv) with the status of the imputation \( g \) hidden \( W \) respectively. The mean square error and absolute bias averaged over the target parameters confidence interval on each parameter, as summarized in Tables A3–A6 of Appendix F for configurations (i)–(iv) respectively. The mean square error and absolute bias averaged over the target parameters

(ii) Take \( P(Y = 1 | W) = g(-0.4W_1 + 0.4W_2 - 0.6W_3 + 0.4W_4) \) and
\[
P(Y = 1 | X) = g(0.4X_1 + 0.3X_2 + 0.5X_3 + 0.3X_4 + 0.15X_1X_2 + 0.15X_2X_3 + 0.2X_3X_4).
\]

(iii) Take \( P(Y = 1 | W) = g(0.25 + 0.4W_1 + 0.5W_2 + 0.4W_4 + 0.25W_1W_2 + 0.15W_2W_3 + r(W_3)) \),
where \( h(X_3) = 0.6\{2\Phi(X_3) - 1\}^2 + \{2\Phi(X_3) - 1\}^3 \) and \( r(W_3) = 0.6\{-1.5\Phi(W_3) + 0.5\}^3 \).

(iv) Take \( P(Y = 1 | W) = g(-0.4X_1 + 0.4X_2 - 0.6X_3 + 0.5X_4) \) and
\[
P(Y = 1 | W) = g(0.5W_1 + 0.5W_2 - 0.6W_3 - 0.3W_4 + 0.15W_1W_2 + 0.25W_2W_3 + 0.2W_3W_4).
\]

For (i)–(iv), we set \( n = 500 \) as the sample size of source data, \( N = 1000 \) for target data, and the goal is to estimate the logistic model on the target population \( T \), i.e. the solution of \( E_T X \{Y - g(X^T \beta)\} = 0 \). Our data generation procedure has a similar spirit as Kang and Schafer (2007) and Tan (2020). In configurations (i) and (ii), model of \( Y \) is constructed directly with the “observed” covariates \( X \) and likely to be characterized by some parametric or semiparametric logistic models with linear and interaction of \( X \). While the importance weight model is constructed using the hidden \( W \) so the parametric or semiparametric models of \( X \) is prone to misspecification. In addition, we add a nonlinear function \( r(X_2) \) to \( E[Y | X] \) in (i), which could be captured by the nonparametric component of our semi-nonparametric nuisance model but missed by the parametric models. Similar logic applies to the configurations (iii) and (iv) with the status of the imputation model and importance weight model interchanged. Accordingly, we consider doubly robust/double machine learning estimators with different construction strategies that remain the same under all configurations, summarized as follows:

(a) Parametric nuisance models (Parametric): the importance weight model is chosen as the logistic model of \( S \) against \( \Psi = X \) and the imputation model is specified as the logistic model of \( Y \) against \( \Phi = (X^T, X_1X_2, X_2X_3, X_3X_4)^T \) on \( S \).

(b) Semi-nonparametric nuisance models (Our method): the importance weight model is specified as a semi-nonparametric logistic model of \( \Psi^T \alpha + h(Z) \) and the imputation model is specified as \( \Phi^T \gamma + r(Z) \), where \( Z = X_2 \) for (i) and (ii) and \( Z = X_3 \) for (iii) and (iv). We include three ways of realizing our approach where \( \hat{a}^{[k]} \) and \( \tilde{\gamma}^{[k]} \) are constructed by “Plug-in”, “Parametric” and “Debiased” respectively, as introduced in Section 2.3

(c) Double machine learning with regularized additive (Additive) model: the nuisance models regress \( Y \) or \( S \) on features combining together \( X \), natural splines of each \( X_j \) with order 5 and all the interaction terms of these natural splines. Due to high dimensionality of the bases, we use a combination of \( \ell_1 \) and \( \ell_2 \) penalties for regularization.

(d) Double machine learning with kernel machine (Kernel machine): both models are estimated using support vector machine with the radial basis function kernel.

More implementing details of (a)–(d) are presented in Appendix F. Performance of the four approaches are evaluated through mean square error, bias and coverage probability of the 95% confidence interval on each parameter, as summarized in Tables A3–A6 of Appendix F for configurations (i)–(iv) respectively.
are summarized in Table I. Our method presented in Tables A3–A6 and I are constructed with the “Plug-in” $\hat{\alpha}^{[-k]}$ and $\hat{\gamma}^{[-k]}$. Though less strict on the asymptotic normality of the parametric components (under misspecified nuisance models), this construction is natural, easy-to-implement and preserves good numerical efficiency and validity as shown in Tables A3–A6 and I (see our discussion later in this section). We compare performance of the three constructions proposed in Section 2.8, i.e. “Plug-in”, “Parametric” and “Debiased” in Tables A7–A10. They show similar performance under all the four configurations while ”Plug-in” has slightly lower mean square errors and bias than the other two on most parameters. Thus, we shall recommend primarily using “Plug-in” for numerical implementation of our method and following discussions on the numerical performance of our method mainly correspond to this version.

Under all configurations, our method has better performance, especially smaller average bias (at least in 50%), than the two double machine learning approaches. Also, our method and Parametric perform well in interval estimation with coverage probabilities on all parameters under all configurations falling in (0.92, 0.98), the ±0.03 of the nominal level. While the two double machine learning approaches fail apparently on interval estimation of certain parameters, for example, both fail on interval estimation of $\beta_3$ under Configuration (i), on $\beta_0$ under (iii), and on $\beta_3$ under (iv). These demonstrate that our method achieves better balance on the model complexity than the fully nonparametric/machine learning constructions, leading to consistently better performance on point and interval estimation under all configurations.

Also, our method has significantly smaller mean square error than Parametric under (i) (relative efficiency being 0.72) and (iii) (relative efficiency being 0.50), with nonlinear effects in the nuisance models captured by our method and missed by the parametric approach. Under these two settings, our method also has (10% under (i) and 61% under (iii)) smaller average absolute bias than Parametric. While for (ii) and (iv) with the nonparametric components in our construction being redundant, performance of our method is close to the parametric approach. Thus, our nonparametric components help to improve estimation efficiency in the presence of nonlinear effects (under (i,iii)) while they do not hurt the efficiency when being redundant (under (ii,iv)). In addition, we find that our method still has slightly lower average mean squared errors than Parametric under (ii) and (iv) without non-linear effects in $E[Y \mid X]$ or $P(S = 1 \mid X)$. It should be due to that including redundant basis in the one nuisance model can effectively reduce the asymptotic variance of the estimator when the other one is wrong [Tsiatis, 2007; Kawakita and Kanamori, 2013].

5 Phenotyping of bipolar disorder under covariates shift

Growing availability of EHR data enables more accurate and efficient phenotyping algorithm in biomedical research [Liao et al., 2019]. Among the extensive (high-throughput) phenotypes studied in this area, bipolar disorder, a heritable mental disorder characterized by mood swings between mania and depression, has attracted great interests on how it is associated with and predicted by certain mental health EHR features [Monteith et al., 2015; Castro et al., 2015; McCoy Jr et al., 2018].

Though highly valuable in practice, constructing phenotyping algorithms with high quality is challenging. On one hand, unsupervised algorithms only based on EHR features [Liao et al., 2019] usually have good prediction performance in terms of receiver operating characteristic but can poorly estimate specific association parameters, i.e. the outcome models of the disease status against the EHR features. On the other hand, supervised methods require the availability of chart review labels for the response, obtained via extensive human efforts. As a result, efficiently utilizing the labels across different populations is crucial for accurate and transportable EHR phenotyping models. And statistical method is needed to properly adjust for extensive and nuisance covariate
Table 1: Average mean square error (MSE) and average absolute bias (Bias) of the doubly robust/double machine learning methods under different configurations. Parametric: doubly robust estimator with parametric nuisance models; Our method: doubly robust estimator using semi-nonparametric nuisance models with “Plug-in” parametric components; Additive: double machine learning estimator constructed with regularized additive nuisance models; Kernel machine: double machine learning estimator of support vector machine with radial basis function kernel. Configurations (i), (ii), (iii) and (iv) are as described in Section 4.

| Configuration | Parametric | Our method | Additive | Kernel machine |
|---------------|------------|------------|----------|----------------|
| (i) MSE       | 0.029      | 0.021      | 0.031    | 0.040          |
| (i) Bias      | 0.033      | 0.030      | 0.067    | 0.082          |
| (ii) MSE      | 0.018      | 0.016      | 0.023    | 0.028          |
| (ii) Bias     | 0.011      | 0.012      | 0.055    | 0.070          |
| (iii) MSE     | 0.038      | 0.019      | 0.044    | 0.033          |
| (iii) Bias    | 0.023      | 0.009      | 0.124    | 0.079          |
| (iv) MSE      | 0.022      | 0.019      | 0.029    | 0.029          |
| (iv) Bias     | 0.009      | 0.012      | 0.072    | 0.095          |

shift across different EHR data sets.

Our application example includes two patients cohorts: Partner Health System (PHS) and Vanderbilt University Medical Center (VUMC). Covariates $X$ at the two sites consists of demographic and EHR features including Age ($X_1$), Gender ($X_2$), Race (white or others, $X_3$), logarithm-count of the diagnostic codes for Bipolar disorder ($X_4$) and logarithm-count of the diagnostic codes for Major depressive disorder (MDD) or Depression ($X_5$). At the source site PHS ($S$), clinical investigators have manually labelled the binary disease status $Y$ for $n = 400$ patients. While the target site VUMC ($T$) has $N = 649$ unlabelled samples. Similar to Section 4, our goal is to learn the $\beta_0$ solving $E_T X \{Y - g(X^T \beta)\} = 0$ where $X = (1, X_1, \ldots, X_5)^T$ and $g(a) = e^a/(1 + e^a)$.

We again implement the doubly robust estimators introduced in Section 4, including Parametric, Our method (in three different versions), Additive and Kernel machine. In addition, we include the logistic model simply fitted on the source data without adjusting for covariate shift, named as Source, as a basic benchmark. The nuisance models of Parametric and the parametric components of Our method are again constructed using the linear terms and certain interaction terms in $X$ (see their implementing details presented in Appendix G). And we take $X_4$: Diagnostic codes for bipolar disorder as the covariate “$Z$” for the nonparametric component in our estimator. We make this choice considering that the main code is typically the most informative predictor for certain phenotype in EHR data, as reflected by magnitudes of the fitted coefficients in Table A11. So its nonlinear effect may be of large impact on the estimator. To illustrate this point, we plot the fitted nonparametric components of the two nuisance models in Figure A1. The fitted curves demonstrate significant nonlinear relationship between $Y$ or $S$ and $X_4$.

For validation, we asked the clinicians to create labels for another 200 patients in VUMC ($T$). We fit a logistic regression using these 200 labelled target samples to obtain a validation estimator (Target), denoted as $\hat{\beta}_{\text{valid}}$, that is free of covariate shift and (asymptotically) valid
for the target parameters. Fitted intercepts and coefficients of all methods are presented alone with their bootstrap standard errors in Table A11 of Appendix G. To measure the estimation performance of an estimator \( \hat{\beta} \), we calculate its relative mean square prediction error to \( \hat{\beta}_{\text{valid}} \) on \( \mathcal{T} \): 
\[
E_T \{ g(X^T\hat{\beta}_{\text{valid}}) - g(X^T\hat{\beta}) \}^2
\]
and the root mean square empirical standard error. Also, we measure its out-of-sample classification and prediction performance on the labelled target samples using receiver operating characteristic. Results are represented in Table 2.

