Sensitivity analysis of unmeasured confounding in tailored treatment rules estimated by dynamic weighted ordinary least squares (dWOLS)

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Abstract

The idea of precision medicine is to use patient-level data to develop personalized treatment regimes for each individual. Dynamic treatment regimes (DTRs) formalize this idea and use statistical tools to learn from data and personalize treatment to optimize treatment decisions. There are different methods to estimate the optimal DTR. We focused on the dynamic weighted ordinary least squares (dWOLS), a regression-based approach to estimating the parameters of a DTR.

In practice, we must often use observational data to determine personalized treatment strategies. This poses several difficulties, particularly due to potential unmeasured confounders which can create biased results. To evaluate the impact of potential unmeasured confounding factors, sensitivity analysis methods are used.

In this thesis, we developed a simple and easy-to-use sensitivity analysis method. We introduced a sensitivity parameter that partially captures the impact of violations of the no unmeasured confounding assumption. The sensitivity parameter is obtained by evaluating the mean of the unmeasured confounder conditional on the measured covariates. The performance of the method is assessed in various scenarios through simulation studies. Finally, we applied this method to the National Health and Nutrition Examination Survey (NHANES) data to examine how physical activity recommendations can be tailored at an individual level while accounting for unmeasured confounding.

Résumé

La notion de la médecine de précision est d'utiliser les données au niveau du patient pour développer des régimes de traitement personnalisés pour chaque individu. Les régimes de traitement dynamiques (RTD) formalisent cette idée et utilisent des outils statistiques pour apprendre des données afin de personnaliser le traitement et d'optimiser les décisions de traitement. Il existe de différentes méthodes pour estimer le RTD optimal. Nous nous sommes concentrés sur la méthode des moindres carrés ordinaires pondérés dynamiques, une approche basée sur la régression pour estimer les paramètres d'un RTD.

En pratique, nous devons souvent utiliser des données non-randomisées pour déterminer des stratégies de traitement personnalisées. Cela pose plusieurs difficultés, notamment en raison de potentiels facteurs de confusion non mesurés qui peuvent mener à des résultats biaisés. Pour évaluer l'impact des facteurs de confusion potentiels non mesurés, des méthodes d'analyse de sensibilité sont utilisées.

Dans cette thèse, nous avons développé une méthode d'analyse de sensibilité simple et facile à utiliser. Nous avons introduit un paramètre de sensibilité qui capture partiellement l'impact des violations de l'hypothèse de l'absence de facteurs de confusion non mesurés. Le paramètre de sensibilité est obtenu en évaluant la moyenne du facteur de confusion non mesuré conditionnellement aux covariables mesurées. Les performances de la méthode sont évaluées dans divers scénarios à l'aide d'études de simulation. Enfin, nous avons appliqué cette méthode aux données de l'Enquête nationale sur la santé et la nutrition (≪ NHANES ≫) pour examiner comment les recommandations d'activité

physique peuvent être adaptées au niveau individuel, tout en tenant compte d’un facteur de confusion non mesuré.

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Contribution of Authors

Dr. Erica Moodie, Dr. Juliana Schulz, and Elham Bahrampour conducted the original research presented in this thesis. Elham Bahrampour authored all the chapters and performed the data analysis. The thesis was reviewed and proofread by Dr. Erica Moodie and Dr. Juliana Schulz.

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Abbreviations

AIPWE augmented inverse probability weighted estimator

BMI body mass index

CDC Centers for Disease Control and Prevention

DGM data generating mechanism

DTR dynamic treatment regime

dWOLS dynamic weighted ordinary least squares

IPW inverse probability weights

IPWE inverse probability weighted estimator

ITR individual treatment rule

MC Monte Carlo

NCHS National Center for Health Statistics

NHANES National Health and Nutrition Examination Survey

NUC no unmeasured confounding

PS propensity score

SD standard deviation

SE standard error

SUTVA stable unit treatment value assumption

Chapter 1

Introduction

In clinical practice, the notion of precision medicine or personalized medicine is that healthcare should be tailored at the individual patient level. Rather than considering a traditional "one size fits all" approach, a personalized strategy suggests that clinicians should tailor medical decisions to account for patient response heterogeneity. The goal of precision medicine is to find the treatment which will optimize a patient's clinical outcome. There are obviously numerous benefits from considering a personalized approach to patient care, including better treatment efficacy, fewer side effects, etc. [4, 41].

