CAUSAL INFERENCE WITH INTERFERENCE

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Abstract

LAN LIU: Causal Inference with Interference
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Recently, increasing attention has focused on making causal inference when interference is possible, i.e., when the potential outcomes of one individual may be affected by the treatment (or exposure) of other individuals. For example, in infectious diseases, whether one individual becomes infected may depend on whether another individual is vaccinated. In the presence of interference, treatment may have several types of effects. We consider inference about such effects when the population consists of groups of individuals where interference is possible within groups but not between groups. In the first part of this research, we assume a two stage randomization design where in the first stage groups are randomized to different treatment allocation strategies and in the second stage individuals are randomized to treatment or control conditional on the strategy assigned to their group in the first stage. For this design, the asymptotic distribution of estimators of the causal effects are derived when either the number of individuals per group or the number of groups grows large. A simulation study is presented showing that in various settings the corresponding asymptotic confidence intervals have good coverage in finite samples and are substantially narrower than exact confidence intervals. The methods are illustrated with two applications which consider the indirect effects of cholera vaccination and an intervention to encourage voting. In the second part of this research, we consider drawing inference about causal effects in the presence of interference when two stage randomization is not possible. Inverse probability weighted and doubly robust estimators are proposed for use in this setting.

These estimators will be used to analyze data from an observational study on rotavirus vaccination in Nicaragua.

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Chapter 1

Introduction and Literature Review

An important problem in epidemiological and clinical studies is how to make causal inferences of treatments or agents; for example, does exposure to high levels of toxic chemicals cause cancer? Does a new drug lead to a longer survival time? To assess the causal effect, traditional literature assumes units are randomly assigned directly to treatment or control. More often than not, the ideal randomization is violated or unethical to implement in scientific studies. However, it is useful to describe methods for drawing valid causal inferences in randomized setting before we consider more complicated settings involving nonrandomized data. Also, in the traditional randomized experiment, the potential outcomes that would be observed for a unit in either the treatment or control condition are assumed not depend on the treatment assignment of other units. Part of this condition is what Rubin (1980) refers to as the 'stable unit treatment value assumption', or SUTVA for short. More recently there has been research on relaxing SUTVA (see Hudgens and Halloran (2008), Tchetgen Tchetgen and VanderWeele (2012) and VanderWeele and Tchetgen Tchetgen (2011)). In this document we first review some classic approaches to making inferences about causal effects using potential outcomes in randomization designed studies and then in observational studies. In Chapter 2, we give the asymptotic distribution of estimators of various causal effects in randomization studies and hence construct the Wald type of confidence

intervals (CI). These CIs are compared to existing exact CIs in simulation studies where Wald CIs are significantly narrower while preserving good coverage. In Chapter 3, we suggest using Hajek type estimators instead of inverse probability weighted estimators in observational studies. Chapter 4 focuses on developing double robust estimators for causal effects.

1.1 Motivating Examples

In the last decade a growing body of research has studied the effects of an intervention when interference is at present. Hong and Raudenbush (2006) investigated an case study of policy of retaining low-achieving children in kindergarten rather than promoting them to first grade. Children were nested in classes and classes were nested in schools. Interference was assumed to happen between children in the same school but not between schools. In econometric studies, Sobel (2006) suggested the decision to move of one household may also depend on other households in the same neighborhood. The randomized trial described in Mvukiyehe and Samii (2011) studies the proximate and medium-term effects of a newly designed intervention that (i) establishes village "security committees" to enhance communication between local communities and a peacekeeping mission and (ii) complements this security-based treatment with civic and peace education. The communities were grouped based on location and proximity to each other into 'clans'. Interference may exist between communities in the same clan. In this section, we introduce three studies that motivate the research in the following chapters.

1.1.1 Herd Immunity Study in Bangladesh

The evaluation of killed oral cholera vaccines, which possess mild direct protection to vaccinees, can also be judged based on indirect or herd protection when high levels

of vaccine coverage are achieved. Ali et al. (2005) analyzed the first year of surveillance data from a placebo-controlled trial of B subunit-killed whole-cell and killed whole-cell-only oral cholera vaccines in children and adult women in Bangladesh. In the triple blinded study (blinded to investigators, statisticians and patients), patients were randomly assigned one of three letter-codes, which corresponded to three agents identical in appearance.

When assessing cholera risk, the researchers grouped patients according to the baris (patrilineally-related households living in clusters) they residing in. To define baris, the authors made use of the Demographic Surveillance System of the region, which has tracked all vital events of the local population since 1966. The bari level of vaccine coverage was calculated as the number of vaccinated individuals divided by the number of people who were eligible for participation in the tria by age and sex criteria. To some extent, we can view the bari level as observational studies. It was assumed that person-to-person transmission of cholera often takes place within these baris but not across baris. Ali et al. (2005) found that the incidence of cholera tended to be lower in unvaccinated individuals within baris with high vaccine coverage compared to unvaccinated individuals within baris with low vaccine coverage.

1.1.2 Voting Encouragement Experiment

The study was carried out prior to the 2002 Congressional Primaries (Nickerson (2008)). Households in Denver, CO, and Minneapolis, MN, with two registered persons were included in the study and randomly assigned to one of the conditions: (1) receive a Get Out the Vote (GOTV) message; (2) receive encouragement to recycle; (3) receive no contact from the campaign. Each appeal was delivered through door-to-door visit. Both Denver and Minneapolis are big cities with high density of two-voters households. There were 486 households received the encouragement to vote and 470 households

received the recycling treatment. The two key features of this study make it possible to draw conclusion about contagion within household: only two-voter households are considered and the treatment is administered to the first person who answers the door. Thus, in a household received encouragement to vote, the coverage of the treatment is exactly 50% in the household while that is 0% for either a placebo household or one that received encouragement to recycle.

Nickerson (2008) found that both cities experienced a significant rise in the percent of people voted in the election from the GOTV campaign. It was reported that 9.8% more people in GOTV households voted compared to that in recycling encouragement household among those who answered the door. The spillover effect was estimated to be 6.0% and it is significant at the 0.1 level, that is for every 100 households that receive the encouragement intervention, on average an additional six individuals will vote despite never coming into direct contact with a canvasser. Thus Nickerson (2008) concluded that interpersonal influence shapes the behaviors of people living in the same household and the atomistic assumption was contradicted.

1.1.3 Diarrhea Vaccine Study in Nicaragua

The study was carried out in León, Nicaragua's second largest city, with an estimated 2010 population of 200,000. The primary goal of the study was to evaluate the efficacy of rotavirus vaccine in preventing and controlling the diarrhea episodes in infants and young kids as well as to find out other characteristic factors that may help reduce the risk of having rotavirus diarrhea.

The rotavirus vaccine was first introduced to León, Nicaragua in October 2006. In 2010, the Health and Demographic Surveillance Site-León (HDSS-León) was employed to obtain a simple random sample of households from about 50 out of 208 randomly selected geographical clusters of equal size (Becker-Dreps et al (2012)). Any child in

the selected family under the age of 5 is eligible to be in the study. Rotavirus vaccine is offered to any eligible child in the study at the age of 2, 4 and 6 months. However, due to various reasons, the coverage of vaccine of at least one dose is about 67% after the implementation of immunization program. Each individuals in the study were visited by a field worker every 2 weeks for about a year (January 2010 to February 2011, except during Christmas break). During each visit, information about the episodes happened in the past 14 days were collected as well as other information about the household such as the sanitation conditions, water source, or that of the mother or the child such as maternal employment or age of the child. To better evaluate the effectiveness of rotavirus vaccine, a historical study started in December 2000 and ended in January 2003 in León, Nicaragua was revisited. Children in this study were viewed as the placebo group. Becker-Dreps et al (2012) concluded that the rotavirus vaccine has a significant indirect effect in that the rotavirus diarrhea incidence of unvaccinated children after the introduction of the vaccine is lower than that before the introduction.

1.2 Causal Inference in Randomized Studies

1.2.1 Classic Causal Inference

As pointed out by Little and Rubin (2000), it is complicated and challenging to define "cause" rigourously, but for empirical research, the idea of the causal effect of an agent or treatment makes it more straightforward and practically useful to quantify "cause." One possible method is to define causal effects by means of potential outcomes. The definition of causal effects using potential outcomes is often referred to as Rubin's Causal Model (Little and Yau (1998), Frangakis and Rubin (2004)), but the formal notation was introduced by Neyman in the context of randomization-based inference (Robins (1989), Rubin (1990)). This framework has been widely employed in empirical research in various fields such as economics (Haavelmo (1944), Robins and Greenland

(1996), Pratt and Schlaifer (1988), Tinbergen (1930)), epidemiology (Greenland and Robins (1986), Robins (2000), Robins et al. (1992), Robins et al. (2000)), social and behavioral sciences (Sobel (1990, 1995), Wilkinson (1999)), statistics (Rubin (2004), Pratt and Schlaifer (1984)) and elsewhere.

The key problem for inference is that once the treatment is adopted, only one of potential outcomes is observed, the one corresponding to the treatment actually assigned. This feature is referred to as "counterfactual" in the causal inference literature (Morgan and Winship (2007)). For example, if we assign vaccine to prevent the flu, then we do not observe the outcome we would have seen if vaccine were not assigned. In other words, the outcomes under control is missing for individuals assigned treatment and that under treatment is missing for individuals in control group. Thus, causal inference can be regarded as a problem of drawing inference when half of the potential outcomes are 'missing'. This viewpoint gave rise to a formal framework that extended the idea beyond randomized experiments to accommodate unexpected missing data and noncompliance (Rubin (1974, 1977, 1978)).

Following the existing literature, with a binary treatment there are two potential outcomes for each individual, one under treatment and the other under control. The potential outcome is well defined in this way only if two conditions are satisfied. First, there are not multiple versions of the treatment. Second, the potential outcomes that would be observed for a unit in either the treatment or control condition do not depend on the overall set of treatment assignments. These two conditions together are what Rubin (1980) refers to as the "stable unit treatment value assumption," or SUTVA. Manski (2012) addressed the latter assumption as "individualistic treatment response" (ITR) and viewed it as a restriction of the form of treatment response function.

Primarily, there are three formal statistical modes of causal inference, one due to Fisher (1932), one due to Neyman (1990) and the third arises from a Bayesian point

of view. The Fisher's sharp null hypothesis states that both treatments have exactly the same outcomes, i.e., $Y(1) = Y(0)$ for all units, where 1 stands for treatment and 0 for placebo. Under the sharp null hypothesis, there is no missing value since all the potential outcomes can be identified from the observed outcome Y^{obs} (note $Y(0) = Y(1) = Y^{obs}$). Furthermore, the value of any test statistic, T, such as $Y(1) - Y(0)$, can be computed and the P value of with can be obtained. Little and Rubin (2000) pointed out that the Fisher's sharp null model is too restricted and a small P value does not necessarily imply that deviations from the null hypothesis are of importance. However, there is still worthwhile to obtain such a P value when one claims evidence for a treatment difference.

Neyman's form of randomization-based inference, on the other hand, has a direct mapping to Neyman's (1934) classic article on randomization-based (also known as design-based) inference in surveys. Essentially, one needs to construct an unbiased estimator of the causal effect and an unbiased (or upwardly biased) variance estimator for it. Central limit theorem can be applied to attain the normality of the estimator when the sample size is large enough and hence a Wald confidence interval (CI) can be construct to assess the region of uncertainty. More explicitly, let $\hat{Y}(0)$ and $\hat{Y}(1)$ denote the sample means of the outcomes of individuals assigned to treatments 0 and 1, respectively. The average causal effect is chosen to be $\overline{Y}(1) - \overline{Y}(0)$, where $\overline{Y}(1)$ is the average outcome among the treated individuals and $\overline{Y}(0)$ is that among the untreated. It can be shown that $\hat{Y}(1) - \hat{Y}(0)$ is unbiased for $\overline{Y}(1) - \overline{Y}(0)$ under simple random assignment of treatments. Let n_1 denote the number of units assigned the first treatment and n_2 units assigned the second treatment, thus the estimated variance is $se^2 = s_1^2/n_1 + s_2^2/n_2$, where s_1 and s_2 are the sample variances of two treatment groups. Unless causal effects are the same across all the individuals (also called 'additivity'), the sample variance se^2 is positively biased. The standard 95% confidence interval for

$Y(1) - Y(0)$ is $\hat{Y}(1) - \hat{Y}(0) \pm 1.96se$, which, in large enough samples, includes $\overline{Y}(1) - \overline{Y}(0)$ in 95% of the possible random assignments. As commented on by Little and Rubin (2000), Neyman's form of inference is aiming at evaluations of procedures for causal inference rather than telling us what to do. The Bayesian approach is beyond the scope of our discussion here. In Chapter 2, we will adopt Neyman's form of randomization-based inference.

1.2.2 Interference

We say 'interference' is present if the treatment of one individual affect the potential outcome of another individual. Experimental and observational studies often involve treatments with effects that 'interfere' across units through spillover or other forms of dependency. Sometimes this interference is a nuisance, in which case we might design the study to isolate units as much as possible from potential interference. This may not always be feasible, however. Also, the spillover effects may be of intrinsic interest. Treatments may be applied to people in an existing network, and we may wish to study how effects transmit to peers in the network.

There are a number of research papers trying to demystify the role of interference in various scientific areas. In infectious disease studies, the susceptibility of an individual to the disease may depend not only on his own vaccine status, but on that of others as well. Halloran and Struchiner (1995) defined 'conditional direct causal effects' to be the averages effects of vaccination conditional on the subject's exposure status. By assuming 'all exposures to infection are discrete and equivalent', they circumvent the interference problem and instead focus on the difference between the transmission probabilities among the vaccinated and unvaccinated individuals. In economics, Angelucci and De Giorgi (2009) employed village-level randomized experiment to demonstrate

that the strong impact of a cash transfer program may be due to large positive spill-overs. More specifically, the comparison between ineligible households from treated villages to households from untreated villages reveal a positive impact on the consumption of ineligible households of the policies. In such randomization study, spill-over effect can be measured directly. Sobel (2006), however, took a different approach by defining unit effects for any allocation of the population units to treatment groups. Based on that, he defined average effects in a specific allocation of the units to treatments. Although his method was illustrated by a "Moving to Opportunity" (MTO) study, such techniques can be apply to other settings as well.

When interference is present, the difficulty of analyzing data in a sensible way increases. The first and foremost problem is how to define the potential outcomes. As mentioned, the classic interference literature assumes that each individual has two potential outcomes. This is generally not true when the interference is at present. Imagine there are two people in the study, the outcome of one individual cannot be fully determined by his own treatment but also by the other's. More generally, in a population of size n, the number of potential outcome for each individual can be as many as 2^n if any interference is possible. Also, as stated by Rosenbaum (2007), simple comparison such as take the difference of the treated and untreated can no longer reflect the treatment effects since the interference makes the effect inherently more complex. Available statistical tools are also limited. For instance, Fisher's sharp null hypothesis of no treatment effect implicitly assumes no interference, thus this randomization test cannot be used to test no effect in the presence of interference.

Hudgens and Halloran (2008) defined the average potential outcome, that is, the expected outcome of an individual given his treatment averaging over all the possible combinations of treatment assignment of others. Thus, there are only two average potential outcome for each individual even when individuals interfere with each other.

Researches on the simplification on the structure of interference are carried out. For example, the stratified interference states that the interference is possible only among the individuals in the same group but not across. Further, Hudgens and Halloran (2008) considered the situation where the outcome of one individual is allowed to depend on his treatment as well as the coverage of the group he belongs to. Thus, under certain randomization, the number of all potential outcome decreases greatly. For a study where individuals interfere with each other, the potential outcomes can be regarded as a function of the treatment vector of other members in the population. Manski (2012) commented that the no interference, the partial interference and other interference structure assumption are merely special cases of the functional form of the potential outcomes. Another commonly used approach assumes that interference is of a simple parametric form confined to units that are near one another in time or space. For example, Verbitsky and Raudenbush (2004) modeled the neighbourhood crime rate in Chicago as a function of community policing implemented in it as well as surrounding areas. This approach is useful when applicable but is of little use when interference may be widespread and of uncertain form. In this case, nonparametric methods that assuming nothing at all about the structure of the interference between units makes more sense.

When the interference exists in the population, there are more effects to investigate before reaching the conclusion of the efficacy of a treatment or intervention. Hudgens and Halloran (2008) defined direct, indirect, total and overall effects and proposed unbiased estimators for them. Under the stratified interference assumption, the variance estimator of those causal effect estimators are also developed. They were shown to be unbiased when the additivity holds and positively biased otherwise. Tchetgen Tchetgen and VanderWeele (2012) relaxed the stratified interference assumption when developing variance estimators. They came up with simple yet conservative estimation of variance,

as an unbiased estimator of an upper bound for the variance is often a useful measure of uncertainty. McConnell et al. (2010) applied multi-level designs to a large-scale voter mobilization experiment conducted in Chicago during a special election in 2009 using the social pressure mailings pioneered by Gerber, Green and Larimer (2008). They found some evidence of within-household spill-overs but no evidence of spill-overs across households. The advantage of their method is the inference is no longer restricted under SUTVA or just interference within group not across groups. However, they adopted a parametric way of analyzing data, which may provide misleading result if confounders are not all taken into considerations.

1.3 Observational Studies

Unlike an ideal randomized trial, the response of individuals in different treatment groups should not be compared directly in observational studies. This is because the units in one treatment group may differ greatly from the units in the other treatment group. An idea is to modify the observational study as much alike as possible into a randomized trial. For example, if (i) the treatment selection mechanism can be predicted by the measured covariates (conditional exchangeability), (ii) the probability of the treatment allocation is positive conditional on covariates (positivity) and (iii) although the treatment are not assigned by the investigator but correspond to certain intervention (consistency), then the observational study can emulate a conditional randomized experiment. That is to say, to endow causal inference from the observational study, one needs to provide an observational study which can be modified into a conditional randomized study and describe the randomization mechanism that one would like to carry out but couldn't. Recall that in an ideal randomization trial, the exchangeability, positivity and consistency are all satisfied. However, in observational studies, these three assumptions, however careful an investigator might be about and no matter how

many covariates have been collected, can never be guaranteed by study design.

In reality, a randomization study can bear the intricateness as much as an observational study. For example, a randomized trial with possible severe adverse events may result in censoring or non-compliance which causes selection bias. Or, some predictor or outcome (e.g., SNPs) maybe unable to observed directly or the study is unable to be blinded which leads to measurement error. Above all, randomization study is not always ethnical, practical or timely to conduct. These problems all beg the need for appropriate analytical method for observational studies.

1.3.1 Classic Methods

As mentioned, once the conditional exchangeability, positivity and consistency are satisfied, an observational study emulates a conditional randomization study, thus the methods of the latter could be applied. Following Rosenbaum (2002), overt bias, defined as visible, recorded pretreatment differences, can be removed by post-study adjustments; hidden bias, defined as unobserved pretreatment differences, must be studied by other technics such as sensitivity analysis. There are two common methods to adjust for the overt bias: the stratification or matching can be used to compute the conditional causal effects in certain subsets of the population while inverse-probability weighting (IPW) (or the equivalent 'standardization' method) can be used to compute the marginal causal effects in the entire population.

Rosenbaum and Rubin (1983) suggested the use of balancing scores, that is to group the individuals that have similar propensity scores. Although such method cannot guarantee the units in different treatment group to be exactly the same in all covariates, it can at least achieve balance in terms of the selection mechanism and thus make the comparison under different treatment exposure meaningful. It has been shown both in theory and in empirical studies that such adjustment is sufficient to eliminate the

bias caused by the observed covariates. More generally, covariate adjustment plays an important role in making inference in non-randomization studies especially when the treatment selection mechanism is unknown. In observational studies with unknown propensity score but without hidden bias, if conditional on a sufficient estimator for the unknown parameters in the propensity model, the conditional assignment follows a known distribution. And thus, the methods and results obtained in randomization studies can be generalized without much difficulty in observational studies.

The IPW estimator for the mean response under treatment z can be described as $\widehat{Y}(z) = \sum_i 1(Z_i = z)Y_i(z)/\{n\Pr(Z_i|L_i)\}$, where Z_i is the random variable of treatment for individual $i = 1, \ldots, n$, $Y_i(z)$ is the potential outcome under treatment z and L_i is the covariates determines the choice of treatment. In the survey sampling literature, the IPW estimator is known as the Horwitz Thompson estimator. The IPW procedure simulates what would have been observed if the covariates had not been used to decide the treatment. Similar as in the randomization studies, there are many settings where the no interference assumption is violated in non-experimental studies. Under ignorability and positivity assumption, Tchetgen Tchetgen and VanderWeele (2012) proved that the average potential outcome can be unbiasedly estimated by the 'generalized IPW estimator' in the presence of interference. In Chapter 3, we propose the Hajek estimator to improve the 'generalized IPW' estimator for observational studies when interference is present. For the following chapters, we always assume that observational studies of interest are free of hidden bias.

1.3.2 Doubly Robust Estimators

There are two main criticism against IPW estimator: one in terms of efficiency and the other of robustness. Note that when the propensity score tends to 0, the estimator is unbounded, which leads to large variance. Empirical studies have shown that, the

IPW estimator is sensitive to the estimation of the propensity score. The doubly robust estimator, on the other hand, is shown both theoretically and empirically to be effective to make the correct inference in observational studies. There are two ways to adjust for the missing outcome when the missing is beyond the control of the investigator. One way is to model the missing mechanism while the other is to impute the missing outcomes through covariates. The doubly robust procedure takes the both models into account and the conclusion is valid when either of the model is right.

Previous literature has developed various doubly robust estimators (Särndal et al. (2003), Lunceford and Davidian (2004), Bang and Robins (2005), Kang and Schafer (2007)). For example, Cassel et al. (1976, 1977) proposed a family of "generalized regression estimators" of population means based both on the outcome predicted and the propensity scores. The estimator can be expressed as $\widehat{Y}_{BC-OLS}(z) = \widehat{Y}_{OLS}(z) + \sum_i 1(Z_i = z)\widehat{\pi}_i^{-1}\widehat{\varepsilon}_i(z)$, where $\widehat{Y}_{OLS}(z)$ is the ordinary least square estimator for the population mean if everyone in the population assigned treatment z, $\widehat{\pi}_i = \Pr(Z_i = z)$ and $\widehat{\varepsilon}_i(z)$ is the estimated residuals. Thus, if the study potential outcome model is true, then $E[\widehat{\varepsilon}_i(z)] = 0$ which leads to the second term in the $\widehat{Y}_{BC-OLS}(z)$ formula 0 for any $\widehat{\pi}_i$. If the propensity score model is true, the the second term consistently estimates the bias of the first term.

As commented by Tsiatis and Davidian (2007), the property of an estimator can be fully understood by investigating the influence function. The situations where either of the potential outcome model or the propensity score is correct can be viewed from a semi-parametric standing where the distribution of covariates are always unspecified. It was shown that when at most one model is misspecified, the standardized DR estimator is asymptotically linear in influence functions and thus achieves consistency and asymptotically normality. However, to our knowledge all methods on DR inference assume no interference. In Chapter 4, we are going to apply the DR procedure for

observational studies when interference is present.

1.4 Summary and Proposed Research

In summary, assessing the causal effect of treatment with interference is an important goal. However, interest in interference can make inference challenging even when randomization is employed. Specifically, previous literature have develop the estimators for different causal effects but further investigation about the asymptotic distribution needs to be undertaken. Additionally, published approaches for analyzing data from observational studies under various types of interference are limited.

Accordingly, we first develop methods for randomization-based causal inference with interference. The asymptotic distribution of various causal effects: direct, indirect, overall and total effect at both individual and group level will be derived. Moreover, Wald type of CI will be proposed and compared to exact CI. The methods are illustrated with two applications which consider the effects of cholera vaccination and an intervention to encourage voting. Second, we propose modified IPW estimators for use in observation studies where interference may be present. The modified IPW estimators will be shown to be asymptotically unbiased and have smaller variance compared to the IPW estimators proposed by Tchetgen Tchetgen and VanderWeele (2012). Lastly, we propose doubly robust estimators for use in observational studies when interference may be present. These estimators are appealing in the sense that the estimators are consistent when either the propensity or the potential outcome model is right. Simulations are carried out to show the bias and mean square error for various estimators. The modified IPW estimators and the doubly robust estimators are illustrated with an application which considers the effects of rotavirus vaccination.

Chapter 2

Large Sample Randomization Inference with Interference

2.1 Introduction

When assessing the causal effect of a treatment or exposure, it is typically assumed that individuals (or units) do not interfere with each other (Cox 1958). This assumption is part of the stable unit treatment value assumption (SUTVA) (Rubin 1980). Under the no interference assumption, the potential outcomes of any individual are assumed to be determined solely by the treatment of that individual, unaffected by the treatment of other individuals under study. However, in many settings this assumption may not hold. For example, in vaccine studies, the outcome of an individual may depend not only on that individual's vaccine status but also on the vaccination status of other individuals (Halloran and Struchiner 1995). In educational studies, a student's academic performance may depend on the retention or promotion of that student as well as of fellow classmates (Hong and Raudenbush 2006). In econometric studies, interference may be present between households in the same neighborhood (Sobel 2006) or other settings where individuals interact socially (Manski 2012). Interference can occur within an individual over time, e.g., as in functional MRI studies (Luo et al. 2012), or between units that are proximal spatially (e.g., Zigler et al. 2012). Rosenbaum (2007) presents several other examples where interference may be present.

Increasing attention has been placed on relaxing the no interference assumption

(see Tchetgen Tchetgen and VanderWeele (2012) and references therein). Inference in this setting is particularly interesting because a treatment may have different types of effects, but challenging because individuals may have many potential outcomes due to interference. One approach has been to consider settings where individuals can be partitioned into groups such that interference is possible between individuals within the same group but not across groups. This is sometimes called 'partial interference' (Sobel 2006), a terminology adopted here. In the nomenclature of Manski (2012), partial interference is an example of a 'constant treatment response' where the 'reference groups' are 'treatment invariant' and 'symmetric'. The partial interference assumption will be reasonable when groups are sufficiently separate socially, temporally, or spatially.

Drawing inference about treatment effects often relies on knowledge or modeling of the mechanism by which individuals are assigned or select treatment. Assuming partial interference, one possible assignment mechanism is a two stage randomization design, where in the first stage groups are randomized to different treatment allocation strategies and in the second stage individuals are randomized to treatment or control conditional on the strategy assigned to their group in the first stage. For example, schools might be randomized to high or low vaccine coverage, and then students in the schools randomized to vaccine or control with vaccination probability dependent on whether their school was assigned to high or low coverage (Longini et al. 1998). Similarly, Borm et al. (2005) described a trial where general practitioners were randomized to two allocation strategies and then different proportions of each practitioner's patients were randomly assigned either a traditional or new method of care. Sinclair et al. (2012) conducted a two stage randomization experiment to determine the direct and indirect (or 'spillover') effects of social pressure mailings on voter mobilization in a special election in 2009. In that study zip-codes were randomly assigned to one of four allocation strategies, and then households within a zip-code were randomly assigned to

receive mailings (postcards) conditional on the allocation strategy assigned to that zip-code. For other examples, see Duflo and Saez (2003) and Ichino and Schündeln (2012). This two-stage randomization design has been referred to as split-plot or pseudo-cluster randomization.

Assuming partial interference and a two stage randomization design, Hudgens and Halloran (2008) proposed unbiased estimators for different causal effects of treatment. They also derived variance estimators which under certain assumptions are conservative unless the corresponding causal effect is additive. These results can be viewed as generalizations of the classic results of Splawa-Neyman (1923) to the setting of interference. In this paper, the large sample distributions of the causal effect estimators proposed by Hudgens and Halloran (2008) are derived for two stage randomization studies. The outline of the remainder of this paper is as follows. In Section 2.2 we introduce notation and define various causal effects. Unbiased estimators of these effects and the corresponding variance estimators are reviewed briefly in Section 2.3.1. The asymptotic distributions of these estimators are then derived when either the number of individuals within the groups grows large (Section 2.3.2.1), or the number of groups grows large (Section 2.3.2.2). These results can be utilized to construct Wald type confidence intervals (CIs) or tests for the different treatment effects. In Section 2.4 a simulation study is presented comparing Wald CIs with CIs based on Hoeffding and Chebyshev inequalities. Section 2.5 includes two applications which consider the various effects of a cholera vaccine and an intervention to encourage voting. Proofs of the results in Section 2.3 and some technical details regarding the voting encouragement analysis are given in the Appendix.

2.2 Notation, Assumptions and Estimands

Consider a population of m groups with n_i individuals in group i for $i = 1, \ldots, m$. Suppose individuals can receive treatment or control, denoted by 1 or 0. Let z_{ij} denote the treatment indicator for individual j in group i, where $z_{ij} = 1$ indicates treatment and $z_{ij} = 0$ denotes control. Let $z_{i(-j)}$ denote the vector of treatment indicators for the individuals in group i other than individual j and let $z_i = (z_{ij}, z_{i(-j)})$ denote the vector of treatment indicators for all individuals in group i. Let $y_{ij}(z_i) = y_{ij}(z_{ij}, z_{i(-j)})$ denote the potential outcome of individual j when individuals in group i receive treatment z_i. Randomization based inference is employed in this paper wherein the potential outcomes are viewed as fixed (i.e., non-random) features of the population of $\sum_{i=1}^{m} n_i$ individuals. Note the notation $y_{ij}(z_i)$ encompasses the partial interference assumption that the outcome for individual j does not depend on the treatment of individuals in groups $i^{'} \neq i$.

Just as individuals can receive treatment or control, suppose groups can take on different treatment allocation strategies corresponding to the proportion of individuals within the group that receive treatment. For simplicity we consider only two allocation strategies, denoted by α_1 and α_0. For instance, α_1 could correspond to assigning treatment to 50% of individuals in a group and α_0 could correspond to assigning treatment to 10% of individuals in a group. Let $g_i = s$ when allocation strategy for group i is α_s and let $g = (g_1, \ldots, g_m)$ denote the vector of group level allocation strategies.