Our method (with Plug-in parametric components) has the smallest relative mean square prediction error among all the estimators, with its relative rate being 0.09/0.13 = 0.69 to Parametric, 0.29 to Additive, 0.39 to Kernel machine and 0.33 to Source. Also, it has smaller empirical standard errors than the other three estimators on all parameters (see Table A11). And it has relative standard errors in average below 0.7 to the others. Thus, by trading-off the nonparametric and parametric modelling strategies in a better way, our method provides the most efficient estimation.

As for the receiver operating characteristic properties, the validation model (Target) achieves the highest (cross-validated) area under the curve. Our method has slightly larger area under the curve than the other doubly robust approaches and all of them has better performance than Source, which does not adjust for the covariate shift between the two health centers at all. Overall, the out-of-sample classification performances of the four doubly robust estimators are basically on the same level and close to the validation estimator: all their receiver operating characteristic measures vary within 11% of the validation estimator. One should note these measures have a different angle with the estimation performance measures presented in the first two rows of Table 2. For example, in our case, estimators \( \hat{\beta} \) and 0.5\( \hat{\beta} \) have the same area under the curve and \( F_{5\%/10\%} \) scores. And our primary goal is still point and interval estimation, on which our method shows better performance than the other methods.

In addition, we study our proposed constructions “Plug-in”, “Parametric” and “Debiased” in terms of their fitted outcomes and on the same performance evaluation in Tables A12 and A13. These three estimators show similar fitted coefficients in Table A13. As shown in Table A12, "Plug-in" and “Parametric” have close estimation and prediction performance on the validation set and the debiased construction has larger errors than them. Though attaining worse performance than "Plug-in" and “Parametric”, “Debiased” still outperforms the (fully nonparametric) machine learning approaches and has an equally well performance as the estimator with parametric nuisance models (see Tables 2 and A12).

Table 2: Estimation and prediction performance of the estimators in bipolar disorder phenotyping. Source: logistic model fitted with the 400 source samples in PHS; Parametric: doubly robust estimator with parametric nuisance models; Our method: doubly robust estimator using semi-nonparametric nuisance models with “Plug-in” parametric components; Additive: double machine learning estimator constructed with regularized additive nuisance models; Kernel machine: support vector machine with radial basis function kernel; Target: logistic model fitted with the 200 validation (labelled) samples in VUMC. RMSPE: relative mean square prediction error; Average SE: root mean square average of (empirical) standard errors; AUC: area under the curve; \( F_{5\%/10\%} \): \( F_1 \)-score (harmonic mean of precision and recall) at the classification cutoff with the false positive rate being 5% or 10%.

|             | Source | Parametric | Our method | Additive | Kernel machine | Target |
|-------------|--------|------------|------------|----------|----------------|--------|
| RMSPE       | 0.27   | 0.13       | 0.09       | 0.31     | 0.23           | N/A    |
| Average SE  | 0.63   | 1.40       | 0.88       | 1.15     | 2.92           | 1.01   |
| AUC         | 0.83   | 0.84       | 0.85       | 0.82     | 0.84           | 0.86   |
| \( F_{5\%} \) | 0.49   | 0.57       | 0.56       | 0.46     | 0.53           | 0.54   |
| \( F_{10\%} \) | 0.65   | 0.60       | 0.67       | 0.64     | 0.69           | 0.62   |
6 Further extension and discussion

6.1 Semi-supervised setting with large amounts of unlabelled data

In the primary application field of this paper, EHR phenotyping, sample size of unlabelled data is usually much larger than the size of labelled data so the semi-supervised setting is of particular interests. We shortly comment on how our method would benefit if there was large amounts of observed $X$ (without $Y$) in the source, target, or both populations. First, when both populations have unlabelled samples with sizes much larger than $n$, one can improve the convergence rate of the estimator $\hat{h}^{[k]}(\cdot)$, which makes Assumption 3(ii) easier to be satisfied. Second, it has been established that semi-supervised learning enables estimating varies types of target parameters more efficiently than the supervised method (Kawakita and Kanamori, 2013; Azriel et al., 2016; Gronsbell and Cai, 2018; Chakrabortty and Cai, 2018, e.g.). However, existing work is restricted to the setting where the unlabelled and labelled data are from the same population. In our case, it is of interests to further investigate whether having $N \gg n$ (unlabelled) target samples would benefit our estimator. As we can tell, if the importance weight model is correct, similar results of Kawakita and Kanamori (2013) and Chakrabortty and Cai (2018) should apply in our case and the asymptotic variance of $c^T\beta_{DR}$ could be reduced if one has $N \gg n$. While future work is needed to study this problem more systematically and rigorously.

6.2 Intrinsic efficiency

When the importance weight model is correctly specified while the imputation model may be wrong, asymptotic efficiency of our doubly robust estimator is dependent of the limiting parameters $\bar{\gamma}$ and $\bar{r}(\cdot)$. Under the parametric setting, there exists estimating equations for constructing the imputation model that grants one to always have the most efficient doubly robust estimator among those with the same specification of the imputation model. This property is referred as intrinsic efficiency (Tan, 2010; Rotnitzky et al., 2012). Under our semi-nonparametric framework, flexibility on specifying the parametric parts of the nuisance models makes the intrinsic efficiency of our proposed estimator worthwhile considering. In Appendix E we introduce a modified construction procedure for $\hat{m}^{[k]}(\cdot)$ that solves its parametric part and calibrates its nonparametric part simultaneously and grants the intrinsic efficiency of the doubly robust estimator of $c^T\beta_0$, and more generally, any continuous differentiable function of $\beta_0$.

6.3 More choices on modelling the nonparametric components

We use kernel smoothing to construct the calibrated estimators $\hat{\gamma}^{[k]}(\cdot)$ and $\hat{h}^{[k]}(\cdot)$, as introduced in Section 2.3. In our general semi-nonparametric framework, the calibration step is not restricted to this and we shall comment on some other potential choices. First, using sieve to represent $r(\cdot)$ and $h(\cdot)$ is natural and pretty close to kernel smoothing conceptually. As an advantage of sieve, it is more simple to implement than kernel, especially for constructing the intrinsic efficient estimator introduced in Section 6.2. We present relevant details in Appendix D.

Second, it is a common way in practice to model a non-linear function of some covariates with their high dimensional basis functions and incorporating high dimensional sparse models of covariates $Z$ with our framework is interesting. We introduce our proposal for specific implementation in Appendix D. We propose two dantzig equations with certain moment constraints to estimate the nuisance models. Our idea is similar to Smucler et al., 2019; Dukes and Vansteelandt, 2020; Tan, 2020, e.g.) who construct certain Karush–Kuhn–Tucker (moment) conditions for bias reduction. Different from them, we require the fixed (low) dimensional parametric estimators $\hat{\gamma}^{[k]}$ and
\( \hat{\alpha}_{[k]} \) to be arbitrary and converge at the parametric rate. To achieve this, we adopt debiased lasso \cite{ZhangZhang2014, JavanmardMontanari2014, VanDeGeeretal2014}. Consequently, our method has an additional flexibility on specifying the parametric parts compared with \cite{Tan2020, e.g.}. This flexibility allows us to use different basis \( \Phi \) and \( \Psi \) in the two nuisance models while they require the two models to have exactly the same covariates. And as discussed in Section 6.2, this flexibility is also useful in improving the intrinsic efficiency of our estimator.

We also note a potentiality of incorporating more complex modern machine learning methods, like random forest and neural network with our framework. Compared with classic nonparametric estimation methods like kernel smoothing and sieve, these approaches are less prone to curse of dimensionality and more applicable in practice. In recent, Liu et al. \cite{Liuetal2020} proposed a double machine learning approach for partial logistic model allowing one to estimate the nonparametric component of a semiparametric logistic model with arbitrary black-box learning algorithms and obtain a \( \sqrt{n} \)-consistent estimator for its parametric components. However, \( \sqrt{n} \)-consistency of their proposed estimator is guaranteed for correct model only. To incorporate such methods with our framework and strictly ensure its theoretical correctness (like our “Debiased” proposal), one needs modify them to guarantee that they output \( \sqrt{n} \)-consistent nuisance parametric estimators even when the nuisance models are wrongly specified.

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A Bias correction of the nuisance parametric estimators

We outline the debiasing procedure used to obtain the nuisance parametric components \( \tilde{\alpha}^{[k]} \) and \( \tilde{\gamma}^{[k]} \) mentioned in Section 2.3 as an alternative method to the natural “plug-in” estimation. It preserves better theoretical guarantee on the asymptotic normality (at rate \( n^{-1/2} \)) of \( \tilde{\alpha}^{[k]} \) and \( \tilde{\gamma}^{[k]} \) when their corresponding nuisance models are wrongly specified. First, inspired by Van de Geer et al. (2014), we introduce a debiasing procedure to estimate \( \gamma \) with arbitrary smooth link function \( g(\cdot) \) and it also works for \( \alpha \) of the logistic importance weight model.

Let \( b(z) \) be some basis function of \( z \), e.g. natural spline or Hermite polynomials, whose dimensionality grows with \( n \) and functional space can well approximate a smooth function of \( z \). For each \( k \in \{1, 2, \ldots, K\} \), randomly and equally split \( \mathcal{I}_k \) into \( \mathcal{I}_{k,1}, \ldots, \mathcal{I}_{k,K} \). Then for each \( \ell \), we solve \( \tilde{\gamma}^{[k,\ell]} \) and \( \tilde{\xi}^{[k,\ell]} \) from:

\[
\frac{K^2}{n(K-1)^2} \sum_{i \in \mathcal{I}_{k,\ell}} \left( \phi_i b(z_i) \right) [y_i - g(\gamma^T \phi_i + \xi^T b(z_i))] + \lambda_1 \nabla \rho_1(\gamma, \xi) = 0,
\]

where \( \rho_1(\gamma, \xi) \) represents some penalty function (for low dimensional \( z \), we recommend using \( \ell_2 \) penalty: \( \rho_1(\gamma, \xi) = \|\gamma\|^2_2 + \|\xi\|^2_2 \)), \( \nabla \rho_1(\gamma, \xi) \) is its gradient (or sub-gradient for \( \ell_1 \) penalty) and \( \lambda_1 \) is some tuning parameter chosen by cross-validation. Denote by

\[
\phi_{i,\gamma,\xi} = (\phi_{ij,\gamma,\xi})^T = \phi_i \hat{g}^{1/2} \{ \gamma^T \phi_i + \xi^T b(z_i) \}; \quad b_{\gamma,\xi}(z_i) = b(z_i) \hat{g}^{1/2} \{ \gamma^T \phi_i + \xi^T b(z_i) \}.
\]

Then for each \( j \in \{1, 2, \ldots, p_{\phi}\} \), fit

\[
\min_u \frac{K^2}{n(K-1)^2} \sum_{i \in \mathcal{I}_{k,\ell}} \left\{ \phi_{ij,\gamma,\xi,\ell} \tilde{\gamma}^{[k,\ell]} - \left( \phi_{ij,\gamma,\xi,\ell}^T, b_{\gamma,\xi} \tilde{\xi}^{[k,\ell]} \right) u \right\}^2 + \lambda_2 \rho_2(u),
\]

(A10)

to obtain the debiasing vector \( \tilde{u}_{[k,\ell]} \). We use cross-fitting to avoid over-fitting. For each \( i \in \mathcal{I}_{k,\ell} \), let \( \tilde{c}_{ij} = \phi_{ij} - (\phi_{ij,\gamma,\xi,\ell}^T, b_{\gamma,\xi}(z_i))^T \tilde{u}_{[k,\ell]} \) and take

\[
\tilde{\sigma}^2_j = \frac{K}{n(K-1)} \sum_{\ell=1}^K \sum_{i \in \mathcal{I}_{k,\ell}} \tilde{c}_{ij}^2 \hat{g} \left\{ \left( \tilde{\gamma}^{[k,\ell]} \right)^T \phi_i + \left( \tilde{\xi}^{[k,\ell]} \right)^T b(z_i) \right\} .
\]

Finally, \( \tilde{\gamma}^{[k]} = (\tilde{\gamma}_1^{[k]}, \ldots, \tilde{\gamma}_p_{\phi}^{[k]})^T \) is obtained through:

\[
\tilde{\gamma}^{[k]}_{ij} = \frac{1}{\tilde{\sigma}^2_j} \sum_{i \in \mathcal{I}_k} \frac{\tilde{c}_{ij}}{\tilde{\sigma}_j} \left[ y_i - g(\gamma^T \phi_i + \xi^T b(z_i)) \right]
\]

for each \( j \in \{1, 2, \ldots, p_{\phi}\} \), where \( \tilde{\gamma}^{[k]}_{ij} = K^{-1} \sum_{\ell=1}^K \tilde{\gamma}^{[k,\ell]}_{ij} \). In the same spirit as Van de Geer et al. (2014), \( \tilde{\gamma}^{[k]} \) can be viewed as an “one-step” estimator initialized at \( \tilde{\gamma}^{[k]}_j \). And its theoretical verification could follow a similar procedure as Van de Geer et al. (2014).