In practice, patient care typically involves several decisions that are made sequentially. As such, personalized treatment strategies will often consist of a sequence of decision rules, where a treatment decision at any given point in time could (and likely will) affect future decisions. The theory of dynamic treatment regime (DTR) formalizes this idea and consists of a general framework for determining the optimal sequence of treatments. The notion of tailored interventions is not limited to medicine or therapeutic treatment of illness. Tailored recommendations can also be used for educational interventions, advertising, or behavioural interventions or recommendations. The latter example will be the focus of the real data analysis undertaken in Chapter 5.

A DTR considers patient information such as medical history, socio-demographic factors, and genetic information as input and recommends a treatment, or sequence of treatments as output. It formalizes the notion of precision medicine by tailoring treatment regimes such that the clinical outcome of interest is optimized [17]. In the illustrative analysis of Chapter 5, tailoring variables are primarily socio-demographic.

There are several statistical approaches that can be used for estimating optimal treatment strategies. There are two broad classes for DTR estimation: regression-based and value search methods. Within the class of regression-based methods, there are also several different approaches including G-estimation [31], Q-learning [40, 47] and dynamic weighted ordinary least squares (dWOLS) [15, 45], the last of which is the focus of this thesis.

In regression-based methods, we model the conditional expectation of the outcome of clinical interest, given patient information and history. The optimal treatment rules are then estimated by sequentially optimizing the outcome at each treatment stage, starting from the last stage and working backwards (full details on estimation will be provided in Chapter 2). The validity of this approach to estimating personalized treatment rules is based on several standard assumptions. One of these assumptions is that of no unmeasured confounding (NUC), an assumption that is often violated in research that relies on non-experimental data such as electronic health records. Violations of the assumption of NUC may lead to biased estimation, thereby yielding sub-optimal treatment strategies.

The issues that arise due to unmeasured confounding have been widely discussed in the literature. Several authors have proposed various sensitivity analyses that can be used to evaluate the impacts of violations to NUC [12,33]. The objective of this thesis is to explore the sensitivity of dWOLS estimation to violations of the NUC assumption [33]. In particular, we propose a sensitivity analysis approach that attempts to capture the effect of an unmeasured confounder in a single sensitivity parameter.

The thesis includes six chapters. In Chapter 2, the literature relevant to dWOLS and sensitivity analyses of unmeasured confounders is reviewed. The basic concepts, notations, and assumptions are also given. Then a new sensitivity analysis approach in the dWOLS framework is proposed in Chapter 3. In Chapter 4, several simulation studies are summarized. The first set of simulations investigates the performance of dWOLS estimators in the presence of unmeasured confounding. The second set of simulations explores incorporating a sensitivity parameter in dWOLS in order to compensate for unmeasured confounding. Chapter 5 considers a real data analysis applying the proposed method to the National Health and Nutrition Examination Survey (NHANES) data. The conclusion and further discussion are presented in Chapter 6.

Chapter 2

Literature Review

In this chapter, we provide a general review of the literature on DTRs as well as estimation methods for determining the optimal treatment strategy. We will focus on regression-based estimation methods, specifically dWOLS. We will then describe some existing approaches for conducting sensitivity analysis which is the main focus of our work. By providing an overview of the literature on dWOLS and sensitivity analysis techniques, we aim to lay the foundation for the methodology proposed in the following chapter.

2.1 Dynamic Treatment Regime

As stated in Chapter 1, a DTR consists of a sequence of treatment rules, each of which uses patient information as input and recommends the treatment which optimizes some outcome of clinical interest. The optimal DTR is determined by comparing the expected response under different treatment strategies, and selecting the regime that leads to the best expected outcome [4]. In the multi-stage setting, the optimal DTR improves the expected outcome in long-term conditions by constructing a sequence of treatment rules that will result in the best outcome over an extended period [26]. In the single-stage setting, on the other hand, the optimal DTR consists of a single decision rule yielding the optimal outcome and is referred to as an individual treatment rule (ITR).