Assume a two-stage randomization design where in the first stage groups are assigned allocation strategies α_1 and α_0. Denote the random assignment indicator for group i by G_i and let $G = (G_1, \ldots, G_m)$. Let $l = \sum_{i=1}^{m} G_i$ denote the number of groups assigned allocation strategy α_1. Assume allocation strategies are assigned using permutation randomization such that l is fixed for some integer $l \in \{1, \ldots, m-1\}$, i.e., $\Pr(G = g) = 1/\binom{m}{l}$ for all g such that $\sum_{i=1}^{m} g_i = l$ and $\Pr(G = g) = 0$ otherwise. In the

second stage of randomization, individuals are randomly assigned treatment or control conditional on $G_i = g_i$ from the first stage. Let the individual treatment assignment of individual j in group i be denoted by Z_{ij} and let $Z_i = (Z_{i1}, \ldots, Z_{in_i})$ such that the observed outcome for individual j is $y_{ij}(Z_i)$. Throughout, it is assumed that the assignment of an individual to a particular treatment is equivalent to receipt of that treatment, i.e., there is perfect compliance. Likewise, it is assumed groups are always compliant with their assigned allocation strategy. Let $k_{i\alpha_s} = \sum_{j=1}^{n_i} Z_{ij}$ denote the number of individuals in group i assigned treatment when group i is assigned allocation strategy α_s. Assume that treatment is assigned using permutation randomization such that $k_{i\alpha_s}$ is fixed given G_i. Let R_k^n denote the set of vectors of length n with elements 0 or 1 that sum to k, i.e., $R_k^n = \{v \in \{0,1\}^n : \sum_{i=1}^n v_i = k\}$. Under the two stage randomization design described above, $g \in R_l^m$, $z_i \in R_{k_{i\alpha_s}}^{n_i}$ and $z_{i(-j)} \in R_{k_{i\alpha_s} - z_{ij}}^{n_i - 1}$.

Define the average potential outcome for individual j in group i when individual j is assigned treatment z and group i is assigned allocation strategy α_1 by

$$\overline{y}_{ij}(z, \alpha_1) = \sum_{z_{i(-j)} \in R_{k_{i\alpha_1} - z}^{n_i - 1}} y_{ij}(z_{ij} = z, z_{i(-j)}) \Pr_{\alpha_1}(Z_{i(-j)} = z_{i(-j)} \mid Z_{ij} = z).$$

See VanderWeele and Tchetgen Tchetgen (2011) for alternative approaches to defining average potential outcomes for an individual. Averaging over individuals, define the group average potential outcome under group allocation α_1 and individual treatment assignment z as $\overline{y}_i(z, \alpha_1) = \sum_{j=1}^{n_i} \overline{y}_{ij}(z, \alpha_1)/n_i$. Similarly, averaging over groups, define the population average potential outcome as $\overline{y}(z, \alpha_1) = \sum_{i=1}^{m} \overline{y}_i(z, \alpha_1)/m$. Define the marginal individual average potential outcome by $\overline{y}_{ij}(\alpha_1) = \sum_{z \in R_{k_{i\alpha_1}}^{n_i}} y_{ij}(z) \Pr_{\alpha_1}(Z_i = z)$, that is, the average potential outcome for individual j in group i when group i is assigned α_1. Similarly, define the marginal group and population average potential

outcomes by $\overline{y}_i(\alpha_1) = \sum_{j=1}^{n_i} \overline{y}_{ij}(\alpha_1)/n_i$ and $\overline{y}(\alpha_1) = \sum_{i=1}^{m} \overline{y}_i(\alpha_1)/m$.

Various causal effects can be defined by considering contrasts of different average potential outcomes. For example, at the group level, a direct effect can be defined as $\overline{DE}_i(\alpha_1) = \overline{y}_i(1,\alpha_1) - \overline{y}_i(0,\alpha_1)$. That is, $\overline{DE}_i(\alpha_1)$ is the difference between the average potential outcome when group i receives allocation strategy α_1 and an individual in that group receives treatment compared to when an individual in that group receives control. At the population level define the direct effect $\overline{DE}(\alpha_s) = \overline{y}(1,\alpha_s) - \overline{y}(0,\alpha_s)$ for $s = 0, 1$, the indirect effect $\overline{IE}(\alpha_1,\alpha_0) = \overline{y}(0,\alpha_1) - \overline{y}(0,\alpha_0)$, the total effect $\overline{TE}(\alpha_1,\alpha_0) = \overline{y}(1,\alpha_1) - \overline{y}(0,\alpha_0)$, and the overall effect $\overline{OE}(\alpha_1,\alpha_0) = \overline{y}(\alpha_1) - \overline{y}(\alpha_0)$. In words, the indirect (or spillover) effect compares the average potential outcome when an individual receives control and their group receives allocation strategy α_1 compared to when their group receives α_0. Because the individual treatment assignment is held fixed, the indirect effect will be non-zero only if interference is present. Note that the indirect effect can also be defined for individuals who receive treatment, i.e., in terms of $\bar{y}(1,\alpha_s)$ for $s = 0, 1$, but for simplicity we do not consider this other indirect effect here. The total effect equals the sum of the direct and indirect effects, while the overall effect provides a single summary measure of the effect of allocation strategy α_1 versus α_0. See Tchetgen Tchetgen and VanderWeele (2012) for further discussion about these estimands.

Assuming only partial interference, an individual in a group with n_i individuals will have 2^{n_i} potential outcomes. For groups of even moderate size the large number of potential outcomes per individual makes inference challenging. One possible additional assumption about the structure of interference that reduces the number of potential outcomes considerably is:

$$y_{ij}(z_i) = y_{ij}(z_i') \text{ for all } z_i, z_i' \in R^{n_i}_{k_i\alpha_s} \text{ such that } z_{ij} = z_{ij}'. \tag{2.1}$$

Assumption (2.1) has been referred to as 'stratified interference' (Hudgens and Halloran

2008) and 'anonymous interaction' (Manski 2012). This assumption might be appropriate when the potential outcome of any individual in a group is thought to be affected only by that individual's treatment and the aggregate treatment assignment of others in the same group. For example, consider a study of vaccines in children attending school and assume no interference between schools. Assumption (2.1) implies the outcome for an individual vaccinated child will be the same when $k-1$ schoolmates receive vaccine regardless of which particular $k-1$ schoolmates are actually vaccinated. Under (2.1), the number of potential outcomes reduces from 2^{n_i} to $2n_i$ for any individual in a group of size n_i. Given permutation allocation strategy α_s is assigned to group i, individual j will have only two potential outcomes depending on whether $z_{ij}=1$ or $z_{ij}=0$. That is, $y_{ij}(z_{ij}, z_{i(-j)}) = \overline{y}_{ij}(z_{ij}, \alpha_s)$ for all $z_i \in R^{n_i}_{k_{i\alpha_s}}$. In the sequel, the stratified interference assumption (2.1) is made throughout. Thus for notational simplicity $\overline{y}_{ij}(z, \alpha_s)$ will be denoted by $y_{ij}(z, \alpha_s)$ for $z, s = 0, 1$.

2.3 Inference

2.3.1 Estimators

Hudgens and Halloran (2008) derived unbiased estimators for the causal estimands defined in Section 2.2 above. Specifically, assuming partial interference and two stage permutation randomization, a conditionally unbiased estimator for $\overline{y}_i(z, \alpha_s)$ given $G_i = s$ is $\widehat{Y}_i(z, \alpha_s) = \sum_{j=1}^{n_i} y_{ij}(Z_i) 1(Z_{ij} = z) / \sum_{j=1}^{n_i} 1(Z_{ij} = z)$ and an unbiased estimator for $\overline{y}(z, \alpha_s)$ is $\widehat{Y}(z, \alpha_s) = \sum_{i=1}^{m} \widehat{Y}_i(z, \alpha_s) 1(G_i = s) / \sum_{i=1}^{m} 1(G_i = s)$, where $1(\cdot)$ is the usual indicator function. At the group level a conditionally unbiased estimator given $G_i = s$ of the direct effect is $\widehat{DE}_i(\alpha_s) = \widehat{Y}_i(1, \alpha_s) - \widehat{Y}_i(0, \alpha_s)$, and at the population level unbiased estimators for the direct, indirect, total, and overall effects are $\widehat{DE}(\alpha_s) = \widehat{Y}(1, \alpha_s) - \widehat{Y}(0, \alpha_s)$ for $s = 0, 1$, $\widehat{IE}(\alpha_1, \alpha_0) = \widehat{Y}(0, \alpha_1) - \widehat{Y}(0, \alpha_0)$, $\widehat{TE}(\alpha_1, \alpha_0) = \widehat{Y}(1, \alpha_1) - \widehat{Y}(0, \alpha_0)$ and $\widehat{OE}(\alpha_1, \alpha_0) = \widehat{Y}(\alpha_1) - \widehat{Y}(\alpha_0)$, where $\widehat{Y}_i(\alpha_1) =$

$\sum_{j=1}^{n_i} y_{ij}(Z_i)/n_i$, $\widehat{Y}(\alpha_1) = \sum_{i=1}^{m} \widehat{Y}_i(\alpha_1) 1(G_i = 1)/\sum_{i=1}^{m} 1(G_i = 1)$ and $\widehat{Y}(\alpha_0)$ is defined analogously.

Hudgens and Halloran also proposed estimators of the variances of these estimators. In particular, under (2.1) unbiased estimators for $Var\{\widehat{Y}_i(1,\alpha_1)|G_i = 1\}$ and $Var\{\widehat{Y}(1,\alpha_1)\}$ are given by $\widehat{Var}\{\widehat{Y}_i(1,\alpha_1)|G_i = 1\} = (1 - k_{i\alpha_1}/n_i)\hat{\sigma}^2_{i1}(\alpha_1)/k_{i\alpha_1}$ where $\hat{\sigma}^2_{i1}(\alpha_1) = \sum_{j=1}^{n_i}\{y_{ij}(Z_i) - \widehat{Y}_i(1,\alpha_1)\}^2 Z_{ij}/(k_{i\alpha_1} - 1)$ and $\widehat{Var}\{\widehat{Y}(1,\alpha_1)\} = (1-l/m)\hat{\sigma}^2_{g1}(\alpha_1)$ $/l + \sum_{i=1}^{m}(1 - k_{i\alpha_1}/n_i)\hat{\sigma}^2_{i1}(\alpha_1)G_i/(k_{i\alpha_1} ml)$ where $\hat{\sigma}^2_{g1}(\alpha_1) = \sum_{i=1}^{m}\{\widehat{Y}_i(1,\alpha_1) - \widehat{Y}(1,\alpha_1)\}^2$ $G_i/(l-1)$. Hudgens and Halloran also proposed estimators of the variance of the various causal effect estimators which are positively biased unless certain additivity conditions hold. For example, if there exist constants $\eta_1, \ldots, \eta_m$ such that $y_{ij}(1,\alpha_s) = y_{ij}(0,\alpha_s) + \eta_i$ for all $i = 1, \ldots, m$ and $j = 1, \ldots, n_i$, then their estimator for the variance of $\widehat{DE}(\alpha_s)$ is unbiased; otherwise their estimator is positively biased. Similar additivity conditions exist for the variance estimators of the other causal effect estimators.

2.3.2 Asymptotic Distributions

Below the asymptotic distributions of the causal effect estimators defined in Section 2.3.1 are derived. In Section 2.3.2.1, the setting where the numbers of individuals per group $n_1, \ldots, n_m$ grow large is considered. These results might be applicable, for instance, when groups are defined to be all individuals in a particular geographic region. For example, Sur et al. (2009) estimated the indirect, total, and overall effects of typhoid vaccination in groups of people within contiguous geographic areas in India, where the average group size was over 700. The results in Section 2.3.2.1 do not require the number of groups to be large. On the other hand, in Section 2.3.2.2 we consider the setting where the number of groups m grows large. These results do not require that the number of individuals per group is large and could be applied, for instance, in household based studies when the households (i.e., groups) are small but the number of

households in the study is large. For example, Millar et al. (2008) studied the indirect effect of vaccination against pneumococcal disease in over 900 households containing on average fewer than four individuals per household.

2.3.2.1 Large Groups

Propositions 1 – 3 below show that under certain conditions the group average potential outcome estimators, group average direct effect estimator and the marginal group average potential outcome estimators are asymptotically Normal (i.e., Gaussian). The notation $\xrightarrow{d}\mathcal{N}(0,1)$ will be used to denote convergence in distribution to a standard Normal random variable.

Proposition 1. *Let* $\upsilon_{ij} = y_{ij}(z,\alpha_s)$ *and* $\upsilon_{i.} = (\upsilon_{i1} + \cdots + \upsilon_{i,n_i})/n_i$ *for* $z,s \in \{0,1\}$. *If*

$$k_{i\alpha_s} \to \infty, n_i - k_{i\alpha_s} \to \infty \tag{2.2}$$

and

$$\frac{\max(\upsilon_{ij}-\upsilon_{i.})^2}{\sum_{j=1}^{n_i}(\upsilon_{ij}-\upsilon_{i.})^2}\max\left\{\frac{n_i-k_{i\alpha_s}}{k_{i\alpha_s}}, \frac{k_{i\alpha_s}}{n_i-k_{i\alpha_s}}\right\} \to 0 \quad \text{as } n_i \to \infty \tag{2.3}$$

where $\max(\upsilon_{ij}-\upsilon_{i.})^2 = \max\{(\upsilon_{ij}-\upsilon_{i.})^2 : j = 1,\ldots,n_i\}$, *then*

$$\left.\frac{\widehat{Y}_i(z,\alpha_s) - \overline{y}_i(z,\alpha_s)}{\sqrt{Var_{\alpha_s}\{\widehat{Y}_i(z,\alpha_s)\}}}\right| G_i = s \xrightarrow{d}\mathcal{N}(0,1)$$

where $Var_{\alpha_s}\{\widehat{Y}_i(z,\alpha_s)\} = Var\{\widehat{Y}_i(z,\alpha_s)|G_i = s\}$.

Proposition 2. *Assume* (2.2) *and that* (2.3) *holds for* $\upsilon_{ij} = y_{ij}(1,\alpha_s)/k_{i\alpha_s} + y_{ij}(0,\alpha_s)/(n_i - k_{i\alpha_s})$. *Then*

$$\left.\frac{\widehat{DE}_i(\alpha_s) - \overline{DE}_i(\alpha_s)}{\sqrt{Var_{\alpha_s}\{\widehat{DE}_i(\alpha_s)\}}}\right| G_i = s \xrightarrow{d}\mathcal{N}(0,1)$$

where $Var_{\alpha_s}\{\widehat{DE}_i(\alpha_s)\} = Var\{\widehat{DE}_i(\alpha_s)|G_i = s\}$.

Proposition 3. *Assume*(2.2) *and that* (2.3) *holds for* $v_{ij} = y_{ij}(1,\alpha_s) - y_{ij}(0,\alpha_s)$. *Then*

$$\left.\frac{\widehat{Y}_i(\alpha_s) - \overline{y}_i(\alpha_s)}{\sqrt{Var_{\alpha_s}\{\widehat{Y}_i(\alpha_s)\}}}\right| G_i = s \ \xrightarrow{d} \mathcal{N}(0,1)$$

where $Var_{\alpha_s}\{\widehat{Y}_i(\alpha_s)\} = Var\{\widehat{Y}_i(\alpha_s)|G_i = s\}$.

Propositions 4.1 – 4.4 below show that, under certain conditions, the population direct, indirect, total and overall effect estimators are asymptotically distributed as a mixture of Normal random variables as the numbers of individuals per group grow large, i.e., as $n_{\min} = \min\{n_1,\ldots,n_m\} \to \infty$. Recall a random variable X follows a finite Normal mixture distribution (McLachlan et al. 1988) if there exists a discrete random variable U with support $u_1,\ldots,u_h$ and parameter vectors $\mu = (\mu^{(1)},\ldots,\mu^{(h)})$ and $\sigma = (\sigma^{(1)},\ldots,\sigma^{(h)})$ such that the density of X satisfies

$$f_X(x) = \sum_{i=1}^{h} \omega^{(i)} f(x|\mu^{(i)},\sigma^{(i)})$$

where $\omega^{(i)} = \Pr(U = u_i)$ and $f(x \mid \mu^{(i)},\sigma^{(i)})$ is the density of a Normal random variable with mean $\mu^{(i)}$ and standard deviation $\sigma^{(i)}$. Equivalently, $(X - \mu^{(i)})/\sigma^{(i)} \mid U = u_i \sim \mathcal{N}(0,1)$ for $i = 1,\ldots,h$. Define a sequence of random variables $\{X_n\}$ to have an asymptotically Normal mixture distribution if there exists a discrete random variable U with support $u_1,\ldots,u_h$ and sequences of parameter vectors $\{\mu_n\}$ and $\{\sigma_n\}$ such that

$$\left.\frac{X_n - \mu_n^{(i)}}{\sigma_n^{(i)}} \right| U = u_i \xrightarrow{d} \mathcal{N}(0,1) \quad \text{as } n \to \infty \tag{2.4}$$

for $i = 1,\ldots,h$, where $\mu_n^{(i)}$ and $\sigma_n^{(i)}$ denote the i^{th} components of μ_n and σ_n. When (2.4) holds, for notational convenience we suppress the subscript n and write $(X - \mu)/\sigma \xrightarrow{d}$

$\mathcal{M}(\omega, h)$. The following proposition is stated in terms of α_1; the analogous result holds for α_0.

Proposition 4.1. *Assume* (2.2) *and that* (2.3) *holds for* $v_{ij} = y_{ij}(1, \alpha_1)/k_{i\alpha_1} + y_{ij}(0, \alpha_1)/(n_i - k_{i\alpha_1})$ *for* $i = 1, \ldots, m$. *Assume for any simple random sample* $\{i_1, \ldots, i_l\}$ *drawn without replacement from* $\{1, \ldots, m\}$ *that* $\lim Var_{\alpha_1}\{\widehat{DE}_i(\alpha_1)\} / \sum_{i \in \{i_1, \ldots, i_l\}} Var_{\alpha_1}\{\widehat{DE}_i(\alpha_1)\}$ *as* $n_{\min} \to \infty$ *exists for* $i \in \{i_1, \ldots, i_l\}$. *Then for* $m < \infty$, $\widehat{DE}(\alpha_1)$ *has an asymptotically Normal mixture distribution, i.e.,*

$$\frac{\widehat{DE}(\alpha_1) - \mu_{DE}}{\sigma_{DE}} \xrightarrow{d} \mathcal{M}(\omega, \binom{m}{l})$$

as $n_{\min} \to \infty$. *The parameter vectors, each of length* $\binom{m}{l}$, *are given by* $\omega = \left(1/\binom{m}{l}\right)$, $\mu_{DE} = \left(\mu_{DE}^{(i_1, \ldots, i_l)}\right)$ *and* $\sigma_{DE} = \left(\sigma_{DE}^{(i_1, \ldots, i_l)}\right)$, *where the elements of the vectors correspond to all possible simple random sample* $\{i_1, \ldots, i_l\}$ *without replacement from* $\{1, \ldots, m\}$, *with* $\mu_{DE}^{(i_1, \ldots, i_l)} = \sum_{i \in \{i_1, \ldots, i_l\}} \overline{DE}_i(\alpha_1)/l$ *and* $\sigma_{DE}^{(i_1, \ldots, i_l)} = \left[\sum_{i \in \{i_1, \ldots, i_l\}} Var_{\alpha_1}\{\widehat{DE}_i(\alpha_1)\}\right]^{1/2} / l$.

Note in Proposition 4.1 and below the dependence of the parameters μ_{DE} and σ_{DE} on α_s and $n_{\min}$ are suppressed for notational convenience. From a single experiment or trial, only one element from each of the vectors μ_{DE} and σ_{DE} is identifiable from the observed data; in particular, only the parameters $\mu_{DE}^{i_1, \ldots, i_l}$ and $\sigma_{DE}^{i_1, \ldots, i_l}$ are identifiable where $\{i_1, \ldots, i_l\} = \{i \in \{1, \ldots, m\} : G_i = 1\}$. Hence the asymptotic distribution of $\widehat{DE}(\alpha_1)$ as the groups grow large is not identifiable without additional assumptions. One special case of Proposition 4.1 occurs when the groups are homogeneous in a certain sense as described by the following corollary.

Corollary 1. *If the assumptions of Proposition 4.1 hold and there exists* $\mu_{DE}^{(0)}$ *and* $\sigma_{DE}^{(0)}$ *such that* $\mu_{DE}^{(i_1, \ldots, i_l)} = \mu_{DE}^{(0)}$ *and* $\sigma_{DE}^{(i_1, \ldots, i_l)} = \sigma_{DE}^{(0)}$ *for all simple random samples* $\{i_1, \ldots, i_l\}$, *then* $\mu_{DE}^{(0)} = \overline{DE}(\alpha_1)$, $\sigma_{DE}^{(0)} = \sqrt{Var\{\widehat{DE}(\alpha_1)\}}$ *and for* $m < \infty$,

$$\frac{\widehat{DE}(\alpha_1) - \overline{DE}(\alpha_1)}{\sqrt{Var\{\widehat{DE}(\alpha_1)\}}} \xrightarrow{d} \mathcal{N}(0,1) \tag{2.5}$$

as $n_{\min} \to \infty$.

Note that the condition $\mu_{DE}^{(i_1,\ldots,i_l)} = \mu_{DE}^{(0)}$ and $\sigma_{DE}^{(i_1,\ldots,i_l)} = \sigma_{DE}^{(0)}$ for all simple random samples $\{i_1,\ldots,i_l\}$ is equivalent to $\overline{DE}_1(\alpha_1) = \cdots = \overline{DE}_m(\alpha_1)$ and $Var_{\alpha_1}\{\widehat{DE}_1(\alpha_1)\} = \cdots = Var_{\alpha_1}\{\widehat{DE}_m(\alpha_1)\}$. In other words, if the group level direct effect estimators have the same mean and variance, then (2.5) holds.

The next three propositions and corollaries give analogous results for the population average indirect, total and overall effect estimators.

Proposition 4.2. *Assume* (2.2) *and that* (2.3) *holds for* $v_{ij} = y_{ij}(0,\alpha_s),\ s = 0,1$. *Assume for any simple random sample* $\{i_1,\ldots,i_l\}$ *drawn without replacement from* $\{1,\ldots,m\}$ *that* $\lim \sqrt{Var_{\alpha_1}\widehat{Y}_i(0,\alpha_1)}/\{l\sigma_{IE}^{(i_1,\ldots,i_l)}\}$ *exists for* $i \in \{i_1,\ldots,i_l\}$ *and* $\lim \sqrt{Var_{\alpha_1}\widehat{Y}_i(0,\alpha_1)}/\{(m-l)\sigma_{IE}^{(i_1,\ldots,i_l)}\}$ *exists for* $i \notin \{i_1,\ldots,i_l\}$ *as* $n_{\min} \to \infty$. *Then for* $m < \infty$,

$$\frac{\widehat{IE}(\alpha_1,\alpha_0) - \mu_{IE}}{\sigma_{IE}} \xrightarrow{d} \mathcal{M}(\omega, \tbinom{m}{l})$$

as $n_{\min} \to \infty$. *The parameter vectors, each of length* $\binom{m}{l}$, *are given by* $\omega = \left(1/\binom{m}{l}\right)$, $\mu_{IE} = \left(\mu_{IE}^{(i_1,\ldots,i_l)}\right)$, $\sigma_{IE} = \left(\sigma_{IE}^{(i_1,\ldots,i_l)}\right)$, *where*

$$\mu_{IE}^{(i_1,\ldots,i_l)} = \sum_{i\in\{i_1,\ldots,i_l\}} \frac{\overline{y}_i(0,\alpha_1)}{l} - \sum_{i\notin\{i_1,\ldots,i_l\}} \frac{\overline{y}_i(0,\alpha_0)}{m-l}$$

$$\sigma_{IE}^{(i_1,\ldots,i_l)} = \left[\sum_{i\in\{i_1,\ldots,i_l\}} \frac{Var_{\alpha_1}\{\widehat{Y}_i(0,\alpha_1)\}}{l^2} + \sum_{i\notin\{i_1,\ldots,i_l\}} \frac{Var_{\alpha_0}\{\widehat{Y}_i(0,\alpha_0)\}}{(m-l)^2}\right]^{\frac{1}{2}}$$

Corollary 2. *If the assumptions of Proposition 4.2 hold and there exists* $\mu_{IE}^{(0)}$ *and* $\sigma_{IE}^{(0)}$ *such that* $\mu_{IE}^{(i_1,\ldots,i_l)} = \mu_{IE}^{(0)}$ *and* $\sigma_{IE}^{(i_1,\ldots,i_l)} = \sigma_{IE}^{(0)}$ *for all* $\{i_1,\ldots,i_l\}$*, then* $\mu_{IE}^{(0)} = \overline{IE}(\alpha_1,\alpha_0)$*,* $\sigma_{IE}^{(0)} = \sqrt{Var\{\widehat{IE}(\alpha_1,\alpha_0)\}}$*, and for* $m<\infty$*,*

$$\frac{\widehat{IE}(\alpha_1,\alpha_0) - \overline{IE}(\alpha_1,\alpha_0)}{\sqrt{Var\{\widehat{IE}(\alpha_1,\alpha_0)\}}} \xrightarrow{d} \mathcal{N}(0,1) \tag{2.6}$$

as $n_{\min}\to\infty$*.*

Proposition 4.3. *Assume* (2.2) *and that* (2.3) *holds for* $v_{ij} = y_{ij}(z,\alpha_s)$*,* $(z,s)\in\{(1,1),(0,0)\}$*. Assume for any simple random sample* $\{i_1,\ldots,i_l\}$ *drawn without replacement from* $\{1,\ldots,m\}$ *that* $\lim\sqrt{Var_{\alpha_1}\widehat{Y}_i(1,\alpha_1)}/\{l\sigma_{TE}^{(i_1,\ldots,i_l)}\}$ *exists for* $i\in\{i_1,\ldots,i_l\}$ *and* $\lim\sqrt{Var_{\alpha_1}\widehat{Y}_i(0,\alpha_1)}/\{(m-l)\sigma_{TE}^{(i_1,\ldots,i_l)}\}$ *exists for* $i\notin\{i_1,\ldots,i_l\}$ *as* $n_{\min}\to\infty$*. Then for* $m<\infty$*,*

$$\frac{\widehat{TE}(\alpha_1,\alpha_0) - \mu_{TE}}{\sigma_{TE}} \xrightarrow{d} \mathcal{M}(\omega,(\tbinom{m}{l}))$$

as $n_{\min}\to\infty$*. The parameter vectors, each of length* $\binom{m}{l}$*, are given by* $\omega = \left(1/\binom{m}{l}\right)$*,* $\mu_{TE} = \left(\mu_{TE}^{(i_1,\ldots,i_l)}\right)$*,* $\sigma_{TE} = \left(\sigma_{TE}^{(i_1,\ldots,i_l)}\right)$*, where*

$$\mu_{TE}^{(i_1,\ldots,i_l)} = \sum_{i\in\{i_1,\ldots,i_l\}} \frac{\overline{y}_i(1,\alpha_1)}{l} - \sum_{i\notin\{i_1,\ldots,i_l\}} \frac{\overline{y}_i(0,\alpha_0)}{m-l}$$

$$\sigma_{TE}^{(i_1,\ldots,i_l)} = \left[\sum_{i\in\{i_1,\ldots,i_l\}} \frac{Var_{\alpha_1}\{\widehat{Y}_i(1,\alpha_1)\}}{l^2} + \sum_{i\notin\{i_1,\ldots,i_l\}} \frac{Var_{\alpha_0}\{\widehat{Y}_i(0,\alpha_0)\}}{(m-l)^2}\right]^{\frac{1}{2}}$$

Corollary 3. *If the assumptions of Proposition 4.3 hold and there exists* $\mu_{TE}^{(0)}$ *and* $\sigma_{TE}^{(0)}$ *such that* $\mu_{TE}^{(i_1,\ldots,i_l)} = \mu_{TE}^{(0)}$ *and* $\sigma_{TE}^{(i_1,\ldots,i_l)} = \sigma_{TE}^{(0)}$ *for all* $\{i_1,\ldots,i_l\}$*, then* $\mu_{TE}^{(0)} = \overline{TE}(\alpha_1,\alpha_0)$*,* $\sigma_{TE}^{(0)} = \sqrt{Var\{\widehat{TE}(\alpha_1,\alpha_0)\}}$ *and for* $m<\infty$*,*

$$\frac{\widehat{TE}(\alpha_1,\alpha_0) - \overline{TE}(\alpha_1,\alpha_0)}{\sqrt{Var\{\widehat{TE}(\alpha_1,\alpha_0)\}}} \xrightarrow{d} \mathcal{N}(0,1) \tag{2.7}$$

as $n_{\min}\to\infty$*.*

Proposition 4.4. *Assume* (2.2) *and that* (2.3) *holds for* $v_{ij} = y_{ij}(1,\alpha_s) - y_{ij}(0,\alpha_s)$*,* $s = 0,1$*. Assume for any simple random sample* $\{i_1,\ldots,i_l\}$ *drawn without replacement from* $\{1,\ldots,m\}$ *that* $\lim\sqrt{Var_{\alpha_1}\widehat{Y}_i(\alpha_1)}/\{l\sigma_{OE}^{(i_1,\ldots,i_l)}\}$ *exists for* $i\in\{i_1,\ldots,i_l\}$ *and* $\lim\sqrt{Var_{\alpha_1}\widehat{Y}_i(\alpha_1)}/\{(m-l)\sigma_{OE}^{(i_1,\ldots,i_l)}\}$ *exists for* $i\notin\{i_1,\ldots,i_l\}$ *as* $n_{\min}\to\infty$*. Then for* $m<\infty$*,*

$$\frac{\widehat{OE}(\alpha_1,\alpha_0) - \mu_{OE}}{\sigma_{OE}} \xrightarrow{d} \mathcal{M}(\omega, \tbinom{m}{l})$$

as $n_{\min}\to\infty$*. The parameter vectors, each of length* $\binom{m}{l}$*, are given by* $\omega = \left(1/\binom{m}{l}\right)$*,* $\mu_{OE} = \left(\mu_{OE}^{(i_1,\ldots,i_l)}\right)$*,* $\sigma_{OE} = \left(\sigma_{OE}^{(i_1,\ldots,i_l)}\right)$*, where*

$$\mu_{OE}^{(i_1,\ldots,i_l)} = \sum_{i\in\{i_1,\ldots,i_l\}} \frac{\overline{y}_i(\alpha_1)}{l} - \sum_{i\notin\{i_1,\ldots,i_l\}} \frac{\overline{y}_i(\alpha_0)}{m-l}$$

$$\sigma_{OE}^{(i_1,\ldots,i_l)} = \left[\sum_{i\in\{i_1,\ldots,i_l\}} \frac{Var_{\alpha_1}\{\widehat{Y}_i(\alpha_1)\}}{l^2} + \sum_{i\notin\{i_1,\ldots,i_l\}} \frac{Var_{\alpha_0}\{\widehat{Y}_i(\alpha_0)\}}{(m-l)^2}\right]^{\frac{1}{2}}$$

Corollary 4. *If the assumptions of Proposition 4.4 hold and there exists* $\mu_{OE}^{(0)}$ *and* $\sigma_{OE}^{(0)}$ *such that* $\mu_{OE}^{(i_1,\ldots,i_l)} = \mu_{OE}^{(0)}$ *and* $\sigma_{OE}^{(i_1,\ldots,i_l)} = \sigma_{OE}^{(0)}$ *for all* $\{i_1,\ldots,i_l\}$*, then* $\mu_{OE}^{(0)} = \overline{OE}(\alpha_1,\alpha_0)$*,* $\sigma_{OE}^{(0)} = \sqrt{Var\{\widehat{OE}(\alpha_1,\alpha_0)\}}$ *and for* $m < \infty$*,*

$$\frac{\widehat{OE}(\alpha_1,\alpha_0) - \overline{OE}(\alpha_1,\alpha_0)}{\sqrt{Var\{\widehat{OE}(\alpha_1,\alpha_0)\}}} \xrightarrow{d} \mathcal{N}(0,1) \tag{2.8}$$

as $n_{\min} \to \infty$*.*

2.3.2.2 Large Number of Groups

In this section the asymptotic distributions of the causal effect estimators are derived when the number of groups m grows large, in particular when $l \to \infty$ and $m - l \to \infty$. These results rely on the following Lindeberg condition (Lehmann 1998, eq. A.128): Let $\{W_h\}$ be a sequence of independent random variables, each having finite expected value μ_h and variance σ_h^2. Define $s_t^2 = \sum_{h=1}^t \sigma_h^2$. If for every $\varepsilon > 0$

$$\lim_{t\to\infty} \frac{1}{s_t^2} \sum_{h=1}^{t} \mathrm{E}\left[(W_h - \mu_h)^2 1\{|W_h - \mu_h| > \varepsilon s_t\}\right] = 0, \tag{2.9}$$

then $\sum_{h=1}^t (W_h - \mu_h)/s_t \xrightarrow{d} \mathcal{N}(0,1)$ as $t \to \infty$. The propositions below indicate that, under different versions of (11), the distributions of the causal effect estimators are approximately Normal as m grows large. These results will have applicability in studies with large numbers of groups even if the groups are small (e.g., households). Unlike in Section 2.3.2.1, here the mean homogeneity assumption is not needed to justify the Normal approximation.