For the logistic importance weight model or the imputation model with logit link \( g(a) = e^a/(1+e^a) \), we propose a debiasing semiparametric logistic regression approach of special form inspired by Tan (2019) and Liu et al. (2020). Compared with the above introduced debiasing approach, this procedure relies on a more reasonable debiasing model without creating the “pseudo-variables” for \( \phi \) and \( b(z) \) in (A10). And it is used for the “Debiased” construction in our simulation and
real example where both nuisance models are logistic models. Let $y_i \in \{0, 1\}$ and again take the imputation model as an example and the importance weight could follow the same procedure.

For each $j$, we first fit a nonparametric model (using either sieve or kernel smoothing) for $\Phi_j \sim Z_j$ with data in $I_{k_j} \cap \{ i : y_i = 0 \}$ to obtain $\hat{d}_{k_j}^{[k]}(z)$, as an estimator of $E[\Phi_j | Z = z, Y = 0]$, and denote by $\bar{d}^{[k]}(z_i) = \{ \hat{d}_{1}^{[k]}(z_i), \ldots, \hat{d}_{p_0}^{[k]}(z_i) \}$. Then we again take $r(z) = \xi^T b(z)$ with $b(z)$ being some basis function of $z$ and solve:

\[
\frac{K}{n(K-1)} \sum_{k=1}^{L} \sum_{i \in I_{k}} \left\{ \phi_i - \frac{\hat{d}^{[k]}(z_i)}{b(z_i)} \right\} [y_i \exp(-\phi_i^T \gamma) - (1 - y_i) \exp(\xi^T b(z_i))] = 0, \tag{A11}
\]

to obtain the debiased estimator $\hat{\gamma}^{[k]}$. One can see Tan (2013) and Liu et al. (2020) for discussion on the theoretical validity of this approach.

\section*{B Proof of Theorem 1}

\textit{Proof.} Without loss of generality, assume $\|c\|_2 = 1$. Inspired by Chen et al. (2016), we expand the left side of (1) as

\[
\frac{1}{n} \sum_{k=1}^{K} \sum_{i \in I_k} \bar{\omega}^{[k]}(x_i) x_i \left\{ y_i - \hat{m}^{[k]}(x_i) \right\} + \frac{1}{N} \sum_{i = n+1}^{N+n} x_i \{ \hat{m}(x_i) - g(x_i^T \beta) \}
\]

\[
= \frac{1}{n} \sum_{i = 1}^{K} \sum_{k=1}^{K} \left\{ \bar{\omega}^{[k]}(x_i) - \hat{\omega}(x_i) \right\} x_i \{ \hat{m}^{[k]}(x_i) - \hat{m}(x_i) \}
\]

\[
+ \frac{1}{n} \sum_{k=1}^{K} \sum_{i \in I_k} \hat{\omega}(x_i) x_i \{ \hat{m}^{[k]}(x_i) - \hat{m}(x_i) \} - \frac{1}{N} \sum_{i = n+1}^{N+n} x_i \{ \hat{m}(x_i) - \hat{m}(x_i) \}
\]

\[
+ \frac{1}{n} \sum_{k=1}^{K} \sum_{i \in I_k} \left\{ \hat{\omega}^{[k]}(x_i) - \hat{\omega}(x_i) \right\} x_i \{ y_i - \hat{m}(x_i) \}
\]

\[
= V(\beta) + \Delta_a + \Delta_b + \Delta_c.
\]

We first prove the consistency of the solution $\hat{\beta}_{DR}$. By Assumption 1 that the covariates belong to compact sets and Assumption 3 that $\hat{\alpha}^{[k]} - \alpha = O_p(1/\sqrt{n})$, $\hat{\gamma}^{[k]} - \gamma = O_p(1/\sqrt{n})$, $\sup_{z \in \mathcal{Z}} |\hat{h}^{[k]}(z) - \bar{h}(z)| = o_p(1)$ and $\sup_{z \in \mathcal{Z}} |\hat{r}^{[k]}(z) - \bar{r}(z)| = o_p(1)$, for each $k$, there exists absolute constant $C > 0$ that

\[
\|\Delta_a\|_\infty \leq n^{-1} \sum_{i = 1}^{n} \bar{\omega}(x_i) \|x_i\|_\infty \cdot \max_{k=1, \ldots, K, i \in I_k} \left| \frac{\bar{\omega}^{[k]}(x_i)}{\omega(x_i)} - 1 \right| \left\{ \hat{m}^{[k]}(x_i) - \hat{m}(x_i) \right\}
\]

\[
\leq C \max_{1 \leq k \leq K, i \in I_k} \left\{ \| \psi_i \|_\infty \| \alpha^{[k]} - \bar{\alpha} \|_1 + |\hat{h}^{[k]}(z_i) - \bar{h}(z_i)| \right\} \left\{ \| \phi_i \|_\infty \| \gamma^{[k]} - \bar{\gamma} \|_1 + |\hat{r}^{[k]}(z_i) - \bar{r}(z_i)| \right\}
\]

\[
+ o_p \left( \max_{k, i \in I_k} \left\{ \| \psi_i \|_\infty \| \alpha^{[k]} - \bar{\alpha} \|_1 + |\hat{h}^{[k]}(z_i) - \bar{h}(z_i)| \right\}^2 \right)
\]

\[
+ o_p \left( \max_{k, i \in I_k} \left\{ \| \phi_i \|_\infty \| \gamma^{[k]} - \bar{\gamma} \|_1 + |\hat{r}^{[k]}(z_i) - \bar{r}(z_i)| \right\}^2 \right)
\]
\[
\|\Delta_0\|_\infty \leq C \left\{ N^{-1} \sum_{i=1}^{N} \|\xi_i\|_\infty + n^{-1} \sum_{i=1}^{n} \tilde{\omega}(\xi_i) \|\xi_i\|_\infty \right\} \max_{k,i \in I_k} \left\| \phi_i \|_\infty \| \hat{\gamma}[k] - \gamma + \tilde{r}[k](z_i) - \bar{r}(z_i) \right\| = o_p(1);
\]

\[
\|\Delta_c\|_\infty \leq C n^{-1} \sum_{i=1}^{n} \tilde{\omega}(\xi_i) \|\xi_i\|_\infty |y_i - \tilde{m}(\xi_i)| \max_{k,i \in I_k} \left\| \psi_i \|_\infty \| \alpha[1,k] - \alpha \|_1 + \hat{h}[k](z_i) - \bar{h}(z_i) \right\| = o_p(1).
\]

Thus, \( \hat{\beta}_{DR} \) solves: \( V(\beta) + o_p(1) = 0 \). Let the solution of \( EV(\beta) = 0 \) be \( \bar{\beta} \). When \( \omega(\cdot) = \omega_0(\cdot) \),

\[
EV(\beta) = E_S \omega_0(X) X \{ Y - g(X^T \beta) \} + E_S \omega_0(X) \{ g(X^T \beta) - \bar{m}(X) \} - E_T \{ g(X^T \beta) - \bar{m}(X) \} = E_T X \{ Y - g(X^T \beta) \} + 0.
\]

When \( \tilde{m}(\cdot) = m_0(\cdot) \), \( EV(\beta) = 0 + E_T \{ m_0(X) - g(X^T \beta) \} \). Both cases lead to solution \( \beta_0 \). So under Assumption 2, we have \( \bar{\beta} = \beta_0 \). Then by Assumption 3 that \( D_0 \) and \( \beta_0 \) belongs to compact sets and the uniform law of large numbers (ULLN) (Pollard, 1990, Theorem 8.2), as \( n \to \infty \), \( \sup_{\beta \in B} \| V(\beta) - EV(\beta) \| = o_p(1) \) and \( \hat{\beta}_{DR} \) converges to \( \beta_0 \) in probability.

Then we consider the asymptotic expansion of \( \hat{\beta}_{DR} \). Noting that \( \hat{\beta}_{DR} \) is consistent for \( \beta_0 \), by Theorem 5.21 of Van der Vaart (2000), we expand (A12) with respect to \( c^T \hat{\beta}_{DR} \) as:

\[
\sqrt{n} (c^T \hat{\beta}_{DR} - c^T \beta_0) = \frac{1}{\sqrt{n}} \sum_{i=1}^{n} \tilde{\omega}(\xi_i) c^T \Sigma^{-1}_{\beta_0} x_i \{ y_i - \tilde{m}(\xi_i) \} + \sqrt{\frac{\rho}{N}} \sum_{i=1}^{N} c^T \Sigma^{-1}_{\beta_0} x_i \{ \tilde{m}(\xi_i) - g(x_i^T \beta_0) \} + \frac{1}{\sqrt{n}} \sum_{k=1}^{K} \sum_{i \in I_k} \{ \tilde{\omega}[k](\xi_i) - \tilde{\omega}(\xi_i) \} c^T \Sigma^{-1}_{\beta_0} x_i \{ y_i - \tilde{m}(\xi_i) \} + \frac{1}{\sqrt{n}} \sum_{k=1}^{K} \sum_{i \in I_k} \{ \tilde{\omega}[k](\xi_i) - \tilde{\omega}(\xi_i) \} \{ \tilde{m}[k](\xi_i) - \bar{m}(\xi_i) \} =: V + \Xi_1 + \Xi_2 + \Delta_3.
\]

Again using Assumptions 1 and 2 and that \( \rho = O(1) \), we have \( EV = 0 \) and \( EV^2 < \infty \). By central limited theory (CLT), \( V \) converges to \( N(0, \sigma^2) \) in distribution where \( \sigma^2 \) represents the asymptotic variance of \( V \) and is order 1. Then we consider the remaining terms separately. First, we have

\[
\Xi_1 = \frac{1}{\sqrt{n}} \sum_{k=1}^{K} \sum_{i \in I_k} \tilde{\omega}(\xi_i) c^T \Sigma^{-1}_{\beta_0} x_i \{ y_i - g(\phi^T \gamma + \bar{r}(z)) \} \left[ \psi_i^T (\hat{\alpha}[1,k] - \alpha) + O_p(\{ \psi_i^T (\hat{\alpha}[1,k] - \alpha) \}^2) \right]
\]

\[
+ \frac{1}{\sqrt{n}} \sum_{k=1}^{K} \sum_{i \in I_k} \tilde{\omega}(\xi_i) c^T \Sigma^{-1}_{\beta_0} x_i \{ y_i - g(\phi^T \gamma + \bar{r}(z)) \} \Delta h[k](z_j) =: U_1 + \Delta_1,
\]

(A14)

where \( \Delta h[k](z_j) = \hat{h}[k](z_i) - \bar{h}(z_i) + O_p(\{ \hat{h}[k](z_i) - \bar{h}(z_i) \})^2 \). By Assumption 3, \( \sqrt{n}(\hat{\alpha}[1,k] - \alpha) \) is asymptotic normal with mean 0 and variance of order 1 and using the regularity condition in
Assumption 1

\[ n^{-1} \sum_{i=1}^{n} \bar{\omega}(x_i) c^T \Sigma_{\beta_0}^{-1} x_i [yi - g(\Phi^T \gamma + \bar{r}(z))] \psi_i = O_p(1), \]

for each \( k \), by law of large number (LLN). Combining these with Slutsky’s Theorem leads to that \( U_1 \) is asymptotically normally distributed with mean 0 and variance of order 1.

