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Doubly Robust Estimation in Observational Studies with Partial Interference

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Summary

Interference occurs when the treatment (or exposure) of one individual affects the outcomes of others. In some settings it may be reasonable to assume individuals can be partitioned into clusters such that there is no interference between individuals in different clusters, i.e., there is partial interference. In observational studies with partial interference, inverse probability weighted (IPW) estimators have been proposed of different possible treatment effects. However, the validity of IPW estimators depends on the propensity score being known or correctly modeled. Alternatively, one can estimate the treatment effect using an outcome regression model. In this paper, we propose doubly robust (DR) estimators which utilize both models and are consistent and asymptotically normal if either model, but not necessarily both, is correctly specified. Empirical results are presented to demonstrate the DR property of the proposed estimators, as well as the efficiency gain of DR over IPW estimators when both models are correctly specified. The different estimators are illustrated using data from a study examining the effects of cholera vaccination in Bangladesh.

Keywords

Causal Inference; Doubly Robust Estimator; Interference; Observational Studies

1 INTRODUCTION

Typically in causal inference it is assumed an individual's potential outcomes do not depend on the treatment (or exposure) of other individuals, i.e., there is no interference (Cox 1958). However, this assumption may not hold in various settings. For example, in a vaccine trial, the infection status of one individual may depend on whether other individuals are vaccinated. Interference may occurs in other areas, such as econometrics (Manski 2013;

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Sobel 2006), education (Basse & Feller 2018; Hong & Raudenbush 2006), and political science (Bowers, Fredrickson, & Panagopoulos 2013; Sinclair, McConnell, & Green 2012).

Recently, inference methods have been proposed for settings where individuals can be partitioned into clusters and possible interference exists only among individuals in the same cluster. This is sometimes called partial interference (Sobel 2006) and can be viewed as a special case of the constant treatment response assumption (Manski 2013). Hudgens and Halloran (2008) proposed estimators of direct, indirect (or spillover), total, and overall causal effects of a treatment for two-stage randomized experiments in the presence of partial interference, and Liu and Hudgens (2014) derived the asymptotic distributions of these estimators. Tchetgen Tchetgen and VanderWeele (2012) proposed inverse probability weighted (IPW) estimators of these causal effects for observational studies with partial interference. However, the validity of these IPW estimators only holds when the propensity score is known or correctly modeled. Moreover, IPW estimators are known to have large variances and be unstable, especially when some propensity scores are close to 0 or 1, which may be common when there is partial interference.

In the absence of interference, doubly robust (DR) estimators are known to have certain advantages over IPW estimators. DR estimators are constructed by utilizing two models: a model for the dependence of treatment on covariates (i.e., propensity score model), and a model for the dependence of the outcome on covariates and treatment. DR estimators are consistent when either, but not necessarily both, of the two models is correct. Thus DR estimators provide some protection against model mis-specification. However, existing DR estimators assume no interference and hence are not applicable in settings such as infectious diseases where interference may be present.

In this paper, several DR estimators are proposed for use in observational studies where there may be partial interference. The outline of the remainder of the paper is as follows. In Section 2, notation, assumptions, and the causal effects of interest are introduced. IPW and regression estimators are defined in Section 3 and various DR estimators are proposed in Section 4. Results from a simulation study are presented in Section 5. The proposed DR estimators are used to analyze data from a cholera vaccine study in Section 6. Finally, Section 7 concludes with a discussion.

2 NOTATION, ASSUMPTIONS AND ESTIMANDS

Consider an observational study where data is observed for individuals who can be partitioned into groups (e.g., students in different schools). Suppose there are k groups of individuals in the study with $N_i > 1$ individuals in group i. For individual j in group i we observe (X_{ij}, A_{ij}, Y_{ij}) for $j = 1, \ldots, N_i$, $i = 1, \ldots, k$, where X_{ij} denotes a vector of pre-treatment covariates, A_{ij} denotes a treatment indicator ($A_{ij} = 1$ if individual receives treatment and $A_{ij} = 0$ otherwise), and Y_{ij} is a univariate outcome of interest, which can be continuous or categorical. Let $X_i = \left(X_{i1}, \ldots, X_{iN_i}\right)$, $A_i = \left(A_{i1}, \ldots, A_{iN_i}\right)$ and $Y_i = \left(Y_{i1}, \ldots, Y_{iN_i}\right)$.

Assume the k groups are a random sample from an infinite super-population of groups such that $O_i = (X_i, A_i, Y_i)$ are independent and identically distributed for $i = 1, \ldots, k$. Define

$A_{i(-j)} = A_i \backslash A_{ij}$, i.e., the vector of treatment indicators for all individuals in group i except individual j. Let a_{ij}, $a_{i(-j)}$ and a_i denote possible realizations of A_{ij}, $A_{i(-j)}$ and A_i. Define $f(a_i|x_i) = \Pr(A_i = a_i|X_i = x_i)$ to be the probability of treatment vector a_i given covariates x_i and similarly define $f(a_{ij}|x_i) = \Pr(A_{ij} = a_{ij}|X_i = x_i)$. Assume $f(a_i|x_i) > 0$ for all x_i in the support of X_i; this is sometimes referred to as the positivity assumption.

Assume there is no interference between individuals in different groups, i.e., partial interference. This assumption may be reasonable in settings where groups are sufficiently separated geographically or in time. Note that no assumption is made about the nature of interference within groups. Indeed one of the primary inferential goals is to assess to what extent there is interference within groups. Assuming partial interference, the potential outcome of one individual may be expressed as a function of their own treatment as well as the treatment of others in the same group. Therefore, the potential outcome for individual j in group i is denoted $Y_{ij}(a_i) = Y_{ij}(a_{ij}, a_{i(-j)})$ for treatment vector a_i. Additionally, we make the causal consistency assumption that the observed outcome Y_{ij} is the same as the potential outcome $Y_{ij}(a_i)$ if treatment $A_i = a_i$, i.e.,$Y_{ij} = \sum_{a_i} 1(A_i = a_i)Y_{ij}(a_i)$. Assume $Y_i() \perp\!\!\!\perp A_i|X_i$, where $Y_i()$ denotes all of the potential outcomes for group i and $\perp\!\!\!\perp$ indicates independence; this assumption is sometimes referred to as conditional exchangeability or ignorability.

Causal effects of treatment are defined by average outcomes under different counterfactual scenarios corresponding to different distributions of treatment in the population. Following Tchetgen Tchetgen and VanderWeele (2012), consider the treatment allocation strategy (or policy) where individuals receive treatment independently with probability α. Under an α allocation strategy, the probability of treatment $A_i = a_i$ for group i is $\pi(a_i; \alpha) = \Pr_\alpha(A_i = a_i) = \prod_j \alpha^{a_{ij}}(1-\alpha)^{1-a_{ij}}$. The α subscript of $\Pr_\alpha$ indicates probability in the counterfactual scenario corresponding to policy α. Similarly, let $\pi(a_{i(-j)}; \alpha) = \Pr_\alpha(A_{i(-j)} = a_{i(-j)}) = \prod_{k\neq j} \alpha^{a_{ik}}(1-\alpha)^{1-a_{ik}}$ denote the probability of treatment $A_{i(-j)} = a_{i(-j)}$ for all individuals in group i other than individual j. Define the average potential outcome in group i when an individual receives treatment a under policy α by $\overline{Y}_i(a, \alpha) = N_i^{-1} \sum_{j=1}^{N_i} \sum_{a_{i(-j)}} Y_{ij}(a, a_{i(-j)})\pi(a_{i(-j)}; \alpha)$, and let $\mu_{a\alpha} = E\{\overline{Y}_i(a, \alpha)\}$ where $E\{\cdot\}$ denotes the expected value in the super-population of groups. Similarly, define $\mu_\alpha = E\{\overline{Y}_i(\alpha)\}$ where $\overline{Y}_i(\alpha) = N_i^{-1} \sum_{j=1}^{N_i} \sum_{a_i} Y_{ij}(a_i)\pi(a_i; \alpha)$ denotes the average outcome in group i under policy α

Following Halloran and Struchiner (1995) and Hudgens and Halloran (2008), define the direct effect of treatment under policy α to be $\overline{DE}(\alpha) = \mu_{1\alpha} - \mu_{0\alpha}$. For policies α_0 and α_1, define the indirect effect $\overline{IE}(\alpha_1, \alpha_0) = \mu_{0\alpha_1} - \mu_{0\alpha_0}$, the total effect $\overline{TE}(\alpha_1, \alpha_0) = \mu_{1\alpha_1} - \mu_{0\alpha_0}$, and

the overall effect $\overline{\mathrm{OE}}(\alpha_1, \alpha_0) = \mu_{\alpha_1} - \mu_{\alpha_0}$. In words, the direct effect is the difference between the average potential outcome when group i receives policy a and an individual in that group receives treatment compared to when an individual in that group receives control. The indirect (or spillover) effect compares the average potential outcome when an individual receives control under different policies a_1 and a_0. The total effect equals the sum of the direct and indirect effects, and the overall effect provides a single summary measure of the effect of policies a_1 versus a_0. See Tchetgen Tchetgen and VanderWeele (2012) for further discussion about these estimands.