Proposition 5.1. *Suppose for any simple random sample* $\{i_1,\ldots,i_l\}$ *that* (2.9) *holds for the sequence* $\{W_h\}$ *defined by* $W_h=\widehat{DE}_{i_h}(\alpha_1)\big|G_{i_1}=\cdots=G_{i_l}=1$ *for* $h=1,\ldots,l$ *and there exists* $\sigma_{DE}^{(0)}$ *such that* $\sigma_{DE}^{(i_1,\ldots,i_l)}=\sigma_{DE}^{(0)}$. *Let* $\tilde{v}_i=\overline{DE}_i(\alpha_1)$ *and* $\tilde{v}_\cdot=(\tilde{v}_1+\ldots+\tilde{v}_m)/m$. *If* $\lim_{m\to\infty}\sigma_{DE}^{(0)}/\sqrt{Var\{\widehat{DE}(\alpha_1)\}}$ *exists and*

$$\frac{\max(\tilde{v}_i-\tilde{v}_\cdot)^2}{\sum_{i=1}^m(\tilde{v}_i-\tilde{v}_\cdot)^2}\max\left\{\frac{m-l}{l},\frac{l}{m-l}\right\}\to 0 \quad \text{as } m\to\infty \tag{2.10}$$

where $\max(\tilde{v}_i-\tilde{v}_\cdot)^2=\max\{(\tilde{v}_i-\tilde{v}_\cdot)^2:i=1,\ldots,m\}$, *then* (2.5) *holds as* $m\to\infty$.

Proposition 5.2. *Suppose for any simple random sample* $\{i_1,\ldots,i_l\}$ *that* (2.9) *holds for the sequence* $\{W_h\}$ *defined by* $W_h=\big\{\widehat{Y}_{i_h}(0,\alpha_1)1(G_{i_h}=1)/l-\widehat{Y}_{i_h}(0,\alpha_0)1(G_{i_h}=0)/(m-l)\big\}\big|G_{i_1}=\cdots=G_{i_l}=1$ *for* $h=1,\ldots,l$ *and there exists* $\sigma_{IE}^{(0)}$ *such that* $\sigma_{IE}^{(i_1,\ldots,i_l)}=\sigma_{IE}^{(0)}$. *If* (2.10) *holds for* $\tilde{v}_i=\overline{y}_i(0,\alpha_1)/l+\overline{y}_i(0,\alpha_0)/(m-l)$ *and* $\lim_{m\to\infty}\sigma_{IE}^{(0)}/\sqrt{Var\{\widehat{IE}(\alpha_1,\alpha_0)\}}$ *exists, then* (2.6) *holds as* $m\to\infty$.

Proposition 5.3. *Suppose for any simple random sample* $\{i_1,\ldots,i_l\}$ *that* (2.9) *holds for the sequence* $\{W_h\}$ *defined by* $W_h=\big\{\widehat{Y}_{i_h}(1,\alpha_1)1(G_{i_h}=1)/l-\widehat{Y}_{i_h}(0,\alpha_0)1(G_{i_h}=0)/(m-l)\big\}\big|G_{i_1}=\cdots=G_{i_l}=1$ *for* $h=1,\ldots,l$ *and there exists* $\sigma_{TE}^{(0)}$ *such that* $\sigma_{TE}^{(i_1,\ldots,i_l)}=\sigma_{TE}^{(0)}$. *If* (2.10) *holds for* $\tilde{v}_i=\overline{y}_i(1,\alpha_1)/l+\overline{y}_i(0,\alpha_0)/(m-l)$ *and* $\lim_{m\to\infty}\sigma_{TE}^{(0)}/\sqrt{Var\{\widehat{TE}(\alpha_1,\alpha_0)\}}$ *exists, then* (2.7) *holds as* $m\to\infty$.

Proposition 5.4. *Suppose for any simple random sample* $\{i_1,\ldots,i_l\}$ *that* (2.9) *holds for the sequence* $\{W_h\}$ *defined by* $W_h=\big\{\widehat{Y}_{i_h}(\alpha_1)1(G_{i_h}=1)/l-\widehat{Y}_{i_h}(\alpha_0)1(G_{i_h}=0)/(m-l)\big\}\big|G_{i_1}=\cdots=G_{i_l}=1$ *for* $h=1,\ldots,l$ *and there exists* $\sigma_{OE}^{(0)}$ *such that* $\sigma_{OE}^{(i_1,\ldots,i_l)}=\sigma_{OE}^{(0)}$. *If* (2.10) *holds for* $\tilde{v}_i=\overline{y}_i(\alpha_1)/l+\overline{y}_i(\alpha_0)/(m-l)$ *and* $\lim_{m\to\infty}\sigma_{OE}^{(0)}/\sqrt{Var\{\widehat{OE}(\alpha_1,\alpha_0)\}}$ *exists, then* (2.8) *holds as* $m\to\infty$.

2.3.3 Confidence intervals and testing

2.3.3.1 Large sample approximations

The results in the previous two sections establish the limiting distributions of the different effect estimators when either the number of individuals per group or the number of groups grows large. These results can be used to construct CIs when the limiting distribution is a single Normal. For example, under the conditions stated in the Corollary to Proposition 4.1, we have $\{\widehat{DE}(\alpha_1) - \overline{DE}(\alpha_1)\}/\sqrt{Var\{\widehat{DE}(\alpha_1)\}} \xrightarrow{d} \mathcal{N}(0,1)$. Thus, by Slutsky's theorem, for $\gamma \in (0,1)$ an asymptotic $1-\gamma$ CI of $\overline{DE}(\alpha_1)$ is

$$\widehat{DE}(\alpha_1) \pm z_{1-\gamma/2}\sqrt{\widehat{Var}\{\widehat{DE}(\alpha_1)\}}$$

where $z_{1-\gamma/2}$ is the $1-\gamma/2$ quantile of the standard Normal distribution and $\widehat{Var}\{\widehat{DE}(\alpha_1)\}$ is a consistent estimator of $Var\{\widehat{DE}(\alpha_1)\}$.

These CIs can be used in the large sample setting to test various null hypotheses about the different treatment effects by examining whether the CI for a particular effect contains the corresponding null value. Equivalently, test statistics can be constructed to directly assess the null hypothesis of interest. For example, consider testing the null hypothesis that the group level direct effects are all zero, i.e., $H_0 : \overline{DE}_1(\alpha_1) = \ldots = \overline{DE}_m(\alpha_1) = 0$. Under the assumption that $Var_{\alpha_1}\{\widehat{DE}_1(\alpha_1)\} = \cdots = Var_{\alpha_1}\{\widehat{DE}_m(\alpha_1)\}$, the statistic $T = \widehat{DE}(\alpha_1)/\sqrt{\widehat{Var}\{\widehat{DE}(\alpha_1)\}}$ will be approximately $\mathcal{N}(0,1)$ under H_0, provided either $n_{\min}$ or l is large.

The Wald CIs are applicable when the groups are homogeneous. Certain of these homogeneity assumptions can be tested. For instance, the assumption that the direct effects are homogeneous across groups can be tested as follows. Suppose $Var_{\alpha_1}\{\widehat{DE}_1(\alpha_1)\} = \cdots = Var_{\alpha_1}\{\widehat{DE}_m(\alpha_1)\} = \sigma^2_{DE}$, where σ^2_{DE} is an unknown constant and the goal is to test $H_{0h} : \overline{DE}_1(\alpha_1) = \cdots = \overline{DE}_m(\alpha_1)$. Let $\widetilde{T} = \sum_{i=1}^{m}\{\widehat{DE}_i(\alpha_1) - \widehat{DE}(\alpha_1)\}^2 1(G_i =$

$1)/\widehat{\sigma}^2_{DE}$, where $\widehat{\sigma}^2_{DE}$ is a consistent estimator for σ^2_{DE}. Then based on Proposition 2, $\widetilde{T} \sim \chi^2_{l-1}$ under H_{0h} as $n_{\min} \to \infty$. Without further assumptions about the potential outcomes, tests of mean homogeneity cannot be developed for indirect, total and overall effects. To see this, consider the homogeneity assumptions given in the Corollary to Proposition 4.2 that are sufficient for the indirect effect estimator to have a single Normal distribution asymptotically. The mean homogeneity assumption that there exists $\mu^{(0)}_{IE}$ such that $\mu^{(i_1,\ldots,i_l)}_{IE} = \mu^{(0)}_{IE}$ for all simple random samples $\{i_1,\ldots,i_l\}$ is equivalent to assuming $\overline{y}_1(0,\alpha_1)+\overline{y}_1(0,\alpha_0) = \cdots = \overline{y}_m(0,\alpha_1)+\overline{y}_m(0,\alpha_0)$. Because only one element of each pair $\{\overline{y}_i(0,\alpha_1),\overline{y}_i(0,\alpha_0)\}$ is identifiable from the observable data, this assumption is not subject to empirical test.

In the absence of homogeneity, the observed data do provide some information about the asymptotic distributions such that inference relying on large sample approximations may still be possible. For instance, CIs can be constructed using Chebyshev's inequality. For example, for the direct effect the interval $\widehat{DE}(\alpha_s) \pm \sqrt{Var\{\widehat{DE}(\alpha_s)\}/\gamma}$ will contain $\overline{DE}(\alpha_s)$ with at least probability $1-\gamma$. Because the Chebyshev inequality holds for all distributions, such CIs are expected to often be conservative, i.e., have coverage probability greater than $1-\gamma$. In practice $Var\{\widehat{DE}(\alpha_s)\}$ will be unknown and can be replaced with a consistent estimator $\widehat{Var}\{\widehat{DE}(\alpha_s)\}$ which asymptotically will still give a $1-\gamma$ CI.

2.3.3.2 Exact method

Rather than relying on large sample approximations, Tchetgen Tchetgen and VanderWeele (2012) derived exact CIs for various casual effects in the setting where the outcome is binary based on the Hoeffding inequality. In particular, they showed under two-stage permutation randomization that for any $\gamma \in (0,1)$, the interval $\widehat{DE}(\alpha_1) \pm \epsilon^*_{DE}(\gamma,\alpha_1,q,m)$ is a $(1-\gamma)$ CI of $\overline{DE}(\alpha_1)$, where

$$\epsilon^*_{DE}(\gamma,\alpha_1,q,m)=\sqrt{\log(2/\gamma)\Big\{4\Big(\frac{1}{q}-1\Big)^2+\sum_{i=1}^{m}\frac{L_{DE,i}(\alpha_1)^2}{q^2m}\Big\}/(2m)}$$

$q=\Pr(G_i=1)=l/m$ and $L_{DE,i}(\alpha_1)=2\Big\{1-1/\binom{n_i}{k_{i\alpha_1}}\Big\}$ for $i=1,\ldots,m$. Similarly, the interval $\widehat{IE}(\alpha_1,\alpha_0)\pm\epsilon^*(\gamma,\alpha_1,\alpha_0,q,m)$ is a $(1-\gamma)$ CI of $\overline{IE}(\alpha_1,\alpha_0)$, where

$$\epsilon^*(\gamma,\alpha_1,\alpha_0,q,m)=\sqrt{\log(2/\gamma)\Big[\max\Big\{\frac{1}{q^2},\frac{1}{(1-q)^2}\Big\}+\sum_{i=1}^{m}L_{IE,i}(\alpha_1,\alpha_0,q)^2/m\Big]/(2m)}$$

and $L_{IE,i}(\alpha_1,\alpha_0,q)=\max\Big[\Big\{1-1/\binom{n_i}{k_{i\alpha_1}}\Big\}/q,\Big\{1-1/\binom{n_i}{k_{i\alpha_0}}\Big\}/(1-q)\Big]$ for $i=1,\ldots,m$. Likewise, exact $(1-\gamma)$ CIs of $\overline{TE}(\alpha_1,\alpha_0)$ and $\overline{OE}(\alpha_1,\alpha_0)$ can be constructed by $\widehat{TE}(\alpha_1,\alpha_0)$ $\pm\epsilon^*(\gamma,\alpha_1,\alpha_0,q,m)$ and $\widehat{OE}(\alpha_1,\alpha_0)\pm\epsilon^*(\gamma,\alpha_1,\alpha_0,q,m)$ respectively. These CIs are exact in the sense that the probability the interval contains the true parameter is at least $1-\gamma$ for any m and $n_1,\ldots,n_m$. The exact CIs are appealing in that the only assumptions required for the intervals to be valid are partial interference and two-stage permutation randomization. However, in the simulation study in Section 2.4 below it is demonstrated these CIs tend to be conservative, i.e., the exact CIs tend to be very wide and cover the target parameter with probability greater than $1-\gamma$. The form of the exact CIs suggests several reasons why they are conservative. First, the widths of the CIs are not data dependent, i.e., they do not depend on the observed outcomes $y_{ij}(Z_i)$. Second, the widths of these CIs do not go to 0 as $\gamma\to 1$. Finally, for any given data set and fixed γ, the widths of the CIs for the indirect, overall, and total effects will be the same.

2.4 Simulations

Simulations were conducted to verify the asymptotic distributions of the causal effect estimators derived in Sections 2.3.2.1 and 2.3.2.2 as well as to evaluate the finite sample performance of the CIs described in Section 2.3.3. Simulations were conducted under four scenarios: (i) continuous outcomes with heterogeneity between groups, (ii) continuous outcomes, homogeneous groups, (iii) binary outcomes, heterogeneous groups, and (iv) binary outcomes, homogeneous groups. For scenario (i), the simulation study was conducted in the following steps:

Step 1: A hypothetical population with $m = 4$ groups and $n_1 = \cdots = n_4 = 1000$ individuals within each group was created as follows. For $i = 1, \ldots, 4$ and $j = 1, \ldots, 1000$, b_{ij} was randomly sampled from $\mathcal{N}(0,1)$. Then for $z_{ij} = 0,1$ and $g_i = 0,1$ the potential outcomes for individual j in group i were set to $y_{ij}(z_{ij}, \alpha_{g_i}) = g_i + 0.7z_{ij} + b_{ij} + b_{ij}z_{ij}$ for $i = 1,2$ and $y_{ij}(z_{ij}, \alpha_{g_i}) = g_i + b_{ij} + b_{ij}z_{ij}$ for $i = 3,4$.

Step 2: Groups were assigned α_1 or α_0 and individuals assigned $z = 1$ or $z = 0$ using two-stage permutation randomization with $l = 2$, $k_{i\alpha_1} = 500$, and $k_{i\alpha_0} = 200$.

Step 3: The various causal effect estimators defined in Section 2.3.1 were calculated based on the observed data from Step 2. The corresponding Wald and Chebyshev CIs as described in Section 2.3.3.1 were also computed, using the variance estimators proposed by Hudgens and Halloran (2008).

Step 4: Steps 2 – 3 were repeated 5000 times.

Note the model used to generate the potential outcomes in Step 1 assumes partial and stratified interference, such that under two-stage permutation randomization each individual has four potential outcomes. The true causal effects for the simulated population were $\overline{DE}(\alpha_1) = \overline{DE}(\alpha_0) = 0.35$, $\overline{IE}(\alpha_1, \alpha_0) = 1.00$, $\overline{TE}(\alpha_1, \alpha_0) = 1.35$, $\overline{OE}(\alpha_1, \alpha_0) = 1.10$.

For these simulation $n_1 = \cdots = n_4 = 1000$, such that the asymptotic results for large

groups derived in Section 2.3.2.1 apply. Figure 2.1 shows the accuracy of the Normal mixture approximation to the distribution of the direct, indirect, total and overall effect estimators. For simplicity, here and in the sequel results for $\widehat{DE}(\alpha_0)$ are omitted. The histograms give the empirical distributions of the estimators based on the 5000 simulated data sets. The solid lines, created using the R package *nor1mix* (Mächler 2011), show the density of the Normal mixtures used to approximate the distributions of the estimators. For the direct effect estimator the $\binom{m}{l} = \binom{4}{2} = 6$ conditional means of the Normal mixture were 0.71, 0.36, 0.35, 0.35, 0.34, -0.01. Because four of these means are nearly identical, the approximate distribution of $\widehat{DE}(\alpha_1)$ is trimodal (Figure 2.1 upper left panel). The distributions of the total and overall effect estimators are similar. From the model in Step 1 above the simulated groups were approximately homogeneous with respect to the indirect effect. For instance, the indirect effect conditional means were 1.02, 1.01, 1.00, 1.00, 0.98 and 0.98. Thus, in accordance with the Corollary to Proposition 4.2, the distribution of $\widehat{IE}(\alpha_1, \alpha_0)$ for large groups is approximately Normal (Figure 2.1 upper right panel).

Additional simulations were conducted under scenario (i) for various values of m and $n_1 = \cdots = n_m$. In each case we let $l = m/2$, $k_{i\alpha_1} = 0.5n_i$, and $k_{i\alpha_0} = 0.2n_i$, with non-integer values rounded up to the nearest integer. Table 2.1 shows the empirical coverage and width (i.e., average length) of the Wald and Chebyshev 95% CIs. Recall that justification of the Wald CIs for small m requires certain mean homogeneity assumptions as stated in the corollaries in Section 2.3.2.1. Therefore, because of the mean heterogeneity between groups for the direct, total, and overall effects in scenario (i), the Wald CIs were not necessarily expected to perform well for small m. Indeed, Table 2.1 shows the Wald CIs for these effects tend to under-cover for $m \leq 10$. These results demonstrate the Wald CIs may not be particularly robust to violation of the mean homogeneity assumption when m is small. On the other hand, the Wald CIs perform

well for $m \geq 30$, corroborating the results in Section 2.3.2.2. In contrast to the other effects, the mean homogeneity assumption does approximately hold for the indirect effect in scenario (i), suggesting that the corresponding Wald CIs should perform well for small m provided n_i is sufficiently large. To the contrary, the results in the bottom of Table 2.1 show the Wald CIs of the indirect effect under-cover for $n_i = 1000$ when m is small. Further investigation revealed this under-coverage was attributable to the estimated variance of the indirect effect estimator; when the true variance was used to construct the Wald CIs, the coverage was approximately 95% (results not shown). The Chebyshev CIs tended to perform better than the Wald CIs for small m, although for $n_i = 1000$ and $m = 4$ the Chebyshev CIs also under-covered due to using the estimated variance. For $m \geq 30$ the Chebyshev CIs were overly conservative, with 100% coverage for all effects for both $n_i = 6$ and $n_i = 1000$.

For scenario (ii), potential outcomes were simulated as above except in Step 1 we let $y_{ij}(z_{ij}, \alpha_{g_i}) = g_i + b_{ij} + b_{ij} z_{ij}$ for $j = 1, \ldots, n_i,\ i = 1, \ldots, m$. Various values of m and $n_1 = \cdots = n_m$ were considered for scenario (ii) as in scenario (i). In this scenario the groups were approximately homogeneous; for example, the direct effects $\overline{DE}_i(\alpha_1)$ for $i = 1, \ldots, m$ were all approximately 0 and the variances of the estimators $Var_{\alpha_1}\{\widehat{\overline{DE}}_i(\alpha_1)\}$ were all approximately the same. Table 2.2 gives the empirical coverage and width of the Wald and Chebyshev CIs for scenario (ii). Results for the indirect effect are identical to those in Table 2.1 because the same values were generated for $y_{ij}(0, \alpha_0)$ and $y_{ij}(0, \alpha_1)$ in scenarios (i) and (ii). For the other effects, coverage for the Wald CIs tends to be slightly better in Table 2.2 compared to Table 2.1 for small m and large n_i, but under-coverage persists despite mean homogeneity; this anti-conservative performance of the Wald CIs can again be attributed to use of the estimated variances. Coverage of the Chebyshev CIs was approximately 0.95 or greater for all effects and all values of n_i and m considered.

For scenario (iii), simulations were conducted as in scenario (i) with $m = 4$ groups each having $n_i = 1000$ individuals but with the first step being replaced by the following:

Step 1: Of the 4000 individuals in the population, randomly assign 480 of the individuals to have $x_{ij} = 0$, 480 of the individuals to have $x_{ij} = 1$, and the remaining individuals to have $x_{ij} = 2$. If $x_{ij} = 2$, the potential outcomes were set to $y_{ij}(z_{ij}, \alpha_{g_i}) = g_i z_{ij}$ for $i = 1, 2$ and $y_{ij}(z_{ij}, \alpha_{g_i}) = g_i(1 - z_{ij})$ for $i = 3, 4$; otherwise $y_{ij}(z_{ij}, \alpha_{g_i}) = x_{ij}$ for $i = 1, \ldots, 4$.

For this scenario there was heterogeneity between groups for the direct, indirect and total effects. Similar to Figure 2.1 for scenario (i), the Normal mixture distributions provided an excellent approximation to the empirical distributions of the estimators (not shown). Simulations were also conducted under scenario (iii) for $m = 6, 10, 30, 100$. Because the outcomes in scenario (iii) were binary, for each simulated data set the exact CIs described in Section 2.3.3.2 were computed in addition to the Wald and Chebyshev CIs. Empirical coverage and width of the three types of CIs are given in Table 2.3. Coverage of the Wald and Chebyshev CIs was similar to scenario (i), which also entailed heterogeneous effects. The exact CIs were very conservative, with 100% coverage for all effects and all values of m considered. Compared to the Wald and Chebyshev CIs, the exact CIs tended to be as wide or wider, especially for the overall effect where the exact CIs were at least an order of magnitude wider than the other CIs.

For scenario (iv), simulations were repeated as in scenario (iii) but the potential outcomes were set to $y_{ij}(z_{ij}, \alpha_{g_i}) = g_i z_{ij}$ if $x_{ij} = 2$ and $y_{ij}(z_{ij}, \alpha_{g_i}) = x_{ij}$ otherwise. In this scenario the groups were approximately homogeneous. Empirical coverage and width of the three CIs are given in Table 2.4. For $m \geq 30$ the Wald CIs gave the correct coverage and were the narrowest. For small m the Chebyshev and exact CIs both provided at least 95% coverage, but the Chebyshev CIs were substantially narrower. The widths of the exact CIs depend only on $m, l, k_{i\alpha_1}, k_{i\alpha_0}, n_i, \gamma$ and thus are the same

for the simulations carried out in scenario (iii) and (iv). Coverage of the exact CIs was always 100% in scenario (iv), as in scenario (iii).

In summary, the simulation results suggest for $m \geq 30$ the Wald CIs tend to yield nominal coverage levels while being narrower than the Chebyshev and exact CIs. For $m < 30$ and continuous outcomes, the simulations suggest the Chebyshev CIs may be preferred, although for $m = 10$ the Wald CIs tend to be narrower while still providing approximately correct coverage. For $m < 30$ and binary outcomes, only the exact CIs tend to provide the correct coverage when the effects are heterogeneous (scenario (iii)), whereas the Chebyshev CIs tend to provide the correct coverage and are narrower than the exact CIs when the effects are homogeneous (scenario (iv)).

2.5 Examples

2.5.1 Cholera Vaccine Trial

The indirect effects of vaccination have important public health implications. In an analysis of data from an individually-randomized, placebo-controlled trial of two oral cholera vaccines in Matlab, Bangladesh, Ali et al. (2005) found a significant association between the level of vaccine coverage (i.e., the proportion of individuals vaccinated) and the incidence of cholera in unvaccinated individuals, suggesting an indirect effect of the vaccines. Motivated by the results given in Ali et al., Hudgens and Halloran (2008, Table 2) provided data from a hypothetical two-stage randomized vaccine trial wherein the first stage $l = 3$ of $m = 5$ geographically separate groups were randomly assigned α_1 and the other two groups α_0, and in the second stage 50% of individuals in groups assigned α_1 were randomly assigned vaccine and 30% of individuals in groups assigned α_0 were randomly assigned vaccine. The number of individuals in the five groups $n_1, \ldots, n_5$ ranged from roughly 19,000 to 36,000 such that the results from Section 3.2.1 apply.

Table 2.5 gives point estimates and Wald, Chebyshev, and exact 95% CIs for the different vaccine effects (cases of cholera per 1000 individuals per year) based on the data from Hudgens and Halloran (2008) (see also VanderWeele and Tchetgen Tchetgen (2011) for an analysis of these data). To obtain the results in Table 2.5 we let $y_{ij}(Z_i) = 1$ if individual j in group i did not develop cholera and $y_{ij}(Z_i) = 0$ otherwise, such that positive values of the estimates reflect beneficial effects of the vaccine. For example, $\widehat{DE}(\alpha_1)$ indicates 1.30 fewer cases of cholera per 1000 person-years would be expected among vaccinated individuals compared to unvaccinated individuals when vaccine coverage is 50%. Wald CIs for the α_0 direct effect, the total effect, and the overall effect all exclude zero. However, the empirical results from Section 2.4 suggest Wald CIs should be interpreted with caution when $m = 5$. The test for mean homogeneity of the direct effect based on $\widetilde{T}$ indicates significant heterogeneity for α_1 ($p = 0.01$) but not for α_0 ($p = 0.54$), providing additional reason to interpret the Wald CI for $\overline{DE}(\alpha_1)$ skeptically. The Chebyshev CI for the α_0 direct effect excludes zero, suggesting the risk of cholera is significantly lower when vaccinated compared to when not vaccinated if the group level coverage is low. The Chebyshev CI for the total effect also excludes zero. In contrast to the Wald and Chebyshev CIs, the exact CIs are very wide and uninformative. As pointed out by Tchetgen Tchetgen and VanderWeele (2012), the width of exact CI is proportional to $1/\sqrt{m}$ and thus is expected to be wide when m is small.

2.5.2 Voting Encouragement Experiment

Assessing the indirect effects on an intervention is important in many areas beyond public health, including econometrics and political science. Nickerson (2008) described an experiment where households in Denver and Minneapolis with two registered voters were randomly assigned to one of three conditions: (i) receive encouragement to vote; (ii) receive encouragement to recycle; or (iii) receive nothing. Households assigned to

(i) or (ii) were contacted one week prior to the 2002 primaries by canvassers knocking on the households' doors. In households where the door was answered, the canvassers provided either voting or recycling encouragement to whichever individual of voting age answered the door and recorded the name of that individual. Whether each registered member of the household subsequently voted in the 2002 primary was then determined by voter turnout records. Nickerson found that individuals not directly contacted by the canvassers tended to vote more often if the individuals belonged to households assigned to voting encouragement compared to households assigned to recycling encouragement. This suggests an indirect effect of the voting encouragement intervention, which Nickerson referred to as a 'secondary effect.'

For the analysis here we take the $m = 392$ households contacted in Minneapolis (excluding one household where apparently both voters in the household were contacted by canvassers) as the finite population of interest. Of these 392 households, 201 or 51.2% were randomly assigned to voting encouragement. The randomization process by which these households were assigned to receive encouragement to vote or recycle was complicated (see Nickerson (2005), (2008) for details); for simplicity we assume each household was independently assigned to receive voting encouragement with probability 0.5. In the nomenclature of Tchetgen Tchetgen and VanderWeele (2012), this corresponds to Bernoulli randomization at the group level. By design, at the individual level exactly one (α_1) or none (α_0) of the $n_i = 2$ registered voters in each of the households received voting encouragement. Although the experimenters did not randomly assign one of the two individuals in the household to receive the intervention, for illustrative purposes assume among households assigned to α_1 that each individual received the intervention with equal probability. Under these assumptions, Wald and Chebyshev CIs can be computed as described in Section 2.3.3.1, with slight modifications owing to Bernoulli randomization at the group level (see the Appendix

for details). Here we let $y_{ij}(Z_i) = 1$ if individual j in group i voted in the election and $y_{ij}(Z_i) = 0$ otherwise, such that positive values of the effects indicate increased voter turnout due to the encouragement intervention. Point estimates as well as Wald and Chebyshev 90% CIs for the different voting encouragement effects are given in Table 2.5 (90% CIs were computed following Nickerson (2008), who interpreted p-values of hypothesis tests for secondary effects at the $\gamma = 0.1$ level). The exact CIs were not computed because permutation randomization was not employed at the group level. The Wald CIs indicate the presence of indirect, total and overall effects. Based on a similar result in the Denver experiment, Nickerson concluded the null hypothesis of no indirect effect was unlikely. That is, there is likely interference between individuals within the same household. The indirect effect estimate suggests that for every 100 households that receive the encouragement intervention, on average an additional eight individuals will vote despite never coming into direct contact with a canvasser.