For \( \Delta_1 \), by Assumption 2, the moment condition:

\[ E_S \left[ \bar{\omega}(X) c^T \Sigma_{\beta_0}^{-1} X (Y - g(\Phi^T \gamma + \bar{r}(Z))) \right] = 0 \]

holds because under Assumption 2(i), both limiting parameters \( \omega^*(\cdot) = \bar{\omega}(\cdot) = \omega_0(\cdot) \) and \( \bar{r}(\cdot) \) solves Assumption 1, by Assumption 2(ii), \( E_S[Y|X] = g(\Phi^T \gamma + \bar{r}(Z)) \), leading to

\[ E_S \left[ \bar{\omega}(X) c^T \Sigma_{\beta_0}^{-1} X (Y - g(\Phi^T \gamma + \bar{r}(Z))) \mid X \right] = 0. \]

Combining this with the fact that \( \hat{h}^{[k]}(\cdot) \) is independent of the data in \( \mathcal{I}_k \) due to the use of cross-fitting, we have that \( \hat{h}^{[k]}(\cdot) \) is asymptotically normally distributed with mean 0 and variance of order 1.

For \( \Delta_2 \), we write \( \Xi_1 \) as

\[ \Xi_1 = \sum_{i=1}^{K} \sum_{k=1}^{N} \bar{\omega}(x_i) c^T \Sigma_{\beta_0}^{-1} x_i g(\Phi^T \gamma + \bar{r}(z)) \Delta h^{[k]}(z_j) \]

\[ O \left( \sum_{1 \leq k \leq K, i \in I_k} | \hat{h}^{[k]}(z_i) - h(z_i) | \cdot \max_{1 \leq i \leq n} | \bar{\omega}(x_i) c^T \Sigma_{\beta_0}^{-1} x_i g(\Phi^T \gamma + \bar{r}(z)) | \right) = o_p(1). \]

Combining this with \( E|Y|^2 < \infty \) by Assumption 1, we use CLT to derive that \( \Delta_1 = o_p(1) \). Thus, by Assumption 1, \( \Xi_1 = o_p(1) \) is asymptotically normal with mean 0.

Similarly, we write \( \Xi_2 \) as

\[ \Xi_2 = \frac{1}{n} \sum_{k=1}^{K} \sum_{i=1}^{n} \bar{\omega}(x_i) c^T \Sigma_{\beta_0}^{-1} x_i g(\Phi^T \gamma + \bar{r}(z)) \left[ \Phi_i^T (\hat{\gamma}^{[k]} - \gamma) + O_p((\Phi_i^T (\hat{\gamma}^{[k]} - \gamma))^2) \right] \]

\[ - \frac{\sqrt{n}}{N} \sum_{i=n+1}^{N+n} c^T \Sigma_{\beta_0}^{-1} x_i g(\Phi^T \gamma + \bar{r}(z)) \left[ K^{-1} \sum_{k=1}^{K} \Phi_i^T (\hat{\gamma}^{[k]} - \gamma) + O_p((\Phi_i^T (\hat{\gamma}^{[k]} - \gamma))^2) \right] \]

\[ + \frac{1}{n} \sum_{k=1}^{K} \sum_{i=1}^{n} \bar{\omega}(x_i) c^T \Sigma_{\beta_0}^{-1} x_i g(\Phi^T \gamma + \bar{r}(z)) \Delta r^{[k]}(z_i) \]

\[ - \frac{\sqrt{n}}{N} \sum_{i=n+1}^{N+n} c^T \Sigma_{\beta_0}^{-1} x_i g(\Phi^T \gamma + \bar{r}(z)) \left[ K^{-1} \sum_{k=1}^{K} \Delta r^{[k]}(z_i) \right] := U_2 + \Delta_2, \]

where \( \Delta r^{[k]}(z_i) = \hat{r}^{[k]}(z_i) - r(z_i) + O_p((\hat{r}^{[k]}(z_i) - r(z_i))^2) \), \( U_2 \) represents the difference of the first two terms and \( \Delta_2 \) represents the difference of the last two terms. Similar to \( U_1 \), by Assumption 1 and LLN,

\[ \frac{1}{n} \sum_{i=1}^{n} \bar{\omega}(x_i) c^T \Sigma_{\beta_0}^{-1} x_i g(\Phi^T \gamma + \bar{r}(z)) \Phi_i = o_p(1); \]

\[ \frac{1}{N} \sum_{i=n+1}^{N+n} c^T \Sigma_{\beta_0}^{-1} x_i g(\Phi^T \gamma + \bar{r}(z)) \Phi_i = o_p(1). \]

Then by Assumption 3(i), \( U_2 \) is asymptotically normal with mean 0. For \( \Delta_2 \), by Assumption 2 and the use of cross-fitting, we have that

\[ E_S \left( \frac{1}{n} \sum_{i=1}^{n} \bar{\omega}(x_i) c^T \Sigma_{\beta_0}^{-1} x_i g(\Phi^T \gamma + \bar{r}(z)) \Delta r^{[k]}(z_i) \right) = E_T \left( \frac{1}{Nk} \sum_{i=n+1}^{N+n} c^T \Sigma_{\beta_0}^{-1} x_i g(\Phi^T \gamma + \bar{r}(z)) \Delta r^{[k]}(z_i) \right). \]
Here, we follow the same logic as that for \( \Delta_1 \): if Assumption (ii) holds, \( \omega(\cdot) = \omega_0(\cdot) \) and

\[
E_S \left[ \exp \{ \Psi^T \hat{\alpha} + \tilde{h}(Z) \} e^T \Sigma_{\beta_0}^{-1} X \hat{g}(m_0(X)) f(X) \right] = E_T \left[ e^T \Sigma_{\beta_0}^{-1} X \hat{g}(m_0(X)) f(X) \right]
\]

holds for all measurable function of \( X, f(\cdot) \); (ii) holds, we have that \( \tilde{h}(\cdot) \) solves (8) by \( m_\ast(\cdot) = \hat{m}(\cdot) = m_0(\cdot) \). Again using Assumption (i) and CLT, we have \( \Delta_2 = o_p(1) \). Thus, \( \Xi_2 \) is asymptotically normal with mean 0 and variance of order 1.

Finally, we consider \( \Delta_3 \) in (A13). By Assumption (i) and Cauchy–Schwarz inequality, we have

\[
|\Delta_3| = O \left( \frac{1}{\sqrt{n}} \sum_{k=1}^{K} \sum_{i \in I_k} |\hat{\omega}^{[k]}(x_i) - \hat{\omega}(x_i)||\hat{m}^{[k]}(x_i) - \hat{m}(x_i)| \right)
\]

\[
= \sqrt{n}O \left( \sum_{k=1}^{K} E_S |\hat{\omega}^{[k]}(X) - \hat{\omega}(X)||\hat{m}^{[k]}(X) - \hat{m}(X)| \right) + o_p(1)
\]

\[
\leq \sqrt{n}O \left( \left[ \sum_{k=1}^{K} E_S |\hat{\omega}^{[k]}(X) - \hat{\omega}(X)|^2 \sum_{k=1}^{K} E_S |\hat{m}^{[k]}(X) - \hat{m}(X)|^2 \right]^{\frac{1}{2}} \right) + o_p(1),
\]

where we combine Assumption (i), Assumption (ii) and CLT for the second equality (\( \hat{\omega}^{[k]} \) and \( \hat{m}^{[k]} \) are independent of \( x_i \in I_k \) and that \( \sup_{x} |\hat{\omega}^{[k]}(x) - \hat{\omega}(x)| = o_p(1) \); \( \sup_{x} |\hat{m}^{[k]}(x) - \hat{m}(x)| = o_p(1) \)). Still using Assumptions (i) and (ii) we have

\[
E_S \{\hat{\omega}^{[k]}(X) - \hat{\omega}(X)\}^2 = E_S \left[ \hat{\omega}^2(X) O_p \left( \left\| \Psi \right\|^2 + \hat{\alpha}^2 + \left[ \tilde{h}^{[k]}(Z) - \tilde{h}(Z) \right]^2 \right) \right]
\]

\[
= E_S \left[ \tilde{h}^{[k]}(Z) - \tilde{h}(Z) \right] + O_p(1/n)
\]

\[
E_S \{\hat{m}^{[k]}(X) - \hat{m}(X)\}^2 = E_S \left[ \hat{g}(\hat{m}(X)) O_p \left( \left\| \Phi \right\|^2 + \hat{\gamma}^2 + \left[ \tilde{r}^{[k]}(Z) - \tilde{r}(Z) \right]^2 \right) \right]
\]

\[
= E_S \left[ \tilde{r}^{[k]}(Z) - \tilde{r}(Z) \right] + O_p(1/n).
\]

Then by Assumption (ii), \( E_S \{\hat{\omega}^{[k]}(X) - \hat{\omega}(X)\}^2 E_S \{\hat{m}^{[k]}(X) - \hat{m}(X)\}^2 = o_p(1/n) \). Therefore, we have \( \Delta_3 = o_p(1) \). Combining these with the asymptotic normality of \( V, \Xi_1 \) and \( \Xi_2 \) and the expansion (A13), \( \sqrt{n}(c^T \beta_{DR} - c^T \beta_0) \) is asymptotic normal with mean 0 and variance of order 1.