3 IPW AND REGRESSION ESTIMATORS

Inverse probability weighting is a common approach to adjusting for observed confounding in observational studies. Heuristically, inverse probability weighting creates a pseudo-population in which there is no confounding such that the average outcome in the pseudo-population approximates the average outcome that would have been observed if treatment has been randomly assigned. Tchetgen Tchetgen and VanderWeele (2012) proposed IPW estimators for μ_{aa} and μ_a defind by $\widehat{\mathrm{Y}}^{\mathrm{ipw}}(\mathrm{a};\alpha) = \sum_{\mathrm{i}=1}^{\mathrm{k}} \widehat{\mathrm{Y}}_{\mathrm{i}}^{\mathrm{ipw}}(\mathrm{a};\alpha)/\mathrm{k}$ and $\widehat{\mathrm{Y}}^{\mathrm{ipw}}(\alpha) = \sum_{\mathrm{i}=1}^{\mathrm{k}} \widehat{\mathrm{Y}}_{\mathrm{i}}^{\mathrm{ipw}}(\alpha)/\mathrm{k}$, where

$$\widehat{\mathrm{Y}}_{\mathrm{i}}^{\mathrm{ipw}}(\mathrm{a},\alpha) = \mathrm{N}_{\mathrm{i}}^{-1} \sum_{\mathrm{j}=1}^{\mathrm{N}_{\mathrm{i}}} 1\left(\mathrm{A}_{\mathrm{ij}} = \mathrm{a}\right) \mathrm{Y}_{\mathrm{ij}}\left(\mathrm{A}_{\mathrm{i}}\right) \pi\left(\mathrm{A}_{\mathrm{i}(-\mathrm{j})};\alpha\right) / \mathrm{f}\left(\mathrm{A}_{\mathrm{i}} \middle| \mathrm{X}_{\mathrm{i}};\hat{\gamma}\right),$$

$$\widehat{\mathrm{Y}}_{\mathrm{i}}^{\mathrm{ipw}}(\alpha) = \mathrm{N}_{\mathrm{i}}^{-1} \sum_{\mathrm{j}=1}^{\mathrm{N}_{\mathrm{i}}} \mathrm{Y}_{\mathrm{ij}}\left(\mathrm{A}_{\mathrm{i}}\right) \pi\left(\mathrm{A}_{\mathrm{i}};\alpha_0\right) / \mathrm{f}\left(\mathrm{A}_{\mathrm{i}} \middle| \mathrm{X}_{\mathrm{i}};\hat{\gamma}\right),$$

and $\mathrm{f}(\mathrm{A}_{\mathrm{i}}|\mathrm{X}_{\mathrm{i}};\ \gamma)$ denotes a propensity score model with finite-dimensional vector of parameters γ and $\hat{\gamma}$ is an estimator of γ. IPW estimators of the direct, indirect, total and overall effect are then defined as $\widehat{\mathrm{DE}}^{\mathrm{ipw}}(\alpha) = \widehat{\mathrm{Y}}^{\mathrm{ipw}}(1,\alpha) - \widehat{\mathrm{Y}}^{\mathrm{ipw}}(0,\alpha)$, $\widehat{\mathrm{IE}}^{\mathrm{ipw}}(\alpha_1,\alpha_0) = \widehat{\mathrm{Y}}^{\mathrm{ipw}}(0,\alpha_1) - \widehat{\mathrm{Y}}^{\mathrm{ipw}}(0,\alpha_0)$, $\widehat{\mathrm{TE}}^{\mathrm{ipw}}(\alpha_1,\alpha_0) = \widehat{\mathrm{Y}}^{\mathrm{ipw}}(1,\alpha_1) - \widehat{\mathrm{Y}}^{\mathrm{ipw}}(0,\alpha_0)$ and $\widehat{\mathrm{OE}}^{\mathrm{ipw}}(\alpha_1,\alpha_0) = \widehat{\mathrm{Y}}^{\mathrm{ipw}}(\alpha_1) - \widehat{\mathrm{Y}}^{\mathrm{ipw}}(\alpha_0)$, respectively. Assuming a correctly specified mixed effects logistic regression model for the propensity score $\mathrm{f}(\mathrm{A}_{\mathrm{i}}|\mathrm{X}_{\mathrm{i}};\ \gamma)$ and $\hat{\gamma}$ equal to the maximum likelihood estimator of γ, Perez-Heydrich et al. (2014) proved the IPW estimators are consistent and asymptotically normal by showing the estimators solve a vector of unbiased estimating equations.

Alternatively, one can adjust for confounding by controlling for observed covariates in an outcome regression model. By the exchangeability assumption,

$$\mathrm{E}\left\{\mathrm{Y}_{\mathrm{ij}}\left(\mathrm{a}_{\mathrm{i}}\right) \middle| \mathrm{X}_{\mathrm{i}}\right\} = \mathrm{E}\left\{\mathrm{Y}_{\mathrm{ij}}\left(\mathrm{a}_{\mathrm{i}}\right) \middle| \mathrm{A}_{\mathrm{i}} = \mathrm{a}_{\mathrm{i}}, \mathrm{X}_{\mathrm{i}}\right\} = \mathrm{E}\left(\mathrm{Y}_{\mathrm{ij}} \middle| \mathrm{A}_{\mathrm{i}} = \mathrm{a}_{\mathrm{i}}, \mathrm{X}_{\mathrm{i}}\right),$$

with the last conditional expectation identifiable from the observable random variables O_i. This motivates constructing estimators by first positing a regression model such as $E(Y_{ij}|A_i=a_i,X_i)=m_{ij}(A_i,X_i;\beta)$ where $m_{ij}(A_i,X_i;\beta)=\beta_1+\beta_{A_{ij}}A_{ij}+\beta^T_{A_{i(-j)}}A_{i(-j)}+\beta^T_{X_i}X_i$ Then let

$\hat{Y}_i^{reg}(a,\alpha)=\sum_{j=1}^{N_i}\sum_{a_{i(-j)}} m_{ij}(a,a_{i(-j)},X_i;\hat{\beta})\pi(a_{i(-j)};\alpha)/N_i$ and

$\hat{Y}_i^{reg}(\alpha)=\sum_{j=1}^{N_i}\sum_{a_i} m_{ij}(a_i,X_i;\hat{\beta})\pi(a_i;\alpha)/N_i$, where $\hat{\beta}$ is the maximum likelihood estimator for β, and define the regression estimators of $\mu_{a\alpha}$ and μ_α to be $\hat{Y}^{reg}(a,\alpha)=\sum_{i=1}^{k}\hat{Y}_i^{reg}(a,\alpha)/k$ and $\hat{Y}^{reg}(\alpha)=\sum_{i=1}^{k}\hat{Y}_i^{reg}(\alpha)/k$ with the corresponding regression causal effect estimators defined analogously to the IPW causal effect estimators defined above. Similar to the IPW estimators, it is straightforward to show that if the outcome regression model is correctly specified, then $\hat{Y}^{reg}(a,\alpha)$ and $\hat{Y}^{reg}(\alpha)$ are consistent and asymptotically normal estimators of $\mu a\alpha$ and $\mu\alpha$ using standard estimating equation theory.

Thus, the various causal effects defined above can be consistently estimated by the IPW estimator if the propensity score model is correctly specified. These effects can also be consistently estimated by the outcome regression estimator if the regression model is correctly specified. In the next section, several DR estimators are proposed which utilize both the propensity score and regression models, and are consistent if either model (but not necessarily both) is correctly specified.

4 DOUBLY ROBUST ESTIMATORS

4.1 Regression estimation with residual bias correction

Define $\hat{Y}^{DR\cdot BC}(a,\alpha)=\sum_{i=1}^{k}\hat{Y}_i^{DR\cdot BC}(a,\alpha)/k$ and $\hat{Y}^{DR\cdot BC}(\alpha)=\sum_{i=1}^{k}\hat{Y}_i^{DR\cdot BC}(\alpha)/k$ to be the residual bias correction DR estimators for $\mu_{a\alpha}$ and μ_α where

$$\hat{Y}_i^{DR\cdot BC}(a,\alpha)=N_i^{-1}\sum_{j=1}^{N_i}\left\{\sum_{a_{i(-j)}} m_{ij}(a,a_{i(-j)},X_i;\hat{\beta})\pi(a_{i(-j)};\alpha)+\frac{1(A_{ij}=a)}{f(A_i|X_i;\hat{\gamma})}\{Y_{ij}(A_i)-m_{ij}(A_i,X_i;\hat{\beta})\}\pi(A_{i(-j)};\alpha)\right\},$$

$$\hat{Y}_i^{DR\cdot BC}(\alpha)=N_i^{-1}\sum_{j=1}^{N_i}\left\{\sum_{a_i} m_{ij}(a,a_i,X_i;\hat{\beta})\pi(a_i;\alpha)+\frac{\{Y_{ij}(A_i)-m_{ij}(A_i,X_i;\hat{\beta})\}}{f(A_i|X_i;\hat{\gamma})}\pi(A_i;\alpha)\right\}.$$

The bias correction DR estimators are motivated by the DR estimators proposed by Scharfstein, Rotnitzky, and Robins (1999) for the setting where there is no interference. The bias correction DR estimators are composed of two parts. The first part is the regression

estimator and the second part entails inverse weighted residuals of the regression estimator. Informally, the DR property of these estimators follows by noting: (i) when the regression estimator is correctly specified, the first part is consistent for the parameter of interest and the second part converges to 0; (ii) when the regression estimator is misspecified but the propensity score model is correctly specified, the first part is biased but the second part consistently estimates the bias of the first term such that the summation is still consistent for the target parameter.