2.6 Discussion

In this paper, we consider inference about treatment effects when the population consists of groups of individuals where interference is possible within groups but not between groups. The asymptotic distributions of effect estimators were derived when either the number of individuals per group or the number of groups grows large. Under certain assumptions about homogeneity across groups, the asymptotic distributions provide justification for Wald type CIs and tests. Empirical results suggest the Wald CIs may be preferred provided there are a large number of groups; otherwise, for a small number of groups, the Chebyshev CIs tend to provide correct coverage while being narrower than the exact CIs.

The asymptotic distributions were derived under several key assumptions, such as

partial and stratified interference. The partial interference assumption may be reasonable when groups are sufficiently separated in space, in time, or socially. Methods for assessing the stratified interference assumption are needed in future research, perhaps building upon VanderWeele et al. (2012). The results in this paper also rely on the assumption that certain two-stage randomization designs are employed to assign groups to allocation strategies and individuals to treatment. Further research remains to be conducted for other randomization designs and for observational studies where interference may be present.

2.7 Tables and Figures

Figure 2.1: Empirical distribution of various estimators

Empirical distribution of the direct effect $\overline{DE}(\alpha_1)$, indirect effect $\overline{IE}(\alpha_1,\alpha_0)$, total effect $\overline{TE}(\alpha_1,\alpha_0)$ and overall effect $\overline{OE}(\alpha_1,\alpha_0)$ estimators forsimulations in scenario (i) with $m = 4$ groups, $n_i = 1000$ individuals per group, and continuous outcomes. The solid line is the density of the approximating distribution.

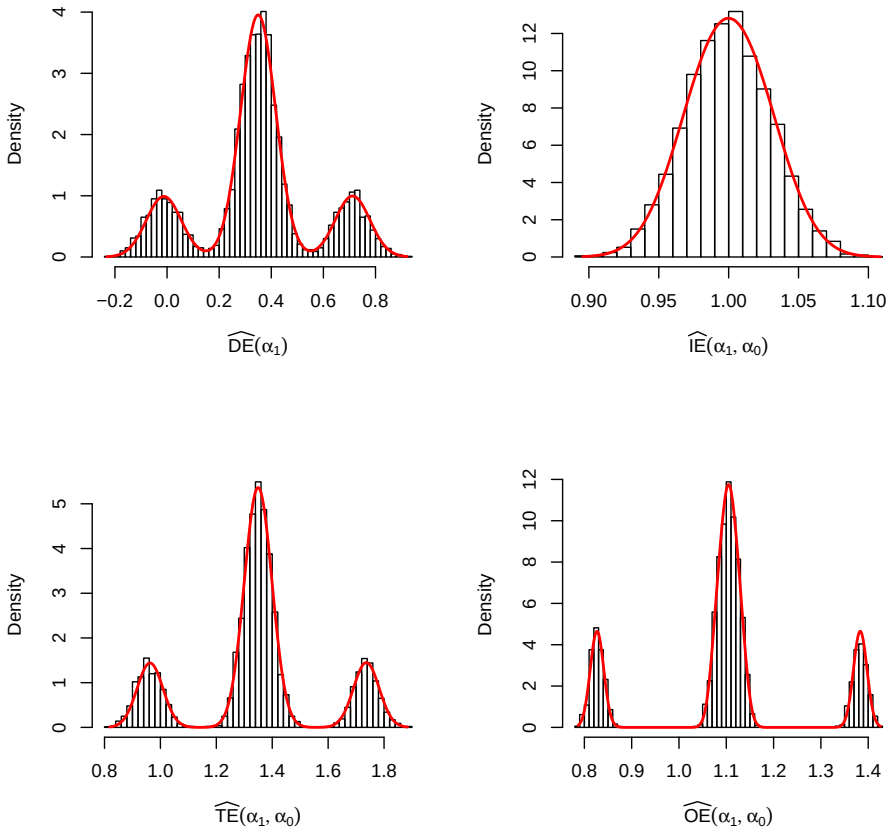

Table 2.1: Comparison among different CIs, continuous outcomes

Empirical width and coverage [in brackets] of Wald (W) and Chebyshev (C) 95% CIs of the direct effect $\overline{DE}(\alpha_1)$, indirect effect $\overline{IE}(\alpha_1,\alpha_0)$, total effect $\overline{TE}(\alpha_1,\alpha_0)$ and overall effect $\overline{OE}(\alpha_1,\alpha_0)$ for simulations under scenario (i) with numbers of groups m, number of individuals per group n_i, and continuous outcomes.

			m				
			4	6	10	30	100
$n_i = 6$	$\overline{DE}(\alpha_1)$	W	3.70[0.88]	2.67[0.91]	2.03[0.93]	1.27[0.95]	0.73[0.95]
		C	8.04[1.00]	5.92[1.00]	4.54[1.00]	2.88[1.00]	1.66[1.00]
	$\overline{IE}(\alpha_1,\alpha_0)$	W	1.89[0.80]	1.60[0.87]	1.26[0.91]	0.88[0.93]	0.42[0.95]
		C	3.92[0.94]	3.49[0.99]	2.82[1.00]	2.01[1.00]	0.96[1.00]
	$\overline{TE}(\alpha_1,\alpha_0)$	W	3.79[0.76]	2.31[0.87]	2.32[0.91]	1.40[0.94]	0.74[0.96]
		C	7.57[0.93]	4.95[0.98]	5.14[1.00]	3.17[1.00]	1.69[1.00]
	$\overline{OE}(\alpha_1,\alpha_0)$	W	2.54[0.77]	1.44[0.88]	1.69[0.90]	1.04[0.94]	0.51[0.94]
		C	5.46[0.94]	3.21[1.00]	3.83[1.00]	2.37[1.00]	1.17[1.00]
$n_i = 1000$	$\overline{DE}(\alpha_1)$	W	0.86[0.66]	0.65[0.90]	0.50[0.90]	0.28[0.94]	0.15[0.95]
		C	1.75[0.74]	1.44[0.91]	1.12[0.99]	0.63[1.00]	0.34[1.00]
	$\overline{IE}(\alpha_1,\alpha_0)$	W	0.12[0.80]	0.10[0.88]	0.11[0.91]	0.06[0.94]	0.03[0.95]
		C	0.24[0.95]	0.22[0.99]	0.25[1.00]	0.14[1.00]	0.08[1.00]
	$\overline{TE}(\alpha_1,\alpha_0)$	W	1.21[0.66]	0.89[0.90]	0.69[0.97]	0.38[0.98]	0.20[0.99]
		C	2.35[0.69]	1.95[0.90]	1.56[0.99]	0.87[1.00]	0.46[1.00]
	$\overline{OE}(\alpha_1,\alpha_0)$	W	0.68[0.66]	0.48[0.90]	0.39[0.92]	0.21[0.96]	0.11[0.97]
		C	1.31[0.66]	1.06[0.90]	0.88[0.99]	0.49[1.00]	0.26[1.00]

Table 2.2: Comparison among different CIs, continuous outcomes (iii)

Empirical width and coverage [in brackets] of Wald (W) and Chebyshev (C) 95% CIs of the direct effect $\overline{DE}(\alpha_1)$, indirect effect $\overline{IE}(\alpha_1,\alpha_0)$, total effect $\overline{TE}(\alpha_1,\alpha_0)$ and overall effect $\overline{OE}(\alpha_1,\alpha_0)$ for simulations under scenario (ii) with numbers of groups m, number of individuals per group n_i, and continuous outcomes.

			m				
			4	6	10	30	100
$n_i = 6$	$\overline{DE}(\alpha_1)$	W	3.51[0.89]	2.72[0.92]	1.92[0.94]	1.27[0.95]	0.71[0.95]
		C	7.66[1.00]	6.05[1.00]	4.32[1.00]	2.87[1.00]	1.62[1.00]
	$\overline{IE}(\alpha_1,\alpha_0)$	W	1.89[0.80]	1.60[0.87]	1.26[0.91]	0.88[0.93]	0.42[0.95]
		C	3.92[0.94]	3.49[0.99]	2.82[1.00]	2.01[1.00]	0.96[1.00]
	$\overline{TE}(\alpha_1,\alpha_0)$	W	3.14[0.78]	2.66[0.87]	2.06[0.91]	1.44[0.95]	0.70[0.95]
		C	6.30[0.94]	5.73[0.98]	4.56[1.00]	3.25[1.00]	1.58[1.00]
	$\overline{OE}(\alpha_1,\alpha_0)$	W	2.01[0.84]	1.81[0.88]	1.50[0.91]	1.09[0.95]	0.48[0.94]
		C	4.38[0.97]	4.05[0.99]	3.40[1.00]	2.47[1.00]	1.10[1.00]
$n_i = 1000$	$\overline{DE}(\alpha_1)$	W	0.27[0.93]	0.22[0.93]	0.18[0.94]	0.10[0.95]	0.06[0.95]
		C	0.60[1.00]	0.49[1.00]	0.40[1.00]	0.23[1.00]	0.13[1.00]
	$\overline{IE}(\alpha_1,\alpha_0)$	W	0.12[0.80]	0.10[0.88]	0.11[0.91]	0.06[0.94]	0.03[0.95]
		C	0.24[0.95]	0.22[0.99]	0.25[1.00]	0.14[1.00]	0.08[1.00]
	$\overline{TE}(\alpha_1,\alpha_0)$	W	0.21[0.78]	0.18[0.85]	0.19[0.91]	0.11[0.94]	0.06[0.95]
		C	0.41[0.93]	0.37[0.98]	0.41[1.00]	0.24[1.00]	0.13[1.00]
	$\overline{OE}(\alpha_1,\alpha_0)$	W	0.11[0.82]	0.10[0.88]	0.13[0.91]	0.07[0.93]	0.04[0.95]
		C	0.23[0.96]	0.22[0.99]	0.30[1.00]	0.17[1.00]	0.09[1.00]

Table 2.3: Comparison among different CIs, binary outcomes (iii)

Empirical width and coverage [in brackets] of Wald (W), Chebyshev (C) and exact (E) 95% CIs of the direct effect $\overline{DE}(\alpha_1)$, indirect effect $\overline{IE}(\alpha_1,\alpha_0)$, total effect $\overline{TE}(\alpha_1,\alpha_0)$ and overall effect $\overline{OE}(\alpha_1,\alpha_0)$ for simulations under scenario (iii) with m groups, $n_i = 1000$ individuals per group, and binary outcomes.

		m				
		4	6	10	30	100
$\overline{DE}(\alpha_1)$	W	1.73[0.67]	1.33[0.90]	0.99[0.79]	0.55[0.98]	0.30[0.93]
	C	3.26[0.67]	2.89[0.90]	2.25[0.99]	1.26[1.00]	0.68[1.00]
	E	6.07[1.00]	4.96[1.00]	3.84[1.00]	2.22[1.00]	1.21[1.00]
$\overline{IE}(\alpha_1,\alpha_0)$	W	1.22[0.67]	0.93[0.90]	0.70[0.99]	0.39[0.98]	0.21[0.99]
	C	2.31[0.67]	2.02[0.90]	1.59[0.99]	0.89[1.00]	0.48[1.00]
	E	3.84[1.00]	3.14[1.00]	2.43[1.00]	1.40[1.00]	0.77[1.00]
$\overline{TE}(\alpha_1,\alpha_0)$	W	1.22[0.67]	0.96[0.90]	0.70[0.99]	0.39[0.98]	0.21[0.99]
	C	2.31[0.67]	2.08[0.90]	1.59[0.99]	0.90[1.00]	0.48[1.00]
	E	3.84[1.00]	3.14[1.00]	2.43[1.00]	1.40[1.00]	0.77[1.00]
$\overline{OE}(\alpha_1,\alpha_0)$	W	0.03[0.85]	0.04[0.87]	0.02[0.92]	0.01[0.95]	0.01[0.96]
	C	0.06[0.98]	0.09[1.00]	0.05[1.00]	0.03[1.00]	0.02[1.00]
	E	3.84[1.00]	3.14[1.00]	2.43[1.00]	1.40[1.00]	0.77[1.00]

Table 2.4: Comparison among different CIs, binary outcomes (iv)

Empirical width and coverage [in brackets] of Wald (W), Chebyshev (C) and exact (E) 95% CIs of the direct effect $\overline{DE}(\alpha_1)$, indirect effect $\overline{IE}(\alpha_1,\alpha_0)$, total effect $\overline{TE}(\alpha_1,\alpha_0)$ and overall effect $\overline{OE}(\alpha_1,\alpha_0)$ for simulations under scenario (iv) with m groups, $n_i = 1000$ individuals per group, and binary outcomes.

		m				
		4	6	10	30	100
$\overline{DE}(\alpha_1)$	W	0.06[0.94]	0.04[0.96]	0.03[0.97]	0.02[0.97]	0.01[0.97]
	C	0.12[1.00]	0.09[1.00]	0.08[1.00]	0.05[1.00]	0.03[1.00]
	E	6.07[1.00]	4.96[1.00]	3.84[1.00]	2.22[1.00]	1.21[1.00]
$\overline{IE}(\alpha_1,\alpha_0)$	W	0.04[0.80]	0.05[0.87]	0.03[0.90]	0.02[0.94]	0.01[0.94]
	C	0.08[0.95]	0.10[0.99]	0.07[1.00]	0.04[1.00]	0.02[1.00]
	E	3.84[1.00]	3.14[1.00]	2.43[1.00]	1.40[1.00]	0.77[1.00]
$\overline{TE}(\alpha_1,\alpha_0)$	W	0.04[0.87]	0.04[0.88]	0.03[0.93]	0.02[0.95]	0.01[0.98]
	C	0.09[0.97]	0.10[0.99]	0.06[1.00]	0.04[1.00]	0.02[1.00]
	E	3.84[1.00]	3.14[1.00]	2.43[1.00]	1.40[1.00]	0.77[1.00]
$\overline{OE}(\alpha_1,\alpha_0)$	W	0.03[0.85]	0.04[0.87]	0.02[0.92]	0.01[0.95]	0.01[0.96]
	C	0.06[0.98]	0.09[1.00]	0.05[1.00]	0.03[1.00]	0.02[1.00]
	E	3.84[1.00]	3.14[1.00]	2.43[1.00]	1.40[1.00]	0.77[1.00]

Table 2.5: Data application

Wald (W), Chebyshev (C) and exact (E) $1-\gamma$ CIs of the direct effect $\overline{DE}(\alpha_s)$, indirect effect $\overline{IE}(\alpha_1,\alpha_0)$, total effect $\overline{TE}(\alpha_1,\alpha_0)$ and overall effect $\overline{OE}(\alpha_1,\alpha_0)$ for the cholera vaccine trial described in Section 2.5.1 and the voting encouragement experiment discussed in Section 2.5.2

		Estimate	W	C	E
Vaccine	$\overline{DE}(\alpha_1)$	1.30	[-0.52, 3.11]	[-2.84, 5.43]	[-3540, 3543]
Trial	$\overline{DE}(\alpha_0)$	3.64	[2.81, 4.46]	[1.75, 5.52]	[-2177, 2184]
$\gamma = 0.05$	$\overline{IE}(\alpha_1,\alpha_0)$	2.81	[-0.63, 6.25]	[-5.03, 10.7]	[-2145, 2150]
	$\overline{TE}(\alpha_1,\alpha_0)$	4.11	[2.50, 5.71]	[0.44, 7.77]	[-2143, 2151]
	$\overline{OE}(\alpha_1,\alpha_0)$	2.37	[0.03, 4.71]	[-2.98, 7.72]	[-2145, 2150]
Voting	$\overline{DE}(\alpha_1)$	0.04	[-2.7e-3, 0.07]	[-0.04, 0.11]	
Experiment	$\overline{IE}(\alpha_1,\alpha_0)$	0.08	[0.01, 0.15]	[-0.06, 0.22]	
$\gamma = 0.1$	$\overline{TE}(\alpha_1,\alpha_0)$	0.12	[0.04, 0.19]	[-0.03, 0.26]	
	$\overline{OE}(\alpha_1,\alpha_0)$	0.09	[0.02, 0.16]	[-0.05, 0.22]	

Chapter 3

On Inverse Probability Weighted Estimators with Interference

3.1 Introduction

Typically in causal inference, each individual is assumed to have two potential outcomes, one under treatment and one in the absence of treatment. This is part of the stable unit treatment value assumption (Rubin 1980). Manski (2013) referred to this as "individualistic treatment response" and viewed it as a restriction of the form of treatment response function. However, the no interference assumption may not hold in various settings. For instance, in infectious disease studies, the vaccination status of one individual may affect whether another individual becomes infected (Halloran and Struchiner 1995). Nickerson (2008) described a voting encouragement study where encouraging individuals to vote increased the likelihood another individual in the same household would vote.

Recently methods have been developed for the setting where individuals can be partitioned into groups such that there may be interference between individuals in the same group but not between individuals in different groups. This is called "partial interferenceąś (Sobel 2006). Assuming partial interference, Hudgens and Halloran (2008) defined the direct, indirect (or spillover), total, and overall causal effects of an intervention. For observational settings where treatment is not randomly assigned, Tchetgen

Tchetgen and VanderWeele (2012) proposed inverse probability weighted (IPW) estimators of these causal effects. These IPW estimators are unbiased when the propensity scores are known and can be viewed as a generalization of the usual IPW estimator of the causal effect of a treatment in the absence of interference. However, in general, IPW estimators are known to have relatively large variance. One possible remedy is to replace the sample size with its estimate in the IPW estimators. The modified estimator is known as a Hajek ratio estimator. Here, we consider the situation where any interference structure is possible and develop Hajek type estimators for various causal effects.

3.2 Notations, Assumptions and Estimands

Consider a population of n individuals. For individual $i = 1, \ldots, n$, let Z_i be the random variable of the received treatment, where $Z_i = 1$ denotes individual i received treatment and $Z_i = 0$ if she received control. Define the interference set $\mathcal{X}_i$ for individual i to be all other individuals such that their treatment received might affect the outcome of individual i. Let $S_i = \{Z_j : j \in \mathcal{X}_i\}$ denote the set of treatment indicators for individuals that possible interfere with individual i. That is, the outcome of individual i is allowed to depend not only on Z_i but also on S_i. For example, if the outcome of individual 1 possibly depends on her own treatment status as well as that of individual 2 and 3, then, $\mathcal{X}_1 = \{2, 3\}$ and $S_1 = \{Z_2, Z_3\}$. Let $y_i(z_i, s_i)$ denote the potential outcome of individual i if she received treatment z_i and her interference group received s_i. Note that the potential outcome notation introduced here is general enough to encompass any possible interference structure of which the partial inference assumption is a special case. Let $Y_i = y_i(Z_i, S_i)$ denote the observed outcome. Let L_i denote the random vector of pre-treatment covariates of individual i. Let $Z = \{Z_1, \ldots, Z_n\}$ denote the random vector of treatment for the entire population and let $L = \{L_1, \ldots, L_n\}$ denote

pre-treatment covariates for the entire population. Let z_i, s_i and z be possible values that Z_i, S_i, Z can take. Let $\sum S_i$ be the sum over all the elements in S_i and $|S_i|$ be the length of the vector. For example, if $S_1 = \{Z_2, Z_3\}$ then $\sum S_1 = Z_2 + Z_3$ and $|S_1| = 2$.

For ease of exposition, we use "allocation strategy α_k" to denote the treatment assignment where each individual is independently assigned treatment with probability α_k. Let $\pi(S_i;\alpha_k) = \alpha_k^{\sum S_i}(1-\alpha_k)^{|S_i|-\sum S_i}$ denote the probability of the interference set being assigned treatment S_i. Let $\pi(Z_i;\alpha_k) = \alpha_k^{Z_i}(1-\alpha_k)^{1-Z_i}$ and $\pi(Z_i, S_i;\alpha_k) = \pi(Z_i;\alpha_k)\pi(S_i;\alpha_k)$ denote respectively the probability of individual i being assigned treatment Z_i and the probability of individual i together with their interference set being randomly assigned joint treatment (Z_i, S_i). Define $\overline{y}_i(z,\alpha_k) = \sum_{s_i} y_i(z_i = z, s_i)\pi(s_i;\alpha_k)$ to be the average potential outcome for individual i under allocation strategy α_k. Returning to the example where $S_1 = \{Z_2, Z_3\}$, the average potential outcome of individual 1 is a weighted average of outcome under different combination of treatment $Z_1 = z$ and $(Z_2, Z_3) \in \{(0,0),(0,1),(1,0),(1,1)\}$. Averaging over all the individuals in the study, define the population average potential outcome as $\overline{y}(z,\alpha_k) = \sum_{i=1}^n \overline{y}_i(z,\alpha_k)/n$. Similarly define the marginal average potential outcome for individual i under allocation strategy α_k by $\overline{y}_i(\alpha_k) = \sum_{z_i,s_i} y_i(z_i,s_i)\pi_i(z_i,s_i;\alpha_k)$ and define the population marginal average potential outcome as $\overline{y}(\alpha_k) = \sum_{i=1}^n \overline{y}_i(\alpha_k)/n$.

Define the direct effect of a treatment under allocation strategy α_k to be $\overline{DE}(\alpha_k) = g\{\overline{y}(1,\alpha_k), \overline{y}(0,\alpha_k)\}$ for $k = 0, 1$, where $g(\cdot,\cdot)$ is some continuous contrast function. For example, a commonly used contrast function is $g(x_1, x_2) = x_1 - x_2$ and in vaccine trials it is typical to use $g(x_1, x_2) = 1 - x_2/x_1$, which can be interpreted as proportion reduction in risk for a binary outcome. The direct effect measures the contrast of average potential outcomes on an individual when applying the treatment directly under allocation strategy α_k. Let $\overline{IE}(\alpha_1,\alpha_0) = g\{\overline{y}(0,\alpha_1), \overline{y}(0,\alpha_0)\}$ be the indirect effect and let $\overline{TE}(\alpha_1,\alpha_0) = g\{\overline{y}(1,\alpha_1), \overline{y}(0,\alpha_0)\}$ be the total effect. The indirect effect measures

the contrast between average potential outcomes of individuals who have the same treatment but under different treatment allocation strategy. Note indirect can also be defined for individuals who receives treatment $z = 1$, for simplicity, we do not consider such indirect effect here. The total effect incorporates both direct and indirect effects, and reflects the difference between the potential outcomes for individuals with treatment under one allocation strategy compared to without treatment under another allocation strategy. Finally, define $\overline{OE}(\alpha_1, \alpha_0) = g\{\overline{y}(\alpha_1), \overline{y}(\alpha_0)\}$ to be the overall effect. The overall effect may be the most relevant for policy making since it describes the difference in outcomes under one allocation strategy relative to another strategy.

Define $f(Z|L) = \Pr(Z|L)$ to be the propensity score. We assume that conditional on covariates L, the probability of any treatment z is non-zero, i.e., $f(Z = z|L = l) > 0$ for all z and l. We also assume that conditional on covariates L, the treatment allocation is independent of the outcome $y(\cdot)$, that is $f(Z|L) = f(Z|L, y_1(\cdot), \ldots, y_n(\cdot))$. We make these two assumptions throughout.

3.3 IPW and Hajek-type Estimators

In this section, we first propose IPW and stablized estimators for $\overline{y}(z, \alpha_k)$ and $\overline{y}(\alpha_k)$ under a completely general interference structure when the propensity scores are known. The stablized estimators are generalizations of Hajek estimators in survey sampling literature. Then we discuss their properties including unbiasedness, consistency and asymptotic Normality. In §3.3.2, we propose estimators when the propensity scores are unknown but correctly modeled and derive the asymptotic Normality under such scenario. In §3.3.3, the IPW and Hajek estimators for the direct, indirect, total, and overall effects are proposed and their the asymptotic properties are derived under both the scenarios where the propensity scores are known or unknown.

3.3.1 Known Propensity

Define the IPW estimator for treatment z under allocation strategy α_k to be

$$\widehat{Y}^{ipw}(z,\alpha_k) = n^{-1}\sum_{i=1}^{n}\frac{y_i(Z_i,S_i)1(Z_i=z)\pi(S_i;\alpha_k)}{f(Z_i,S_i|L_i)} \tag{3.1}$$

and define the IPW marginal estimator under allocation strategy α_k to be

$$\widehat{Y}^{ipw}(\alpha_k) = n^{-1}\sum_{i=1}^{n}\frac{y_i(Z_i,S_i)\pi(Z_i,S_i;\alpha_k)}{f(Z_i,S_i|L_i)} \tag{3.2}$$

where $f(Z_i,S_i|L_i) = \int f(Z|L_i)d\tilde{Z}_i$ and the integral is taken over $\tilde{Z}_i = Z/(Z_i,S_i)$ which is the treatment of all individuals other than individual i and those in the interference set of i. Tchetgen Tchetgen and VanderWeele (2012) proposed an IPW estimator when the partial interference assumption holds. When the interference set of each individual is assumed to be the treatment vector of individuals in the same group and if the groups are of the same size, then the IPW estimator defined here is the same as the IPW estimator proposed by Tchetgen Tchetgen and VanderWeele. If $f(Z_i,S_i|L_i)$ is known for all i, $\widehat{Y}^{ipw}(z,\alpha_k)$ is an unbiased estimator for $\overline{y}(z,\alpha_k)$ and $\widehat{Y}^{ipw}(\alpha_k)$ is unbiased for $\overline{y}(\alpha_k)$ as shown in the following Proposition.

Proposition 1. *$E\{\widehat{Y}^{ipw}(z,\alpha_k)\} = \overline{y}(z,\alpha_k)$ and $E\{\widehat{Y}^{ipw}(\alpha_k)\} = \overline{y}(\alpha_k)$*

It is well known that IPW estimators have large variance (Särndal et al. 2003 chap. 5.7) and thus may lead to imprecise inferences when the sample size is small. One possible remedy is to replace the population size with an estimator of n. The classic Hajek estimator (Hájek 1971) when there is no interference uses the marginal distribution $f(Z_i|L_i)$ to estimate n. That is, $\hat{n}_{1,z} = \sum_{i=1}^{n} 1(Z_i=z)/f(Z_i|L_i)$, and it is easy to see that $E\{\hat{n}_{1,z}\} = n$. In the presence of interference, $E\{\hat{n}_{1,z}\} = n$ still holds, thus, by replacing n with $\hat{n}_{1,z}$ in (3.1) and (3.2) one can get a Hajek type of estimator

in the presence of interference. Alternatively, notice the inverse weights in the IPW estimators defined previously, involve the joint distribution $f(Z_i, S_i|L_i)$ which suggests the use of the joint distribution in constructing the estimate for population size n. Let $\hat{n}_{2,z} = \sum_{i=1}^{n} 1(Z_i = z)\pi(S_i; \alpha_k)/f(Z_i, S_i|L_i)$ and we have $E\{\hat{n}_{2,z}\} = n$. Define the Hajek estimators of the population average outcome of treatment z with allocation strategy α_k to be

$$\widehat{Y}_h^{haj}(z, \alpha_k) = \hat{n}_{h,z}^{-1} \sum_{i=1}^{n} \frac{y_i(Z_i, S_i)1(Z_i = z)\pi(S_i; \alpha_k)}{f(Z_i, S_i|L_i)} \tag{3.3}$$

Let $\hat{n}_1 = \sum_{i=1}^{n} \pi(Z_i; \alpha_k)/f(Z_i|L_i)$ and $\hat{n}_2 = \sum_{i=1}^{n} \pi(Z_i, S_i; \alpha_k)/f(Z_i, S_i|L_i)$ then $E\{\hat{n}_h\} = n$ for $h = 1, 2$. Define the population marginal outcome with allocation strategy α_k to be

$$\widehat{Y}_h^{haj}(\alpha_k) = \hat{n}_h^{-1} \sum_{i=1}^{n} \frac{y_i(Z_i, S_i)\pi(Z_i, S_i; \alpha_k)}{f(Z_i, S_i|L_i)} \tag{3.4}$$

for $k = 0, 1$ and $h = 1, 2$. Note both $\hat{n}_{h,z}$ and $\hat{n}_h$ depend on α_k, but we suppress this dependence for notational convenience. We call $\widehat{Y}_1^{haj}(\cdot)$ and $\widehat{Y}_2^{haj}(\cdot)$ "Hajek 1ąś and "Hajek 2ąś estimator respectively.

An appealing property of $\widehat{Y}_2^{haj}(z, \alpha_k)$ and $\widehat{Y}_2^{haj}(\alpha_k)$ is the preservation of the bounds of the potential outcome $y_i(\cdot)$. Specifically, suppose there exists $M_l \leq M_u$ such that $M_l \leq y_i(\cdot) \leq M_u$ for $i = 1, \ldots, n$; then one can show that $M_l \leq \widehat{Y}_2^{haj}(z, \alpha_k) \leq M_u$ and $M_l \leq \widehat{Y}_2^{haj}(\alpha_k) \leq M_u$. For example, if $y_i(\cdot)$ is binary, then $\widehat{Y}_2^{haj}(z, \alpha_k), \widehat{Y}_2^{haj}(\alpha_k) \in [0,\ 1]$. In contrast, this is not guaranteed for $\widehat{Y}^{ipw}(\cdot)$ or $\widehat{Y}_1^{haj}(\cdot)$.

Another property of $\widehat{Y}_2^{haj}(z, \alpha_k)$ and $\widehat{Y}_2^{haj}(\alpha_k)$ is that a linear transformation on the outcome y will result in the same linear transformation on $\widehat{Y}_2^{haj}(z, \alpha_k)$ and $\widehat{Y}_2^{haj}(\alpha_k)$. Let $\widehat{Y}(\cdot; y)$ denote the dependence of an estimator $\widehat{Y}$ on the outcome y. Then for a linear transformation $\mathcal{L}(x) = ax + b$, we have $\widehat{Y}_2^{haj}(\cdot; \mathcal{L}(y)) = \mathcal{L}(\widehat{Y}_2^{haj}(\cdot; y))$ for any $a, b \in \mathcal{R}$. This property indicates that a linear transformation on the coding of y (e.g.,

centering or scaling) results in the same linear transformation on the Hajek 2 estimator. This relationship holds for the IPW and Hajek 1 estimator only when $b = 0$. One ramification of this property will become evident when we consider the different causal effect estimators in §3.3.3 below.