Determining the optimal DTR raises some challenges, as past treatments impact both present and future treatment decisions, therefore, there is a need for sophisticated models [46]. There exists several statistical frameworks for estimating the optimal DTR, including value-search techniques and regression-based methods. This work will focus on the latter approach, particularly dWOLS, as will be discussed in more detail in Section 2.3. Before discussing the methods for determining the optimal DTR, we will first discuss the type of data typically used in such problems, the required notations, and the assumptions that are necessary for DTR estimation and inference.

2.2 Data Type, Notation, and Assumptions

To estimate an optimal DTR, data must provide sufficient information. Different components must be considered and recorded to obtain the optimal DTR, including patient treatment history, the outcome variable of interest, covariates that predict the outcome, and any potential confounders. The goal is to provide treatment recommendations at critical decision points, namely at the time that a treatment decision is made. In this thesis, we consider a binary "treatment" variable that refers to either receiving the treatment or not. Ideally, the covariates summarize all relevant patient information and history, not only for tailoring treatment but also for predicting the outcome and controlling confounding. The final component is the outcome, that is, the response variable of interest, which is impacted by covariates and treatment.

Data Type

A data source may be categorized as either experimental or observational (i.e., not randomized or non-experimental), and the latter is the focus of this thesis. Observational studies are commonly used in clinical research, particularly when randomized experiments are not feasible. Examples of observational data sources include electronic health records, cohort studies, and case-control studies.

Working with observational data can be challenging and, when not analyzed carefully, can lead to biased inference. Such biases include detection bias, recall bias, and selection bias, all of which can lead to biases in estimations [16]. Under certain assumptions, however, unbiased estimation is still possible when using observational data.

Observational data are also subject to confounding, which happens when the effect of the treatment is mixed with the effect of another covariate. In general, confounding occurs when the relationship between the treatment and outcome is distorted by the confounding variable(s). Failure to account for confounding can lead to biased estimates of the treatment effect on the outcome. Therefore, identifying and adjusting for confounding variables is essential in any causal analysis [11].

In this thesis, we aim to develop a sensitivity analysis approach for adjusting for unmeasured confounders. As such, the methods developed in this thesis are relevant in the case of observational data, that is, in the absence of randomization.

Notation

In DTR, the decision points or time points at which a treatment decision is made, are defined as stages. In a multi-stage setting, a DTR consists of a set of decision rules for all stages. Throughout this thesis, the random variables and observed values are indicated by upper case and lower case letters, respectively. We will consider the following notation in a multi-stage DTR:

- X_j: the covariates before beginning the j^{th} treatment
- A_j: a binary variable representing assigned treatment at the j^{th} stage
- H_j: the patient history before the j^{th} treatment i.e., $H_j = (X_1, ..., X_j, A_1, ..., A_{j-1})$
- Y: the final outcome measuring the patient's response to the sequence of treatment.

In this thesis, the notation $Y(a)$ represents the potential outcome that would be observed if the individual receives treatment a. In the case of binary treatment, $Y(1)$ signifies the potential outcome in the presence of treatment, whereas $Y(0)$ corresponds to the potential outcome in the absence of treatment.

Figure 2.1 shows the causal diagram of a simplified two-stage study with no unmeasured confounders. In this thesis, we focus primarily on the single-stage setting, although we also consider some cases with two stages in the simulations.

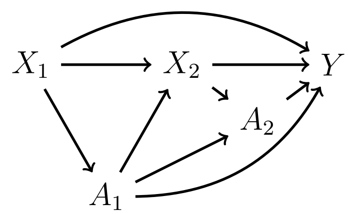

Figure 2.1: Causal diagram for a two-stage example with no unmeasured confounders. The interactions are not shown in this graph.

Assumptions

Several standard assumptions are required for estimating the optimal treatment strategy, as will now be detailed for a one-stage setting. An essential assumption is the axiom of consistency. It states that the potential outcome is equal to the observed outcome when we have observed treatment, i.e.,

$$Y = AY(1) + (1 - A)Y(0).$$

Another assumption is known as the stable unit treatment value assumption (SUTVA), stability, or "no interference" assumption by some authors. By this assumption, there is no interaction between units such that one person's outcome is not affected by other individuals' treatments [4]. The next assumption is positivity which means that all treatment levels are possible for any covariate combination [32]. In causal inference, positivity means we only assess causal effects in people who are eligible for all levels of treatment.