The bias correction DR causal effect estimators are defined similarly to the IPW and regression causal effect estimators in Section 3. For example, the bias correction DR direct effect estimator is $\widehat{\mathrm{DE}}^{\mathrm{DR\cdot BC}}(\alpha) = \widehat{\mathrm{Y}}^{\mathrm{DR\cdot BC}}(1,\alpha) - \widehat{\mathrm{Y}}^{\mathrm{DR\cdot BC}}(0,\alpha)$. To derive the asymptotic distribution of the bias correction direct effect estimator, let $\mathrm{G}_{\mathrm{a}\alpha}^{\mathrm{DR\cdot BC}}\left(\mathrm{O}_{\mathrm{i}};\mu,\beta,\gamma\right) = \widehat{\mathrm{Y}}_{\mathrm{i}}^{\mathrm{DR\cdot BC}}(\mathrm{a},\alpha) - \mu$ and let $\mathrm{G}_{\beta}(\mathrm{O}_{\mathrm{i}};\boldsymbol{\beta})$ and $\mathrm{G}_{\gamma}(\mathrm{O}_{\mathrm{i}};\boldsymbol{\gamma})$ denote the estimating functions corresponding to $\hat{\beta}$ and $\hat{\gamma}$, such that $\hat{\theta}^{\mathrm{DR\cdot BC}} = \left\{\widehat{\mathrm{Y}}^{\mathrm{DR\cdot BC}}(0,\alpha) - \widehat{\mathrm{Y}}^{\mathrm{DR\cdot BC}}(1,\alpha), \hat{\beta}, \hat{\gamma}\right\}$ is the solution to the vector equation $\sum_{\mathrm{i}=1}^{\mathrm{k}} \mathrm{G}_{\alpha}^{\mathrm{D,\,DR\cdot BC}}\left(\mathrm{O}_{\mathrm{i}};\theta\right) = 0$ where $\theta = (\mu_{0\alpha}, \mu_{1\alpha}, \beta, \gamma)$ and $\mathrm{G}_{\alpha}^{\mathrm{D,\,DR\cdot BC}}(\mathrm{O};\theta) = \left\{\mathrm{G}_{0\alpha}^{\mathrm{DR\cdot BC}}\left(\mathrm{O};\mu_{0\alpha},\beta,\gamma\right), \mathrm{G}_{1\alpha}^{\mathrm{DR\cdot BC}}\left(\mathrm{O};\mu_{1\alpha},\beta,\gamma\right), \mathrm{G}_{\beta}(\mathrm{O};\beta), \mathrm{G}_{\gamma}(\mathrm{O};\gamma)\right\}^{\mathrm{T}}$. The following proposition shows the DR property and the asymptotic normality of the bias correction DR estimator for the direct effect; the proof, including regularity conditions, is in the Appendix. The DR property and asymptotic normality for the other bias correction DR causal effect estimators can be derived similarly.

Proposition 1. If either $\mathrm{f}(\mathrm{A}_{\mathrm{i}}|\mathrm{X}_{\mathrm{i}};\ \boldsymbol{\gamma})$ or $\mathrm{m}_{\mathrm{ij}}(\mathrm{A}_{\mathrm{i}}, \mathrm{X}_{\mathrm{i}};\boldsymbol{\beta})$ is correctly specified, then $\mathrm{k}^{1/2}\left\{\widehat{DE}^{\mathrm{DR\cdot BC}}(\alpha) - \overline{DE}(\alpha)\right\}$ converges in distribution to $\mathrm{N}\left(0, \sum_0^{\mathrm{D}}\right)$ as $\mathrm{k} \to \infty$ where $\sum^{\mathrm{D}} = \tau \mathrm{U}^{-1}\mathrm{V}\mathrm{U}^{-\mathrm{T}}\tau^{\mathrm{T}}$, $\mathrm{U} = -\mathrm{E}\left\{\partial \mathrm{G}_{\alpha}^{\mathrm{D,\,DR\cdot BC}}\left(\mathrm{O}_{\mathrm{i}};\theta\right)/\partial\theta\right\}$, $\mathrm{V} = \mathrm{E}\left\{\mathrm{G}_{\alpha}^{\mathrm{D,\,DR\cdot BC}}\left(\mathrm{O}_{\mathrm{i}};\theta\right)^{\otimes 2}\right\}$, $\boldsymbol{\tau} = (1, -1, 0, \ldots, 0)$ and $\mathrm{A}^{\otimes 2} = \mathrm{A} \otimes \mathrm{A}^{\mathrm{T}}$ denotes the Kronecker product of A and A^{T}.

A consistent estimator of the asymptotic variance of $\widehat{\mathrm{DE}}^{\mathrm{DR\cdot BC}}(\alpha)$ can be constructed by replacing expectations in U and V with their empirical counterparts. Consistent variance estimators of other bias correction DR causal effect estimators can be constructed similarly.

In practice, the summation terms of the form $\sum_{\mathrm{a_i}} \mathrm{m}_{\mathrm{ij}}\left(\mathrm{a}_{\mathrm{i}}, \mathrm{X}_{\mathrm{i}};\hat{\beta}\right)\pi\left(\mathrm{a}_{\mathrm{i}};\alpha\right)$ in the bias correction DR estimators may be computationally challenging to calculate since the summation is over all possible value of a_{i}. However, a Monte Carlo approximation can be employed by: (i) independently sampling $\widetilde{\mathrm{A}}_{\mathrm{ij}}$ from a Bernoulli distribution with mean α for $\mathrm{j} = 1, \ldots, \mathrm{N}_{\mathrm{i}}$; (ii) calculating $\mathrm{m}_{\mathrm{ij}}\left(\left(\widetilde{\mathrm{A}}_{\mathrm{i1}}, \ldots, \widetilde{\mathrm{A}}_{\mathrm{iN}_{\mathrm{i}}}\right), \mathrm{X}_{\mathrm{i}};\hat{\beta}\right)$; (iii) repeating steps (i) and (ii) MC times; and (iv) averaging the MC values of $\mathrm{m}_{\mathrm{ij}}\left(\left(\widetilde{\mathrm{A}}_{\mathrm{i1}}, \ldots, \widetilde{\mathrm{A}}_{\mathrm{iN}_{\mathrm{i}}}\right), \mathrm{X}_{\mathrm{i}};\hat{\beta}\right)$. This will provide an unbiased estimate of $\sum_{\mathrm{a_i}} \mathrm{m}_{\mathrm{ij}}\left(\mathrm{a}_{\mathrm{i}}, \mathrm{X}_{\mathrm{i}};\hat{\beta}\right)\pi\left(\mathrm{a}_{\mathrm{i}};\alpha\right)$, with larger values of MC resulting in smaller variability of the approximation.

4.2 Regression estimation with inverse-propensity weighted coefficients

In this section we consider a second DR estimator which can be viewed as a generalization of the weighted least squares estimator in Kang and Schafer (2007) to the partial interference setting. Let $L_{ij} = (1, A_{i(-j)}, X_i)$ denote the row vector of all regressors including the intercept in an outcome regression model conditional on $A_{ij} = a$, which for simplicity, we write as $m_{ij}(a, A_{i(-j)}, X_i; \beta) = m_{ij}(a, L_{ij}; \beta)$. Let β_a denote the solution to the equation $\int G_a^{reg}(o; \beta) dF(o) = 0$ where F is the distribution function of O,

$$G_a^{reg}(O_i; \beta) = L_i^T \Lambda_i (A_i, X_i, \omega_i)\{Y_i - m_i(a, L_i; \beta)\}^T,$$

$L_i = \left(L_{i1}^T, \ldots, L_{iN_i}^T\right)^T$, $m_i = \left(m_{i1}, \ldots, m_{iN_i}\right)$, and

$\Lambda_i (A_i, X_i, \omega_i) = \text{diag}\left\{1(A_{i1} = a)\omega_{i1}(L_i), \ldots, 1\left(A_{iN_i} = a\right)\omega_{iN_i}(L_i)\right\}$ for any user specified vector-valued function $\omega_i = \left(\omega_{i1}, \ldots, \omega_{iN_i}\right)$ where in general $\text{diag}(x_1, \ldots, x_n)$ denotes an $n \times n$ diagonal matrix with entries $x_1, \ldots, x_n$ along the diagonal. The choice $\omega_{ij} = 1$ corresponds to the normal equations of the standard least squares estimator. To achieve the DR property, we use

$$\omega_i^{WLS} = \left\{ \frac{\pi\left(A_{i(-1)}; \alpha\right)}{f\left(a, A_{i(-1)} \middle| X_i; \gamma\right)}, \ldots, \frac{\pi\left(A_{i(-N_i)}; \alpha\right)}{f\left(a, A_{i(-N_i)} \middle| X_i; \gamma\right)} \right\},$$

and let

$$G_{a\alpha}^{reg \cdot WLS}(O_i; \beta, \gamma) = L_i^T \Lambda_i \left(A_i, X_i, \omega_i^{WLS}; \alpha, \gamma\right)\{Y_i - m_i(a, L_i; \beta)\}^T.$$

As shown below, this construction yields another DR estimator. Define the weighted coefficients DR estimator by $\widehat{Y}^{DR \cdot WLS}(a, \alpha) = \sum_{i=1}^{k} \widehat{Y}_i^{DR \cdot WLS}(a, \alpha)/k$ where

$$\widehat{Y}_i^{DR \cdot WLS}(a, \alpha) = N_i^{-1} \sum_{j=1}^{N_i} \left\{ \sum_{a_{i(-j)}} m_{ij}\left(a, a_{i(-j)}, X_i; \widehat{\beta}_{a,\alpha}^{WLS}\right) \pi\left(a_{i(-j)}; \alpha\right) \right\},$$

and $\widehat{\beta}_{a,\alpha}^{WLS}$ is obtained by solving

$$\sum_{i=1}^{k} G_{a\alpha}^{reg \cdot WLS}(O_i; \beta, \widehat{\gamma}) = 0. \quad (1)$$

Define $\widehat{\mathrm{Y}}^{\mathrm{DR}\cdot\mathrm{WLS}}(\alpha)$ and the causal effect estimators accordingly.