### C Justification on the calibration estimators in Section 2.3

In this section, we provide justification for the error rate of the calibrated estimators introduced in Section 2.3. Throughout, we let the dimension of \( z \): \( p_z = 1 \), as set in our numerical studies. Our deduction is heuristic as we do not bother on the strict regularity and smoothness conditions for \( \tilde{r}(\cdot) \) and \( \tilde{h}(\cdot) \), but consider the asymptotic expansion of \( \tilde{r}^{[k]}(\cdot) \) solving

\[
\frac{K}{n(K-1)} \sum_{i \in I_k} \hat{\omega}^{[k]}(x_i) x_i y_i - \hat{m}^{[k]}(x_i) + \frac{1}{N} \sum_{i=n+1}^{N} x_i \hat{m}^{[k]}(x_i) - g(x_i^T \beta) = 0,
\]

and \( \tilde{r}^{[k]}(\cdot), \tilde{h}^{[k]}(\cdot) \) solving the estimating equations in (8), to analyze their error rate. Assume the initial nuisance estimators satisfy that \( \sup_{z \in Z} |\tilde{r}^{[k]}(z) - r^\ast(z)| = o_p(1) \), \( \sup_{z \in Z} |\tilde{h}^{[k]}(z) - h^\ast(z)| = o_p(1) \),
$\alpha_p(1)$ and there exists some $a_n, b_n \to 0$ satisfying that
\[
\|\hat{\gamma}^{[k]} - \gamma^*\|^2 + E_S\{\hat{r}^{[k]}(Z) - r^*(Z)\}^2 = O_p(a_n^2);
\]
\[
\|\hat{\alpha}^{[k]} - \alpha^*\|^2 + E_S\{\hat{h}^{[k]}(Z) - h^*(Z)\}^2 = O_p(b_n^2).
\]

Define that $\hat{r}^{[k]}(z)$ and $\hat{h}^{[k]}(z)$ respectively solve:
\[
\frac{K}{n(K - 1)h^p} \sum_{i \in L_k} K_h(z_i - z)\omega^*(x_i)c^T\Sigma_{\beta_0}^{-1}x_i [y_i - g\{\phi_i^T\hat{\gamma} + r(z)\}] = 0;
\]
\[
\frac{K}{n(K - 1)h^p} \sum_{i \in L_k} K_h(z_i - z)\exp(\psi_i^T\hat{\alpha})c^T\Sigma_{\beta_0}^{-1}x_i\hat{g}\{m^*(x_i)\}\exp(h(z))
\]
\[
= 1 \frac{N h^p}{n(K - 1)} \sum_{i = n + 1}^{n + N} K_h(z_i - z)c^T\Sigma_{\beta_0}^{-1}x_i\hat{g}\{m^*(x_i)\},
\]
\]

When the weights in (A16) are regular, e.g. all $c^T\Sigma_{\beta_0}^{-1}x_i$ are positive and $\omega^*(x_i), \exp(\psi_i^T\hat{\alpha})$ and $c^T\Sigma_{\beta_0}^{-1}x_i$ are bounded away from 0 and $\infty$ (one may have weaker regularity conditions for unbounded covariates and we already introduced in Section 2.3 how to handle the case that $c^T\Sigma_{\beta_0}^{-1}x_i$ is not always positive/negative), it is natural to assume the two regularity conditions:
\[
\frac{K}{n(K - 1)h^p} \sum_{i \in L_k} K_h(z_i - z)\omega^*(x_i)c^T\Sigma_{\beta_0}^{-1}x_i\hat{g}\{\phi_i^T\hat{\gamma} + \hat{r}(z)\} = \Theta_p(1);
\]
\[
\frac{K}{n(K - 1)h^p} \sum_{i \in L_k} K_h(z_i - z)\exp(\psi_i^T\hat{\alpha})c^T\Sigma_{\beta_0}^{-1}x_i\hat{g}\{m^*(x_i)\}\exp(h(z)) = \Theta_p(1),
\]
\]

uniformly for all $z \in Z$. Consequently, it is reasonable to assume $\hat{r}^{[k]}(z)$ and $\hat{h}^{[k]}(z)$ have the same convergence properties (to different limiting parameters) as $\hat{r}^{[k]}(\cdot)$ and $\hat{h}^{[k]}(\cdot)$ respectively: $\sup_{z \in Z} |\hat{r}^{[k]}(z) - \hat{r}(z)| = o_p(1)$, $\sup_{z \in Z} |\hat{h}^{[k]}(z) - \hat{h}(z)| = o_p(1)$ and
\[
E_S\{\hat{r}^{[k]}(Z) - \hat{r}(Z)\}^2 = O_p(a_n^2);
\]
\[
E_S\{\hat{h}^{[k]}(Z) - \hat{h}(Z)\}^2 = O_p(b_n^2),
\]

noting the estimating equations (A16) for $\hat{r}^{[k]}(z)$ and $\hat{h}^{[k]}(z)$ do not involve nuisance models or parameters estimated empirically.

Without loss of generality, assume that $a_n, b_n = \Omega(1/\sqrt{n})$. Under Assumptions 1, 2 and 3(i) and the assumptions introduced above, we justify in this section that the calibrated estimators defined in Section 2.3 satisfy: $\sup_{z \in Z} |\hat{r}^{[k]}(z) - \hat{r}(z)| = o_p(1), \sup_{z \in Z} |\hat{h}^{[k]}(z) - \hat{h}(z)| = o_p(1)$ and
\[
E_S\{\hat{r}^{[k]}(Z) - \hat{r}(Z)\}^2 = O_p(a_n^2 + b_n^2);
\]
\[
E_S\{\hat{h}^{[k]}(Z) - \hat{h}(Z)\}^2 = O_p(a_n^2 + b_n^2),
\]
\]

which reveals that both $a_n^2$ and $b_n^2$ only needs to be $o(1/\sqrt{n})$ to ensure the rate doubly robust condition, i.e. Assumption 3(ii) in this scenario. This requirement is mild and reasonable for the sieve or kernel estimators (Newey, 1997; Shen, 1997; Chen and Shen, 1998). Now we present the proof as follows.

Proof. Similar to the proof of Theorem 1 we can show that
\[
E_S\{\hat{m}^{[k]}(X) - m^*(X)\}^2 = O_p(a_n^2);
\]
\[
E_S\{\omega^{[k]}(X) - \omega^*(X)\}^2 = O_p(b_n^2).
Also similar to the proof of Theorem 1, we have \( \tilde{\beta}^{[k]} - \beta_0 = o_p(1) \) by ULLN and the expansion

\[
\tilde{\beta}^{[k]} - \beta_0 = \frac{K}{n(K-1)} \sum_{i \in L_k} \omega^*(x_i) \Sigma^{-1}_{\beta_0} x_i \{ y_i - m^*(x_i) \} + \frac{1}{N} \sum_{i=n+1}^{N+n} \Sigma^{-1}_{\beta_0} x_i \{ m^*(x_i) - g(x_i^T \beta_0) \}
\]

\[
+ \frac{K}{n(K-1)} \sum_{i \in L_k} \{ \tilde{\omega}^{[k]}(x_i) - \omega^*(x_i) \} \Sigma^{-1}_{\beta_0} x_i \{ y_i - m^*(x_i) \}
\]

\[
+ \frac{K}{n(K-1)} \sum_{i \in L_k} \omega^*(x_i) \Sigma^{-1}_{\beta_0} x_i \{ \tilde{m}^{[k]}(x_i) - m^*(x_i) \} - \frac{1}{N} \sum_{i=n+1}^{N+n} \Sigma^{-1}_{\beta_0} x_i \{ \tilde{m}^{[k]}(x_i) - m^*(x_i) \}
\]

\[
+ \frac{K}{n(K-1)} \sum_{i \in L_k} \Sigma^{-1}_{\beta_0} x_i \{ \tilde{\omega}^{[k]}(x_i) - \omega^*(x_i) \} \{ \tilde{m}^{[k]}(x_i) - m^*(x_i) \}
\]

\[=: \tilde{V} + \tilde{\Delta}_1 + \tilde{\Delta}_2 + \tilde{\Delta}_3. \tag{A19} \]

When at least one nuisance model is correct, i.e. either \( \omega^*(\cdot) = \omega_0(\cdot) \) or \( m^*(\cdot) = m_0(\cdot) \), the expectation of \( V \) is 0 and \( \| V \|_2 = O_p(1/\sqrt{n}) \). And

\[
\| \tilde{\Delta}_1 \|_2 \leq \frac{K}{n(K-1)} \left[ \sum_{i \in L_k} \{ \tilde{\omega}^{[k]}(x_i) - \omega^*(x_i) \}^2 \right]^{\frac{1}{2}} \left[ \sum_{i \in L_k} \left\| \Sigma^{-1}_{\beta_0} x_i \{ y_i - m^*(x_i) \} \right\|_2^2 \right]^{\frac{1}{2}}
\]

\[= O_p \left( \left\| E_S \{ \tilde{\omega}^{[k]}(X) - \omega^*(X) \} \right\|_2^2 \right) = O_p(\beta_n); \]

\[
\| \tilde{\Delta}_2 \|_2 = O_p \left( \left\| E_S \{ \tilde{m}^{[k]}(X) - m^*(X) \} \right\|_2^2 \right) = O_p(a_n); \]

\[
\| \tilde{\Delta}_3 \|_2 = O_p \left( \left\| E_S \{ \tilde{m}^{[k]}(X) - m^*(X) \}^2 E_S \{ \tilde{\omega}^{[k]}(X) - \omega^*(X) \} \right\|_2 \right) = O_p(a_n b_n).
\]

So we have \( \| \tilde{\beta}^{[k]} - \beta_0 \|_2 = O_p(a_n + b_n) \).

Then we compare the estimating equations in (17) with (A19). For \( r(\cdot) \), since \( \tilde{\omega}^{[k]}(\cdot), \tilde{\beta}^{[k]} \) and \( \tilde{\gamma}^{[k]} \) are consistent, we have \( \sup_{z \in \mathcal{Z}} | \tilde{r}^{[k]}(z) - \bar{r}(z) | = o_p(1) \) using the assumption that \( \bar{r}^{[k]}(\cdot) \) is (uniformly) consistent and consider the asymptotic expansion of \( \tilde{\gamma}^{[k]}(\cdot) \) on (17):

\[0 = \frac{K}{n(K-1)h^p} \sum_{i \in L_k} K_h(z_i - z) \tilde{\omega}^{[k]}(x_i) c^T \tilde{\Sigma}^{-1}_{\beta_0} x_i \{ y_i - g \left\{ \phi_i^T \tilde{\gamma}^{[k]} + \tilde{r}^{[k]}(z) \right\} \}
\]

\[= \frac{K}{n(K-1)h^p} \sum_{i \in L_k} K_h(z_i - z) \omega^*(x_i) c^T \Sigma^{-1}_{\beta_0} x_i \{ y_i - g \left\{ \phi_i^T \gamma + \bar{r}(z) \right\} - \hat{g} \left\{ \phi_i^T \gamma + \bar{r}(z) \right\} \{ \tilde{r}^{[k]}(z) - \bar{r}(z) \} \}
\]

\[+ O_p \left( \left\| E_S \{ \tilde{m}^{[k]}(X) - m^*(X) \} \right\|_2 \right) \frac{1}{2} + O_p \left( \left\| E_S \{ \tilde{\omega}^{[k]}(X) - \omega^*(X) \} \right\|_2 \right) \frac{1}{2} + \| \tilde{\beta}^{[k]} - \beta_0 \|_2 + \| \tilde{\gamma}^{[k]} - \gamma \|_2
\]

\[+ O_p \left( \left\| \tilde{r}^{[k]}(z) - \bar{r}(z) \right\|_2 \right)
\]

\[= \frac{K}{n(K-1)h^p} \sum_{i \in L_k} K_h(z_i - z) \omega^*(x_i) c^T \Sigma^{-1}_{\beta_0} x_i \{ y_i - g \left\{ \phi_i^T \gamma + \bar{r}(z) \right\} - \hat{g} \left\{ \phi_i^T \gamma + \bar{r}(z) \right\} \{ \tilde{r}^{[k]}(z) - \bar{r}(z) \} \}
\]

\[+ O_p(a_n + b_n) + O_p \left( \left\| \tilde{r}^{[k]}(z) - \bar{r}(z) \right\|_2 \right), \]
Compare this with the expansion of $\tilde{r}^{[k]}(z)$ on (A16):

\[
0 = \frac{K}{n(K-1)h^p} \sum_{i \in I_k} K_h(z_i - z) \omega^{*}(x_i) c^T \Sigma_{\beta_0}^{-1} x_i \left[ y_i - g \left\{ \phi_i^T \hat{\gamma} + \hat{r}(z) \right\} - \hat{g} \left\{ \phi_i^T \hat{\gamma} + \hat{r}(z) \right\} \right] \{ \tilde{r}^{[k]}(z) - \hat{r}(z) \} \\
+ O_p \left( [\tilde{r}^{[k]}(z) - \hat{r}(z)]^2 \right).
\]