Anyone who would either always, or never, receive the treatment should be excluded from the study. Thus, the positivity assumption ensures that every combination of covariates in a population has a non-zero probability of treatment, i.e.,

$$P(A = a|X = x) > 0 \quad \forall a \in \{0, 1\} \quad \text{and} \quad \forall x.$$

We also assume that the treatment and potential outcome conditional on covariates are independent [30]; this is known as no unmeasured confounding (NUC) which is a type of exchangeability property i.e.,

$$A \perp Y(A)|X.$$

A violation of this assumption typically implies that there is at least one variable C that is associated with both outcome and treatment [36], though other structures in causal diagrams can lead to NUC violations as well. We refer to such variables C as unmeasured confounders. Recall that a confounder C is such that it is associated with the outcome and treatment, but is not on the causal pathway between the treatment and outcome. In this sense, the time-ordering or direction of association plays an important role: a confounder must occur before receiving the treatment and is thus not influenced by the treatment itself. Note that if a variable lies on the causal pathway between the treatment and outcome, it is referred to as a mediator. The assumption of NUC is also known as strong ignorability.

To estimate the optimal DTR, many estimation approaches rely on confounding adjustment methods via the "treatment model" or "propensity score (PS)" which is defined as the coarsest function

$$\pi(x) = P(A = 1|X = x)$$

where A is a binary treatment and X is a set of the measured covariates. The PS models the probability of a patient receiving a treatment based on confounding variables.

It ensures that covariate distributions are balanced between treatment groups, allowing matching on it for estimation of treatment effects that is not biased by confounding. To estimate the PS, logistic regression models are often used [35].

Having discussed the notations and required assumptions, in the next section, we review the dynamic weighted ordinary least squares (dWOLS) method for estimating the optimal DTR, which is the focus of this work.

2.3 dWOLS Methods

Different statistical approaches can be used for estimating optimal treatment strategies. Two main classes to estimate the optimal DTR are value search methods [27, 32, 48] and regression-based methods [15, 26, 31, 40, 45, 47]. Value search methods parameterize the treatment rules and find the expected outcome associated with each regime. In other words, the value search approach focuses on the parameters of the treatment rule rather than the parameters of the mean outcome model [32]. The optimal treatment strategy is then determined by comparing the expected outcome (value) of each treatment rule, and selecting the rule with the highest expected value. The inverse probability weighted estimator (IPWE) [32] and the augmented inverse probability weighted estimator (AIPWE) [48] are two methods that fall within the value search class.

In this thesis, we focus on regression-based methods which involve using regression models to estimate the effect of treatment on patient outcome. Regression-based methods model the contrast between optimal and observed treatment and find the treatment that optimizes the estimated mean outcome. In a multi-stage setting, these methods begin with the optimal DTR estimation of the last stage and move backward to the first stage using regressions.

In regression-based approaches for estimating the optimal DTR, the blip function is the main modelling component pertinent to DTR estimation. In a single-stage setting, the blip function $\gamma(X, A; \psi)$ is defined as the difference between the expected outcome under treatment a and the expected outcome under a^{ref}, i.e.,

$$\gamma(x, a; \psi) = E[Y(a) - Y(a^{ref})|X = x].$$

In this method, the outcome model $E[Y|X = x, A = a; \beta, \psi]$ is written as $m(X; \beta) + \gamma(X, A; \psi)$, where $m(X; \beta)$ is the treatment-free model defined as the expected outcome under the baseline treatment (typically, $a^{ref} = 0$). We thus use a classical outcome model with a new notation. The advantage of this structure is its ability to isolate the crucial terms that require precise specification (blip function). In the context of DTR, blip parameters ψ represent critical parameters for decision-making, while treatment-free model parameters β are considered nuisance parameters. A related concept to the blip function is the regret function which is the difference between the expected outcome under the optimal treatment (a^{opt}) and the expected outcome under the assigned treatment a and is defined as