To show the DR property of the weighted coefficients DR estimators, notice (1) implies

$$\sum_{\mathrm{i}=1}^{\mathrm{k}}\mathrm{N}_{\mathrm{i}}^{-1}\sum_{\mathrm{j}=1}^{\mathrm{N}_{\mathrm{i}}}\left[\frac{1\left(\mathrm{A}_{\mathrm{ij}}=\mathrm{a}\right)}{\mathrm{f}\left(\mathrm{A}_{\mathrm{i}}\middle|\mathrm{X}_{\mathrm{i}};\hat{\gamma}\right)}\left\{\mathrm{Y}_{\mathrm{ij}}\left(\mathrm{A}_{\mathrm{i}}\right)-\mathrm{m}_{\mathrm{ij}}\left(\mathrm{A}_{\mathrm{i}},\mathrm{X}_{\mathrm{i}};\hat{\beta}_{\mathrm{a},\alpha}^{\mathrm{WLS}}\right)\right\}\pi\left(\mathrm{A}_{\mathrm{i}(-\mathrm{j})};\alpha\right)\right]=0.$$

Thus, the weighted coefficients DR estimator can be written as

$$\widehat{\mathrm{Y}}^{\mathrm{DR}\cdot\mathrm{WLS}}(\mathrm{a},\alpha)=\mathrm{k}^{-1}\sum_{\mathrm{i}=1}^{\mathrm{k}}\mathrm{N}_{\mathrm{i}}^{-1}\sum_{\mathrm{j}=1}^{\mathrm{N}_{\mathrm{i}}}\left\{\sum_{\mathrm{a}_{\mathrm{i}(-\mathrm{j})}}\mathrm{m}_{\mathrm{ij}}\left(\mathrm{a},\mathrm{a}_{\mathrm{i}(-\mathrm{j})},\mathrm{X}_{\mathrm{i}};\hat{\beta}_{\mathrm{a},\alpha}^{\mathrm{WLS}}\right)\pi\left(\mathrm{a}_{\mathrm{i}(-\mathrm{j})};\alpha\right)+\frac{1\left(\mathrm{A}_{\mathrm{ij}}=\mathrm{a}\right)}{\mathrm{f}\left(\mathrm{A}_{\mathrm{i}}\middle|\mathrm{X}_{\mathrm{i}};\hat{\gamma}\right)}\left\{\mathrm{Y}_{\mathrm{ij}}\left(\mathrm{A}_{\mathrm{i}}\right)-\mathrm{m}_{\mathrm{ij}}\left(\mathrm{A}_{\mathrm{i}},\mathrm{X}_{\mathrm{i}};\hat{\beta}_{\mathrm{a},\alpha}^{\mathrm{WLS}}\right)\right\}\pi\left(\mathrm{A}_{\mathrm{i}(-\mathrm{j})};\alpha\right)\right\},$$

which has the same form as the bias correction DR estimator and the DR property can be shown in a similar fashion. In particular, let $\hat{\theta}^{\mathrm{DR}\cdot\mathrm{WLS}}=\left\{\widehat{\mathrm{Y}}^{\mathrm{DR}\cdot\mathrm{WLS}}(0,\alpha),\widehat{\mathrm{Y}}^{\mathrm{DR}\cdot\mathrm{WLS}}(1,\alpha),\hat{\beta}_{0,\alpha}^{\mathrm{WLS}},\hat{\beta}_{1,\alpha}^{\mathrm{WLS}},\hat{\gamma}\right\}$, which is the solution to the estimating equation $\sum_{\mathrm{i}=1}^{\mathrm{k}}\mathrm{G}_{\alpha}^{\mathrm{D},\mathrm{DR}\cdot\mathrm{WLS}}\left(\mathrm{O}_{\mathrm{i}};\theta\right)=0$, where

$$\mathrm{G}_{\alpha}^{\mathrm{D},\mathrm{DR}\cdot\mathrm{WLS}}(\mathrm{O};\theta)=\left\{\mathrm{G}_{0\alpha}^{\mathrm{DR}\cdot\mathrm{WLS}}\left(\mathrm{O};\mu_{0\alpha},\beta,\gamma\right),\mathrm{G}_{1\alpha}^{\mathrm{DR}\cdot\mathrm{WLS}}\left(\mathrm{O};\mu_{1\alpha},\beta,\gamma\right),\mathrm{G}_{0\alpha}^{\mathrm{reg}\cdot\mathrm{WLS}}(\mathrm{O};\beta,\gamma),\mathrm{G}_{1\alpha}^{\mathrm{reg}\cdot\mathrm{WLS}}(\mathrm{O};\beta,\gamma),\mathrm{G}_{\gamma}(\mathrm{O};\gamma)\right\}^{\mathrm{T}}$$

and $\mathrm{G}_{\mathrm{a}\alpha}^{\mathrm{DR}\cdot\mathrm{WLS}}\left(\mathrm{O}_{\mathrm{i}};\mu_{\mathrm{a},\alpha},\beta,\gamma\right)=\widehat{\mathrm{Y}}_{\mathrm{i}}^{\mathrm{DR}\cdot\mathrm{WLS}}(\mathrm{a},\alpha)-\mu_{\mathrm{a},\alpha}$. The DR property and asymptotic normality of the weighted direct effect estimator are formally stated in the following proposition.

Proposition 2. If either $\mathrm{f}(\mathrm{A}_{\mathrm{i}}|\mathrm{X}_{\mathrm{i}};\gamma)$ or $\mathrm{m}_{\mathrm{ij}}(\mathrm{A}_{\mathrm{i}},\mathrm{X}_{\mathrm{i}};\beta)$ is correctly specified, then $\mathrm{k}^{1/2}\left\{\widehat{DE}^{\mathrm{DR}\cdot\mathrm{WLS}}(\alpha)-\overline{DE}(\alpha)\right\}$ converges in distribution to $\mathrm{N}\left(0,\sum_{0}^{\mathrm{D}}\right)$ as $\mathrm{k}\to\infty$ where $\sum^{\mathrm{D}}=\tau\mathrm{U}^{-1}\mathrm{V}\mathrm{U}^{-\mathrm{T}}\tau^{\mathrm{T}}$, $\mathrm{U}=-\mathrm{E}\left\{\partial\mathrm{G}_{\alpha}^{\mathrm{D},\mathrm{DR}\cdot\mathrm{WLS}}\left(\mathrm{O}_{\mathrm{i}};\theta\right)/\partial\theta\right\}$, $\mathrm{V}=\mathrm{E}\left\{\mathrm{G}_{\alpha}^{\mathrm{D},\mathrm{DR}\cdot\mathrm{WLS}}\left(\mathrm{O}_{\mathrm{i}};\theta\right)^{\otimes 2}\right\}$ and $\tau=(1,-1,0,\ldots,0)$.

4.3 Regression estimation with propensity based covariates

In this section, a third DR estimator is considered which is constructed by including the inverse of the estimated propensity score in the regression model. Specifically, define the propensity based covariate DR estimator by $\widehat{\mathrm{Y}}^{\mathrm{DR}\cdot\pi\mathrm{cov}}(\mathrm{a},\alpha)=\sum_{\mathrm{i}=1}^{\mathrm{k}}\widehat{\mathrm{Y}}_{\mathrm{i}}^{\mathrm{DR}\cdot\pi\mathrm{cov}}(\mathrm{a},\alpha)/\mathrm{k}$ where

$$\widehat{\mathrm{Y}}_{\mathrm{i}}^{\mathrm{DR}\cdot\pi\mathrm{cov}}(\mathrm{a},\alpha)=\mathrm{N}_{\mathrm{i}}^{-1}\sum_{\mathrm{j}=1}^{\mathrm{N}_{\mathrm{i}}}\left\{\sum_{\mathrm{a}_{\mathrm{i}(-\mathrm{j})}}\mathrm{m}_{\mathrm{ij}}\left(\mathrm{a},\mathrm{a}_{\mathrm{i}(-\mathrm{j})},\mathrm{X}_{\mathrm{i}};\hat{\beta}_{\mathrm{a}\alpha}^{\pi\mathrm{cov}}\right)\pi\left(\mathrm{a}_{\mathrm{i}(-\mathrm{j})};\alpha\right)\right\},$$

$\hat{\beta}_{a\alpha}^{\pi cov}$ is obtained by solving $\sum_{i=1}^{k} G_{a\alpha}^{reg \cdot \pi cov}(O_i; \beta, \hat{\gamma}) = 0$,

$$G_{a\alpha}^{reg \cdot \pi cov}(O_i; \beta, \gamma) = \tilde{L}_i^T \Lambda_i(A_i, X_i, 1)\{Y_i - m_i(a, \tilde{L}_i; \beta, \gamma)\},$$

$\tilde{L}_{ij} = \{1, A_{i(-j)}, X_i, \pi(A_{i(-j)}; \alpha)/f(a, A_{i(-j)}|X_i; \hat{\gamma})\}$, $\tilde{L}_i = (\tilde{L}_{i1}^T, \ldots, \tilde{L}_{iN_i}^T)^T$ and $\Lambda_i(A_i, X_i, 1) = \text{diag}\{1(A_{i1} = a), \ldots, 1(A_{iN_i} = a)\}$. That is, an addiional covariate $\pi(A_{i(-j)}; \alpha)/f(a, A_{i(-j)}|X_i; \hat{\gamma})$ is included in the outcome regression model for Y_{ij}.Define $\hat{Y}^{DR \cdot \pi cov}(\alpha)$ accordingly. To gain some intuition for this type of DR estimator, note it is straightforward to show that conditional exchangeability implies $A_i \perp\!\!\!\perp Y_{ij}(a_i)|f(a_i|X_i)$, and therefore it is sufficient to model $E\{Y_{ij}|A_{ij} = a, A_{i(-j)} = a_{i(-j)}, f(a, a_{i(-j)}|X_i)\}$. The DR property of this estimator can be shown as in Section 4.2 by noting $\hat{Y}^{DR \cdot \pi cov}(a, \alpha)$ can also be written in the same form as the bias correction DR estimator. This DR estimator can be viewed as a generalization of the DR estimator proposed by Scharfstein et al. (1999) to the interference setting.