We take the difference of the two equations to obtain that

\[
\frac{K}{n(K-1)h^p} \sum_{i \in I_k} K_h(z_i - z) \omega^{*}(x_i) c^T \Sigma_{\beta_0}^{-1} x_i \hat{g} \left\{ \phi_i^T \hat{\gamma} + \hat{r}(z) \right\} \{ \tilde{r}^{[k]}(z) - \hat{r}^{[k]}(z) \}
= O_p(a_n + b_n) + O_p \left( [\tilde{r}^{[k]}(z) - \hat{r}(z)]^2 \right)
\]

Then using the first equation in (A17), $|\tilde{r}^{[k]}(z) - \hat{r}(z)| = o_p(1)$ uniformly for all $z$ belonging to the compact domain $Z$ and the estimation assumption $E_S \{ \tilde{r}^{[k]}(Z) - \hat{r}(Z) \}^2 = O_p(a_n^2)$, we conclude that

\[
E_S \{ \tilde{r}^{[k]}(Z) - \hat{r}(Z) \}^2 = O_p(a_n^2 + b_n^2).
\]

For $h(\cdot)$, we follow the same strategy to show $\sup_{z \in Z} |\tilde{h}^{[k]}(z) - \hat{h}(z)| = o_p(1)$ by using consistency of $\tilde{h}^{[k]}(\cdot)$ and the plug-in estimators in the second equation of (7). Then we similarly consider the difference between the second two lines of equations (7) and (A16) to derive that

\[
\frac{K}{n(K-1)h^p} \sum_{i \in I_k} K_h(z_i - z) \exp(\psi_i^T \alpha \sigma x_i^T \exp(h(z))) \exp(\tilde{m}^{[k]}(z)) \{ \tilde{h}^{[k]}(z) - \hat{h}^{[k]}(z) \}
= O_p \left( E_S \{ \tilde{m}^{[k]}(X) - m^*(X) \}^2 \right) + O_p \left( E_S \{ \tilde{\omega}^{[k]}(X) - \omega^*(X) \}^2 \right) + O_p \left( E_S \| \tilde{\beta}^{[k]} - \beta_0 \|_2^2 \right)
= O_p(a_n + b_n) + O_p \left( [\tilde{h}^{[k]}(z) - \hat{h}(z)]^2 \right).
\]

Then by $E_S \{ \tilde{h}^{[k]}(Z) - \hat{h}(Z) \}^2 = O_p(a_n^2)$ and the second line of (A17), we have $E_S \{ \tilde{h}^{[k]}(Z) - \hat{h}(Z) \}^2 = O_p(a_n^2 + b_n^2)$. Thus we have finally proved (A18) for each $k \in \{1, \ldots, K\}$.

\[\square\]

**D Details of the extension discussed in Section 6.3**

First, we consider using sieve to model and calibrate the nonparametric components: $r(z) = \xi^T b(z)$ and $h(z) = \eta^T b(z)$ where $b(z)$ represents some prespecified basis function of $z$, e.g. natural spline or Hermite polynomials, of dimensionality diverging with $n$. In analog to (7), one can estimate the coefficients $\xi$ and $\eta$ by solving

\[
\frac{K}{n(K-1)} \sum_{i \in I_k} \tilde{\omega}^{[k]}(x_i) c^T \Sigma_{\beta_0}^{-1} x_i b(z_i) \left[ y_i - g \left\{ \phi_i^T \tilde{\gamma}^{[k]} + \xi^T b(z_i) \right\} \right] = 0;
\]

\[
\frac{K}{n(K-1)} \sum_{i \in I_k} c^T \Sigma_{\beta_0}^{-1} x_i \hat{g} \left\{ \tilde{m}^{[k]}(x_i) \right\} \exp(\psi_i^T \hat{\alpha}^{[k]} + \eta^T b(z_i)) b(z_i) = \frac{1}{N} \sum_{i=n+1}^{n+N} c^T \Sigma_{\beta_0}^{-1} x_i \hat{g} \left\{ \tilde{m}^{[k]}(x_i) \right\} b(z_i).
\]

For one-dimensional $Z$ occurring in our numerical studies, this sieve approach should have similar performance as kernel smoothing. While if $p_z > 1$, fully nonparametric approaches like kernel
smoothing usually have poor performance due to the curse of dimensionality. We recommend using additive model of \( Z \) instead to avoid excessive model complexity. This can be more simply implemented with sieve by binding the basis of each covariate in \( Z \) together to form \( b(Z) \).

Second, we introduce the way to combine \( \ell_1 \)-regularized \( M \)-estimation with our semi-nonparametric framework. Let \( Z \) be some high dimensional features with \( p_z \gg n \) and assume \( r(z) = u^T z \) and \( h(z) = v^T z \) with some sparse coefficients \( u \) and \( v \). We then propose to realize the moment conditions (3) and (4) through dantzig selectors:

\[
\begin{align*}
\min_{u \in \mathbb{R}^{p_z}} \|u\|_1; \quad & \text{s.t.} \quad \frac{K}{n(K - 1)} \sum_{i \in I_k} \tilde{\omega}^{[k]}(x_i)c^T \tilde{\Sigma}^{-1}_p x_i z_i \left[ y_i - g\left( \phi_i^T \tilde{\gamma}^{[k]} + u^T z_i \right) \right] \leq \lambda_u \\
\min_{v \in \mathbb{R}^{p_z}} \|v\|_1; \quad & \text{s.t.} \quad \frac{K}{n(K - 1)} \sum_{i \in I_k} c^T \tilde{\Sigma}^{-1}_p x_i \tilde{g}\left( \tilde{m}^{[k]}(x_i) \right) \exp\{\psi_i^T \tilde{\alpha}^{[k]} + v^T z_i\} z_i \\
& \quad - \frac{1}{N} \sum_{i = n + 1}^{n + N} c^T \tilde{\Sigma}^{-1}_p x_i \tilde{g}\left( \tilde{m}^{[k]}(x_i) \right) z_i \leq \lambda_v,
\end{align*}
\]

(A20)

where \( \lambda_u \) and \( \lambda_v \) are two tuning parameters of order \( \{\log(p_z)/n\}^{1/2} \). Motivated by Smucler et al. (2019); Tan (2020), the \( \| \cdot \|_\infty \) constraints of the first and second optimization problems in (A20) help to remove the bias incurred by the estimation errors of \( v \) and \( u \) respectively.

We require the fixed (low) dimensional parametric estimators \( \tilde{\gamma}^{[k]} \) and \( \tilde{\alpha}^{[k]} \) to converge at parametric rates. To realize this, we first estimate the regularized estimators for \( \tilde{\gamma} \) and \( \tilde{\alpha} \) via some \( \ell_1 \)-regularized regression procedures for the response \( Y \) against basis \( (\Phi^T, Z^T)^T \) and the target indicator \( T \) against \( (\Psi^T, Z^T)^T \). Then we use debiased lasso (Zhang and Zhang, 2014; Javanmard and Montanari, 2014; Van de Geer et al., 2014) to correct for the bias of the obtained \( \ell_1 \)-regularized estimators for \( \tilde{\gamma} \) and \( \tilde{\alpha} \), and use the resulted debiased estimators \( \hat{\gamma}^{[k]} \) and \( \hat{\alpha}^{[k]} \) as the parametric components in (A20) and finally in the estimating equation (9). As was studied in existing literature (Javanmard and Montanari, 2014; Bühlmann and van de Geer, 2015), \( \hat{\gamma}^{[k]} \) and \( \hat{\alpha}^{[k]} \) obtained in this way satisfy Assumption (3(i)) under certain regularity and sparsity conditions.

### E Details of the extension discussed in Section 6.2

In this section, we introduce the intrinsic efficient construction procedure of the imputation model under our framework. For simplicity, we consider a semi-supervised setting with \( n \) (labelled) source samples and \( N \gg n \) unlabelled target samples. Method proposed by Shu and Tan (2018) may be useful for handling the \( N \times n \) case. For some given \( h(\cdot) \), let the estimating equation of \( \hat{\alpha}^{[k]} \) be

\[
\sum_{i \in \{n + 1, \ldots, n + N\} \cup I_k} S\{\delta_i, x_i; \alpha, h(\cdot)\} = 0,
\]

with \( S\{\delta_i, x_i; \alpha, h(\cdot)\} \) representing the score function. For example, one can take

\[
S\{\delta_i, x_i; \alpha, h(\cdot)\} = \delta_i \exp\{\psi_i^T \alpha + h(z_i)\} \psi_i - |I_k| (1 - \delta_i) \psi_i / N.
\]

Denote that \( s_i = S\{\delta_i, x_i; \hat{\alpha}^{[k]}, \hat{h}^{[k]}(\cdot)\} \) and let \( \Pi_{I_k}(\epsilon_i; s_i) \) be the empirical projection operator of any \( \epsilon_i \) to the space spanned by \( s_i \) on the samples \( I_k \) and \( \Pi_{I_k}^{\perp}(\epsilon_i; s_i) = \epsilon_i - \Pi_{I_k}(\epsilon_i; s_i) \). As the
importance weight model is correctly specified, the empirical asymptotic variance for \( c^T \hat{\beta}_{DR} \) can be expressed as

\[
\frac{K}{n(K-1)} \sum_{i \in I_k} \left[ \tilde{\omega}^{[-k]}(x_i) \Pi_{I_k}^\perp \left( c^T \hat{\Sigma}_{-\beta}^{-1}[-k] x_i [y_i - g(\phi_i^T \gamma + r(z_i))]; s_i \right) \right]^2.
\]  

(A21)

Then the intrinsically efficient construction of the imputation model is given by minimizing (A21) subject to the moment constraint:

\[
\frac{1}{|I_k \cap I_a|} \sum_{i \in I_k \cap I_a} K_h(z_i - z) \tilde{\omega}^{[-k]}(x_i) c^T \hat{\Sigma}_{-\beta}^{-1}[-k] x_i [y_i - g(\phi_i^T \gamma + r(z))] = 0,
\]

which is the same as the first equation of (1) except that both \( \gamma \) and \( r(z) \) are unknown here. This optimization problem could be solved with methods like profile kernel and back-fitting (Lin and Carroll, 2006). Alternatively and more conveniently, one could use sieve, as discussed in Section 6.3 and Appendix D, to model \( r(z_i) \) and use a constrained least square regression: let \( b(z) \) be some basis function of \( z \) and solve

\[
\min_{\gamma, \xi} \sum_{i \in I_k \cap I_a} \left[ \tilde{\omega}^{[-k]}(x_i) \Pi_{I_k}^\perp \left( c^T \hat{\Sigma}_{-\beta}^{-1}[-k] x_i [y_i - g(\phi_i^T \gamma + b^T(z_i) \xi)]; s_i \right) \right]^2;
\]

s.t. \[
\sum_{i \in I_k \cap I_a} b(z_i) \tilde{\omega}^{[-k]}(x_i) c^T \hat{\Sigma}_{-\beta}^{-1}[-k] x_i [y_i - g(\phi_i^T \gamma + b^T(z_i) \xi)] = 0,
\]

to obtain \( \tilde{\gamma}^{[-k]} \) and \( \tilde{\gamma}^{[-k]}(z) = b^T(z) \tilde{\gamma}^{[-k]} \) simultaneously. Again, one can either take \( \tilde{\gamma}^{[-k]} = \tilde{\gamma}^{[-k]} \) corresponding to the “Plug-in” proposal in Section 2.3 or further correct for the bias of \( \tilde{\gamma}^{[-k]} \) to obtain the “Debiased” \( \tilde{\gamma}^{[-k]} \).