$$\mu(x, a; \psi) = E[Y(a^{opt}) - Y(a)|X = x].$$

The regret is related to the blip function, specifically,

$$\mu(x, a; \psi) = \gamma(x, a^{opt}; \psi) - \gamma(x, a; \psi).$$

Thus, the regression-based methods for DTR estimation separate the linear terms that interact with the treatment in the outcome model. In most cases, the forms of $\psi^T a x^{\psi}$ and $\beta^T x^{\beta}$ are considered for $\gamma(X = x, A = a; \psi)$ and $m(X = x; \beta)$, respectively. Notations of x^{ψ} and x^{β} refer to the variables that are included in the models, i.e., X^{ψ} and X^{β} are the subsets of the covariate X relevant for the blip and treatment-free models, respectively.

G-estimation [31], Q-learning [40,47], and dWOLS [15,45] are examples of regression-based estimation methods. In Q-learning method, the focus is on the quality function

(Q-function) defined as

$$Q(X = x, A = a; \beta, \psi) = E[Y|X = x, A = a].$$

For a one-stage setting, the estimation process is then using a linear regression

$$Q(x, a; \beta, \psi) = \beta^T x^\beta + \psi^T a x^\psi$$

and the optimal DTR is the one which maximizes the Q-function, i.e.,

$$\widehat{a^{opt}} = argmax_a Q(x, a; \hat{\beta}, \hat{\psi}).$$

For a one-stage example, the G-estimation method defines the functions

$$G(X; \beta) = Y - \gamma(X, A; \psi) \quad \text{and} \quad S(X, A) = \frac{\partial}{\partial \psi} \gamma(X, A; \psi).$$

We then posit a model for $E[G(X; \psi)|X; \beta]$ which can be a linear model

$$E[G(x; \psi)|x; \beta] = \beta^T x^\beta.$$

The $\hat{\psi}$ can then be obtained by solving the equation

$$U(\psi) = \sum_{i=1}^{n} (G(\psi) - E[G(X = x, \psi; \beta)])(S(A, X) - E[S(A, X)|X = x]) = 0.$$

G-estimation and Q-learning are similar in concept, but we need more modeling in G-estimation which provides increased robustness to model miss-specification. G-estimation in the form shown above is doubly-robust in that the blip parameter estimators are consistent if at least one of the treatment or treatment-free models is correctly specified under the NUC assumption since the two terms in parentheses are then conditionally independent ensuring a zero mean estimating function. The Q-learning method is relatively simple but is not doubly-robust, and depends on correctly specifying the Q-function models [31]. The dWOLS method is, in some sense, a combination of these two methods: it borrows the doubly-robustness feature of G-estimation and the intuitiveness of Q-learning. In this thesis, we focus on the dWOLS approach, as it is doubly-robust and easy to implement [45].

The dWOLS approach, first introduced by Wallace and Moodie [45], considers weighted regression models for estimating the optimal DTR. More specifically, dWOLS associates specific weights to observations and fits a weighted regression model for the outcome given (i.e., conditional on) the covariates and treatment allowing for interactions between treatment and (typically a subset) of these covariates.

In the dWOLS framework, another assumption is required, in addition to the identifiability assumptions (SUTVA, positivity, and NUC) discussed in Section 2.2. We assume that the blip function is correctly specified and its form is linear. Further, we require that all tailoring variables are also included in the treatment-free model.

Under the above assumptions, the blip parameter estimates are doubly-robust when the weights satisfy the balancing property defined as

$$(1-\pi(X=x))w(A=0,X=x)=\pi(X=x)w(A=1,X=x). \tag{2.1}$$

Wallace and Moodie [45] explored several different weight functions that satisfy the balancing property within the dWOLS framework. This thesis utilizes two commonly employed weights, namely, the absolute value weights and the inverse probability weights (IPW). The former is specified as $w(A=a,X=x)=|a-P(A=1|X=x)|$ and the latter is defined as $w(A=a,X=x)=\frac{1}{P(A=a|X=x)}$.