Propensity based covariate DR estimators can be constructed for the various causal effects, and these estimators are DR and asymptotically normal. This result for the direct effect estimator is stated formally by the following proposition. Let $\hat{\theta}^{DR \cdot \pi cov} = \{\hat{Y}^{DR \cdot \pi cov}(0, \alpha), \hat{Y}^{DR \cdot \pi cov}(1, \alpha), \hat{\beta}_{0\alpha}^{\pi cov}, \hat{\beta}_{1\alpha}^{\pi cov}, \hat{\gamma}\}$, which is the the solution to the estimating equation $\sum_{i=1}^{k} G_{\alpha}^{D, DR \cdot \pi cov}(O_i; \theta) = 0$, where

$G_{\alpha}^{D, DR \cdot \pi cov}(O;\theta)$
$= \{G_{0\alpha}^{DR \cdot \pi cov}(O; \mu_{0\alpha}, \beta, \gamma), G_{1\alpha}^{DR \cdot \pi cov}(O; \mu_{1\alpha}, \beta, \gamma), G_{0\alpha}^{reg \cdot \pi cov}(O; \beta, \gamma), G_{1\alpha}^{reg \cdot \pi cov}(O; \beta, \gamma), G_{\gamma}(O;\gamma)\}^T$
and $G_{a\alpha}^{DR \cdot \pi cov}(O_i; \mu, \beta, \gamma) = \hat{Y}_i^{DR \cdot \pi cov}(a, \alpha) - \mu$.

Proposition 3. If either $f(A_i|X_i;\gamma)$ or $m_{ij}(A_i,X_i;\beta)$ is correctly specified, then $k^{1/2}\{\widehat{DE}^{DR \cdot \pi cov}(\alpha) - \overline{DE}(\alpha)\}$ converges in distribution to $N(0, \sum_0^D)$ as $k \to \infty$ where $\sum^D = \tau U^{-1} V U^{-T} \tau^T$, $U = -E\{\partial G_{\alpha}^{D, DR \cdot \pi cov}(O_i; \theta)/\partial\theta\}$, $V = E\{G_{\alpha}^{D, DR \cdot \pi cov}(O_i; \theta)^{\otimes 2}\}$, and $\boldsymbol{\tau} = (1, -1, 0, \ldots, 0)$.

5 SIMULATIONS

Simulations were conducted to assess the finite sample bias of the IPW, regression and DR estimators given in Sections 3 and 4 as well as to compare their efficiency and robustness when the models are either correct or mis-specified. Simulations were conducted under four scenarios: (i) both the propensity model and the outcome model were correct, (ii) the propensity model was wrong but the outcome model was correct, (iii) the propensity model was correct but the outcome model was wrong, and (iv) neither the propensity model or the

outcome model was correct. For scenario (i), the simulation study was conducted in the following steps:

Step 1: We first generated a population with k = 100 groups and $N_i = 30$ individuals in each group. The vector X_{ij} of pre-treatment covariates for individual j in group i was generated by letting $X_{ij} = (X_{1ij}, X_{2ij})$ where X_{1ij} and X_{2ij} were independently sampled from a standard normal distribution and a Bernoulli distribution with expectation 0.5, respectively.

Step 2: The treatment A_{ij} was generated from the mixed effect logistic regression model $\text{logit}\{\Pr(A_{ij} = 1|X_{ij}, b_i)\} = 0.1 + 0.2|X_{1ij}| + 0.2|X_{1ij}|X_{2ij} + b_i$ where b_i were independently and identically sampled from the normal distribution N(0, 0.3).

Step 3: The outcome Y_{ij} was generated from $Y_{ij} = 2 + 2A_{ij} + p(A_i) - 1.5|X_{1ij}| + 2X_{2ij} - 3|X_{1ij}|X_{2ij} + \varepsilon_{ij}$ where ε_{ij} independently and identically follow N(0, 1) and $p(A_i)$ was the proportion of subjects in group i who received treatment.

Step 4: A correct outcome model $E\{Y_{ij}|X_{ij}, A_i\} = \beta_0 + \beta_1 A_{ij} + \beta_2 p(A_i) + \beta_3|X_{1ij}| + \beta_4 X_{2ij} + \beta_5|X_{1ij}|X_{2ij}$ was fit and $m_{ij}(a_i, X_i; \hat{\beta})$ was calculated.

Step 5: A correct propensity model $\text{logit}\{\Pr(A_{ij} = 1|X_{ij}, b_i)\} = \gamma_0 + \gamma_1|X_{1ij}| + \gamma_2|X_{1ij}|X_{2ij} + b_i$ was fit to calculate the MLE $\hat{\gamma}$ and propensity score estimate $f(A_i|X_i; \hat{\gamma})$

Step 6: The IPW, regression and DR estimators were calculated according to Sections 3 and 4 with $\alpha = 0.5$.

Scenario (ii) was carried out similar to scenario (i) except Step 5 was replaced with

Step 5∗: A mis-specified propensity model $\text{logit}\{\Pr(A_{ij} = 1|X_{ij}, b_i)\} = \gamma_0 + \gamma_1 X_{1ij} + b_i$ was fit to calculate the MLE $\hat{\gamma}$ and propensity score estimate $f(A_i|X_i; \hat{\gamma})$.

Scenarios (iii) was carried out similar to scenario (i) except Step 4 was replaced with

Step 4∗: A mis-specified outcome model $E\{Y_{ij}|X_{ij}, A_i\} = \beta_0 + \beta_1 A_{ij} + \beta_2 p(A_i) + \beta_3 X_{1ij} + \beta_4 X_{2ij}$ was fit and $m_{ij}(a_i, X_i; \hat{\beta})$ was calculated.

Scenario (iv) was carried out similar to scenario (i) with Steps 4 and 5 replaced with Steps 4∗ and 5∗, respectively. The simulations were carried out 1400 times for the scenario with both component models correctly specified in order to accurately estimate confidence interval coverage to the second decimal. For the other scenarios where one or both of the component models was misspecified, the simulations were carried out 700 times. For each scenario, two simulated data sets caused computational issues and were excluded from the results presented below. The propensity based covariate DR estimators were excluded from the simulations due to the computational burden of evaluating these estimators.

Simulation results for the target parameter $\mu_{1,0.5}$ are presented in Figure 1. When the treatment model (i.e., propensity score) is correct, the IPW and the DR estimators have small bias while when the outcome model is correct, the regression and DR estimators have small bias. For example, for scenario (i) the bias of IPW, regression, residual bias correction DR and the weighted coefficients DR estimators are 0.001, −0.02, −0.02 and −0.02, respectively.

The residual bias correction DR and weighted coefficients DR estimators have smaller empirical variances (average estimated standard error (ASE) = 0.053 and 0.055) than that of the IPW estimators (ASE = 0.21) when both the treatment and the outcome regression model model is correct. When the regression model is correctly specified, the regression estimator has the smallest variance. These comparisons of variances align with the results without the interference as reported in Kang and Schafer (2007). In our simulations, when both models are mis-specified, the DR estimators have substantial bias (−0.18 for both) as do the IPW and regression estimators (−0.15 and −0.18).

Wald-type 95% confidence intervals (CIs) were also constructed using empirical sandwich variance estimates as described in Section 4. Empirical coverages of the CIs are shown at the bottom of the Figure 1. As expected, when the corresponding models are correctly specified for the IPW and regression estimators, the Wald CIs have coverage approximately equal to the 0.95. When either model is correctly specified for the DR estimators, the coverages are also approximately 0.95. When the models are mis-specified for the IPW and regression estimators or when neither of the models is correct for the DR estimators, the coverages are well below the nominal level. For example, when both models are wrong, the coverages are 0.75, 0.27, 0.38, and 0.46 for IPW, regression, residual bias correction DR and the weighted coefficients DR estimators, respectively.

6 APPLICATION

A cholera vaccine trial was carried out in Matlab, Bangladesh (Clemens et al. 1988). All children (2–15 yrs old) and women (>15 yrs old) were randomized with equal probability to one of three treatments: one of two types of cholera vaccine or a placebo. Following Perez-Heydrich et al. (2014), in the analysis presented here no distinction is made between the two cholera vaccines. Although the treatments were randomized, not all the eligible individuals participated. Those who did not participate in the randomized trial were followed for the primary outcome and included in the analysis; hence there is an observational aspect to these data.