The Hajek-type of estimator is not unbiased in general. However, noting that $\widehat{Y}_h^{haj}(z;\alpha_k) = \widehat{Y}^{ipw}(z;\alpha_k)n/\hat{n}_{h,z}$, it follows from Särndal et al. (2003) p. 176 §5.6 that

$$\frac{|E\{\widehat{Y}_h^{haj}(z;\alpha_k)\} - \overline{y}(z;\alpha_k)|}{\sqrt{Var\{\widehat{Y}_h^{haj}(z;\alpha_k)\}}} \leq n^{-1}\sqrt{Var\{\hat{n}_{h,z}\}}$$

Thus, if $Var\{\hat{n}_{h,z}\} = o(n^2)$, then bias ratio $|E\{\widehat{Y}_h^{haj}(z;\alpha_k)\} - \overline{y}(z;\alpha_k)|/\sqrt{Var\{\widehat{Y}_h^{haj}(z;\alpha_k)\}}$ goes to 0 as $n \to \infty$. Note $Var\{\hat{n}_{1,z}\} = \sum_{i,i'=1}^{n}\{f_{i,i'} - f_i f_{i'}\}/\{f_i f_{i'}\}$ where $f_i = f(Z_i = z|L)$ and $f_{i,i'} = f(Z_i = z, Z_{i'} = z|L)$. Thus, if conditional on covariates L, the treatment allocation is independent between individuals with probability $f(Z_i = z|L)$ for individual i then $Var\{\hat{n}_1\} = \sum_{i=1}^{n}\{1 - f(Z_i = z|L)\} = O(n)$ and thus is also $o(n^2)$. The formulas of $Var\{\hat{n}_{2,z}\}$ and $Var\{\hat{n}_2\}$ are more complicated and involve higher order moments of the joint treatment allocation probability.

Using Taylor linearization, one can compare the asymptotic variance for $\widehat{Y}_h^{haj}(z;\alpha_k)$ and $\widehat{Y}^{ipw}(z;\alpha_k)$. Define $\widehat{Y}_{h,0}^{haj}(z;\alpha_k)$ to be the first order Taylor expansion of $\widehat{Y}_h^{haj}(z;\alpha_k) = \widehat{Y}^{ipw}(z;\alpha_k)n/\hat{n}_{h,z}$ at $\overline{y}(a;\alpha_k)$ and n for $\widehat{Y}^{ipw}(z;\alpha_k)$ and $\hat{n}_{h,z}$ respectively, then $\widehat{Y}_{h,0}^{haj}(z;\alpha_k) = \overline{y}(z;\alpha_k) + \widehat{Y}^{ipw}(z;\alpha_k) - \overline{y}(z;\alpha_k)\hat{n}_{h,z}/n$. Thus $Var\{\widehat{Y}_{h,0}^{haj}(z;\alpha_k)\} = Var\{\widehat{Y}_i^{ipw}(z;\alpha_k)\} + \overline{y}^2(z;\alpha_k)Var(\hat{n}_{h,z}/n) - 2\overline{y}(z;\alpha_k)Cov\{\widehat{Y}^{ipw}(z;\alpha_k), \hat{n}_{h,z}/n\}$. For random variable X, define $CV(X) = \sqrt{VarX}/EX$ to be the coefficient of variation of X. Suppose $CV(\hat{n}_{h,z})/CV\{\widehat{Y}^{ipw}(z,\alpha_k)\} \leq 2Corr\{\hat{n}_{h,z}, \widehat{Y}^{ipw}(z,\alpha_k)\}$ then $Var\{\widehat{Y}_{h,0}^{haj}(z;\alpha_k)\} \leq Var\{\widehat{Y}^{ipw}(z;\alpha_k)\}$. In the extreme case, if $CV(\hat{n}_{h,z})/CV\{\widehat{Y}^{ipw}(z,\alpha_k)\} = 2Corr\{\hat{n}_{h,z}, \widehat{Y}^{ipw}(z,\alpha_k)\}$ then $Var\{\widehat{Y}_{h,0}^{haj}(z;\alpha_k)\} = Var\{\widehat{Y}^{ipw}(z;\alpha_k)\} - \overline{y}^2(z;\alpha_k)Var\{\hat{n}_{h,z}/n\}$.

For simplification, we make the following assumptions when we derive the asymptotic distribution of the IPW and Hajek estimators.

Assumption 1. *There exists a partition* $\{C_v\}_{v=1}^m$ *of* $\{1,\ldots,n\}$ *such that* $i \notin \mathcal{X}_{i'}$ *for any* $i \in C_v$, $i' \in C_{v'}$ *and* $v \neq v'$ *for* $m \in \mathcal{N}$.

Assumption 2. *Suppose* $f(Z_1,\ldots,Z_n|L) = \prod_{v=1}^m f(\{Z_i : i \in C_v\}|L)$ *and that* $f(Z_i,S_i|L)$ *is the same for all* $i \in C_v$.

Assumption 1 is the partial interference assumption, i.e., the study population can be partitioned into clusters and individuals in same cluster may interfere with each other. Assumption 2 conjectures that the treatment selection has "cliqueąś structure, i.e., dependence of treatment selection exists within cluster not across and interference within clusters is symmetric in the sense that the propensity scores are the same for individuals in the same cluster. Additionally, we assume clusters are i.i.d.. The following proposition shows the asymptotic Normality of $\widehat{Y}^{ipw}(z,\alpha_k)$ and $\widehat{Y}_h^{haj}(z,\alpha_k)$, the proofs of which are provided in the Appendix. For notational convenience, we write $\widehat{Y}_i^{ipw}(z,\alpha_k) = y_i(Z_i,S_i)1(Z_i=z)\pi(S_i;\alpha_k)/f(Z_i,S_i|L_i)$ and we suppress the dependence of variance for IPW and Hajek estimators on z and α_k when there is no confusion. For the rest of the paper, assume that $m = O(n)$ and $m \neq o(n)$.

Proposition 2. *If the propensity scores are known and Assumptions 1 and 2 hold, then as* $n \to \infty$,

(a) $\sqrt{n}\{\widehat{Y}^{ipw}(z,\alpha_k) - \overline{y}(z,\alpha_k)\}/\sigma^{ipw} \xrightarrow{d} N(0,1)$, *where* $\sigma^{ipw} = \sqrt{\sum_{v=1}^m E\psi_v^2/n}$, $\psi_v = \psi_v^{ipw}(z,\alpha_k) = \sum_{i\in C_v}\{\widehat{Y}_i^{ipw}(z,\alpha_k) - \overline{y}_i(z,\alpha_k)\}$;

(b) $\sqrt{n}\{\widehat{Y}_1^{haj}(z,\alpha_k) - \overline{y}(z,\alpha_k)\}/\sigma_1^{haj} \xrightarrow{d} N(0,1)$, *where* $\sigma_1^{haj} = \sqrt{\sum_{v=1}^m E\psi_v^2/n}$, $\psi_v = \psi_{1,v}^{haj}(z,\alpha_k) = \sum_{i\in C_v}\{\widehat{Y}_i^{ipw}(z,\alpha_k) - \overline{y}_i(z,\alpha_k)\pi(Z;\alpha_k)/f(Z_i|L_i)\} - \{\overline{y}_i(z,\alpha_k) - \overline{y}(z,\alpha_k)\}$;

(c) $\sqrt{n}\{\widehat{Y}_2^{haj}(z,\alpha_k) - \overline{y}(z,\alpha_k)\}/\sigma_2^{haj} \xrightarrow{d} N(0,1)$, *where* $\sigma_2^{haj} = \sqrt{\sum_{v=1}^m E\psi_v^2/n}$, $\psi_v = \psi_{2,v}^{haj}(z,\alpha_k) = \sum_{i\in C_v}\{\widehat{Y}_i^{ipw}(z,\alpha_k) - \overline{y}_i(z,\alpha_k)1(Z_i=z)\pi(S_i;\alpha_k)/f(Z_i,S_i|L_i)\} - \{\overline{y}_i(z,\alpha_k) - \overline{y}(z,\alpha_k)\}$;

Note if $\overline{y}_1(z,\alpha_k) = \cdots = \overline{y}_n(z,\alpha_k)$, then a consistent estimator for $(\sigma^{ipw})^2$ is $(\hat{\sigma}^{ipw})^2 = \sum_{v=1}^m \hat{\psi}_v^2/n$, where $\hat{\psi}_v = \sum_{i\in C_v}\{\widehat{Y}_i^{ipw}(z,\alpha_k) - \widehat{Y}^{ipw}(z,\alpha_k)\}$. Similarly, a consistent estimator for $(\sigma_1^{haj})^2$ is $(\hat{\sigma}_1^{haj})^2 = \sum_{v=1}^m \hat{\psi}_v^2/n$, where $\hat{\psi}_v = \sum_{i\in C_v}\{\widehat{Y}_i^{ipw}(z,\alpha_k) - \widehat{Y}_1^{haj}(z,\alpha_k)$ $1(Z_i = z)/f(Z_i|L_i)\}$ and for $(\sigma_2^{haj})^2$ is $(\hat{\sigma}_2^{haj})^2 = \sum_{v=1}^m \hat{\psi}_v^2/n$, where $\hat{\psi}_v = \sum_{i\in C_v}\{\widehat{Y}_i^{ipw}(z,\alpha_k)$ $- \widehat{Y}_2^{haj}(z,\alpha_k)1(Z_i = z)\pi(S_i;\alpha_k)/f(Z_i,S_i|L_i)\}$.

3.3.2 Unknown Propensity

All of the above results assume the propensity scores $f(Z_i|L_i)$ or $f(Z_i,S_i|L_i)$ are known. We now generate these results when the propensity score is not known but can be consistently estimated. The IPW and Hajek estimators are defined similarly as in (3.1)-(3.4) except that the propensity scores $f(Z_i|L_i)$ and $f(Z_i,S_i|L_i)$ are replaced by their estimates $\hat{f}(Z_i|L_i)$ and $\hat{f}(Z_i,S_i|L_i)$. For simplicity, we only discuss the case where we have partial interference. Similar results and derivations hold in the more general situation (given in the Appendix). Routinely, one would fit a parametric model for the propensity scores, e.g., a logistic regression with a random effect adjusting for the correlation within same clusters, and thus estimate the propensity scores by maximum likelihood. The log likelihood function $l(\gamma,\sigma_b^2) = \sum_{v=1}^m l_v(\gamma,\sigma_b^2)$, where $l_v(\gamma,\sigma_b^2) = \log f(Z_i,S_i|L_i)$ for $i \in C_v$, and the maximum likelihood estimators of γ and σ_b^2 are solutions to the estimating equations $\partial l(\gamma,\sigma_b^2)/\partial\gamma = 0$ and $\partial l(\gamma,\sigma_b^2)/\partial\sigma_b^2 = 0$. The next proposition (under some additional regularity conditions) establishes the asymptotic Normality of $\hat{Y}^{ipw}(z,\alpha_k)$ and for its normalized variance we have $(\sigma_*^{ipw}(z,\alpha_k))^2 = Var\{\sqrt{n}\hat{Y}^{ipw}(z,\alpha_k)\} \leq (\sigma^{ipw}(z,\alpha_k))^2$, which is a well known result in the absence of interference. This relationship in variance when the propensity scores are known compared to unknown but correctly modeled also holds for the Hajek 2 estimators but not necessarily for Hajek 1 estimators.

Proposition 3. *If Assumptions 1 and 2 hold, then as* $n \to \infty$

(a) $\sqrt{n}\{\hat{Y}^{ipw}(z,\alpha_k)-\overline{y}(z,\alpha_k)\}/\sigma_*^{ipw} \xrightarrow{d} N(0,1)$, *where* $(\sigma_*^{ipw})^2=(\sigma^{ipw})^2-H^{ipw^T}V^{-1}_{\gamma,\sigma_b^2}H^{ipw}$, $H^{ipw}=\sum_{v=1}^m|C_v|E\hat{Y}_v^{ipw}(z,\alpha_k)\partial l_v/n$ *and* $V_{\gamma,\sigma_b^2}=\sum_{v=1}^m E\partial l_v^T\partial l_v/n$.

(b) $\sqrt{n}\{\hat{Y}_1^{haj}(z,\alpha_k)-\overline{y}(z,\alpha_k)\}/\sigma_{1,*}^{haj} \xrightarrow{d} N(0,1)$, *where* $(\sigma_{1,*}^{haj})^2=(\sigma_1^{haj})^2+2A^TV^{-1}_{\gamma,\sigma_b^2}H_1^{haj}+H_1^{haj^T}V^{-1}_{\gamma,\sigma_b^2}H_1^{haj}$, *where* $A=\sum_{v=1}^m E\psi_{1,v}^{haj}\partial l_v^T/n$ *and* $H_1^{haj}=\sum_{v=1}^m E\partial\psi_{1,v}^{haj^T}/n$.

(c) $\sqrt{n}\{\hat{Y}_2^{haj}(z,\alpha_k)-\overline{y}(z,\alpha_k)\}/\sigma_{2,*}^{haj} \xrightarrow{d} N(0,1)$, *where* $(\sigma_{2,*}^{haj})^2=(\sigma_2^{haj})^2-H_2^{haj^T}V^{-1}_{\gamma,\sigma_b^2}H_2^{haj}$ *and* $H_2^{haj}=\sum_{v=1}^m E\psi_{2,v}^{haj}\partial l_v^T/n$.

If $\overline{y}_1(z,\alpha_k)=\cdots=\overline{y}_n(z,\alpha_k)$, a consistent estimator for $(\sigma_*^{ipw})^2$ is given by $(\hat{\sigma}_*^{ipw})^2=(\hat{\sigma}^{ipw})^2-\hat{H}^{ipwT}\hat{V}^{-1}_{\gamma,\sigma_b^2}\hat{H}^{ipw}$, where $\hat{H}^{ipw}=\sum\limits_{v=1}^m|C_v|\hat{Y}_v^{ipw}(z,\alpha_k)\hat{\partial}l_v^T/n$, $\hat{V}_{\gamma,\sigma_b^2}=\sum_{v=1}^m\hat{\partial}l_v^T\hat{\partial}l_v/n$ and $\hat{\partial}l_v(\gamma,\sigma_b^2)=\partial l_v(\hat{\gamma},\hat{\sigma}_b^2)$. A consistent estimator for H_1^{haj} is $\hat{H}_1^{haj}=-\sum_{v=1}^m|C_v|\hat{\partial}l_v^T\hat{Y}_v^{ipw}(z,\alpha_k)/n+\widehat{Y}_1^{haj}(z,\alpha_k)\sum_{i=1}^n\pi(Z_i;\alpha_k)\hat{\partial}\log f(Z_i|L_i)^T/n$ where $\hat{\partial}\log f(Z_i|L_i)=\partial\log f(Z_i|L_i)|_{f=\hat{f}}$. And a consistent estimator for H_2^{haj} is $\hat{H}_2^{haj}=-\sum_{v=1}^m|C_v|\{\hat{Y}_v^{ipw}(z,\alpha_k)-\widehat{Y}_2^{haj}(z,\alpha_k)1(Z_i=z)\pi(S_i;\alpha_k)/\hat{f}(Z_i,S_i|L_i)\}\hat{\partial}l_v/n$. Thus, one can construct a consistent estimator for $(\sigma_{1,*}^{haj})^2$ and $(\sigma_{2,*}^{haj})^2$.

For example, the propensity score can be estimated by a mixed effects logistic regression model:

$$\log\{e_i/(1-e_i)\}=L_i\gamma+b_v \tag{3.5}$$

where $e_i=f(Z_i=1|L_i,b_v)$ for $i\in C_v$ and b_v i.i.d $\sim N(0,\sigma_b^2)$. The variance of the IPW and Hajek estimators and their variance estimators are given in the Appendix.

3.3.3 Causal Effect Estimators

In this section, we first give the results of IPW and Hajek causal effect estimators assuming the propensity scores are known. Then their counterparts are given when the propensity scores are unknown but correctly modeled. Define $\widehat{DE}^{ipw}(\alpha_k)=g\{\widehat{Y}^{ipw}(1,\alpha_k),\widehat{Y}^{ipw}(0,\alpha_k)\}$ to be the IPW estimator for the direct effect. Also define

$\widehat{IE}^{ipw}(\alpha_1,\alpha_0)=g\{\widehat{Y}^{ipw}(0,\alpha_1),\widehat{Y}^{ipw}(0,\alpha_0)\}$, $\widehat{TE}^{ipw}(\alpha_1,\alpha_0)=g\{\widehat{Y}^{ipw}(1,\alpha_1),\widehat{Y}^{ipw}(0,\alpha_0)\}$ and $\widehat{OE}^{ipw}(\alpha_1,\alpha_0)=g\{\widehat{Y}^{ipw}(\alpha_1),\widehat{Y}^{ipw}(\alpha_0)\}$ to be the indirect, total and overall effect IPW estimators. Hajek-type causal effect estimators can be defined similarly. For example define the Hajek-type of direct effect estimator to be $\widehat{DE}_h^{haj}(\alpha_k)=g(\widehat{Y}_h^{haj}(1,\alpha_k),$ $\widehat{Y}_h^{haj}(0,\alpha_k))$. If the contrast function $g(x_1,x_2)$ is linear in x_1 and x_2, then the IPW causal effect estimators are all unbiased estimators for the corresponding causal effects and both types of Hajek estimators are asymptotically unbiased.

Recall that the Hajek 2 estimators defined in §3.3.1 and §3.3.2 preserve linear transformation on the outcome. Further, if the contrast function $g(x_1,x_2)=x_1-x_2$ and then the absolute value of Hajek 2 causal effects estimators are invariant under location shift. For example, for the direct effect we have $\widehat{DE}_2^{haj}(\alpha_k;y+c)=\widehat{DE}_2^{haj}(\alpha_k;y)$. Further note that for the binary outcome y, we have $\widehat{DE}_2^{haj}(\alpha_k;1-y)=-\widehat{DE}_2^{haj}(\alpha_k;y)$. The same relationship holds for other Hajek 2 causal effect estimators. That is, for binary outcome, the coding of the outcome will only change the sign of the causal effect estimators but not the magnitude. This is not the case for IPW and the Hajek 1 causal effect estimators; how the sign and the magnitude will change depends on the propensity scores as well.

The results for average mean outcome estimators in §3.3.1 and §3.3.2 can be generalized to causal effect estimators. Let $\bigtriangledown g=(\partial g/\partial x_1,\partial g/\partial x_2)$ denote the gradient of function g. For the direct effect, we have

Proposition 4. *If the propensity score is known and Assumptions 1 and 2 hold then as* $n\to\infty$

(a) $\sqrt{n}\{\widehat{DE}^{ipw}(\alpha_k)-\overline{DE}(\alpha_k)\}/\sigma^{D,ipw}\xrightarrow{d}N(0,1)$, *where* $\sigma^{D,ipw}=\sqrt{\sum_{v=1}^{m}E\psi_v^2/n}$ *and* $\psi_v=\psi_v^{D,ipw}(\alpha_k)=\bigtriangledown g(\psi_v^{ipw}(1,\alpha_k),\psi_v^{ipw}(0,\alpha_k))^T$;

(b) $\sqrt{n}\{\widehat{DE}_1^{haj}(\alpha_k)-\overline{DE}(\alpha_k)\}/\sigma_1^{D,haj}\xrightarrow{d}N(0,1)$, *where* $\sigma_1^{D,haj}=\sqrt{\sum_{v=1}^{m}E\psi_v^2/n}$ *and* $\psi_v=\psi_{1,v}^{D,haj}(\alpha_k)=\bigtriangledown g(\psi_{1,v}^{haj}(1,\alpha_k),\psi_{1,v}^{haj}(0,\alpha_k))^T$;

(c) $\sqrt{n}\{\widehat{DE}_2^{haj}(\alpha_k) - \overline{DE}(\alpha_k)\}/\sigma_2^{D,haj} \xrightarrow{d} N(0,1)$, *where* $\sigma_2^{D,haj} = \sqrt{\sum_{v=1}^{m} E\psi_v^2/n}$ *and* $\psi_v = \psi_{2,v}^{D,haj}(\alpha_k) = \bigtriangledown g(\psi_{2,v}^{haj}(1,\alpha_k), \psi_{2,v}^{haj}(0,\alpha_k))^T$;

And when the propensity scores are unknown we have:

Proposition 5. *If Assumptions 1 and 2 hold, then as* $n \to \infty$

(a) $\sqrt{n}\{\widehat{DE}_v^{ipw}(\alpha_k) - \overline{DE}(\alpha_k)\}/\sigma_*^{ipw} \xrightarrow{d} N(0,1)$, *where* $(\sigma_*^{D,ipw})^2 = (\sigma^{D,ipw})^2 - H^{D,ipw^T} V_{\gamma,\sigma_b^2}^{-1} H^{D,ipw}$, $H^{D,ipw} = \sum_{v=1}^{m} E\psi_v^{D,ipw}(\alpha_k)\partial l_v/n$ *and* $V_{\gamma,\sigma_b^2} = \sum_{v=1}^{m} E\partial l_v^T \partial l_v/n$

(b) $\sqrt{n}\{\widehat{DE}_1^{haj}(\alpha_k) - \overline{DE}(\alpha_k)\}/\sigma_{1,*}^{D,haj} \xrightarrow{d} N(0,1)$, *where* $(\sigma_{1,*}^{D,haj})^2 = (\sigma_1^{D,haj})^2 + 2A^T V_{\gamma,\sigma_b^2}^{-1} H_1^{D,haj} + H_1^{D,haj^T} V_{\gamma,\sigma_b^2}^{-1} H_1^{D,haj}$, *where* $A = \sum_{v=1}^{m} E\psi_{1,v}^{D,haj}(\alpha_k)\partial l_v^T/n$ *and* $H_1^{D,haj} = \sum_{v=1}^{m} E\partial\psi_{1,v}^{D,haj}(\alpha_k)/n$

(c) $\sqrt{n}\{\widehat{DE}_2^{haj}(\alpha_k) - \overline{DE}(\alpha_k)\}/\sigma_{2,*}^{D,haj} \xrightarrow{d} N(0,1)$, *where* $(\sigma_{2,*}^{D,haj})^2 = (\sigma_2^{D,haj})^2 - H_2^{D,haj^T} V_{\gamma,\sigma_b^2}^{-1} H_2^{D,haj}$ *and* $H_2^{D,haj} = \sum_{v=1}^{m} E\psi_{2,v}^{D,haj}(\alpha_k)\partial l_v/n$.

The results can be derived similarly for indirect, total and overall effects estimators.

3.4 Simulation Study

A simulation study was conducted to investigate the bias, empirical square error (ESE) and average estimated square error (ASE) of the different estimators discussed in §3.3. Thus, in the simulations, $\widehat{Y}^{ipw}(z,\alpha_0)$, $\widehat{Y}_1^{haj}(z,\alpha_0)$ and $\widehat{Y}_2^{haj}(z,\alpha_0)$ were computed with the (i) known propensity score, (ii) estimated by a correct model and (iii) estimated by a misspecified model. Simulations were conducted for both continuous and binary outcomes. Let $\lceil a \rceil$ denote the smallest integer greater than or equal to a and let $\lfloor a \rfloor$ denote the largest integer smaller than or equal to a. The simulation study for a continuous outcome was carried out in the following steps:

Step 1: A hypothetical population with $n = 2000$ individuals was created as follows. For $i = 1,\ldots,n$, ε_i was randomly sampled from $\mathcal{N}(0,1)$. Then for $z_i = 0,1$ the potential outcomes for individual i were set to $y_i = 5 + 3z_i + 2\sum s_i + \varepsilon_i$,

where $s_i = \{z_{4\lfloor (i-1)/4 \rfloor + 1}, \ldots, z_{4\lceil i/4 \rceil}\} \backslash z_i$. For example, $s_1 = \{z_2, z_3, z_4\}$, $s_2 = \{z_1, z_3, z_4\}$, $s_3 = \{z_1, z_2, z_4\}$, $s_4 = \{z_1, z_2, z_3\}$ and $|s_i| = 3$.

Step 2: Randomly generate covariate vector $(L_{1i}, \ldots, L_{4i})$ i.i.d from $N(0, I_4)$ for $i = 1, \ldots n$, where I_4 represents the 4 by 4 identity matrix. Let $X_{1i} = \exp(L_{1i}/2)$, $X_{2i} = L_{2i}/\{1 + \exp(L_{1i}/2)\} + 10$, $X_{3i} = (L_{1i}L_{3i}/25 + 0.6)^3$ and $X_{4i} = (L_{1i} + L_{4i} + 20)^2$ be transformed covariates to be used in a misspecified propensity score model.

Step 3: Let $\gamma = (\gamma_0, \gamma_1, \gamma_2, \gamma_3, \gamma_4) = (0.5, -1, 0.5, -0.25, -0.1)$ and $\text{logit}\{f(Z_i = z|b, L)\} = \gamma_0 + \gamma_1 L_{1i} + \gamma_2 L_{2i} + \gamma_3 L_{3i} + \gamma_4 L_{4i} + b_{\lceil i/4 \rceil}$ where b_v i.i.d. follows $N(0, 1)$ for $v = 1, \ldots, 500$ is the random effect and $\lceil i/4 \rceil$ denotes the smallest integer greater than or equal to $i/4$. Simulate Z_i for $i = 1, \ldots, n$ from the mixed effects logistic distribution.

Step 4: Since the propensity scores are not known, we fit the correctly specified mixed effects logistic regression model $\text{logit}\{f^{tru}(Z_i = z|b, L)\} = \gamma_0 + \gamma_1 L_{1i} + \gamma_2 L_{2i} + \gamma_3 L_{3i} + \gamma_4 L_{4i} + b_{\lceil i/4 \rceil}$ and a misspecified mixed effects logistic regression model $\text{logit}\{f^{mis}(Z_i = z|b, L)\} = \gamma_0 + \gamma_1 X_{1i} + \gamma_2 X_{2i} + \gamma_3 X_{3i} + \gamma_4 X_{4i} + b_{\lceil i/4 \rceil}$. Plugging in the regression coefficient estimate $\hat{\gamma}$ and numerically integrating over the estimated distribution of random effect b, we obtain $\hat{f}(Z_i = z|L) = \int f(Z_i = z|b, L, \hat{\gamma}) \phi(b, \hat{\sigma}_b^2) db$ for the two models.

Step 5: Calculate the $\widehat{Y}^{ipw}(z, \alpha_0)$, $\widehat{Y}_1^{haj}(z, \alpha_0)$ and $\widehat{Y}_2^{haj}(z, \alpha_0)$ for $z = 0, 1$ using (i) the known propensity score, (ii) the estimated propensity score from a correctly specified mixed effects model and (iii) the estimated propensity score from a misspecified mixed effects model.

Step 6: Repeat Step 3-5 1000 times and calculate the empirical bias, variance and mean square error (MSE) of the estimators in Step 5.

Table 3.1 shows the simulation results for a continuous outcome. All three estimators are approximately unbiased when the propensity scores are known or when the propensity score is correctly modeled but bias if incorrectly modeled. Also note that $\widehat{Y}_2^{haj}(\cdot)$ has substantially smaller empirical square error (ESE) than $\widehat{Y}^{ipw}(\cdot)$ and $\widehat{Y}_1^{haj}(\cdot)$. For example, when $\alpha = 0.1$, the ESE of $\widehat{Y}^{ipw}(1,\alpha)$ is 1.48 when propensity scores are known, 1.14 when the propensity score models are correctly specified and 1.79 if the covariates are not correctly specified. The ESE of $\widehat{Y}_1^{haj}(1,\alpha)$ is similar to that of $\widehat{Y}^{ipw}(\cdot)$ while that of $\widehat{Y}_2^{haj}(1,\alpha)$ is around 0.03. This can be explained by the larger variance of $\hat{n}_{2,z}$ compared with $\hat{n}_{1,z}$, i.e., the denominator and numerator of the Hajek 2 vary together. Also, in this simulation study, the $\widehat{Y}_2^{haj}(\cdot)$ is more robust than $\widehat{Y}^{ipw}(\cdot)$ and $\widehat{Y}_1^{haj}(\cdot)$ when the propensity model is misspecified.

For binary outcome, the simulations were conducted similarly as for continuous outcome but with the first step being replaced by the following:

Step 1: Of the 2000 individuals in the population, randomly assign 400 of the individuals to have $y_i = 0$, 400 of the individuals to have $y_i = 1$, and the remaining individuals to have $y_i = 1(z_i = 1)1(s_i = |s_i|)$ for $i = 1, \ldots, n$.

The simulation results in this scenario are given in Table 3.2. Similar to the continuous outcome simulations, the ESE for $\widehat{Y}_2^{haj}(\cdot)$ is smaller ESE than $\widehat{Y}^{ipw}(\cdot)$ and $\widehat{Y}_1^{haj}(\cdot)$ under all three scenarios.

3.5 Rotavirus Vaccine Study in Nicaragua

Rotavirous is a major health problem in Nicaragua (Espinoza 1997). A rotavirus vaccine study was carried out in León, Nicaragua's second largest city with an estimated 2010 population of close to 200,000. The rotavirus vaccine was first introduced in León in October 2006. Starting October 2006, any eligible child in the study at the age of 2, 4 and 6 months were offered rotavirus vaccine. However, for various reasons, the coverage of vaccine of at least one dose was 67% after the implementation of the immunization

program. In 2010, the Health and Demographic Surveillance Site-León (HDSS-León) was employed to obtain a simple random sample of households from about 50 out of 208 randomly selected geographical clusters of equal size (Becker-Dreps et al 2013). For the illustration purpose, we ignored the cluster sampling of households and the study population is chosen to be 826 children from the households selected. There were 530 households in the study and any child in the selected household under the age of 5 was eligible to participate. Each individual in the study was visited by a field worker every two weeks for about a year (January 2010 to February 2011, except during Christmas break). Information about the diarrhea episodes in past 14 days was recorded as well as other information about the household such as the sanitation conditions, household water source, maternal employment, and age of the child. Every child that participated study is included in the analysis. There are around 300 children being the only kid in the family. Including them will not be a problem for two reasons: First, they do contribute to the direct effect. And second, in the IPW estimator they cancelled out when calculating the indirect effect since the contrast function for all causal effects used here is $g(x_1, x_2) = x_1 - x_2$. The outcome is set to be whether a child had at least one rotavirus diarrhea episode during the study.