To get the intrinsic efficient estimator for a nonlinear but differentiable function \( \ell(\beta_0) \), with its gradient being \( \dot{\ell}(\cdot) \), we first estimate the entries \( \beta_{0i} \) using our proposed method for every \( i \in \{1, 2, \ldots, d\} \) and use them to form an initial \( \sqrt{n} \)-consistent estimator \( \hat{\beta}_{(init)} \). Then we estimate the linear function \( \beta_0^T \dot{\ell}(\hat{\beta}_{(init)}) \) with the intrinsically efficient estimator and utilize the expansion \( \ell(\beta_0) \approx \ell(\hat{\beta}_{(init)}) + \{\beta_0 - \hat{\beta}_{(init)}\}^T \dot{\ell}(\hat{\beta}_{(init)}) \) for an one-step update.
Implementing details and additional results of simulation

To obtain the initial estimators $\tilde{\omega}^{[k]}(\cdot)$ and $\tilde{m}^{[k]}(\cdot)$ of our method, we use semiparametric logistic regression with covariates including the parametric basis and the natural splines of the nonparametric components $Z$ with order $[n^{1/5}]$ for the imputation model and $[(N + n)^{1/5}]$ for the importance weight model. In this process, we add ridge penalty with tuning parameter of order $n^{-2/3}$ (below the parametric rate) to enhance the training stability. We use sieve instead of kernel smoothing purely because it is more convenient to implement and the two approaches should have close performance.

Then as mentioned in Sections 2.3 and 4, we separately use three ways, "Plug-in", "Parametric" and “Debiased” to construct the nuisance parametric components. For “Plug-in”, we directly take $\hat{\gamma}^{[k]} = \tilde{\gamma}^{[k]}$ and $\hat{\alpha}^{[k]} = \tilde{\alpha}^{[k]}$. For “Parametric”, we fit parametric logistic models for $S_i \sim \psi_i$ and $y_i \sim \phi_i$ to obtain $\hat{\gamma}^{[k]}$ and $\hat{\alpha}^{[k]}$. For “Debiased”, we use the special doubly-robust form of logistic regression to obtain the bias corrected $\hat{\gamma}^{[k]}$ and $\hat{\alpha}^{[k]}$, as introduced in Section A. Finally, we use the kernel methods described by (8) in Section 2.3 to calibrate the nonparametric parts.

We set the loading vector $c$ as $(1, 0, 0, 0, 0)^T$, $(0, 1, 0, 0, 0)^T$, ..., $(0, 0, 0, 0, 1)^T$ to estimate $\beta_0, \ldots, \beta_4$ separately. For $\beta_1, \ldots, \beta_4$, the weights $\mathbf{c}^T \hat{\Sigma}_\beta^{-1} \mathbf{x}_i$’s are not positive (or negative) definite so we split the source and target samples as $\mathcal{I}^+ = \{i : \mathbf{c}^T \hat{\Sigma}_\beta^{-1} \mathbf{x}_i \geq 0\}$ and $\mathcal{I}^- = \{i : \mathbf{c}^T \hat{\Sigma}_\beta^{-1} \mathbf{x}_i < 0\}$, and use (8) to estimate their nonparametric components. For $\beta_0$, we find that $\mathbf{c}^T \hat{\Sigma}_\beta^{-1} \mathbf{x}_i$ is nearly positive definite under all configurations but these weights are sometimes of high variation. So we also split the source/target samples by cutting the $\mathbf{c}^T \hat{\Sigma}_\beta^{-1} \mathbf{x}_i$’s with their median, to reduce the variance of weights at each fold and improve the effective sample size.

We use cross-fitting with $K = 5$ folds for our method and the two double machine learning estimators. And all the tuning parameters including the bandwidth of our method and kernel machine and the coefficients of the penalty functions are selected by 5-folded cross-validation on the training samples.

We present the estimation performance (mean square error, bias and coverage probability) on each parameter in Tables A3–A6, for the four configurations separately. In Tables A3–A6 the parametric components of our method are estimated using the "Plug-in" procedure. Meanwhile, we compare the three construction strategies of our method with the parametric components estimated with "Plug-in", “Parametric” and “Debiased”, under Configurations (i)–(iv) in Tables A7–A10.
Table A3: Estimation performance of the methods on parameters $\beta_0, \ldots, \beta_4$ under Configuration (i) described in Section 4. Parametric: doubly robust estimator with parametric nuisance models; Our method: doubly robust estimator using semi-nonparametric nuisance models with “Plug-in” parametric components; Additive: double machine learning estimator of additive models regularized with $\ell_1+\ell_2$ penalty; Kernel machine: support vector machine with radial basis function kernel. MSE: mean square error; CP: coverage probability of the 95% confidence interval.

| Covariates | Estimator       | Parametric | Our method | Additive | Kernel machine |
|------------|----------------|------------|------------|----------|---------------|
| $\beta_0$  | MSE            | 0.012      | 0.014      | 0.021    | 0.024         |
|            | Bias           | -0.023     | -0.046     | -0.079   | -0.027        |
|            | CP             | 0.96       | 0.94       | 0.96     | 0.99          |
| $\beta_1$  | MSE            | 0.054      | 0.025      | 0.024    | 0.041         |
|            | Bias           | -0.056     | -0.017     | -0.015   | 0.120         |
|            | CP             | 0.94       | 0.95       | 0.99     | 0.95          |
| $\beta_2$  | MSE            | 0.023      | 0.021      | 0.034    | 0.082         |
|            | Bias           | -0.036     | -0.038     | -0.085   | -0.164        |
|            | CP             | 0.94       | 0.95       | 0.97     | 1.00          |
| $\beta_3$  | MSE            | 0.024      | 0.019      | 0.026    | 0.026         |
|            | Bias           | 0.020      | 0.020      | 0.040    | 0.023         |
|            | CP             | 0.96       | 0.97       | 0.99     | 1.00          |
| $\beta_4$  | MSE            | 0.030      | 0.023      | 0.049    | 0.028         |
|            | Bias           | 0.032      | 0.027      | 0.116    | 0.077         |
|            | CP             | 0.95       | 0.94       | 0.95     | 0.98          |
Table A4: Estimation performance of the methods on parameters $\beta_0, \ldots, \beta_4$ under Configuration (ii) described in Section 4. Parametric: doubly robust estimator with parametric nuisance models; Our method: doubly robust estimator using semi-nonparametric nuisance models with “Plug-in” parametric components; Additive: double machine learning estimator of additive models regularized with $\ell_1+\ell_2$ penalty; Kernel machine: support vector machine with radial basis function kernel. MSE: mean square error; CP: coverage probability of the 95% confidence interval.

| Covariates | Estimator | Parametric | Our method | Additive | Kernel machine |
|------------|-----------|------------|------------|----------|----------------|
| $\beta_0$  | MSE       | 0.011      | 0.012      | 0.039    | 0.052          |
|            | Bias      | $-0.004$   | $0.100$    | $0.155$  | $0.147$        |
|            | CP        | 0.96       | 0.96       | 0.77     | 0.97           |
| $\beta_1$  | MSE       | 0.021      | 0.018      | 0.018    | 0.023          |
|            | Bias      | $-0.012$   | $-0.009$   | $-0.021$ | $0.082$        |
|            | CP        | 0.94       | 0.93       | 0.98     | 0.92           |
| $\beta_2$  | MSE       | 0.020      | 0.016      | 0.016    | 0.024          |
|            | Bias      | $-0.011$   | $-0.012$   | 0.023    | $-0.066$       |
|            | CP        | 0.95       | 0.95       | 0.98     | 0.99           |
| $\beta_3$  | MSE       | 0.023      | 0.020      | 0.025    | 0.022          |
|            | Bias      | $-0.008$   | $-0.013$   | $-0.071$ | $-0.037$       |
|            | CP        | 0.96       | 0.95       | 0.97     | 0.97           |
| $\beta_4$  | MSE       | 0.016      | 0.014      | 0.016    | 0.017          |
|            | Bias      | $-0.019$   | $-0.016$   | $-0.005$ | $-0.020$       |
|            | CP        | 0.95       | 0.95       | 0.97     | 0.99           |
Table A5: Estimation performance of the methods on parameters $\beta_0, \ldots, \beta_4$ under Configuration (iii) described in Section 4. Parametric: doubly robust estimator with parametric nuisance models; Our method: doubly robust estimator using semi-nonparametric nuisance models with “Plug-in” parametric components; Additive: double machine learning estimator of additive models regularized with $\ell_1+\ell_2$ penalty; Kernel machine: support vector machine with radial basis function kernel. MSE: mean square error; CP: coverage probability of the 95% confidence interval.

| Covariates | Estimator  | Parametric | Our method | Additive | Kernel machine |
|------------|------------|------------|------------|----------|----------------|
|            | $\beta_0$  | MSE        | 0.013      | 0.012    | 0.111          | 0.078          |
|            |            | Bias       | 0.008      | -0.007   | -0.308         | -0.194         |
|            |            | CP         | 0.97       | 0.96     | 0.32           | 1.00           |
|            | $\beta_1$  | MSE        | 0.024      | 0.016    | 0.052          | 0.042          |
|            |            | Bias       | -0.037     | -0.003   | -0.178         | -0.093         |
|            |            | CP         | 0.97       | 0.96     | 0.88           | 0.99           |
|            | $\beta_2$  | MSE        | 0.061      | 0.026    | 0.022          | 0.014          |
|            |            | Bias       | -0.032     | 0.009    | -0.066         | 0.016          |
|            |            | CP         | 0.96       | 0.95     | 0.97           | 0.98           |
|            | $\beta_3$  | MSE        | 0.054      | 0.024    | 0.018          | 0.015          |
|            |            | Bias       | -0.030     | 0.009    | 0.032          | 0.048          |
|            |            | CP         | 0.96       | 0.94     | 0.98           | 0.97           |
|            | $\beta_4$  | MSE        | 0.037      | 0.019    | 0.018          | 0.013          |
|            |            | Bias       | 0.008      | -0.017   | -0.038         | -0.046         |
|            |            | CP         | 0.98       | 0.95     | 0.98           | 0.98           |
Table A6: Estimation performance of the methods on parameters $\beta_0, \ldots, \beta_4$ under Configuration (iv) described in Section 4. Parametric: doubly robust estimator with parametric nuisance models; Our method: doubly robust estimator using semi-nonparametric nuisance models with “Plug-in” parametric components; Additive: double machine learning estimator of additive models regularized with $\ell_1+\ell_2$ penalty; Kernel machine: support vector machine with radial basis function kernel. MSE: mean square error; CP: coverage probability of the 95% confidence interval.

| Covariates | Estimator   | Parametric | Our method | Additive | Kernel machine |
|------------|-------------|------------|------------|----------|----------------|
| $\beta_0$  | MSE         | 0.011      | 0.014      | 0.040    | 0.030          |
|            | Bias        | 0.006      | -0.035     | -0.146   | -0.091         |
|            | CP          | 0.96       | 0.95       | 0.89     | 0.98           |
| $\beta_1$  | MSE         | 0.031      | 0.023      | 0.028    | 0.036          |
|            | Bias        | 0.001      | -0.004     | -0.072   | 0.133          |
|            | CP          | 0.93       | 0.95       | 0.98     | 0.93           |
| $\beta_2$  | MSE         | 0.024      | 0.020      | 0.037    | 0.037          |
|            | Bias        | -0.016     | 0.006      | 0.13     | 0.132          |
|            | CP          | 0.95       | 0.96       | 0.90     | 0.90           |
| $\beta_3$  | MSE         | 0.027      | 0.022      | 0.022    | 0.023          |
|            | Bias        | 0.013      | 0.002      | -0.008   | -0.076         |
|            | CP          | 0.96       | 0.96       | 1.00     | 0.94           |
| $\beta_4$  | MSE         | 0.016      | 0.015      | 0.017    | 0.020          |
|            | Bias        | 0.011      | 0.013      | -0.002   | 0.043          |
|            | CP          | 0.97       | 0.96       | 1.00     | 0.97           |
Table A7: Comparison of three construction strategies of our method with the parametric components obtained with “Plug-in”, “Debiased” and “Parametric” estimation procedure as introduced in Section 2.3 respectively. Their performance are evaluated on $\beta_0, \ldots, \beta_4$ and average on them, in terms of mean square error (MSE), bias and coverage probability of the 95% confidence interval (CP), under Configuration (i) described in Section 4.