Among the 121,982 eligible individuals, 49,300 individuals received at least two doses of vaccines. Previous analyses of these data suggest the risk of cholera among unvaccinated individuals was associated with the vaccine coverage in neighboring households or in their social network (Ali et al. 2005; Root, Giebultowicz, Ali, Yunus, & Emch 2011). Perez-Heydrich et al. (2014) utilized the inverse probability weighted (IPW) estimators proposed by Tchetgen Tchetgen and VanderWeele (2012) to assess the direct, indirect, total and overall causal effect of cholera vaccines. Here, we demonstrate the proposed DR estimators and compare to the IPW estimator and the outcome regression estimator.

Perez-Heydrich et al. (2014) used a spatial clustering algorithm to group individuals into 700 groups. Large groups cause significant computational burden for the outcome regression estimator. Since our primary purpose is a comparison of estimators, groups with more than 100 individuals were excluded from the analysis. This resulted in 14,589 individuals in 425 groups. Age in decades and distance to the nearest river were included as covariates in both the treatment and outcome models.

Figures 2 and 3 compare the four estimators of the direct effect $\overline{\mathrm{DE}}(\alpha)$, indirect effect $\overline{\mathrm{IE}}(0.1,\alpha)$, total effect $\overline{\mathrm{TE}}(0.4,\alpha)$ and overall effect $\overline{\mathrm{OE}}(0.4,\alpha)$. The estimates and confidence intervals using the IPW, regression, and DR estimators are similar to Perez-Heydrich et al. (2014). While the point estimates using the weighted coefficients DR estimator are generally similar, the confidence intervals using this estimator are as much as 11 times wider than other methods. This could be due to numerical approximations in estimating the covariance matrix. The estimating functions for this estimator correspond to 20 total target and nuisance parameters, compared to 8, 9, and 13 parameters for the IPW, regression, and residual bias DR estimators respectively.

As vaccine coverage a increases, the point estimate of the direct effect decreases among all estimators. For instance, when a = 0.3, the point estimate of the four estimators are approximately 3.4, 3.8, 3.4, and 5.0 for IPW, regression, biased correction DR and weighted coefficients DR estimators, respectively. This implies when the vaccine coverage is 30%, we would expect to see about 3 or 4 fewer cases of cholera per 1000 person-years among the vaccinated individuals compared to unvaccinated ones. In comparison, when the vaccine coverage is around 60%, the point estimates are approximately 1.1, 2.0, 0.6, and 3.0 for IPW, regression, biased correction DR and weighted coefficients DR estimators, respectively, indicating smaller change in the cases of cholera per 1000 person-years among the vaccinated individuals compared to unvaccinated ones.

Unlike the direct effect, the indirect, total, and overall effect estimates incorporate interference, if present. The indirect effect estimate is negative when $a < 0.4$ and positive when $a > 0.4$, suggesting it is less likely for an unvaccinated individual to be infected when the vaccine coverage in their group is higher. The estimates of the total effect $\overline{\mathrm{TE}}(0.4,\alpha)$, which incorporate both the direct and indirect effects, are relatively constant as a increases, reflecting decreasing direct effect estimates offsetting increasing the indirect effect estimates. The overall effect is in general higher for higher coverage groups as compared with lower coverage groups. For example, when the vaccine coverage is 30% compared to 40%, the overall effect is estimated to be −0.51, 0.65, 0.18, and −0.38 for IPW, regression, biased correction DR and weighted coefficients DR estimators, respectively, while when the vaccine coverage is 60%, those are 1.8, 1.8, 1.9 and 2.3. Point estimates and 95% Wald-type confidence intervals of the IPW, regression and DR estimators for various effects are given in Table 1.

7 DISCUSSION

In this paper several DR estimators are proposed for causal effects in the presence of partial interference. The estimators are shown to be consistent and asymptotically normal if either the propensity model or the outcome regression model, but not necessarily both, is correctly specified. Empirical results demonstrate the DR property of the proposed estimators and possible efficiency gains over a previously proposed IPW estimator when both models are correctly specified.

Application of the proposed methods to the cholera vaccine study provides robust evidence corroborating previous analyses that population- level vaccination affords a protective

indirect effect to unvaccinated individuals. As in Perez-Heydrich et al. (2014), the analysis presented here demonstrates how considering only the direct effect of a vaccine may fail to capture the totality of effects afforded by vaccination at the population level. Note the formulation in this paper considers the direct effect to be a function of vaccine coverage. That is, there is not a single direct effect, but rather a direct effect curve which describes the individual effect of vaccination for a given level of vaccine coverage in the population. Traditionally the direct effect of a vaccine refers to the direct protection for a vaccinated individual owing only to vaccine-induced immunity in that individual (Clemens, Shin, & Ali 2011); in the current formulation, this would correspond to the direct effect when the level of vaccine coverage is 0%. In settings where interference is present, the direct effect curve may vary with vaccine coverage, in which case simple analyses about the direct effect from studies with high levels of vaccine coverage may mislead about the standard interpretation of the direct effect of a vaccine. On the other hand, the methods developed in this paper permit robust inference of the direct effect curve, providing public health officials and policy makers with a more complete picture of how the individual effect of vaccination changes with vaccine coverage.

There are several areas of possible future research related to the methods developed here. For instance, whether any of the DR estimators proposed are semiparametric efficient remains to be investigated. In the absence of interference, DR estimators have the appealing property of achieving parametric rates of convergence (i.e., $n^{1/2}$) even if the working outcome and propensity models are non-parametric provided the estimators of the working model parameters (i.e., nuisance parameters) converge at rate greater than $n^{1/4}$ (Naimi & Kennedy 2017), allowing data-adaptive methods for fitting the working models. Whether the DR estimators proposed in this paper also have this property remains to be determined. When no interference is assumed, DR estimators have been proposed which have certain efficiency properties even if the outcome model is mis-specified (Rotnitzky, Lei, Sued, & Robins 2012; Tan 2010); extensions of these DR estimators to the partial interference setting could be considered. Future research could also entail developing DR estimators in the setting where there is general interference, similar to the IPW estimator for general interference proposed by Liu, Hudgens, and Becker-Dreps (2016).

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APPENDIX

Proof of Proposition 1

To prove double robustness of the bias correction DR estimators, let γ_0 and β_0 denote the true values of the parameters in the propensity score and outcome regression models. Define β^* to be such that $E\{G_\beta(O_i; \beta^*)\} = 0$; note here and below the expectation is taken with respect to the true parameters. Likewise, define γ^* to be such that $E\{G_\gamma(O_i; \gamma^*)\} = 0$. If the propensity score (or outcome regression model) is correctly specified, then $\gamma^* = \gamma_0$ (or $\beta^* = \beta_0$).

If $\gamma^* = \gamma_0$, then $f(A_i|X_i;\ \gamma^*) = f(A_i|X_i;\ \gamma_0)$ and following Tchetgen Tchetgen and VanderWeele (2012)

$$E\left\{N_i^{-1}\sum_{j=1}^{N_i}\frac{1\left(A_{ij}=a\right)Y_{ij}\left(A_i\right)}{f\left(A_i|X_i;\gamma^*\right)}\pi\left(A_{i(-j)};\alpha\right)\right\} = E\left\{N_i^{-1}\sum_{j=1}^{N_i}\sum_{a_i}\frac{1\left(a_{ij}=a\right)Y_{ij}\left(a_i\right)}{f\left(a_i|X_i;\gamma^*\right)}\pi\left(a_{i(-j)};\alpha\right)\Pr\left(A_i=a_i|X_i\right)\right\}$$

$$= \mu_{a\alpha}.$$

By similar reasoning

$$E\left[N_i^{-1}\sum_{j=1}^{N_i}\left\{\sum_{a_{i(-j)}}m_{ij}\left(a,a_{i(-j)},X_i;\beta^*\right)\pi\left(a_{i(-j)};\alpha\right)-\frac{1\left(A_{ij}=a\right)m_{ij}\left(A_i,X_i;\beta^*\right)}{f\left(A_i|X_i;\gamma^*\right)}\pi\left(A_{i(-j)};\alpha\right)\right\}\right]=0$$

which implies $E\left\{G_{a\alpha}^{DR\cdot BC}\left(O_i;\mu_{a\alpha},\beta^*,\gamma^*\right)\right\}=0$ On the other hand, if $\beta^*=\beta_0$, then

$$E\left\{N_i^{-1}\sum_{j=1}^{N_i}\sum_{a_{i(-j)}}m_{ij}\left(a,a_{i(-j)},X_i;\beta^*\right)\pi\left(a_{i(-j)};\alpha\right)\right\} = E\left\{N_i^{-1}\sum_{j=1}^{N_i}\sum_{a_{i(-j)}}E\left\{Y_{ij}\left(a,a_{i(-j)}\right)|X_i\right\}\pi\left(a_{i(-j)};\alpha\right)\right\}$$

$$= \mu_{a\alpha},$$

and

$$E\left\{N_i^{-1}\sum_{j=1}^{N_i}\frac{1\left(A_{ij}=a\right)\left\{Y_{ij}\left(A_i\right)-m_{ij}\left(A_i,X_i;\beta^*\right)\right\}}{f\left(A_i|X_i;\gamma^*\right)}\pi\left(A_{i(-j)};\alpha\right)\right\}=0,$$

implying $E\left\{G_{a\alpha}^{DR\cdot BC}\left(O_i;\mu_{a\alpha},\beta^*,\gamma^*\right)\right\}=0$. Thus, $E\left\{G_{a\alpha}^{DR\cdot BC}\left(O_i;\mu_{a\alpha},\beta^*,\gamma^*\right)\right\}=0$ when either the propensity score model or the outcome regression model is correctly specified.