For a one-stage setting, dWOLS estimation consists of fitting a weighted linear regression model of the form

$$E(Y|x,a;\beta,\psi)=\beta^T x^\beta+\psi^T a x^\psi,$$

and the optimal DTR is the one which maximizes the blip function, i.e.,

$$\widehat{a^{opt}} = argmax_a \gamma(x, a; \hat{\psi}).$$

In a multi-stage setting of DTR, dWOLS starts from the last stage and sequentially works backward to the first stage. In evaluating the impact of stage-specific treatments, the potential outcome approach is utilized to determine the hypothetical outcome if all subsequent decisions were made optimally. Here, a pseudo-outcome $\tilde{Y}_j$ is considered for stage j, assuming that the patient will follow the optimal treatment plan from that stage forward. Considering a J-stage example, the pseudo-outcome at the j^{th} stage is defined as

$$\tilde{Y}_j = Y + \sum_{k=j+1}^{J} \mu_k(X_k, A_k; \hat{\psi}_k).$$

The last stage pseudo-outcome is the observed outcome, i.e., $\tilde{Y}_J = Y$.

Note that in a multi-stage setting, a similar approach to creating a pseudo-outcome is considered in G-estimation and Q-learning, however, the exact calculations are not identical (though they are the same in expectation under the correct specification of the outcome model). In Q-learning, the pseudo-outcome is calculated as the predicted outcome under the optimal treatment, relying on the $\hat{\beta}$ and is defined as the maximum of $Q_{j+1}(X_{j+1}, a_{j+1}; \hat{\beta}_{j+1}, \hat{\psi}_{j+1})$ for $j = 1, ..., J-1$ i.e.,

$$\tilde{Y}_j^{\textit{Q-learning}} = max_{a_{j+1}} Q_{j+1}(X_{j+1}, a_{j+1}; \hat{\beta}_{j+1}, \hat{\psi}_{j+1}),$$

and $\tilde{Y}_J^{\textit{Q-learning}} = Y$.

In G-estimation, the pseudo-outcome is the observed outcome removing the expected effect of observed treatment and adding the expected effect of the optimal treatment. Similarly to dWOLS method, the pseudo-outcome can be expressed as regret functions as

$$\tilde{Y}_j^{\textit{G-estimation}} = Y + \sum_{k=j+1}^{J} \mu_k(X_k, A_k; \hat{\psi}_k)$$

for $j = 1, ..., J-1$ and $\tilde{Y}_J^{\textit{G-estimation}} = Y$.

In summary, in the dWOLS method, we need to specify a treatment model $\pi(x)$, a linear blip function $\gamma(x, a; \psi) = \psi^T a x^\psi$, and the treatment-free model $m(x; \beta) = \beta^T x^\beta$ for each stage. The stage j blip parameter estimators $\hat{\psi}_j$ are then obtained by a weighted regression of the pseudo-outcome $\tilde{Y}_j$ and finally, the stage j optimal treatment $\widehat{a_j^{opt}}$ is calculated. The sequence of optimal decisions at each stage creates the optimal DTR $\widehat{a^{opt}} = (\widehat{a_1^{opt}}, \widehat{a_2^{opt}}, ..., \widehat{a_{J-1}^{opt}}, \widehat{a_J^{opt}})$.

Consider a two-stage example and assume that a larger value of Y is more beneficial in a clinical sense. To find the optimal DTR, we begin by modelling the observed outcome at the second stage (Y). If $\hat{\psi}_2$ is the estimated parameter, the backward dynamic programming strategy will be $\widehat{a_2^{opt}} = argmax_a \gamma_2(x_2, a_2; \hat{\psi}_2)$. The inference for the first stage will then be based on the pseudo-outcome at first stage $\tilde{Y}_1 = Y + \mu_2(x_2, a_2; \hat{\psi}_2)$ which accounts for the estimated optimal stage two treatment $\widehat{a_2^{opt}}$. The optimal stage one treatment will be $\widehat{a_1^{opt}} = argmax_a \gamma_1(x_1, a_1; \hat{\psi}_1)$ where $\hat{\psi}_1$ is the dWOLS estimated parameter using $\tilde{Y}_1$. Therefore, the optimal decision rule for a two-stage regime is $\widehat{a^{opt}} = (\widehat{a_1^{opt}}, \widehat{a_2^{opt}})$. Algorithm 1 shows the dWOLS method in a two-stage example, where a higher value of Y is considered more beneficial, and the blip function is assumed to be linear in the form of $\gamma_i(x_i, a_i; \psi) = \psi^T a_i x_i^\psi$ for $i = 1, 2$.