We set the interference set to be children in the same household. A mixed effects logistic regression model of the probability of choosing fully vaccination (individuals are categorized as fully vaccinated, i.e., those who have all three doses and not fully vaccinated, i.e., those who have less than three doses) at baseline was fitted conditional on a subset of covariates available at baseline: child's age (categorized into 0-11 months, 12-23 months and 24-59 months), mother's education level, floor (dirt floor or not dirt floor), season, household sanitation (indoor toilet, latrine or none), water (indoor municipal water supply or not) and breastfeeding (yes or no). The likelihood ratio test from the fitted logistic mixture model indicated that the probability of having all three

doses of vaccine is higher among those whose mother is more educated (OR=1.96 with p value= 0.01) or living in a house with better sanitation (OR=1.5 with p value=0.05), the more likely a child would be vaccinated with all three doses. Table 3.3 shows the estimates and the estimated SE of the IPW and two Hajek estimators. Results of IPW and Hajek 1 are similar. The Hajek 2 estimates are closer to the null and as expected have 15%-20% smaller SE than the IPW and Hajek 1 estimates. The direct effect estimate curve and contour plots for indirect, total and overall effect estimators are given in Figure 3.1. While the estimated direct effect declines as α increased, the indirect, total and overall effect estimates became larger with increases in α_1 for a given level of α_0. The rate of decline for the direct effect estimator is smaller as α increases. Lines in the contour plot for the indirect effect estimates are not parallel and are getting closer at the upper right corner, e.g., 10% of increase of vaccine coverage at high coverage are estimated to have a stronger indirect effect compared to at low coverage. This means that as the vaccine coverage for vaccinated children increased, the risk of having rotavirus diarrhea among unvaccinated children decreased. The contour plot lines are nearly vertical for the total effect estimates, indicating the vaccine coverage does not have much effect on the risk of a vaccinated child having rotavirus diarrhea. The Hajek 2 overall effect estimate provides a simple summary comparison of the two strategies, indicating that, on average, 5.12 fewer cases per 100 individuals in a household with coverage 0.8 compared with a household with coverage 0.1.

3.6 Tables and Figures

Figure 3.1: Hajek 2 causal effect estimators for the rotavirus vaccine study

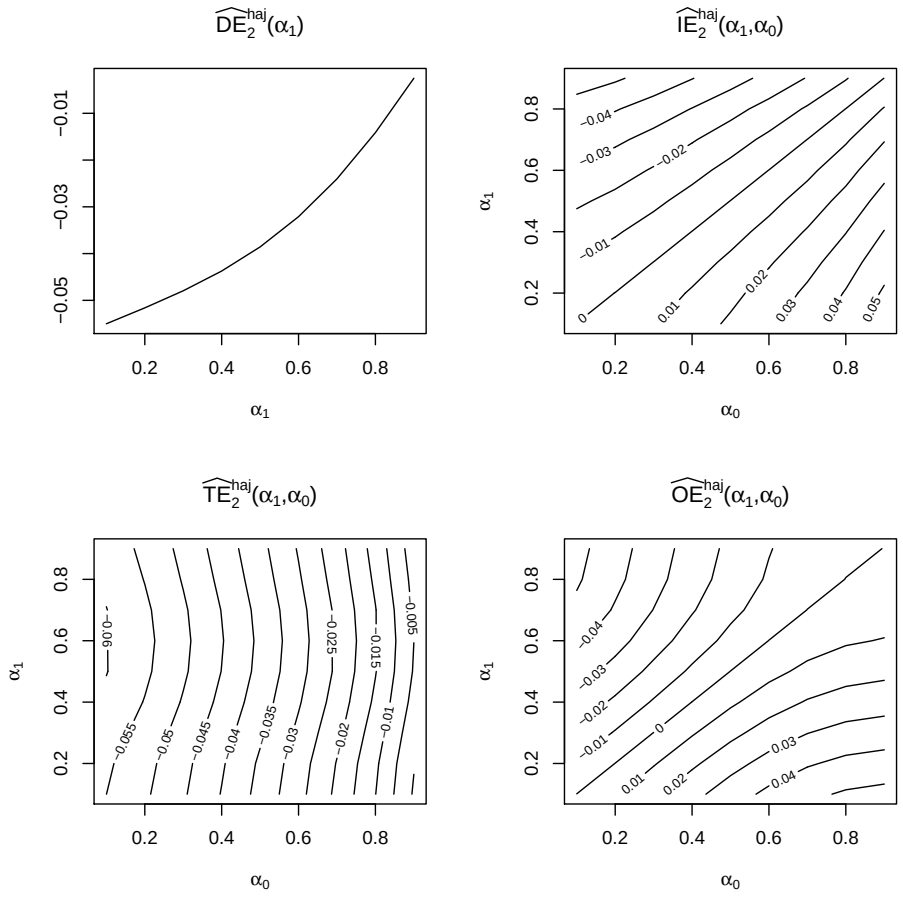

Table 3.1: Comparison among Estimators, continuous outcome

Empirical Bias, empirical standard error (ESE) and the average estimated standard error (ASE) of IPW and Hajek estimators for a continuous outcome with different α when the propensity scores are known (Known f), unknown but correctly modeled (Correct f), and unknown but incorrectly modeled (Mis f)

	α								
	0.1			0.5			0.9		
Known f	Bias	ESE	ASE	Bias	ESE	ASE	Bias	ESE	ASE
$\hat{Y}^{ipw}(1,\alpha)$	0.035	1.48	1.46	0.004	0.68	0.68	0.029	1.57	1.57
$\hat{Y}_1^{haj}(1,\alpha)$	0.050	1.61	1.60	0.008	0.58	0.59	0.037	1.04	1.03
$\hat{Y}_2^{haj}(1,\alpha)$	0.009	0.03	0.03	0.001	0.02	0.02	0.005	0.01	0.01
Correct f	Bias	ESE	ASE	Bias	ESE	ASE	Bias	ESE	ASE
$\hat{Y}^{ipw}(1,\alpha)$	0.036	1.14	1.06	0.151	0.34	0.30	0.442	0.67	0.60
$\hat{Y}_1^{haj}(1,\alpha)$	0.039	1.14	1.12	0.154	0.33	0.37	0.436	0.62	0.69
$\hat{Y}_2^{haj}(1,\alpha)$	0.008	0.03	0.03	0.023	0.01	0.01	0.032	0.01	0.01
Mis f	Bias	ESE	ASE	Bias	ESE	ASE	Bias	ESE	ASE
$\hat{Y}^{ipw}(1,\alpha)$	0.566	1.79	1.25	0.154	2.53	1.45	1.574	13.74	9.28
$\hat{Y}_1^{haj}(1,\alpha)$	0.721	1.43	1.23	0.387	1.21	0.95	1.224	5.68	5.08
$\hat{Y}_2^{haj}(1,\alpha)$	0.007	0.03	0.02	0.112	0.03	0.02	0.071	0.01	0.01

Table 3.2: Comparison among estimators, binary outcome

Empirical Bias (×10), empirical standard error (ESE) (×10) and the average estimated standard error (ASE) (×10) of IPW and Hajek estimators for a binary outcome with different α when the propensity scores are known (Known f), unknown but correctly modeled (Correct f), and unknown but incorrectly modeled (Mis f)

	α								
	0.1			0.5			0.9		
Known f	Bias	ESE	ASE	Bias	ESE	ASE	Bias	ESE	ASE
$\hat{Y}^{ipw}(1,\alpha)$	0.013	0.68	0.68	0.004	0.27	0.27	0.022	0.71	0.71
$\hat{Y}_1^{haj}(1,\alpha)$	0.010	0.68	0.68	0.004	0.25	0.25	0.027	0.61	0.61
$\hat{Y}_2^{haj}(1,\alpha)$	0.021	0.56	0.54	0.001	0.23	0.22	0.019	0.24	0.24
Correct f	Bias	ESE	ASE	Bias	ESE	ASE	Bias	ESE	ASE
$\hat{Y}^{ipw}(1,\alpha)$	0.019	0.72	0.69	0.005	0.23	0.24	0.279	0.49	0.46
$\hat{Y}_1^{haj}(1,\alpha)$	0.020	0.72	0.70	0.004	0.23	0.24	0.275	0.47	0.48
$\hat{Y}_2^{haj}(1,\alpha)$	0.018	0.58	0.54	0.052	0.22	0.20	0.078	0.20	0.20
Mis f	Bias	ESE	ASE	Bias	ESE	ASE	Bias	ESE	ASE
$\hat{Y}^{ipw}(1,\alpha)$	0.145	0.60	0.55	0.079	0.58	0.48	0.914	1.99	1.65
$\hat{Y}_1^{haj}(1,\alpha)$	0.181	0.56	0.53	0.015	0.41	0.39	0.743	1.35	1.27
$\hat{Y}_2^{haj}(1,\alpha)$	0.013	0.49	0.45	0.149	0.28	0.25	0.167	0.30	0.30

Table 3.3: Rotavirus Vaccine Study

IPW and Hajek estimates (Est) and estimated standard error (SE) per 100 individuals for the rotavirus vaccine study

	α							
	0.2		0.4		0.6		0.8	
	Est	SE	Est	SE	Est	SE	Est	SE
$\widehat{DE}^{ipw}(\alpha)$	-7.94	20.3	-6.15	15.2	-4.20	10.4	-1.85	6.82
$\widehat{DE}_1^{haj}(\alpha)$	-8.11	20.4	-6.30	15.3	-4.33	10.6	-1.96	7.05
$\widehat{DE}_2^{haj}(\alpha)$	-5.16	17.3	-4.37	13.0	-3.21	9.21	-1.41	6.45
$\widehat{IE}^{ipw}(\alpha,0.1)$	-1.32	2.59	-4.04	7.78	-6.88	13.0	-9.82	18.4
$\widehat{IE}_1^{haj}(\alpha,0.1)$	-1.32	2.58	-4.06	7.77	-6.92	13.0	-9.88	18.4
$\widehat{IE}_2^{haj}(\alpha,0.1)$	-0.42	2.43	-1.53	6.96	-2.85	11.4	-4.49	15.8
$\widehat{TE}^{ipw}(\alpha,0.1)$	-9.26	22.8	-10.2	22.6	-11.1	22.6	-11.7	22.7
$\widehat{TE}_1^{haj}(\alpha,0.1)$	-9.43	22.9	-10.4	22.7	-11.3	22.7	-11.9	22.7
$\widehat{TE}_2^{haj}(\alpha,0.1)$	-5.58	19.5	-5.90	19.4	-6.06	19.4	-5.90	19.5
$\widehat{OE}^{ipw}(\alpha,0.1)$	-2.00	4.30	-5.60	11.4	-8.49	16.4	-10.4	19.5
$\widehat{OE}_1^{haj}(\alpha,0.1)$	-2.03	4.31	-5.67	11.4	-8.60	16.5	-10.5	19.5
$\widehat{OE}_2^{haj}(\alpha,0.1)$	-0.88	3.76	-2.70	9.82	-4.24	14.1	-5.12	16.8

Chapter 4

Doubly Robust Estimation with Interference

4.1 Introduction

In causal inference, it is typically assumed that individual's potential outcome depends only on the her own treatment assignment. This is part of the stable unit treatment value assumption (Rubin 1980). However, this assumption does not hold in various settings. For example, in a vaccine trial, the infection status of one individual depends on her vaccination status as well as the vaccination of people she commonly contact with. In econometrics, the house mobility may depends on the distribution of voucher in the neighbourhood (Sobel 2006). Recently, the situation has been studied where the study population can be divided into clusters and possible interference exists only among individuals in the same cluster. This is called 'partial interference' (Sobel 2006) and can be viewed as a special case of 'constant treatment response' (Manski 2013). Assuming partial interference, Hudgens and Halloran (2008) defined the direct, indirect (or spillover), total, and overall causal effects of an intervention and Tchetgen Tchetgen and VanderWeele (2012) proposed inverse probability weighted (IPW) estimators of these causal effect for observational studies. However, the validity of IPW estimators only holds when the propensity score is known or correctly modeled. Moreover, IPW estimators are known to have large variance and are unstable to small propensity scores which are quite common in a study with interference. Thus, new

methods need to be developed to improve the efficiency and stabilize IPW estimators.

In the absence of interference, doubly robust (DR) procedure are known to be effective in improving on the IPW estimators. Usually, when the missing mechanism of outcomes are beyond the control of the investigators, there are two ways of adjusting for potential confounders. One is to model the relationship between covariates and potential outcomes and the other is to predict the missing mechanism using the information available. IPW estimators only use the second model while DR estimators apply both model and is proved to be consistent when either of the two models is correct (Robins and Rotnitzky 1995). In practice, neither the model for the propensity score nor the counterfactual outcome model is known to investigators. Thus, the DR estimator provides 2 chances to get a right answer. However, the literature of DR procedure all make the no interference between units assumption and hence there is a need to generalize the DR estimator in the presence of interference.

In this paper, we develop the DR estimators for causal effects in studies assuming partial interference. The outline of the remainder of the paper is as follows. In Section 4.2 we introduce notation and define various causal effects. The IPW and regression estimators are defined in Section 4.3.1 and the DR estimator is derived in Section 4.3.2. Results from a simulation study are presented in Section 4.4. The rotavirus vaccine study is introduced in Section 4.5. Method will be illustrated in an application to this study. Finally, we discuss some limitations and propose future research in Section 4.6.

4.2 Notations, Assumptions and Estimands

Let Y be the continuous or discrete outcome and let X denote the pre-exposure covariates. Let A be the random variable for the treatment received and let $A = 1$ if individual receives treatment and $A = 0$ otherwise. Suppose there are m groups in the study with n_i individuals in group i. For each individual, a copy of (X_{ij}, A_{ij}, Y_{ij}) will be

observed for $j = 1, \ldots, n_i$, $i = 1, \ldots, m$. Let $X_i = (X_{i1}, \ldots, X_{in_i})$ and $Y_i = (Y_{i1}, \ldots, Y_{in_i})$ be the random vector of the covariates and outcome for all individuals in group i. Let $A_i = (A_{i1}, \ldots, A_{in_i})$ denote the random vector of treatment received for all n_i individuals in group i and $A_{i(-j)} = A_i \backslash A_{ij}$ be the subvector of A_i denoting the random vector of treatment for all individuals other than the j^{th} one. Let a_{ij}, $a_{i(-j)}$ and a_i denote the possible value A_{ij}, $A_{i(-j)}$ and A_i can take. Define $f(A_i|X_i) = \Pr(A_i|X_i)$ to be the probability of treatment vector given the covariates (also known as propensity score) and let $f(A_{ij}|X_i) = \Pr(A_{ij}|X_i)$ be the probability of treatment received by an individual. A special interference structure is that individuals interfere with each other within the same group but not across groups. This is called partial interference assumption and we make this assumption throughout. Under partial interference assumption, let $Y(a_i) = Y(a_{ij}, a_{i(-j)})$ be the potential outcome under treatment allocation a_i, and thus $Y = \sum_{a_i} 1(A_i = a_i) Y(a_i)$. In a study with partial interference, the copies (X_{ij}, A_{ij}, Y_{ij}) may be dependent but identically distributed and (X_i, A_i, Y_i) are indeed independent. We assume that conditional on covariates L_i, the treatment allocation is positive, i.e., $f(A_i = A_i|X_i) > 0$ with probability 1. We also make the exchangeability assumption that $f(A_i|L_i) = f(A_i|X_i, Y_i(\cdot))$. This is also known as the ignorability assumption in missing data literature. We make these two assumptions throughout.

We say the treatment assignment is 'allocation strategy α_k' if individuals are independently assigned treatment with probability α_k. Under allocation strategy α_k, the probability of having treatment A_i in group i is $\pi(A_i; \alpha_k) = \Pr(A_i; \alpha_k) = \prod_j \alpha_k^{A_{ij}} (1 - \alpha_k)^{1 - A_{ij}}$ and that of the individuals other than individual j is $\pi(A_{i(-j)}; \alpha_k) = \Pr(A_{i(-j)}; \alpha_k)$

$= \prod_{j' \neq j} \alpha_k^{A_{ij'}} (1-\alpha_k)^{1-A_{ij'}}$. Define the average potential outcome under allocation strategy α_k as $\overline{y}(a, \alpha_k) = \sum_{a_{i(-j)}} EY(a, a_{i(-j)}) \pi(a_{i(-j)}; \alpha_k)$ is the average potential outcome conditional on covariates X_i when individual is assigned treatment a under allocation strategy α_k. Define the average potential outcome conditional on covariates X_i under allocation α_k to be $\overline{y}(\alpha_0) = \sum_{a_i} EY(a_i) \pi(a_i; \alpha_0)$. Following Halloran and Struchiner (1995) and Hudgens and Halloran (2006) , we define the direct effect of a treatment under allocation strategy α_k to be $\overline{DE}(\alpha_k) = \overline{y}(1, \alpha_k) - \overline{y}(0, \alpha_k)$ for $k = 0, 1$, the indirect effect $\overline{IE}(\alpha_1, \alpha_0) = \overline{y}(0, \alpha_1) - \overline{y}(0, \alpha_0)$, the total effect $\overline{TE}(\alpha_1, \alpha_0) = \overline{y}(1, \alpha_1) - \overline{y}(0, \alpha_0)$, and the overall effect $\overline{OE}(\alpha_1, \alpha_0) = \overline{y}(\alpha_1) - \overline{y}(\alpha_0)$. In words, the direct effect is the effect of applying treatment directly. Indirect (or spillover) effect compares the average potential outcome when an individual receives control under different allocation strategy α_1 and α_0. The total effect equals the sum of the direct and indirect effects, while the overall effect provides a single summary measure of the effect of allocation strategy α_1 versus α_0. See Tchetgen Tchetgen and VanderWeele (2012) for further discussion about these estimands.

4.3 Estimators

4.3.1 IPW and Regression Estimators

One way to adjust for the confounding in observational studies is to use inverse-weighting. Inverse probability weighting creates a pseudo-population, in which there is no confounding thus the weighted average represent the average in a population where the treatment is randomly assigned. Under no unmeasured confounders assumption, $Y(a_i)$ is independent with A_i given $f(A_i|X_i)$. However, the propensity score is usually not known but estimated. For example, after fitting the regression model $f(A_i|X_i) = \exp(\gamma_1 + \gamma_{X_i} X_i + \gamma_{A_i} A_i) / \{1 + \exp(\gamma_1 + \gamma_{X_i} X_i + \gamma_{A_i} A_i)\}$, the maximum

likelihood estimates (MLE) $\hat{\gamma} = (\hat{\gamma}_1, \hat{\gamma}_{X_i}, \hat{\gamma}_{A_i})$ for $\gamma = (\gamma_1, \gamma_{X_i}, \gamma_{A_i})$ can be calculated and thus $\hat{f}(A_i|X_i)$ can be obtained. Tchetgen Tchetgen and VanderWeele (2012) proposed group level generalized IPW estimator as $\widehat{Y}_i^{ipw}(a;\alpha_k) = n_i^{-1}\sum_{j=1}^{n_i} 1(A_{ij} = a)Y_{ij}(A_i)\pi(A_{i(-j)};\alpha_k)/\hat{f}(A_i|X_i)$ and $\widehat{Y}_i^{ipw}(\alpha_k) = n_i^{-1}\sum_{j=1}^{n_i} Y_{ij}(A_i)\pi(A_i;\alpha_0)/\hat{f}(A_i|X_i)$. The population level IPW estimators were $\widehat{Y}^{ipw}(a;\alpha_k) = \sum_{i=1}^{m}\widehat{Y}_i^{ipw}(a;\alpha_k)/m$ and $\widehat{Y}^{ipw}(\alpha_k) = \sum_{i=1}^{m}\widehat{Y}_i^{ipw}(\alpha_k)/m$. It has been showed that when the propensity score is known, the generalized IPW estimators $\widehat{Y}_i^{ipw}(a,\alpha_k)$ and $\widehat{Y}_i^{ipw}(\alpha_k)$ are unbiased for $\overline{y}(a,\alpha_k)$ and $\overline{y}(\alpha_k)$, $k = 0, 1$. We assume under certain regularity conditions, there exists γ^* such that $\hat{\gamma} \to \gamma^*$ as $m \to \infty$, that is the estimator $\hat{\gamma}$ will converge no matter the propensity model is correct or not. Thus, if the if the propensity score $f(A_i|X_i)$ is unknown but correctly modeled, i.e., $\gamma^* = \gamma_0$ where γ_0 is the true parameter then $\widehat{Y}^{ipw}(a,\alpha_k) \xrightarrow{p} \overline{y}(a,\alpha_k)$ and $\widehat{Y}^{ipw}(\alpha_k) \xrightarrow{p} \overline{y}(\alpha_k)$ as $m \to \infty$.

Alternatively, one can adjust for potential confounders using a regression estimator based on the imputed value of potential outcomes. For example, suppose the true regression model for $Y(A_i)$ is $\mu(A_i, X_i) = E[Y(A_i)|A_i, X_i] = \beta_0 + \beta_{A_i}A_i + \beta_{X_i}X_i$. Then, the group level regression estimators are defined as $\widehat{Y}_i^{reg}(a;\alpha_k) = \sum_{j=1}^{n_i}\sum_{a_{i(-j)}}\hat{\mu}_{ij}(a, a_{i(-j)}, X_i)$ $\pi(a_{i(-j)};\alpha_k)/n_i$ and $\widehat{Y}_i^{reg}(\alpha_k) = \sum_{j=1}^{n_i}\sum_{a_i}\hat{\mu}_i(a_i, X_i)\pi(a_i;\alpha_k)/n_i$ where $\hat{\mu}_{ij}(a_{ij}, a_{i(-j)}, X_i)$ $= \hat{\mu}_{ij}(a_i, X_i) = \hat{\beta}_1 + \hat{\beta}_{A_i}a_i + \hat{\beta}_{X_i}X_i$ and $\hat{\beta} = (\hat{\beta}_1, \hat{\beta}_{A_i}, \hat{\beta}_{X_i})$ are MLE for $\beta = (\beta_1, \beta_{A_i}, \beta_{X_i})$. The population level regression estimators are defined as $\widehat{Y}^{reg}(a;\alpha_k) = \sum_{i=1}^{m}\widehat{Y}_i^{reg}(a;\alpha_k)/m$ and $\widehat{Y}^{reg}(\alpha_k) = \sum_{i=1}^{m}\widehat{Y}_i^{reg}(\alpha_k)/m$. We assume under certain regularity conditions, there exist β^* such that $\hat{\beta} \to \beta^*$ as $m \to \infty$. Note that if the potential outcome model $m(a_i, X_i)$ is consistently estimated by $\hat{m}(a_i, X_i)$, i.e., $\beta^* = \beta_0$ where β_0 is the true parameter, then $\widehat{Y}^{reg}(a,\alpha_k) \xrightarrow{p} \overline{y}(a,\alpha_k)$ and $\widehat{Y}^{reg}(\alpha_k) \xrightarrow{p} \overline{y}(\alpha_k)$ as $m \to \infty$.

We can define various causal effect estimators based on the IPW and regression estimators introduced in this section. For example, define $\widehat{DE}^{ipw}(\alpha_k) = \widehat{Y}^{ipw}(1,\alpha_k) - \widehat{Y}^{ipw}(0,\alpha_k)$ for $k = 0, 1$ to be the IPW estimator for direct effect, $\widehat{IE}^{ipw}(\alpha_1, \alpha_0) =$

$\widehat{Y}^{ipw}(0,\alpha_1)-\widehat{Y}^{ipw}(0,\alpha_0)$, $\widehat{TE}^{ipw}(\alpha_1,\alpha_0)=\widehat{Y}^{ipw}(1,\alpha_1)-\widehat{Y}^{ipw}(0,\alpha_0)$ and $\widehat{OE}^{ipw}(\alpha_1,\alpha_0)=\widehat{Y}^{ipw}(\alpha_1)-\widehat{Y}^{ipw}(\alpha_0)$ to be the IPW estimators for indirect, total and overall effects. The regression causal effect estimators can be defined similarly. Note that these estimators are consistent estimator for corresponding causal effects when the model required is correctly specified.

4.3.2 Doubly Robust Estimators

In Section 4.3.1, we have shown that in an observational study with interference, the parameter of interest $\overline{y}(a,\alpha_k)$ and $\overline{y}(\alpha_k)$ can be consistently estimated by the estimator based on regression modeling if the regression model is correct or by the estimator based on inverse propensity weighting if the propensity score model is correct. The doubly robust estimators utilize both models and are consistent if either model is correct. We propose doubly robust estimators as follows:

$$\begin{aligned}\widehat{Y}_i^{DR}(a,\alpha_k) &= n_i^{-1}\sum_{j=1}^{n_i}\Bigg\{\frac{1(A_{ij}=a)\{Y_{ij}(A_i)-\hat{\mu}_{ij}(A_i,X_i)\}}{\hat{f}(A_i|X_i)}\pi(A_{i(-j)};\alpha_k)\\ &\quad+\sum_{a_{i(-j)}}\hat{\mu}_{ij}(a,a_{i(-j)},X_i)\pi(a_{i(-j)};\alpha_k)\Bigg\}\end{aligned}$$

$$\widehat{Y}_i^{DR}(\alpha_k)=n_i^{-1}\sum_{j=1}^{n}\left\{\frac{\{Y_{ij}(A_i)-\hat{\mu}_{ij}(A_i,X_i)\}}{\hat{f}(A_i|X_i)}\pi(A_i;\alpha_k)+\sum_{a_i}\hat{\mu}_{ij}(a_i,X_i)\pi(a_i;\alpha_k)\right\}$$

where $\hat{f}(A_i|X_i)$ and $\hat{\mu}_{ij}(a_i,X_i)$ are parametric model built for propensity score and the outcome. Under certain regularity conditions For the group level and $\widehat{Y}^{DR}(a,\alpha_k)=\sum_{i=1}^{m}\widehat{Y}_i^{DR}(a,\alpha_k)/m$ and $\widehat{Y}^{DR}(\alpha_k)=\sum_{i=1}^{m}\widehat{Y}_i^{DR}(\alpha_k)/m$ at the population level. The following Proposition shows that the DR estimators are indeed doubly robust.

Proposition 1. *If either $\gamma^*=\gamma_0$ or $\beta^*=\beta_0$ hold, then*

(a) $\sqrt{m}\{\widehat{Y}^{DR}(a,\alpha_k)-\overline{y}(a,\alpha_k)\}/\sigma^{DR}(a,\alpha_k)\xrightarrow{d}N(0,1)$ as $m\to\infty$, where $(\sigma^{DR}(a,\alpha_k))^2$

$= m^{-1}\sum_{i=1}^{m}\psi_i^2(\overline{y}(a,\alpha_k),\gamma^*,\beta^*)$ *and* $\psi_i(\eta,\gamma,\beta) = \sum_{j=1}^{n_i}[1(A_{ij}=a)\{Y(A_i)-\mu(A_i,X_i|\beta)\}$ $\pi(A_{i(-j)};\alpha_0)/\{n_i f(A_i|X_i,\gamma)\}+\sum_{a_{i(-j)}}\mu(a,a_{i(-j)},X_i|\beta)\pi(a_{i(-j)};\alpha_0)]-\eta$

(b) $\sqrt{m}\{\widehat{Y}^{DR}(\alpha_k)-\overline{y}(\alpha_k)\}/\sigma^{DR}(\alpha_k)\xrightarrow{d}N(0,1)$ *as* $m\to\infty$, *where* $(\sigma^{DR}(\alpha_k))^2 = m^{-1}\sum_{i=1}^{m}\varphi_i^2(\overline{y}(\alpha_k),\gamma^*,\beta^*)$ *and* $\varphi_i(\eta,\gamma,\beta) = n_i^{-1}\sum_{j=1}^{n_i}[\{Y(A_i)-\mu(A_i,X_i|\beta)\}\pi(A_{i(-j)};\alpha_0)/$ $f(A_i|X_i,\gamma)+\sum_{a_i}\mu(a_i,X_i|\beta)\pi(a_i;\alpha_0)]-\eta$.

The proof of Proposition 1 is given in the Appendix. It can also be concluded from the proof that $\sigma^{DR}(a,\alpha_k)$ and $\sigma^{DR}(\alpha_k)$ stay the same whether γ and β are known or estimated. To estimate the variance, note that $\psi_i(\widehat{Y}^{DR}(a,\alpha_k),\hat{\gamma},\hat{\beta}) = \widehat{Y}_i^{DR}(a,\alpha_k)-\widehat{Y}^{DR}(a,\alpha_k)$, thus, $(\hat{\sigma}^{DR}(a,\alpha_k))^2 = m^{-1}\sum_{i=1}^{m}(\widehat{Y}_i^{DR}(a,\alpha_k)-\widehat{Y}^{DR}(a,\alpha_k))^2$ is a consistent estimator for $(\sigma^{DR}(a,\alpha_k))^2$. Similarly, $(\hat{\sigma}^{DR}(\alpha_k))^2 = m^{-1}\sum_{i=1}^{m}(\widehat{Y}_i^{DR}(\alpha_k)-\widehat{Y}^{DR}(\alpha_k))^2$ estimates $(\sigma^{DR}(\alpha_k))^2$ consistently.

Doubly robust causal effect estimators can be defined similarly as the IPW estimators in Section 4.3.1. For example, define $\widehat{DE}^{DR}(\alpha_k) = \widehat{Y}^{DR}(1,\alpha_k)-\widehat{Y}^{DR}(0,\alpha_k)$ to be the DR estimator for direct effect. And it follows from Proposition 1 that $\widehat{DE}^{DR}(\alpha_k)$, $\widehat{IE}^{DR}(\alpha_1,\alpha_0)$, $\widehat{TE}^{DR}(\alpha_1,\alpha_0)$ and $\widehat{OE}^{DR}(\alpha_1,\alpha_0)$ are consistent estimators for the corresponding causal effects when either the propensity or the potential outcome model is correct. Thus, these estimators are doubly robust as well.

Proposition 2. *If either* $\gamma^*=\gamma_0$ *or* $\beta^*=\beta_0$ *hold, then*

(a) $\sqrt{m}\{\widehat{DE}^{DR}(\alpha_k)-\overline{DE}(\alpha_k)\}/\sigma_D^{DR}\xrightarrow{d}N(0,1)$ *as* $m\to\infty$, *where* $(\sigma_D^{DR})^2 = m^{-1}\sum_{i=1}^{m}$ $\{\psi_i(\overline{y}(1,\alpha_k),\gamma^*,\beta^*)-\psi_i(\overline{y}(0,\alpha_k),\gamma^*,\beta^*)\}^2$

(b) $\sqrt{m}\{\widehat{IE}^{DR}(\alpha_1,\alpha_0)-\overline{IE}(\alpha_1,\alpha_0)\}/\sigma_I^{DR}\xrightarrow{d}N(0,1)$ *as* $m\to\infty$, *where* $(\sigma_I^{DR})^2 = m^{-1}\sum_{i=1}^{m}\{\psi_i(\overline{y}(0,\alpha_1),\gamma^*,\beta^*)-\psi_i(\overline{y}(0,\alpha_0),\gamma^*,\beta^*)\}^2$

(c) $\sqrt{m}\{\widehat{TE}^{DR}(\alpha_1,\alpha_0)-\overline{TE}(\alpha_1,\alpha_0)\}/\sigma_T^{DR}\xrightarrow{d}N(0,1)$ *as* $m\to\infty$, *where* $(\sigma_T^{DR})^2 = m^{-1}\sum_{i=1}^{m}\{\psi_i(\overline{y}(1,\alpha_1),\gamma^*,\beta^*)-\psi_i(\overline{y}(0,\alpha_0),\gamma^*,\beta^*)\}^2$

(d) $\sqrt{m}\{\widehat{OE}^{DR}(\alpha_1,\alpha_0)-\overline{OE}(\alpha_1,\alpha_0))\}/\sigma_O^{DR}\xrightarrow{d}N(0,1)$ *as* $m\to\infty$, *where* $(\sigma_O^{DR})^2 = m^{-1}\sum_{i=1}^{m}\{\varphi_i(\overline{y}(\alpha_1),\gamma^*,\beta^*)-\varphi_i(\overline{y}(\alpha_0),\gamma^*,\beta^*)\}^2$

Following a similar argument as previously, a consistent estimator for $(\sigma_D^{DR})^2$ is $(\hat{\sigma}_D^{DR})^2 = (\widehat{DE}_i^{DR}(\alpha_k) - \widehat{DE}^{DR}(\alpha_k))^2$. Consistent variance estimator for the other three causal effects can be construct similarly.