Let $\theta_0=\left(\mu_{0\alpha},\mu_{1\alpha},\beta^*,\gamma^*\right)$ and $\dot{G}_\alpha^{D,\,DR\,\cdot\,BC}\left(O;\theta_0\right)=\partial G_\alpha^{D,\,DR\,\cdot\,BC}\left(O;\theta_0\right)/\partial\theta_0$. Assume: $E\left\{\dot{G}_\alpha^{D,\,DR\,\cdot\,BC}\left(O;\theta_0\right)\right\}$ exists and is non-singular; $G_\alpha^{D,\,DR\,\cdot\,BC}(o;\theta)$ is twice continuously differentiable with regard to θ for every o; $\left|\partial^2 G_\alpha^{D,\,DR\,\cdot\,BC}(o;\theta)/\left(\partial\theta_i\partial\theta_j\right)\right|\le\psi(o)$ for some integrable measurable function ψ; $E\left\|G_\alpha^{D,\,DR\,\cdot\,BC}\left(O;\theta_0\right)\right\|^2<\infty$ where $\left\|v\right\|^2=v_1^2+\cdots+v_p^2$ for any vector v of length p; and $\sum_{i=1}^{k}G_\alpha^{D,\,DR\,\cdot\,BC}\left(O_i;\theta\right)=0$ has a unique solution for any k. Then by standard estimating equation theory (Stefanski and Boos, 2002; van der Vaart, A. 1998 Ch. 5) it follows that $k^{1/2}\left\{\hat{\theta}^{DR\cdot BC}-\theta_0\right\}$ converges in distribution to N(0, Σ) as $k\rightarrow\infty$

where $\Sigma = U^{-1}VU^{-T}$ $U = -E\left\{\partial G_{\alpha}^{D,DR\cdot BC}(O_i;\theta)/\partial\theta\right\}$ and $V = E\left\{G_{\alpha}^{D,DR\cdot BC}(O_i;\theta)^{\otimes 2}\right\}$. Asymptotic normality $\widehat{DE}^{DR\cdot BC}(\alpha)$ follows from the delta method

Proof of Proposition 2

As in the proof of Proposition 1, let γ_0 and β_{a0} for a = 0,1 denote the true values of the parameters in the propensity score and outcome regression models. Define $\beta^*_{a\alpha}$ and $\gamma^*$to be such that $E\left\{G_{a\alpha}^{reg\cdot WLS}(O_i;\beta^*_{a\alpha},\gamma^*)\right\} = 0$ and $E\left\{G_{\gamma}(O_i;\gamma^*)\right\} = 0$ Note $E\left\{G_{a\alpha}^{reg\cdot WLS}(O_i;\beta^*_{a\alpha},\gamma^*)\right\} = 0$ implies

$$E\left\{N_i^{-1}\sum_{j=1}^{N_i}\frac{1(A_{ij}=a)\left\{Y_{ij}(A_i)-m_{ij}(A_i,X_i;\beta^*_{a\alpha})\right\}}{f(A_i|X_i;\gamma^*)}\pi(A_{i(-j)};\alpha)\right\} = 0.$$

Therefore showing $E\left\{G_{a\alpha}^{DR\cdot WLS}(O_i;\mu_{a\alpha},\beta^*,\gamma^*)\right\} = 0$ is equivalent to showing

$$E\left\{N_i^{-1}\sum_{j=1}^{N_i}\left\{\sum_{a_{i(-j)}}m_{ij}(a,a_{i(-j)},X_i;\beta^*_{a\alpha})\pi(a_{i(-j)};\alpha)+\frac{1(A_{ij}=a)\left\{Y_{ij}(A_i)-m_{ij}(A_i,X_i;\beta^*_{a\alpha})\right\}}{f(A_i|X_i;\gamma^*)}\pi(A_{i(-j)};\alpha)\right\}\right.$$

$$\left. = \mu_{a\alpha},\right.$$

which, by the proof of Proposition 1, will be true if $\gamma^*=\gamma_0$ or $\beta^*_{a\alpha} = \beta_{a0}$. Thus, when either the propensity score model or the outcome regression model is correctly specified, $E\left\{G_{a\alpha}^{DR\cdot WLS}(O_i;\mu_{a\alpha},\beta^*,\gamma^*)\right\} = 0$. Asymptotic normality of $\widehat{DE}^{DR\cdot WLS}(\alpha)$ follows along the same lines as the proof of Proposition 1.

Proof of Proposition 3

The proof of the DR property of $\widehat{DE}^{DR\cdot\pi cov}(\alpha)$ follows from the proof of Proposition 2 by replacing $G_{a\alpha}^{reg\cdot WLS}$, $G_{a\alpha}^{DR\cdot WLS}$, and $\widehat{DE}^{DR\cdot WLS}(\alpha)$ with $G_{a\alpha}^{reg\cdot\pi cov}$, $G_{a\alpha}^{DR\cdot\pi cov}$, and $\widehat{DE}^{DR\cdot\pi cov}(\alpha)$, respectively.

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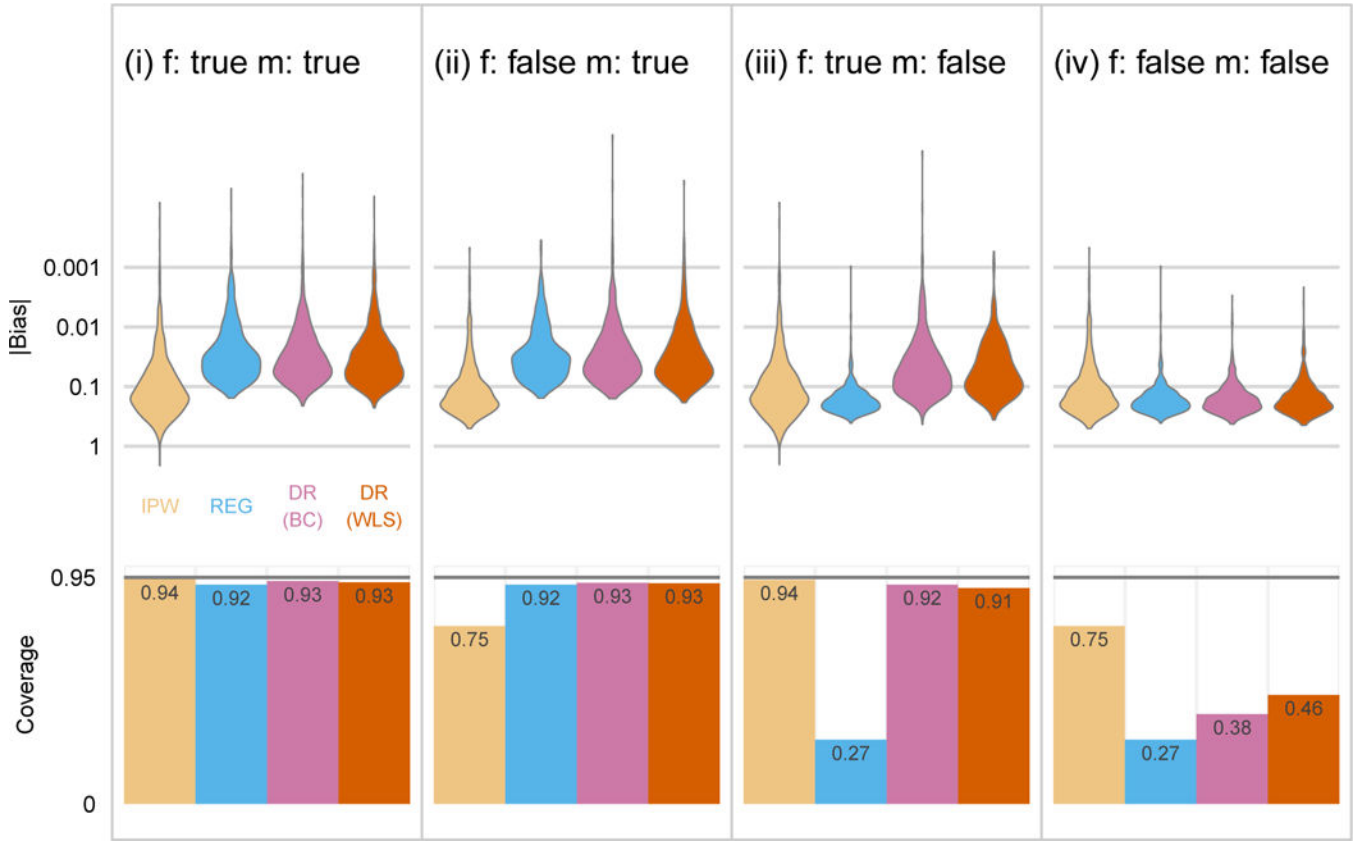

FIGURE 1.