Note that the dWOLS method in Wallace and Moodie [45] was developed specifically for binary treatment and a continuous outcome. Schulz and Moodie [37] proposed a generalized dWOLS method appropriate for both continuous or categorical treatment. Other extensions have since been developed for censored outcomes [38] and discrete outcomes [3].

Regarding the DTR in software, Wallace et al. [46] introduced DTRreg, an R package, which implements the dWOLS. To perform the simulation analysis in Section 4.1, the DTRreg package is used. In the next section, an examination of the existing literature pertaining to sensitivity analysis is presented.

Algorithm 1 dWOLS Method: two-stage example

1: Specify the following
   - second-stage treatment model ($\pi_2(x_2)$)
   - second-stage blip function ($\gamma_2(x_2, a_2; \psi)$)
   - second-stage treatment-free model ($m_2(x_2; \beta)$)

2: Calculate weights w_2 that satisfy equation 2.1

3: Estimate $\hat{\psi}_2$ by performing a weighted regression of Y using the second-stage blip and second-stage treatment-free functions in the model

4: Construct the second-stage optimal treatment

$$\widehat{a_2^{opt}} = \begin{cases} 1, & x_2^{\psi} \hat{\psi}_2 > 0 \\ 0, & otherwise \end{cases}$$

5: Calculate the first-stage pseudo-outcome

$$\tilde{Y} = Y + \mu_2(x_2, a_2; \hat{\psi}_2)$$

6: Specify the followings
   - first-stage treatment model ($\pi_1(x_1)$)
   - first-stage blip function ($\gamma_1(x_1, a_1; \psi)$)
   - first-stage treatment-free model ($m_1(x_1; \beta)$)

7: Calculate weights w_1 that satisfy equation 2.1

8: Estimate $\hat{\psi}_1$ by performing a weighted regression of $\tilde{Y}$ using the first-stage blip and first-stage treatment-free functions in the model

9: Construct the first-stage optimal treatment

$$\widehat{a_1^{opt}} = \begin{cases} 1, & x_1^{\psi} \hat{\psi}_1 > 0 \\ 0, & otherwise \end{cases}$$

10: Obtain the optimal DTR $\widehat{a^{opt}} = (\widehat{a_1^{opt}}, \widehat{a_2^{opt}})$

2.4 Sensitivity Analysis

Observational studies require careful consideration since they are subject to hidden biases. While conducting such a study, the analyst must identify and account for all potential confounding factors that could distort the treatment effect. Confounding variables can be measured or unmeasured. Age, gender, and socioeconomic status (income, education level, occupation, wealth, etc.) are typical examples of measured confounders that can be adjusted for in various ways. Unmeasured confounders, on the other hand, are variables that affect both the treatment and the outcome but were not documented and therefore cannot be directly adjusted for.

In general, sensitivity analysis is a technique used in various fields, including engineering, economics, politics, epidemiology, and physics [6, 13, 20, 24], to assess how changes in the variables or assumptions of a model can affect the outcome. Sensitivity analysis can thus be used to assess the robustness of estimators to potential sources of unmeasured confounding by examining the impact of unmeasured confounders. By assessing the potential impact of unmeasured confounders on outcomes, a sensitivity analysis can provide additional insights that can inform decision-making [1, 29].

There are several methods for conducting sensitivity analyses, which can be classified as either probabilistic or deterministic [28]. This thesis focuses on a probabilistic sensitivity analysis, which involves positing probability distributions of unknown covariates to examine bias and using these distributions to conduct sensitivity analysis.

In contrast, deterministic sensitivity analysis involves varying one or more parameters of interest in a fixed manner rather than considering them as arising or being drawn from probability distributions [28]. A deterministic sensitivity analysis is limited by the fact that it treats parameters as though they are known, which is not always the case, especially when dealing with unmeasured confounders.