| Covariates | Estimator       | Plug-in | Debiased | Parametric |
|------------|-----------------|---------|----------|------------|
| $\beta_0$  | MSE             | 0.014   | 0.017    | 0.014      |
|            | Bias            | -0.046  | -0.012   | -0.025     |
|            | CP              | 0.94    | 0.94     | 0.93       |
| $\beta_1$  | MSE             | 0.025   | 0.029    | 0.028      |
|            | Bias            | -0.017  | -0.009   | -0.022     |
|            | CP              | 0.95    | 0.95     | 0.96       |
| $\beta_2$  | MSE             | 0.021   | 0.030    | 0.023      |
|            | Bias            | -0.038  | -0.055   | -0.040     |
|            | CP              | 0.95    | 0.96     | 0.93       |
| $\beta_3$  | MSE             | 0.019   | 0.023    | 0.023      |
|            | Bias            | 0.020   | 0.025    | 0.025      |
|            | CP              | 0.97    | 0.97     | 0.94       |
| $\beta_4$  | MSE             | 0.023   | 0.027    | 0.027      |
|            | Bias            | 0.027   | 0.026    | 0.029      |
|            | CP              | 0.94    | 0.95     | 0.95       |
| Average    | MSE             | 0.021   | 0.025    | 0.023      |
|            | Bias            | 0.030   | 0.025    | 0.028      |
|            | CP              | 0.95    | 0.95     | 0.94       |
Table A8: Comparison of three different versions of our method with the parametric components obtained with “Plug-in”, “Debiased” and “Parametric” estimation procedure as introduced in Section 2.3 respectively. Their performance are evaluated on $\beta_0, \ldots, \beta_4$ and average on them, in terms of mean square error (MSE), bias and coverage probability of the 95% confidence interval (CP), under Configuration (ii) described in Section 4.

| Covariates | Estimator | Plug-in | Debiased | Parametric |
|------------|-----------|---------|----------|------------|
| $\beta_0$  | MSE       | 0.012   | 0.015    | 0.012      |
|            | Bias      | 0.010   | -0.006   | 0.013      |
|            | CP        | 0.96    | 0.98     | 0.96       |
| $\beta_1$  | MSE       | 0.018   | 0.023    | 0.019      |
|            | Bias      | -0.009  | -0.006   | -0.008     |
|            | CP        | 0.93    | 0.94     | 0.94       |
| $\beta_2$  | MSE       | 0.016   | 0.020    | 0.016      |
|            | Bias      | -0.012  | -0.013   | -0.012     |
|            | CP        | 0.95    | 0.96     | 0.95       |
| $\beta_3$  | MSE       | 0.020   | 0.023    | 0.022      |
|            | Bias      | -0.013  | -0.011   | -0.012     |
|            | CP        | 0.95    | 0.96     | 0.95       |
| $\beta_4$  | MSE       | 0.014   | 0.016    | 0.016      |
|            | Bias      | -0.016  | -0.010   | -0.017     |
|            | CP        | 0.95    | 0.95     | 0.95       |
| Average    | MSE       | 0.016   | 0.019    | 0.017      |
|            | Bias      | 0.012   | 0.009    | 0.012      |
|            | CP        | 0.95    | 0.96     | 0.95       |
Table A9: Comparison of three construction strategies of our method with the parametric components obtained with “Plug-in”, “Debiased” and “Parametric” estimation procedure as introduced in Section 2.3, respectively. Their performance are evaluated on $\beta_0, \ldots, \beta_4$ and average on them, in terms of mean square error (MSE), bias and coverage probability of the 95% confidence interval (CP), under Configuration (iii) described in Section 4.

| Covariates | | Estimator | |
|------------|-----------|-----------|-----------|
|            | Plug-in   | Debiased  | Parametric|
| $\beta_0$  | MSE       | 0.012     | 0.015     | 0.013     |
|            | Bias      | -0.007    | 0.004     | 0.013     |
|            | CP        | 0.96      | 0.98      | 0.96      |
| $\beta_1$  | MSE       | 0.016     | 0.023     | 0.019     |
|            | Bias      | -0.003    | -0.015    | -0.013    |
|            | CP        | 0.96      | 0.96      | 0.97      |
| $\beta_2$  | MSE       | 0.026     | 0.034     | 0.034     |
|            | Bias      | 0.009     | -0.002    | -0.003    |
|            | CP        | 0.95      | 0.96      | 0.96      |
| $\beta_3$  | MSE       | 0.024     | 0.031     | 0.029     |
|            | Bias      | 0.009     | 0.016     | 0.001     |
|            | CP        | 0.94      | 0.93      | 0.93      |
| $\beta_4$  | MSE       | 0.019     | 0.024     | 0.022     |
|            | Bias      | -0.017    | -0.011    | -0.012    |
|            | CP        | 0.95      | 0.96      | 0.95      |
| Average    | MSE       | 0.019     | 0.025     | 0.023     |
|            | Bias      | 0.009     | 0.010     | 0.008     |
|            | CP        | 0.95      | 0.96      | 0.95      |
Table A10: Comparison of three construction strategies of our method with the parametric components obtained with “Plug-in”, “Debiased” and “Parametric” estimation procedure as introduced in Section 2.3 respectively. Their performance are evaluated on $\beta_0, \ldots, \beta_4$ and average on them, in terms of mean square error (MSE), bias and coverage probability of the 95% confidence interval (CP), under Configuration (iv) described in Section 4.

| Covariates | MSE | Bias | CP |
|------------|-----|------|----|
| $\beta_0$  | 0.014 | 0.016 | 0.013 |
|            | $-0.035$ | $-0.022$ | 0.008 |
|            | 0.95  | 0.97  | 0.95  |
| $\beta_1$  | 0.023 | 0.025 | 0.026 |
|            | $-0.004$ | $-0.008$ | $-0.009$ |
|            | 0.95  | 0.94  | 0.91  |
| $\beta_2$  | 0.02  | 0.024 | 0.023 |
|            | 0.006 | $-0.003$ | $-0.009$ |
|            | 0.96  | 0.97  | 0.94  |
| $\beta_3$  | 0.022 | 0.026 | 0.024 |
|            | 0.002 | 0.006 | 0.004 |
|            | 0.96  | 0.95  | 0.92  |
| $\beta_4$  | 0.015 | 0.017 | 0.016 |
|            | 0.013 | 0.016 | 0.013 |
|            | 0.96  | 0.98  | 0.90  |
| Average    | 0.019 | 0.021 | 0.020 |
|            | 0.012 | 0.011 | 0.009 |
|            | 0.96  | 0.96  | 0.93  |
Implementing details and additional results of real example

For the real example, the implementing procedures remain the same for the methods except that the bases in the nuisance models of Parametric and Our method are slightly different: we take $\Psi = X$ for the importance weight model and

$$\Phi = (X^T, X_1 X_4, X_2 X_4, X_3 X_4, X_1 X_5, X_2 X_5, X_3 X_5)^T$$

for the imputation model (interaction effects include the terms between {Age, Gender, Race} and the two diagnostic code features). At last, we present the plot of fitted nonparametric components $h(Z)$ and $r(Z)$ where $Z = X_4$ in Figure A1, the fitted coefficients of the methods in comparison and their bootstrap standard errors in Table A11, evaluation parameters in terms of the estimation and prediction performance of the three construction strategies of our method in Table A12 and the fitted coefficients and bootstrap standard errors of them in Table A13.

Figure A1: Curves of the nonparametric components $r(Z)$ and $h(Z)$ against $Z = X_4$, the diagnostic code for bipolar disorder (log-count), estimated by the initial semiparametric models using natural splines.
Table A11: Fitted outcome coefficients and in parentheses are their bootstrap standard errors. Source: logistic model fitted with the 400 source samples in PHS; Parametric: doubly robust estimator with parametric nuisance models; Our method: doubly robust estimator using semi-nonparametric nuisance models with “Plug-in” parametric components; Additive: double machine learning estimator of additive models regularized with ℓ₁ + ℓ₂ penalty; Kernel machine: support vector machine with radial basis function kernel; Target: logistic model fitted with the 200 validation (labelled) samples in VUMC.

|        | Source | Parametric | Our method | Additive | Kernel machine | Target |
|--------|--------|------------|------------|----------|----------------|--------|
| β₀     | -0.88 (0.36) | -0.27 (0.66) | -0.66 (0.49) | -0.82 (0.61) | -0.79 (1.23) | -1.59 (0.59) |
| β₁     | 0.12 (0.14) | -0.62 (0.41) | -0.29 (0.16) | 0.09 (0.29) | -0.07 (0.55) | -0.18 (0.22) |
| β₂     | 0.41 (0.27) | -0.26 (0.59) | -0.11 (0.37) | 0.29 (0.47) | 0.03 (1.19) | 0.24 (0.42) |
| β₃     | 0.67 (0.36) | 0.94 (0.73) | 0.78 (0.49) | 0.63 (0.43) | 1.12 (0.77) | 1.15 (0.53) |
| β₄     | 1.5 (0.16) | 1.92 (0.63) | 1.71 (0.29) | 2.04 (0.55) | 1.71 (1.72) | 2.08 (0.31) |
| β₅     | -1.09 (0.15) | -0.55 (0.29) | -0.79 (0.22) | -1.60 (0.40) | -0.98 (1.33) | -0.37 (0.27) |

Table A12: Estimation and prediction performance of the three construction strategies of our method in bipolar disorder phenotyping. RMSPE: relative mean square prediction error; Average SE: root mean square average of (empirical) standard errors; AUC: area under the curve; F₁₅%/₁₀%: F₁-score (harmonic mean of precision and recall) at the classification cutoff with the false positive rate being 5% or 10%.

|                | Plug-in | Debiased | Parametric | Target |
|----------------|---------|----------|------------|--------|
| RMSPE          | 0.09    | 0.14     | 0.09       | N/A    |
| Average SE     | 0.88    | 1.39     | 1.04       | 1.01   |
| AUC            | 0.85    | 0.84     | 0.85       | 0.86   |
| F₁₅%           | 0.56    | 0.54     | 0.56       | 0.54   |
| F₁₀%           | 0.67    | 0.65     | 0.64       | 0.62   |

Table A13: Fitted coefficients of our method with different construction procedures for the nuisance parametric components and in parentheses are their bootstrap standard errors.

|        | Plug-in | Debiased | Parametric | Target |
|--------|---------|----------|------------|--------|
| β₀     | -0.66 (0.49) | -0.24 (0.73) | -0.69 (0.57) | -1.59 (0.59) |
| β₁     | -0.29 (0.16) | -0.46 (0.29) | -0.28 (0.16) | -0.18 (0.22) |
| β₂     | -0.11 (0.37) | -0.40 (0.54) | -0.26 (0.41) | 0.24 (0.42) |
| β₃     | 0.78 (0.49) | 0.72 (0.79) | 0.91 (0.63) | 1.15 (0.53) |
| β₄     | 1.71 (0.29) | 1.90 (0.44) | 1.72 (0.35) | 2.08 (0.31) |
| β₅     | -0.79 (0.22) | -0.9 (0.45) | -0.81 (0.23) | -0.37 (0.27) |