Absolute bias and confidence interval coverage for the IPW, regression (REG), residual bias correction DR (DR (BC)) and weighted coefficients DR (DR (WLS)) estimators of $\mu_{1,0.5}$

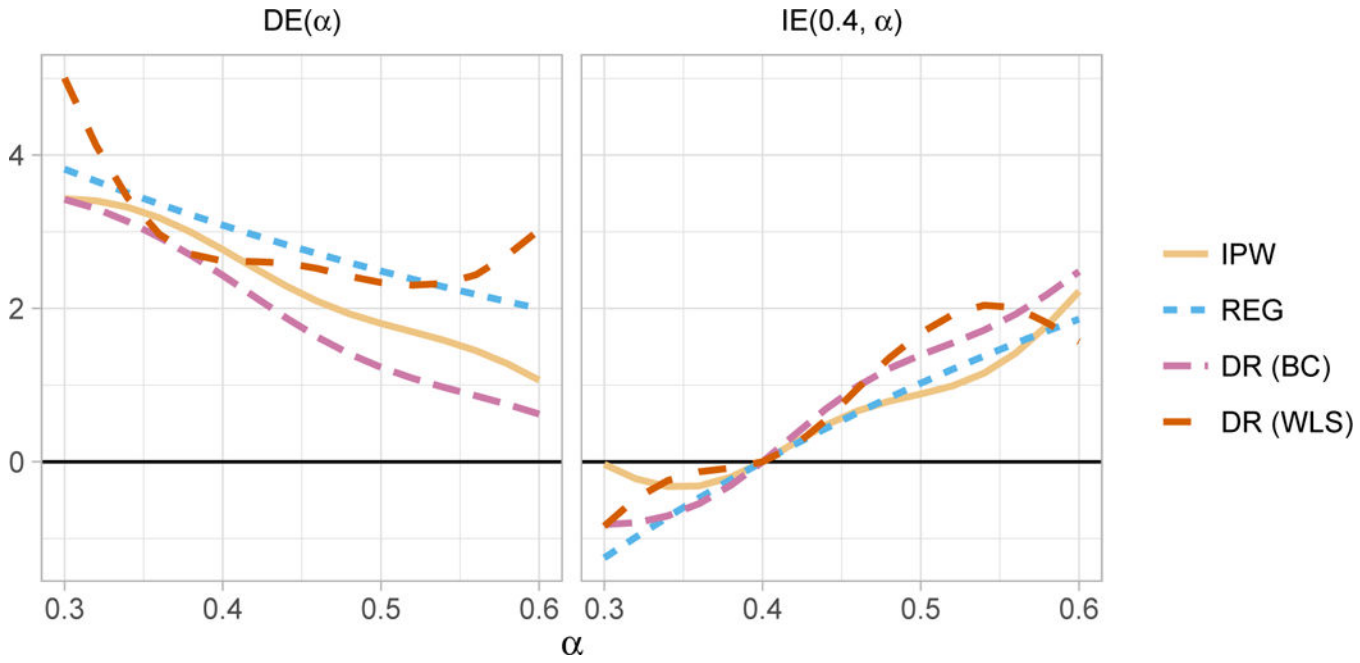

FIGURE 2.

Estimates of the direct $(\overline{\mathrm{DE}}(\alpha))$ and indirect $(\overline{\mathrm{IE}}(0.4, \alpha))$ for the IPW, regression (REG), bias correction DR (DR (BC)) and weighted coefficient DR (DR (WLS)) estimators.

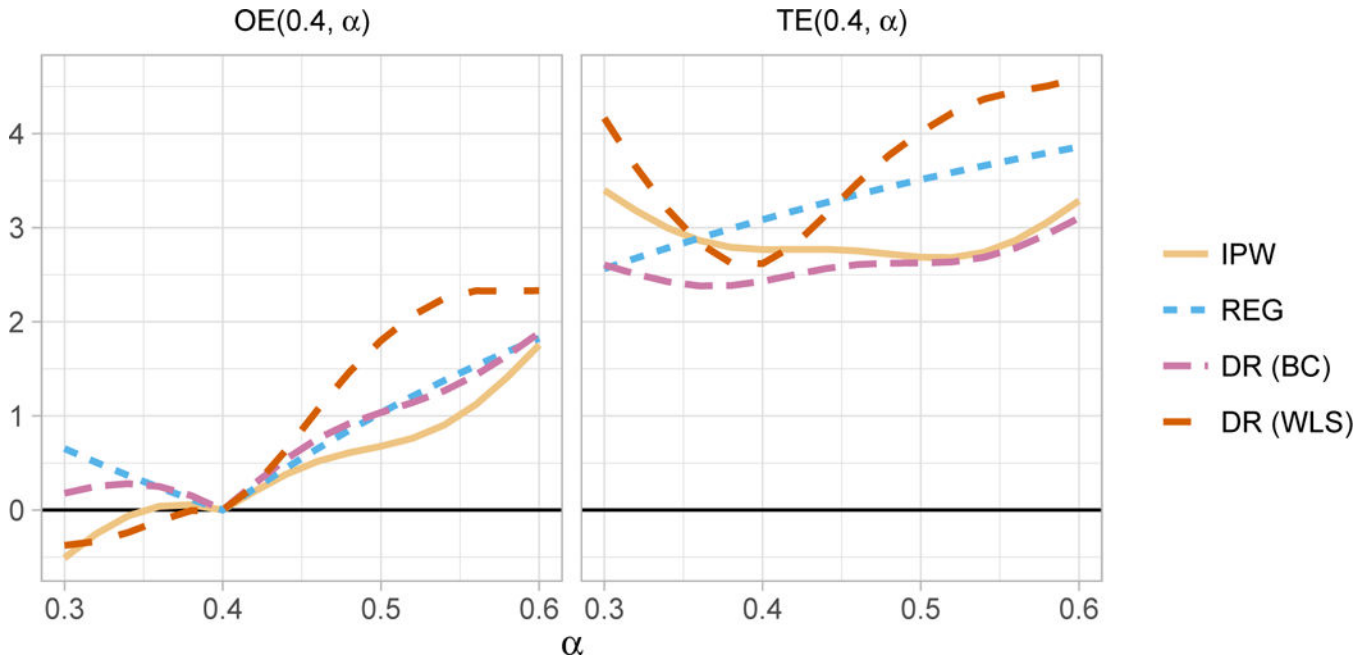

FIGURE 3.

Estimates of the total $\left(\overline{\mathrm{TE}}(0.4,\alpha)\right)$ and overall effects $\left(\overline{\mathrm{OE}}(0.4,\alpha)\right)$ for the IPW, regression (REG), bias correction DR (DR (BC)) and weighted coefficient DR (DR (WLS)) estimators.

TABLE 1

Estimates and 95% Wald-type confidence intervals of the direct $(\overline{\mathrm{DE}}(\alpha))$, indirect $(\overline{\mathrm{IE}}(0.4,\alpha))$, total $(\overline{\mathrm{TE}}(0.4,\alpha))$ and overall effects $(\overline{\mathrm{OE}}(0.4,\alpha))$ for the IPW, regression (REG), bias correction DR (DR (BC)) and weighted coefficient DR (DR (WLS)) estimators

	IPW	REG	DR (BC)	DR (WLS)
$(\overline{\mathrm{DE}}(\alpha))$				
$\alpha = 0.30$	3.4 (0.0, 6.9)	3.8 (1.0, 6.7)	3.4 (–0.2, 7.0)	5.0 (–1.2, 11.2)
$\alpha = 0.44$	2.3 (–1.1, 5.7)	2.8 (0.8, 4.8)	1.9 (–1.5, 5.3)	2.6 (–2.1, 7.3)
$\alpha = 0.60$	1.1 (–1.8, 3.9)	2.0 (0.5, 3.5)	0.6 (–2.3, 3.5)	3.0 (–1.3, 7.3)
$(\overline{\mathrm{IE}}(0.4,\alpha))$				
$\alpha = 0.30$	0.0 (–1.9, 1.8)	–1.3 (–2.4, –0.1)	–0.8 (–2.5, 0.9)	–0.8 (–6.0, 4.3)
$\alpha = 0.44$	0.5 (–0.2, 1.2)	0.4 (0.1, 0.8)	0.7 (0.1, 1.3)	0.5 (–2.7, 3.8)
$\alpha = 0.60$	2.2 (–0.2, 4.6)	1.9 (0.5, 3.2)	2.5 (0.2, 4.8)	1.6 (–5.8, 0.0)
$(\overline{\mathrm{TE}}(0.4,\alpha))$				
$\alpha = 0.30$	3.4 (0.0, 6.8)	2.6 (0.1, 5.0)	2.6 (–1.0, 6.2)	4.2 (–2.4, 10.7)
$\alpha = 0.44$	2.8 (–0.7, 6.3)	3.3 (1.1, 5.4)	2.6 (–0.9, 6.1)	3.1 (–3.4, 9.7)
$\alpha = 0.60$	3.3 (–0.1, 6.6)	3.9 (1.8, 5.9)	3.1 (–0.2, 6.4)	4.6 (–1.7, 10.9)
$(\overline{\mathrm{OE}}(0.4,\alpha))$				
$\alpha = 0.30$	–0.5 (–1.8, 0.8)	0.7 (–0.2, 1.5)	0.2 (–1.0, 1.4)	–0.4 (–3.9, 3.1)
$\alpha = 0.44$	0.4 (–0.1, 0.9)	0.4 (0.2, 0.7)	0.5 (0.1, 1.0)	0.6 (–1.4, 2.7)
$\alpha = 0.60$	1.8 (0.1, 3.4)	1.8 (0.8, 2.8)	1.9 (0.3, 3.5)	2.3 (–2.0, 6.7)