4.4 Simulations

Simulations were conducted to verify the unbiasedness and consistency of the IPW, regression and DR robust estimators given in Sections 4.3.1 and 4.3.2 as well as to compare their efficiency and robustness when the model is either correctly or mistakenly specified. Simulations were conducted under four scenarios: (i) the propensity model is correct but the potential outcome model is wrong, (ii) the propensity model is wrong but the potential outcome model is correct, (iii) both the propensity model and the potential outcome model are correct, and (iv) neither the propensity model or the potential outcome model is correct. For scenario (i), the simulation study was conducted in the following steps:

Step 1: Covariates $(Z_{1ij}, Z_{2ij}, Z_{3ij}, Z_{4ij})$ were independently sampled from N(0,I_4) for $j = 1,\ldots,n_i,\ i = 1,\ldots,m$, where I_4 are 4 by 4 identity matrix. Let $X_{1ij} = \exp(Z_{1ij}/2)$, $X_{2ij} = Z_{2ij}/\{1+\exp(Z_{1ij})\}+10$, $X_{3ij} = (Z_{1ij}Z_{3ij}/25+0.6)^3$ and $X_{4ij} = (Z_{1ij}+Z_{4ij}+20)^2$.

Step 2: Let $\operatorname{logit}\Pr(A_{ij}=1|Z_{1i},\ldots,Z_{4i},b_i) = -Z_{1ij}+2Z_{2ij}-1.25Z_{3ij}-0.1Z_{4ij}+b_i$ where b_i i.i.d. follows $N(0,1)$ for $i = 1,\ldots,500$ is the random effect. Simulate A_{ij} from the mixed effect logistic distribution.

Step 3: Let $\mu_{ij} = 2 - Z_{1ij} - 2.7Z_{2ij} + 3Z_{3ij} - Z_{4ij} + 0.5A_{ij} + 6f(A_{i(-j)})/n_i + A_{ij}Z_{1ij} + 8f(A_{i(-j)})Z_{2ij}$ where $f(A_{i(-j)}) = \sum_{j'=1,j'\neq j}^{n_i} A_{ij'}/n_i$ is proportion of treatment received among people in the rest of group i. Randomly sample ε_i from N(0,1) and let $Y_{ij} = \mu_{ij} + \varepsilon_{ij}$.

Step 4: Fit the correct potential outcome model $E\{Y_{ij}|Z_{1i},\ldots,Z_{4i},A_i\} = \beta_1 + \beta_1 Z_{1ij} +$

$\beta_2 Z_{2ij}+\beta_3 Z_{3ij}+\beta_4 Z_{4ij}+\beta_5 A_{ij}+\beta_6 f(A_{i(-j)})+\beta_7 A_{ij}Z_{1ij}+\beta_8 f(A_{i(-j)})Z_{2ij}$ and the mis-specified propensity model $\text{logit}\Pr(A_{ij}=1|X_{1i},\ldots,X_{4i},b_i)=\gamma_1 X_{1ij}+\gamma_2 X_{2ij}+\gamma_3 X_{3ij}+\gamma_4 X_{4ij}+b_i$. Calculate the MLE $\hat{\beta}$ and $\hat{\gamma}$ and thus obtain the estimated outcome $\hat{m}_{ij}(a_i,X_i)$ and propensity score $\hat{f}(A_{ij}=1|X_i)$ for $j=1,\ldots,n_i$, $i=1,\ldots,m$.

Step 5: Calculate the IPW, regression and DR estimators according to Section 4.3.1 and 4.3.2.

Step 6: Repeat Step 1-5 for 500 times and calculate the empirical mean and variance of these estimators.

The simulation was carried out for $n_i=4$, $m=500$ and α_0 took the value 0.1, 0.5 and 0.9. Scenario (ii) was carried out similar as Scenario (i) except replace Step 4 with

Step 4: Fix the mis-specified potential outcome model $E\{Y_{ij}|X_{1i},\ldots,X_{4i},A_i\}=\beta_1+\beta_1 X_{1ij}+\beta_2 X_{2ij}+\beta_3 X_{3ij}+\beta_4 X_{4ij}+\beta_5 A_{ij}+\beta_6 f(A_{i(-j)})+\beta_7 A_{ij}X_{1ij}+\beta_8 f(A_{i(-j)})X_{2ij}$ and the correct propensity model $\text{logit}\Pr(A_{ij}=1|Z_{1i},\ldots,Z_{4i},b_i)=\gamma_1 Z_{1ij}+\gamma_2 Z_{2ij}+\gamma_3 Z_{3ij}+\gamma_4 Z_{4ij}+b_i$. Calculate the MLE $\hat{\beta}$ and $\hat{\gamma}$ and thus obtain the estimated outcome $\hat{m}_i(a_i,X_i)$ and propensity score $\hat{f}(A_{ij}=1|X_i)$ for $j=1,\ldots,n_i$, $i=1,\ldots,m$.

And Scenario (iii) and (iv) were carried out using the corresponding regression model.

The simulation result is presented in Table 4.1. As expected, when the π model is correct, the IPW, hajek and the DR estimators have small bias while when the μ model is correct, the regression and DR estimators have small bias. Note that the DR estimator has a smaller variance than that of the IPW estimators when the π model is correct; the DR estimator has a smaller variance than that of both the regression estimators when the μ model is correct. That is when one of the model is correct, the other model in DR estimator, although mis-specified, helps increase the efficiency. When both models are correct, the DR estimator has even smaller bias and variance.

However, when both models are wrong, the DR estimator has as big or even bigger bias when using the IPW and regression estimators. This is also observed by who pointed out that 'two wrong models are not better than one'.

4.5 Rotavirus Vaccine Study in Nicaragua

Rotavirous is a major health problem in Nicaragua (Espinoza 1997). A rotavirus vaccine study was carried out in León, Nicaragua's second largest city, with an estimated 2010 population of close to 200,000. The rotavirus vaccine was first introduced in León in October 2006. In 2010, the Health and Demographic Surveillance Site-León (HDSS-León) was employed to obtain a simple random sample of households from about 50 out of 208 randomly selected geographical clusters of equal size (Becker-Dreps et al 2013). There were 530 households in the study and any child in the selected household under the age of 5 was eligible to participate. Starting October 2006, any eligible child in the study at the age of 2, 4 and 6 months were offered rotavirus vaccine. However, due to various reasons, the coverage of vaccine of at least one dose was about 67% after the implementation of immunization program. Each individual in the study was visited by a field worker every two weeks for about a year (January 2010 to February 2011, except during Christmas break). During each visit, information about the diarrhea episodes in the past 14 days was recorded as well as other information about the household such as the sanitation conditions, water source, or the mother or the child such as maternal employment or age of the child. Every child participated study is included in the analysis. There are around 300 children out 826 children being the only kid in the family. Including them will not be a problem for two reasons: First, they do contribute to the direct effect. And second, in the IPW estimator they cancelled out when calculating the indirect effect since the contrast function for all causal effects used here is $g(x_1, x_2) = x_1 - x_2$. The outcome is set to be whether one child ever had rotavirus diarrhea episode during the study.

A logistic regression model of the probability of choosing vaccine (all three doses) at baseline was fitted on the covariates available at baseline: child's age (categorized into 0-11 months, 12-23 months and 24-59 months), mother's education level, floor (dirt floor or not dirt floor), season, household sanitation (indoor toilet, latrine or none), water (indoor municipal water supply or not) and breastfeeding (yes or no). The likelihood ratio test from the fitted logistic mixture model indicated that the probability of having all three doses of vaccine is higher among those whose mother has a higher education level categorized age variable has p value 0.001. Also, the more educated the mother (OR=1.96 with p value= 0.01) or those in a house with better sanitation (OR=1.5 with p value=0.05). Then we fit a linear regression model for outcomes. Apart from all the covariates included in the propensity score model, we include individual vaccine status (all 3 doses) and the proportion of vaccine received in the household. Compared with 24-59 month old children, infants are more likely to have rotavirus diarrhea (OR=1.09 with p value 0.02). Also, rotavirus diarrhea is more likely to happen in the dry season (OR=1.11 with p value¡0.001). Mothers with a higher education level or those breastfeeding their children are more likely to report diarrhea. Table 4.2 shows the estimates of IPW, regression and DR estimators.

4.6 Discussion

So far, we have proposed to extend the doubly robust estimators in the presence of interference. The DR estimators of various causal effects were proposed and showed to be consistent and asymptotical normally distributed. The DR estimators we proposed use only one model for propensity score and one for potential outcome. However, it was suggested in the absence of interference that estimators using multiple models for both the propensity score and potential outcome are more robust than DR (Han and Wang 2013). Also, Tsiatis (2006) proposed DR estimator that achieved the semiparametric

efficiency bound. How these results can be generated in the presence of interference is left for future work.

4.7 Tables and Figures

Table 4.1: Bias and SE of Estimators
Empirical bias and standard error (in parentheses) of different estimators when interference is at present, $n_i = 4$ and $m = 500$

	α								
	0.1			0.5			0.9		
π_tru μ_mis	Bias	ESE	ASE	Bias	ESE	ASE	Bias	ESE	ASE
$\hat{Y}^{ipw}(1,\alpha_0)$	0.032	0.77	0.80	0.066	0.29	0.31	0.198	0.38	0.42
$\hat{Y}^{reg}(1,\alpha_0)$	0.284	0.71	0.17	0.220	0.40	0.11	0.157	0.27	0.14
$\hat{Y}^{DR}(1,\alpha_0)$	0.013	0.55	0.55	0.004	0.19	0.19	0.007	0.19	0.18
π_mis μ_tru	Bias	ESE	ASE	Bias	ESE	ASE	Bias	ESE	ASE
$\hat{Y}^{ipw}(1,\alpha_0)$	0.706	0.70	0.83	0.139	3.05	4.37	0.756	2.29	3.10
$\hat{Y}^{reg}(1,\alpha_0)$	0.004	0.14	0.10	0.002	0.09	0.08	0.001	0.11	0.10
$\hat{Y}^{DR}(1,\alpha_0)$	0.005	0.20	0.20	0.010	0.23	0.23	0.000	0.19	0.19
π_tru μ_tru	Bias	ESE	ASE	Bias	ESE	ASE	Bias	ESE	ASE
$\hat{Y}^{DR}(1,\alpha_0)$	0.006	0.17	0.17	0.001	0.09	0.09	0.003	0.11	0.11
π_mis μ_mis	Bias	ESE	ASE	Bias	ESE	ASE	Bias	ESE	ASE
$\hat{Y}^{DR}(1,\alpha_0)$	0.501	0.76	0.79	0.246	2.07	2.08	0.094	1.29	1.28

Table 4.2: Estimators for Rotavirus Vaccine Study

IPW, regression and DR estimates (Est) and estimated standard error (SE) per 100 individuals for the rotavirus vaccine study

	α_1							
	0.2		0.4		0.6		0.8	
	Est	SE	Est	SE	Est	SE	Est	SE
$\widehat{DE}^{ipw}(\alpha_1)$	-6.30	10.30	-3.90	7.90	-1.60	5.80	0.80	4.30
$\widehat{DE}^{reg}(\alpha_1)$	5.30	4.70	5.30	4.70	5.30	4.70	5.30	4.70
$\widehat{DE}^{DR}(\alpha_1)$	-6.10	10.10	-4.20	7.90	-2.10	5.90	0.40	4.40
$\widehat{IE}^{ipw}(\alpha_1, 0.1)$	-1.20	1.30	-3.50	3.90	-5.80	6.50	-8.20	9.10
$\widehat{IE}^{reg}(\alpha_1, 0.1)$	2.20	2.30	6.70	6.90	11.10	11.50	15.60	16.10
$\widehat{IE}^{DR}(\alpha_1, 0.1)$	1.30	1.20	3.70	3.70	6.10	6.10	8.50	8.50
$\widehat{TE}^{ipw}(\alpha_1, 0.1)$	-7.40	11.50	-7.40	11.50	-7.50	11.50	-7.40	11.50
$\widehat{TE}^{reg}(\alpha_1, 0.1)$	7.50	5.50	12.00	8.80	16.40	12.90	20.90	17.30
$\widehat{TE}^{DR}(\alpha_1, 0.1)$	-4.90	11.30	-0.50	11.30	4.10	11.30	8.90	11.30
$\widehat{OE}^{ipw}(\alpha_1, 0.1)$	-1.70	2.10	-4.30	5.70	-6.10	8.20	-6.90	9.80
$\widehat{OE}^{reg}(\alpha_1, 0.1)$	2.80	2.40	8.30	7.20	13.80	12.00	19.30	16.80
$\widehat{OE}^{DR}(\alpha_1, 0.1)$	0.70	2.10	2.80	5.50	5.60	8.00	9.50	9.60

Chapter 5

Conclusion

To summarize, assessing the causal effect in the presence of interference can be difficult in many settings. We have provided methodology to make causal inference about treatment effects when the population consists of groups of individuals where interference is possible within groups but not between groups. The asymptotic distributions of effect estimators were derived when either the number of individuals per group or the number of groups grows large. Under certain assumptions about homogeneity across groups, the asymptotic distributions provide justification for Wald type CIs and tests. A simulation study was presented showing that in some settings the Wald CIs have good coverage in finite samples and are substantially narrower than exact CIs.

Additionally, we generalized the IPW estimator proposed by Tchetgen Tchetgen and VanderWeele (2012) for general interference structure in observational studies. Specifically, first we propose generalized IPW estimators that do not require the partial interference; rather any form of interference between individuals is permitted. Second, two stabilized IPW estimators are proposed based on the classic Hajek estimator from survey sampling. Third, we develop the asymptotic distribution of IPW estimators and Hajek estimators and propose consistent variance estimators assuming partial interference. Empirical results are presented demonstrating one of the Hajek estimators can have substantially smaller variance than the other IPW estimators.

Chapter 4 provides a way to construct doubly robust estimators for causal effects in the presence of interference. These estimators are generalization of doubly robust estimator for average treatment effect. The doubly robust estimators proposed are shown to be consistent and asymptotically normally distributed when either the propensity score or the potential outcome is correctly modeled. Both the Hajek estimators and the DR estimators are illustrated using data from a recent study examining the effects of rotavirus vaccination in Nicaragua.

Appendix I

Proofs from Chapter 2

Proof of Propositions 1-3

Proposition 1 follows directly from Lehmann (1998) Appendix 4 Theorem 6. To prove Proposition 2, set $S_{n_i}(\alpha_1) = \sum_{j=1}^{n_i} \upsilon_{ij} 1(Z_{ij} = 1)$ and note the same theorem from Lehmann (1998) implies

$$[S_{n_i}(\alpha_1) - E_{\alpha_1}\{S_{n_i}(\alpha_1)\}]/\sqrt{Var_{\alpha_1}\{S_{n_i}(\alpha_1)\}} \xrightarrow{d} \mathcal{N}(0,1) \tag{5.1}$$

where $E_{\alpha_1}\{S_{n_i}(\alpha_1)\} = E\{S_{n_i}(\alpha_1)|G_i = 1\}$. Next note that

$$\begin{aligned}
& \widehat{DE}_i(\alpha_1) = \widehat{Y}_i(1,\alpha_1) - \widehat{Y}_i(0,\alpha_1) \\
= \;& \frac{1}{k_{i\alpha_1}} \sum_{j=1}^{n_i} y_{ij}(1,\alpha_1) 1(Z_{ij}=1) - \frac{1}{n_i - k_{i\alpha_1}} \sum_{j=1}^{n_i} y_{ij}(0,\alpha_1) 1(Z_{ij}=0) \\
= \;& \frac{1}{k_{i\alpha_1}} \sum_{j=1}^{n_i} y_{ij}(1,\alpha_1) 1(Z_{ij}=1) - \frac{1}{n_i - k_{i\alpha_1}} \sum_{j=1}^{n_i} y_{ij}(0,\alpha_1) \{1 - 1(Z_{ij}=1)\} \\
= \;& \sum_{j=1}^{n_i} \left\{ \frac{1}{k_{i\alpha_1}} y_{ij}(1,\alpha_1) + \frac{1}{n_i - k_{i\alpha_1}} y_{ij}(0,\alpha_1) \right\} 1(Z_{ij}=1) - \frac{1}{n_i - k_{i\alpha_1}} \sum_{j=1}^{n_i} y_{ij}(0,\alpha_1)
\end{aligned}$$

implying

$$\begin{aligned}
\widehat{DE}_i(\alpha_1) - \overline{DE}_i(\alpha_1) \;=\; & \sum_{j=1}^{n_i} \left\{ \frac{1}{k_{i\alpha_1}} y_{ij}(1,\alpha_1) + \frac{1}{n_i - k_{i\alpha_1}} y_{ij}(0,\alpha_1) \right\} 1(Z_{ij}=1) \\
& - \frac{1}{n_i - k_{i\alpha_1}} \sum_{j=1}^{n_i} y_{ij}(0,\alpha_1) - \frac{1}{n_i} \sum_{j=1}^{n_i} y_{ij}(1,\alpha_1) + \frac{1}{n_i} \sum_{j=1}^{n_i} y_{ij}(0,\alpha_1) \\
= \;& \sum_{j=1}^{n_i} \left\{ \frac{1}{k_{i\alpha_1}} y_{ij}(1,\alpha_1) + \frac{1}{n_i - k_{i\alpha_1}} y_{ij}(0,\alpha_1) \right\} 1(Z_{ij}=1) \\
& - \sum_{j=1}^{n_i} \left\{ \frac{1}{k_{i\alpha_1}} y_{ij}(1,\alpha_1) + \frac{1}{n_i - k_{i\alpha_1}} y_{ij}(0,\alpha_1) \right\} \frac{k_{i\alpha_1}}{n_i}
\end{aligned}$$

such that $\widehat{DE}_i(\alpha_1) - \overline{DE}_i(\alpha_1) = S_{n_i}(\alpha_1) - E_{\alpha_1}\{S_{n_i}(\alpha_1)\}$. Also note $\widehat{DE}_i(\alpha_1) = S_{n_i}(\alpha_1) - \sum_{j=1}^{n_i} y_{ij}(0,\alpha_1)/(n_i - k_{i\alpha_1})$, i.e., $\widehat{DE}_i(\alpha_1)$ and $S_{n_i}(\alpha_1)$ differ by a constant. Therefore $Var_{\alpha_1}\{\widehat{DE}_i(\alpha_1)\} = Var_{\alpha_1}\{S_{n_i}(\alpha_1)\}$, implying

$$\frac{\widehat{DE}_i(\alpha_1) - \overline{DE}_i(\alpha_1)}{\sqrt{Var_{\alpha_1}\{\widehat{DE}_i(\alpha_1)\}}} = \frac{S_{n_i}(\alpha_1) - E_{\alpha_1}\{S_{n_i}(\alpha_1)\}}{\sqrt{Var_{\alpha_1}\{S_{n_i}(\alpha_1)\}}}$$

which by (5.1) completes the proof of Proposition 2. Using the fact that $\widehat{Y}_i(\alpha_s) - \overline{Y}_i(\alpha_s) = \sum_{j=1}^{n_i}\Big\{y_{ij}(1,\alpha_s) - y_{ij}(0,\alpha_s)\Big\}\Big\{1(Z_{ij}=1) - k_{i\alpha_s}/n_i\Big\}/n_i$, Proposition 3 can be proved similarly to Proposition 2.

Proof of Propositions 4.1-4.4

To prove Proposition 4.1, let $\{i_1,\ldots,i_l\} = \{i \in \{1,\ldots,m\} : G_i = 1\}$ and let $c_i = \lim \sqrt{Var_{\alpha_1}\{\widehat{DE}_i(\alpha_1)\}}/\sqrt{\sum_{i\in\{i_1,\ldots,i_l\}} Var_{\alpha_1}\{\widehat{DE}_i(\alpha_1)\}}$ as $n_{\min} \to \infty$ for $i \in \{i_1,\ldots,i_l\}$. By assumption $c_{i_1},\ldots,c_{i_l}$ exist. Then conditional on $G_1 = g_1, ..., G_m = g_m$,

$$\begin{aligned}
\frac{\widehat{DE}(\alpha_1) - \mu_{DE}^{(i_1,\ldots,i_l)}}{\sigma_{DE}^{(i_1,\ldots,i_l)}} &= \frac{\sum\limits_{i\in\{i_1,\ldots,i_l\}} [\widehat{DE}_i(\alpha_1) - E_{\alpha_1}\{\widehat{DE}_i(\alpha_1)\}]}{\sqrt{\sum\limits_{i\in\{i_1,\ldots,i_l\}} Var_{\alpha_1}\{\widehat{DE}_i(\alpha_1)\}}} \\
&= \sum_{i\in\{i_1,\ldots,i_l\}} \frac{[\widehat{DE}_i(\alpha_1) - E_{\alpha_1}\{\widehat{DE}_i(\alpha_1)\}]}{\sqrt{Var_{\alpha_1}\{\widehat{DE}_i(\alpha_1)\}}} \frac{\sqrt{Var_{\alpha_1}\{\widehat{DE}_i(\alpha_1)\}}}{\sqrt{\sum\limits_{i\in\{i_1,\ldots,i_l\}} Var_{\alpha_1}\{\widehat{DE}_i(\alpha_1)\}}} \\
&\xrightarrow{d} \sum_{i\in\{i_1,\ldots,i_l\}} Z_i c_i \sim \mathcal{N}(0,1)
\end{aligned}$$

where $Z_{i_1},\ldots,Z_{i_l}$ are i.i.d $\mathcal{N}(0,1)$ and the last line follows from Proposition 2 and that $\sum_{i\in\{i_1,\ldots,i_l\}} c_i^2 = 1$.

To prove Proposition 4.2, note that

$$\begin{aligned}\widehat{IE}(\alpha_1,\alpha_0) &= \widehat{Y}(0,\alpha_1)-\widehat{Y}(0,\alpha_0)\\ &= \sum_{i=1}^{m}\left\{\frac{\widehat{Y}_i(0,\alpha_1)}{l}1(G_i=1)-\frac{\widehat{Y}_i(0,\alpha_0)}{m-l}1(G_i=0)\right\}\end{aligned}$$

Thus conditional on $\left\{G_i=1:i\in\{i_1,\ldots,i_l\}\right\}$,

$$\begin{aligned}&\frac{\widehat{IE}(\alpha_1,\alpha_0)-\mu_{IE}^{\{i_1,\ldots,i_l\}}}{\sigma_{IE}^{\{i_1,\ldots,i_l\}}}\\ =\;& \sum_{i\in\{i_1,\ldots,i_l\}}\frac{\widehat{Y}_i(0,\alpha_1)-\overline{y}_i(0,\alpha_1)}{l\sigma_{IE}^{\{i_1,\ldots,i_l\}}}-\sum_{i\notin\{i_1,\ldots,i_l\}}\frac{\widehat{Y}_i(0,\alpha_0)-\overline{y}_i(0,\alpha_0)}{(m-l)\sigma_{IE}^{\{i_1,\ldots,i_l\}}}\\ =\;& \sum_{i\in\{i_1,\ldots,i_l\}}\frac{\widehat{Y}_i(0,\alpha_1)-\overline{y}_i(0,\alpha_1)}{\sqrt{Var_{\alpha_1}\widehat{Y}_i(0,\alpha_1)}}\frac{\sqrt{Var_{\alpha_1}\widehat{Y}_i(0,\alpha_1)/l^2}}{\sigma_{IE}^{\{i_1,\ldots,i_l\}}}\\ -\;& \sum_{i\notin\{i_1,\ldots,i_l\}}\frac{\widehat{Y}_i(0,\alpha_0)-\overline{y}_i(0,\alpha_0)}{\sqrt{Var_{\alpha_1}\widehat{Y}_i(0,\alpha_1)}}\frac{\sqrt{Var_{\alpha_1}\widehat{Y}_i(0,\alpha_1)/(m-l)^2}}{\sigma_{IE}^{\{i_1,\ldots,i_l\}}}\\ \xrightarrow{d}\;& \sum_{i\in\{i_1,\ldots,i_l\}}Z_i\frac{\sqrt{Var_{\alpha_1}\widehat{Y}_i(0,\alpha_1)/l^2}}{\sigma_{IE}^{\{i_1,\ldots,i_l\}}}-\sum_{i\notin\{i_1,\ldots,i_l\}}Z_i\frac{\sqrt{Var_{\alpha_1}\widehat{Y}_i(0,\alpha_1)/(m-l)^2}}{\sigma_{IE}^{\{i_1,\ldots,i_l\}}}\\ \sim\;& \mathcal{N}(0,1)\end{aligned}$$

where the penultimate step follows from Proposition 1. The proofs for Propositions 4.3 and 4.4 are similar.

Proof of Propositions 5.1-5.4

To prove Proposition 5.1, let $\mu_{DE}^G=\sum_{i=1}^m\overline{DE}_i(\alpha_1)1(G_i=1)/l$ and $\tilde{\sigma}_{DE}^2=Var\{\mu_{DE}^G\}$. Note $\mu_{DE}^G=E\{\widehat{DE}(\alpha_1)|G_1,\ldots,G_m\}$ and the assumptions of Proposition 5.1 imply that $\sigma_{DE}^{(0)}=\sqrt{Var\{\widehat{DE}(\alpha_1)|G_1,\ldots,G_m\}}$. Therefore, because we assume that (2.9) holds for

the sequence $W_h = \widehat{DE}_{i_h}(\alpha_1)\Big|G_{i_1} = \cdots = G_{i_l} = 1,\ h = 1,\ldots,l$ for any $i_1 \neq \ldots \neq i_l$, it follows that $\{\widehat{DE}(\alpha_1) - \mu^G_{DE}\}/\sigma^{(0)}_{DE}\Big|G_{i_1} = \cdots = G_{i_l} = 1 \xrightarrow{d} N(0,1)$ for any $i_1 \neq \ldots \neq i_l$. Because the limiting distribution is the same regardless of $G_1,\ldots,G_m$, it follows that $\{\widehat{DE}(\alpha_1) - \mu^G_{DE}\}/\sigma^{(0)}_{DE} \xrightarrow{d} N(0,1)$. Note also this indicates that $\{\widehat{DE}(\alpha_1) - \mu^G_{DE}\}/\sigma^{(0)}_{DE}$ is asymptotically independent of $G_1,\ldots,G_m$ and thus asymptotically independent of $\{\mu^G_{DE} - \overline{DE}(\alpha_1)\}/\tilde{\sigma}_{DE}$, which is a function of $G_1,\ldots,G_m$. Next note that because we assume $\overline{DE}_i(\alpha_1)$ satisfies (2.10), Lehmann (1998) Appendix 4 Theorem 6 implies $\{\mu^G_{DE} - \overline{DE}(\alpha_1)\}/\tilde{\sigma}_{DE} \xrightarrow{d} N(0,1)$. Note $Var\{\widehat{DE}(\alpha_1)\} = \sigma^{(0)2}_{DE} + \tilde{\sigma}^2_{DE}$ such that

$$\frac{\widehat{DE}(\alpha_1) - \overline{DE}(\alpha_1)}{\sqrt{Var\{\widehat{DE}(\alpha_1)\}}} = \frac{\sigma^{(0)}_{DE}}{\sqrt{\sigma^{(0)2}_{DE} + \tilde{\sigma}^2_{DE}}} \frac{\widehat{DE}(\alpha_1) - \mu^G_{DE}}{\sigma^{(0)}_{DE}} + \frac{\tilde{\sigma}_{DE}}{\sqrt{\sigma^{(0)2}_{DE} + \tilde{\sigma}^2_{DE}}} \frac{\mu^G_{DE} - \overline{DE}(\alpha_1)}{\tilde{\sigma}_{DE}}$$

Following Slutsky's theorem, (2.5) is obtained. The proofs of Propositions 5.2-5.4 can be derived along the same lines.

Details for Voting Experiment Analysis

For the voting experiment described in Section 2.5.2, we assume households were independently assigned encouragement to vote with probability 0.5. This group-level Bernoulli type randomization is different from the permutation randomization assumed throughout the rest of the paper and therefore some adaptations of the various results are needed. First, it is helpful to re-express the estimators in an inverse probability weighted (IPW) form. Namely, now define $\widehat{Y}(z,\alpha_s) = \sum_{i=1}^m \widehat{Y}_i(z,\alpha_s)1(G_i = s)/\{m\Pr(G_i = s)\}$ and $\widehat{Y}(\alpha_s) = \sum_{i=1}^m \widehat{Y}_i(\alpha_s)1(G_i = s)/\{m\Pr(G_i = s)\}$, where $\widehat{Y}_i(z,\alpha_s)$ and $\widehat{Y}_i(\alpha_s)$ are defined as before. When the group-level assignment entails permutation randomization, these IPW estimators are equivalent to those presented in Section 2.3.1. Assuming group-level Bernoulli randomization, it is straightforward to show the IPW estimators are unbiased. Deriving the limiting distributions of the IPW estimators is

also straightforward because $G_1,\ldots,G_n$ are independent under group-level Bernoulli randomization. For example, if (2.9) holds for $W_h = \widehat{DE}_h(\alpha_1)1(G_h=1)/\Pr(G_h=1)$, $h=1,\ldots,m$, then it follows immediately that (2.5) holds as $m\to\infty$; similarly, if (2.9) holds for $W_h = \widehat{Y}_h(0,\alpha_1)1(G_h=1)/\Pr(G_h=1) - \widehat{Y}_h(0,\alpha_0)1(G_h=0)/\Pr(G_h=0)$, then it follows immediately that (2.6) holds as $m\to\infty$. Similar results can be obtained for the total and overall effect IPW estimators. Note that no homogeneity assumptions are required here, in contrast to when there is permutation group-level randomization.

Computing Wald and Chebyshev CIs requires estimating the variances of the different IPW estimators. For the direct effect one possible estimator is $\widehat{Var}\{\widehat{DE}(\alpha_1)\} = \sum_{i=1}^m \widehat{DE}_i^2(\alpha_1)1(G_i=1)/\{m^2\Pr(G_i=1)^2\}$, which is a positively biased estimator for $Var\{\widehat{DE}(\alpha_1)\}$ with bias $\sum_{i=1}^m \overline{DE}_i^2(\alpha_1)/m^2$. To see this, note

$$\begin{aligned}
Var\{\widehat{DE}(\alpha_1)\} &= E\Big[Var\{\widehat{DE}(\alpha_1)|G_1,\ldots,G_m\}\Big] + Var\Big[E\{\widehat{DE}(\alpha_1)|G_1,\ldots,G_m\}\Big] \\
&= \sum_{i=1}^m \frac{E\Big[Var_{\alpha_1}\widehat{DE}_i(\alpha_1)1(G_i=1)\Big]}{m^2\Pr(G_i=1)^2} + \sum_{i=1}^m Var\Big[\frac{\overline{DE}_i(\alpha_1)1(G_i=1)}{m\Pr(G_i=1)}\Big] \\
&= \sum_{i=1}^m \frac{Var_{\alpha_1}\widehat{DE}_i(\alpha_1)}{m^2\Pr(G_i=1)} + \sum_{i=1}^m \frac{\overline{DE}_i^2(\alpha_1)\{1-\Pr(G_i=1)\}}{m^2\Pr(G_i=1)} \\
&= \sum_{i=1}^m \frac{E_{\alpha_1}\widehat{DE}_i^2(\alpha_1)}{m^2\Pr(G_i=1)} - \sum_{i=1}^m \frac{\overline{DE}_i^2(\alpha_1)}{m^2} \\
&= E\Big\{\sum_{i=1}^m \frac{\widehat{DE}_i^2(\alpha_1)1(G_i=1)}{m^2\Pr(G_i=1)^2}\Big\} - \sum_{i=1}^m \frac{\overline{DE}_i^2(\alpha_1)}{m^2}
\end{aligned}$$

where $E_{\alpha_1}\widehat{DE}_i^2(\alpha_1) = E\{\widehat{DE}_i^2(\alpha_1)|G_i=1\}$. Similarly, one can define $\widehat{Var}\{\widehat{IE}(\alpha_1,\alpha_0)\} = \sum_{i=1}^m \widehat{Y}_i^2(0,\alpha_1)1(G_i=1)/\{m^2\Pr^2(G_i=1)\} + \widehat{Y}_i^2(0,\alpha_0)1(G_i=0)/\{m^2\Pr^2(G_i=0)\}$, $\widehat{Var}\{\widehat{TE}(\alpha_1,\alpha_0)\} = \sum_{i=1}^m \widehat{Y}_i^2(1,\alpha_1)1(G_i=1)/\{m^2\Pr^2(G_i=1)\} + \widehat{Y}_i^2(0,\alpha_0)1(G_i=0)/\{m^2\Pr^2(G_i=0)\}$ and $\widehat{Var}\{\widehat{OE}(\alpha_1,\alpha_0)\} = \sum_{i=1}^m \widehat{Y}_i^2(\alpha_1)1(G_i=1)/\{m^2\Pr^2(G_i=1)\} + \widehat{Y}_i^2(\alpha_0)1(G_i=0)/\{m^2\Pr^2(G_i=0)\}$, as positively biased estimators for $Var\{\widehat{IE}(\alpha_1,\alpha_0)\}$, $Var\{\widehat{TE}(\alpha_1,\alpha_0)\}$ and $Var\{\widehat{OE}(\alpha_1,\alpha_0)\}$ with bias $\sum_{i=1}^m\{\overline{y}_i(0,\alpha_1) - \overline{y}_i(0,\alpha_0)\}^2/m^2$,

$\sum_{i=1}^{m}\{\overline{y}_i(1,\alpha_1)-\overline{y}_i(0,\alpha_0)\}^2/m^2$ and $\sum_{i=1}^{m}\{\overline{y}_i(\alpha_1)-\overline{y}_i(\alpha_0)\}^2/m^2$ respectively. Because these variance estimators are positively biased, Wald and Chebyshev CIs constructed using these estimators (as in the lower part of Table 2.5) are expected in practice to be conservative, i.e., cover with probability greater $1-\gamma$.

Appendix II

Proofs from Chapter 3

Proof of Proposition 1

Note

$$\begin{aligned} E\widehat{Y}^{ipw}(z,\alpha_k) &= E\Big[E\{\widehat{Y}^{ipw}(z,\alpha_k)|L_i\}\Big] \\ &= n^{-1}E\sum_{i=1}^{n}\sum_{z_i,s_i}\frac{y_i(z_i,s_i)1(z_i=z)\pi(s_i,\alpha_k)}{f(z_i,s_i|L_i)}f(z_i,s_i|L_i) \\ &= n^{-1}E\sum_{i=1}^{n}\sum_{s_i}y_i(z,s_i)\pi(s_i,\alpha_k) \\ &= \overline{y}(z,\alpha_k) \end{aligned}$$

The unbiasness for $\widehat{Y}^{ipw}(\alpha_k)$ can be proved in the same line

Proof of Proposition 2

To prove the asymptotic Normality of $\widehat{Y}^{ipw}(z,\alpha_k)$, note that this estimator is the solution to estimating equation $G_n^{ipw}(\mu)=0$ where

$$G_n^{ipw}(\mu) = \sum_{i=1}^{n}\left\{\frac{y_i(Z_i,S_i)1(Z_i=z)\pi(S_i;\alpha_k)}{f(Z_i,S_i|L_i)}-\mu\right\}$$

Large-sample properties for IPW estimators follow from the general framework of M-estimation thoery (Stefanski and Boos 2002 and Lunceford and Davidian 2004). We only sketch out some key steps here. By Taylor expansion, $0=G_n^{ipw}(\hat{\mu})=G_n^{ipw}(\mu)+\dot{G}_n^{ipw}(\mu)(\hat{\mu}-\mu)+o_p(1)$, we have $\sqrt{n}(\hat{\mu}-\mu)=\{-\dot{G}_n^{ipw}(\mu)/n\}^{-1}n^{-1/2}G_n^{ipw}(\mu)+o_p(1)$.

Note that $\dot{G}_n^{ipw}(\mu)/n \to E\{\dot{G}_n^{ipw}(\mu)/n\}$ and that $n^{-1/2}G_n^{ipw}(\mu) \xrightarrow{d} N(0, Var\{G_n^{ipw}(\mu)\}/n)$ as $n \to \infty$ thus $\sqrt{n}(\hat{\mu}-\mu)/\sigma^{ipw} \xrightarrow{d} N(0,1)$, where $(\sigma^{ipw})^2 = Var\{G_n^{ipw}(\mu)\}E\{-\dot{G}_n^{ipw}(\mu)/n\}^{-2}$ $/n = Var\{G_n^{ipw}(\mu)\}/n = E\{G_n^{ipw}(\mu)\}^2/n = \sum_{v=1}^m E\psi_v^2/n$. Similarly, note that $\widehat{Y}_h^{haj}(z,\alpha_k)$ is the solution of the estimating equation $G_{h,n}^{haj}(\mu) = 0$, where

$$G_{h,n}^{haj}(\mu) \;=\; \sum_{i=1}^{n} \frac{y_i(Z_i,S_i)\pi(S_i;\alpha_k)1(Z_i=z)}{f(Z_i,S_i|L_i)} - \mu\hat{n}_{h,z}$$

The remainder of the proof of (b) and (c) follows along the same lines as the proof of (a).

Proof of Proposition 3

To prove (a), let $\theta = (\mu, \gamma, \sigma_b^2)^T$, then $\hat{\theta} = \{\hat{Y}^{ipw}(z,\alpha_k), \hat{\gamma}, \hat{\sigma}_b^2\}^T$ is the solution of the vector equation $G_n^{ipw} = 0$, where $G_n^{ipw} = \sum_{v=1}^m \{|C_v|(\hat{Y}_v^{ipw}(z,\alpha_k) - \mu), \partial l_v\}^T$, where for the notation convenience we write $\partial\cdot = \{\partial\cdot/\partial\gamma, \partial\cdot/\partial\sigma_b^2\}$. Then

$$\begin{aligned}
\frac{\partial \hat{Y}_v^{ipw}(z,\alpha_k)}{\partial\gamma} &= |C_v|^{-1}\frac{\partial}{\partial\gamma}\sum_{i\in C_v}\frac{y_i(Z_i,S_i)1(Z_i=z)\pi(S_i;\alpha_k)}{f(Z_i,S_i|L_i)} \\
&= -|C_v|^{-1}\sum_{i\in C_v}\frac{y_i(Z_i,S_i)1(Z_i=z)\pi(S_i;\alpha_k)}{f^2(Z_i,S_i|L_i)}\frac{\partial f(Z_i,S_i|L_i)}{\partial\gamma} \\
&= -|C_v|^{-1}\sum_{i\in C_v}\frac{y_i(Z_i,S_i)1(Z_i=z)\pi(S_i;\alpha_k)}{f(Z_i,S_i|L_i)}\frac{\partial/\partial\gamma f(Z_i,S_i|L_i)}{f(Z_i,S_i|L_i)} \\
&= -|C_v|^{-1}\sum_{i\in C_v}\frac{y_i(Z_i,S_i)1(Z_i=z)\pi(S_i;\alpha_k)}{f(Z_i,S_i|L_i)}\frac{\partial l_v}{\partial\gamma} = -\hat{Y}_v^{ipw}(z,\alpha_k)\frac{\partial l_v}{\partial\gamma}
\end{aligned}$$

Similarly, $\partial\hat{Y}_v^{ipw}(z,\alpha_k)/\partial\sigma_b^2 = -\hat{Y}_v^{ipw}(z,\alpha_k)\partial l_v/\partial\sigma_b^2$, i.e., $\partial\hat{Y}_v^{ipw}(z,\alpha_k) = -\hat{Y}_v^{ipw}(z,\alpha_k)\partial l_v$. Thus,

$$E\left\{\frac{\partial G_n^{ipw}}{\partial\theta}\right\} = -\sum_{v=1}^{m}\begin{pmatrix} |C_v| & |C_v|E\hat{Y}_v^{ipw}(z,\alpha_k)\partial l_v \\ 0 & E\partial l_v^T\partial l_v \end{pmatrix}$$

$$= -\begin{pmatrix} n & \sum_{v=1}^{m}|C_v|E\hat{Y}_v^{ipw}(z,\alpha_k)\partial l_v \\ 0 & \sum_{v=1}^{m}E\partial l_v^T\partial l_v \end{pmatrix}$$

i.e.,

$$\left\{-E\frac{\partial G_n^{ipw}}{\partial\theta}\right\}^{-1} = \begin{pmatrix} n^{-1} & -\sum\limits_{v=1}^{m}|C_v|E\hat{Y}_v^{ipw}(z,\alpha_k)\partial l_v/n\{\sum\limits_{v=1}^{m}E\partial l_v^T\partial l_v\}^{-1} \\ 0 & \{\sum\limits_{v=1}^{m}E\partial l_v^T\partial l_v\}^{-1} \end{pmatrix}$$

Note that

$$E\{G_n^{ipw}G_n^{ipw^T}\} = \sum_{v=1}^{m}\begin{pmatrix} |C_v|^2E(\hat{Y}_v^{ipw}(z,\alpha_k)-\mu)^2 & |C_v|E(\hat{Y}_v^{ipw}(z,\alpha_k)-\mu)\partial l_v \\ |C_v|E(\hat{Y}_v^{ipw}(z,\alpha_k)-\mu)\partial l_v & E\partial l_v^T\partial l_v \end{pmatrix}$$

$$= \sum_{v=1}^{m}\begin{pmatrix} |C_v|^2E(\hat{Y}_v^{ipw}(z,\alpha_k)-\mu)^2 & |C_v|E\hat{Y}_v^{ipw}(z,\alpha_k)\partial l_v \\ |C_v|E\hat{Y}_v^{ipw}(z,\alpha_k)\partial l_v^T & E\partial l_v^T\partial l_v \end{pmatrix}$$

Thus,

$$\Big\{\frac{1}{n}E\frac{\partial G_n^{ipw}}{\partial\theta}\Big\}^{-1}E\{G_n^{ipw}G_n^{ipw^T}/n\}\Big\{\frac{1}{n}E\frac{\partial G_n^{ipw}}{\partial\theta}\Big\}^{-T} = \begin{pmatrix} (\sigma^{ipw})^2 - H^{ipw^T}V_{\gamma,\sigma_b^2}^{-1}H^{ipw} & * \\ * & * \end{pmatrix}$$

where $H^{ipw} = \sum_{v=1}^{m}E\hat{Y}_v^{ipw}(z,\alpha_k)\partial l_v^T/n$ is a vector, $V_{\gamma,\sigma_b^2} = \sum_{v=1}^{m}E\partial l_v^T\partial l_v/n$ and $*$ denotes some number which we do not express explicitly. Thus, when the propensity scores are unknown, we have $(\sigma_*^{ipw})^2 = (\sigma^{ipw})^2 - H^{ipw^T}V_{\gamma,\sigma_b^2}^{-1}H^{ipw}$. And since V_{γ,σ_b^2} is positive

definite, so does $V^{-1}_{\gamma,\sigma_b^2}$ and thus $H^{ipw^T} V^{-1}_{\gamma,\sigma_b^2} H^{ipw} \geq 0$, which concludes $(\sigma_*^{ipw})^2 \leq (\sigma^{ipw})^2$.

To prove (b), note that $\hat{\theta} = \{\hat{Y}_1^{haj}(z,\alpha_k), \hat{\gamma}, \hat{\sigma}_b^2\}^T$ is the solution to the vector equation $G_{1,n}^{haj} = 0$, where $G_{1,n}^{haj} = \sum_{v=1}^m \{|C_v| \hat{Y}_v^{ipw}(z,\alpha_k) - \mu \sum_{i \in C_v} \pi(Z_i;\alpha_k)/f(Z_i|L_i), \partial l_v\}$. Also note that

$$E \frac{\partial}{\partial \gamma} \left\{ \hat{Y}_v^{ipw}(z,\alpha_k) - \mu \frac{\pi(Z_i;\alpha_k)}{f(Z_i|L_i)} \right\} = -E \left\{ \hat{Y}_v^{ipw}(z,\alpha_k) \frac{\partial l_v}{\partial \gamma} - \mu \pi(Z_i;\alpha_k) \frac{\partial}{\partial \gamma} \log f(Z_i|L_i) \right\}$$

Similarly, we have $\partial\{\hat{Y}_v^{ipw}(z,\alpha_k) - \mu\pi(Z_i;\alpha_k)/f(Z_i|L_i)\}/\partial\sigma_b^2 = -\{\hat{Y}_v^{ipw}(z,\alpha_k)\partial l_v/\partial\sigma_b^2 - \mu\pi(Z_i;\alpha_k)\partial \log f(Z_i|L_i)/\partial\sigma_b^2\}$. Thus,

$$E\left\{ \frac{\partial G_{1,n}^{haj}}{\partial \theta} \right\} = - \begin{pmatrix} n & -\sum_{v=1}^m E\partial\psi_{1,v}^{haj} \\ 0 & \sum_{v=1}^m E\partial l_v^T \partial l_v \end{pmatrix}$$

where $E\partial\psi_{1,v}^{haj} = E\partial\{|C_v|\hat{Y}_v^{ipw}(z,\alpha_k) - \sum_{i\in C_v} \mu\pi(Z_i;\alpha_k)/f(Z_i|L_i)\} = -E\{|C_v|\hat{Y}_v^{ipw}(z,\alpha_k)\partial l_v - \sum_{i\in C_v} \partial \log f(Z_i|L_i)\mu\pi(Z_i;\alpha_k)\}$. i.e.,

$$\left\{ -E\frac{\partial G_{1,n}^{haj}}{\partial \theta} \right\}^{-1} = \begin{pmatrix} n^{-1} & \sum_{v=1}^m E\partial\psi_{1,v}^{haj}/n\{\sum_{v=1}^m E\partial l_v^T \partial l_v\}^{-1} \\ 0 & \{\sum_{v=1}^m E\partial l_v^T \partial l_v\}^{-1} \end{pmatrix}$$

Note that

$$E\{G_{1,n}^{haj} G_{1,n}^{haj^T}\} = \sum_{v=1}^m \begin{pmatrix} E(\psi_{1,v}^{haj})^2 & E\psi_{1,v}^{haj}\partial l_v \\ E\psi_{1,v}^{haj}\partial l_v^T & E\partial l_v^T \partial l_v \end{pmatrix}$$

Thus, $(\sigma_{1,*}^{haj})^2 = (\sigma_1^{haj})^2 + 2A^T V^{-1}_{\gamma,\sigma_b^2} H_1^{haj} + H_1^{haj^T} V^{-1}_{\gamma,\sigma_b^2} H_1^{haj}$, where $A = \sum_{v=1}^m E\psi_{1,v}^{haj}\partial l_v^T/n$ and $H_1^{haj} = \sum_{v=1}^m E\partial\psi_{1,v}^{haj^T}/n$.

To prove (c), note that $\hat{\theta} = \{\hat{Y}_2^{haj}(z,\alpha_k), \hat{\gamma}, \hat{\sigma}_b^2\}^T$ is the solution to the vector equation

$G_{2,n}^{haj}=0$, where $G_{2,n}^{haj}=\sum_{v=1}^{m}\{|C_v|[\hat{Y}_v^{ipw}(z,\alpha_k)-\mu 1(Z_i=z)\pi(S_i;\alpha_k)/f(Z_i,S_i|L_i)],\partial l_v\}^T$. Also note that

$$\frac{\partial}{\partial\gamma}\left\{\hat{Y}_v^{ipw}(z,\alpha_k)-\mu\frac{1(Z_i=z)\pi(S_i;\alpha_k)}{f(Z_i,S_i|L_i)}\right\} = -\left\{\hat{Y}_v^{ipw}(z,\alpha_k)-\mu\frac{1(Z_i=z)\pi(S_i;\alpha_k)}{f(Z_i,S_i|L_i)}\right\}\frac{\partial l_v}{\partial\gamma}$$

Similar as in the proof for Proposition 3, we have $(\sigma_{2,*}^{haj})^2=(\sigma_2^{haj})^2-H_2^{haj^T}V_{\gamma,\sigma_b^2}^{-1}H_2^{haj}$, where $H_2^{haj}=\sum_{v=1}^{m}E\{\hat{Y}_v^{ipw}(z,\alpha_k)-\mu 1(Z_i=z)\pi(S_i;\alpha_k)/f(Z_i,S_i|L_i)\}\partial l_v/n$.

Derivations for variance of IPW and Hajek estimators and their estimators assuming (3.5)

We derive the formula for ∂l_v. Recall that $l_v=l_v(\gamma,\sigma_b^2)=\log\int\prod_{i\in C_v}e_i^{Z_i}(1-e_i)^{1-Z_i}\phi(b_v)db_v$, where $e_i=\exp\{L_i\gamma+b_v\}/(1+\exp\{L_i\gamma+b_v\})$ and $\phi(\cdot)$ denotes the density function of $N(0,\sigma_b^2)$. we have $\partial e_i/\partial\gamma=e_i(1-e_i)L_i$ and that

$$\begin{aligned}\frac{\partial l_v}{\partial\gamma} &= \frac{1}{f(\{Z_i:i\in C_v\}|L_i)}\int\prod_{i\in C_v}e_i^{Z_i}(1-e_i)^{1-Z_i}\{\sum_{i\in C_v}\frac{Z_i-e_i}{e_i(1-e_i)}\frac{\partial e_i}{\partial\gamma}\}\phi(b_v)db_v\\ &= \frac{1}{f(\{Z_i:i\in C_v\}|L_i)}\int\prod_{i\in C_v}e_i^{Z_i}(1-e_i)^{1-Z_i}\{\sum_{i\in C_v}(Z_i-e_i)L_i\}\phi(b_v)db_v\\ &= \sum_{i\in C_v}Z_iL_i-\frac{\int f(\{Z_i:i\in C_v\}|L_i,b_v)\phi(b_v)\{\sum_{i\in C_v}e_iL_i\}db_v}{f(\{Z_i:i\in C_v\}|L_i)}\end{aligned}$$

Note that $\partial\phi(b_v)/\partial\sigma_b^2=\sigma_b^{-2}\phi(b_v)\{b_v^2/\sigma_b^2-1\}/2$ and thus

$$\frac{\partial l_v}{\partial\sigma_b^2}=\frac{\int f(\{Z_i:i\in C_v\}|L_i,b_v)\phi(b_v)b_v^2db_v}{2\sigma_b^4f(\{Z_i:i\in C_v\}|L_i)}-\frac{1}{2\sigma_b^2}$$

Similarly, we have

$$\frac{\partial \log f(Z_i|L_i)}{\partial \gamma} = Z_i L_i - \frac{\int f(Z_i|L_i, b_v)\phi(b_v) e_i L_i db_v}{f(Z_i|L_i)}$$

and that

$$\frac{\partial \log f(Z_i|L_i)}{\partial \sigma_b^2} = \frac{\int f(Z_i|L_i, b_v)\phi(b_v) b_v^2 db_v}{2\sigma_b^4 f(Z_i|L_i)} - \frac{1}{2\sigma_b^2}$$

Finally, note that $\hat{H}^{ipw} = \sum_{v=1}^{m} \hat{Y}_v^{ipw}(z, \alpha_k)\hat{\partial} l_v^T / n$, $\hat{V}_{\gamma,\sigma_b^2} = \sum_{v=1}^{m} \hat{\partial} l_v^T \hat{\partial} l_v / n$ are consistent estimators for H^{ipw}, V_{γ,σ_b^2}, where $\hat{\partial} l_v(\gamma, \sigma_b^2) = \partial l_v(\hat{\gamma}, \hat{\sigma}_b^2)$.

Proof of Propositions 4-5

To prove (a) in Proposition 4, recall that $\widehat{DE}_h^{haj}(\alpha_k) = g(\widehat{Y}_h^{haj}(1, \alpha_k), \widehat{Y}_h^{haj}(0, \alpha_k))$ and note that $\hat{\mu} = \{\hat{\mu}_1, \hat{\mu}_0\}^T$ for $\hat{\mu}_z = \widehat{Y}^{ipw}(z, \alpha_k)$ is the solution for estimating equation $G_n^{ipw}(\mu) = \{G_n^{ipw}(\mu_1), G_n^{ipw}(\mu_0)\}^T = 0$, where $G_n^{ipw}(\mu_z) = \sum_{v=1}^{m} |C_v|(\hat{Y}_v^{ipw}(z, \alpha_k) - \mu_z)$. Similar as in the proof of Proposition 2, we have $\sqrt{n}(\hat{\mu} - \mu) = \{-\dot{G}_n^{ipw}(\mu)\}^{-1}\sqrt{n} G_n^{ipw}(\mu) + o_p(1)$. The Normality of $\hat{\mu}$ and thus $\widehat{DE}^{ipw}(\alpha_k) = g(\hat{\mu}_1, \hat{\mu}_0)$ is obtained for continuous function g. Further we have $(\sigma^{D,ipw})^2 = \nabla g Var\{G_{h,n}^{haj}(\mu)\}\nabla g^T / n = \sum_{v=1}^{m} E\psi_v^2 / n$, where $\psi_v = \psi_v^{D,ipw}(\alpha_k) = \bigtriangledown g(\psi_v^{ipw}(1, \alpha_k), \psi_v^{ipw}(0, \alpha_k))^T$. The proofs of Propositions 4(b), 4(c) and 5 can be derived similarly.

Appendix III

Proofs from Chapter 4

Proof of Proposition 1

To prove (a), notice that $\hat{\theta} = (\widehat{Y}^{DR}(a, \alpha_k), \hat{\gamma}, \hat{\beta})^T$ is the solution of estimating equation $G_m(\theta) = (\sum_{i=1}^m \psi_i(\eta, \gamma, \beta), S_\gamma, S_\beta)^T = 0$, S_γ and S_β are log-likelihood functions from which we obtained $\hat{\gamma}$ and $\hat{\beta}$. By Taylor expansion, $0 = G_m(\hat{\theta}) = G_m(\theta) + \dot{G}_m(\theta)(\hat{\theta} - \theta) + o_p(1)$, we have $\sqrt{m}(\hat{\theta} - \theta) = \{-\dot{G}_m(\theta)/m\}^{-1} m^{-1/2} G_m(\theta) + o_p(1)$. Note that $m^{-1/2}\{G_m(\theta) - EG_m(\theta)\} \xrightarrow{d} N(0, \Sigma)$, where $\Sigma = \lim_{m\to\infty} EG_m(\theta)G_m^T(\theta)/m$. Since $ES_\gamma = 0$ and $ES_\beta = 0$, we next show that $E\psi_i(\eta, \gamma, \beta) \to 0$ and thus $EG_m(\theta) \to 0$ when either $\gamma^* = \gamma_0$ or $\beta^* = \beta_0$.

If $\hat{\gamma} \to \gamma_0$, then $\hat{f}(A_i|X_i) \xrightarrow{p} f(A_i|X_i)$ and thus

$$E\left\{ \frac{1(A = a)Y(A_i)}{\hat{f}(A_i|X_i)} \pi(A_{i(-j)}; \alpha_0) \right\} \to \overline{y}(a, \alpha_0)$$

Also note that

$$\begin{aligned}
& E\left\{ \sum_{a_{i(-j)}} \hat{\mu}(a_i, X_i)\pi(a_{i(-j)}; \alpha_0) - \frac{1(A = a)\hat{\mu}(A_i, X_i)}{\hat{f}(A_i|X_i)} \pi(A_{i(-j)}; \alpha_0) \right\} \\
= \; & E\left\{ \sum_{a_{i(-j)}} \hat{\mu}(a_i, X_i)\pi(a_{i(-j)}; \alpha_0) \right\} - E\left\{ \frac{1(A = a)\hat{\mu}(A_i, X_i)}{\hat{f}(A_i|X_i)} \pi(A_{i(-j)}; \alpha_0) \right\} \\
= \; & E\left\{ \sum_{a_{(-i)}} \hat{\mu}(a_i, X_i)\pi(a_{i(-j)}; \alpha_0) \right\} - E\left\{ \sum_{a_i} \frac{\hat{\mu}(a, a_{i(-j)}, X_i)}{\hat{f}(a, a_{i(-j)}|X_i)} \pi(a_{i(-j)}; \alpha_0) \Pr(a, a_{i(-j)}|X_i) \right\} \\
\to \; & E\left\{ \sum_{a_{(-i)}} \hat{\mu}(a_i, X_i)\pi(a_{i(-j)}; \alpha_0) \right\} - E\left\{ \sum_{a_{i(-j)}} \hat{\mu}(a, a_{i(-j)}, X_i)\pi(a_{i(-j)}; \alpha_0) \right\} = 0
\end{aligned}$$

which leads to $E\psi_i \to 0$.

If $\beta^* \to \beta_0$ then $\hat{\mu}(a_i, X_i) \xrightarrow{p} \mu(a_i, X_i)$ and thus

$$E\left\{\sum_{a_{i(-j)}} \hat{\mu}(a, a_{i(-j)}, X_i)\pi(a_{i(-j)};\alpha_0)\right\} \to \overline{y}(a,\alpha_0)$$

Also note that

$$E\left\{\frac{1(A_{ij}=a)\{Y(A_i)-\hat{\mu}(A_i,X_i)\}}{\hat{f}(A_i|X_i)}\pi(A_{i(-j)};\alpha_0)\right\} \to 0$$

which also leads to $E\psi_i \to 0$. Thus, we have $m^{-1/2}G_m(\theta) \xrightarrow{d} N(0,\Sigma)$.

We next derive $\dot{G}_m(\theta)$. Note that $\partial\psi_i/\partial\eta = -1$ and that

$$\begin{aligned}
& m^{-1}\sum_{i=1}^{m}\frac{\partial\psi_i}{\partial\gamma} \\
\xrightarrow{p} \; & m^{-1}\sum_{i=1}^{m}E\frac{\partial\psi_i}{\partial\gamma} \\
= \; & \frac{1}{n_i}\sum_{j=1}^{n_i}E\left\{-\frac{1(A_{ij}=a)}{f(A_i|X_i)}\frac{\partial\mu(A_i,X_i)}{\partial\gamma}+\sum_{a_{i(-j)}}\frac{\partial\mu(a,a_{i(-j)},X_i)}{\partial\gamma}\pi(a_{i(-j)};\alpha_0)\right\} \\
= \; & 0
\end{aligned}$$

Similarly,

$$\begin{aligned}
& m^{-1}\sum_{i=1}^{m}\frac{\partial\psi_i}{\partial\beta} \\
\xrightarrow{p} \; & m^{-1}\sum_{i=1}^{m}E\frac{\partial\psi_i}{\partial\beta} \\
= \; & \frac{1}{n_i}\sum_{j=1}^{n_i}E\left\{\frac{1(A_{ij}=a)\{Y(A_i)-\mu(A_i,X_i)\}}{\hat{f}(A_i|X_i)}\frac{\partial\log f(A_i|X_i)}{\partial\beta}\pi(A_{i(-j)};\alpha_0)\right\} \\
= \; & \frac{1}{n_i}\sum_{j=1}^{n_i}E\left\{\frac{1(A_{ij}=a)E\{Y(A_i)-\mu(A_i,X_i)|A_i,X_i\}}{\hat{f}(A_i|X_i)}\frac{\partial\log f(A_i|X_i)}{\partial\beta}\pi(A_{i(-j)};\alpha_0)\right\} \\
= \; & 0
\end{aligned}$$

Thus,

$$\dot{G}_m(\theta)/m \xrightarrow{p} - \begin{pmatrix} 1 & 0 & 0 \\ 0 & * & * \\ 0 & * & * \end{pmatrix}$$

i.e.,

$$\{\dot{G}_m(\theta)/m\}^{-1} \xrightarrow{p} - \begin{pmatrix} 1 & 0 & 0 \\ 0 & * & * \\ 0 & * & * \end{pmatrix}$$

where $*$ denotes some number we do not express explicitly. Thus, we have the desired result. The proof for (b) can be obtained in a similar fashion.

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