In clinical research, the idea of sensitivity analysis was first introduced by Cornfield et al. [5] in 1959, when they investigated the relationship between smoking and lung cancer and assessed whether unknown variables could have confounded the association. Their main question was, "How strong should the unmeasured confounder be in order to explain away the association between the treatment and outcome?" They concluded that if the strength of the unmeasured confounder that is required to explain away the association is too large, then the association between the treatment and the outcome cannot be explained only by one factor. Instead, it suggests a causal relationship between the treatment and outcome. Since then, various methods have been proposed to conduct sensitivity analyses. Rosenbaum and Rubin [34] focused on the effect of unmeasured confounders on the relationship between a binary treatment and a binary outcome. They examined the relationship by adjusting for both a binary unmeasured confounder and an observed categorical covariate. They performed a sensitivity analysis by assessing the odds ratios between the unmeasured confounder and both the treatment and the outcome, determining the values at which the causal effect becomes insignificant.

In the presence of unmeasured confounding in observational studies, several methods are available to conduct sensitivity analyses and assess the impact of this confounding on the outcome. These methods include the use of E-values, Bayesian approaches, Monte Carlo (MC) methods, and G-estimation. In the following sections, we will provide a concise discussion of each of these approaches.

The E-value is a measure that determines the minimum strength of association required between an unmeasured confounding variable and both the treatment A and outcome Y to account for the observed relationship between A and Y. VanderWeele et al. [43] stated that sensitivity analysis could be employed with this approach to assess how strong an unmeasured confounder would have to be to explain away an observed treatment–outcome relationship.

There are different formulas to calculate the E-value for an estimate such as risk ratio, odds ratio, hazard ratio, etc. For instance, for an observed risk ratio (RR), the E-value is calculated based on the following formula

$$\mathrm{E-value} = \begin{cases} \mathrm{RR} + \sqrt{\mathrm{RR}(\mathrm{RR}-1)}, & \mathrm{RR} > 1 \\ \frac{1}{\mathrm{RR}} + \sqrt{\frac{1}{\mathrm{RR}}(\frac{1}{\mathrm{RR}}-1)}, & \mathrm{RR} < 1. \end{cases}$$

Suppose for example that an observed risk ratio is 3 ($\mathrm{RR} = 3$), using the E-value, the analyst can make statements such as: "The observed risk ratio of 3 could be explained away by an unmeasured confounder that was associated with both A and Y by a risk ratio of 5.45 each, but weaker confounding could not do so" [43]. Some more examples and discussions on this method are provided in [19, 22].

Ioannidis et al. [14] raised some concerns about the limitations and potential misinterpretation of the E-value method. They pointed out that certain unrealistic assumptions are made when using E-values, notably that there is only one unmeasured confounder. Another assumption is that the unmeasured confounder C is equally associated with the treatment A and outcome Y, which is often not the case. Additionally, the assumption that a single variable can capture the effects of multiple confounders is implausible, as is the assumption that there is no interaction between the effects of the unmeasured confounder C and the treatment A and the outcome Y. VanderWeele et al. provided guidance on how to avoid the potential misuse of the E-value approach in [7, 44].

Bayesian approaches and MC methods are probabilistic sensitivity analyses to assess the impact of any potential unmeasured confounding on the outcome. Bayesian sensitivity analyses use a statistical framework based on prior probabilities and likelihood functions to estimate the treatment effect, while MC sensitivity analysis is a simulation-based approach that uses random sampling to estimate the causal effect [39]. More specifically, MC sensitivity analysis can involve randomly sampling values from the probability distributions for the parameters influencing bias caused by unmeasured confounder and then evaluating the model outcome for each sample. By repeating this process many times, a distribution of model outcomes is generated, which can be used to estimate how the treatment effect changes due to the unmeasured confounding and the uncertainty associated with this bias. The Bayesian sensitivity analysis method, on the other hand, involves specifying a prior distribution for the unmeasured confounder, creating a model for the probability of the data given the unmeasured confounder, and finally, using Bayes' theorem, calculating the posterior distribution of the causal effect that accounts for the bias due to unmeasured confounding [23, 39].

G-estimation has also been used to carry out sensitivity analyses. Hernán and Robins employed G-estimation to examine the sensitivity of effect estimates to different assumptions [12]. To perform a sensitivity analysis using G-estimation, they created a candidate potential outcome defined as $H(\psi) = Y - \gamma(X, A; \psi)$, and considered the model

$$\text{logit}[\text{P}(A = 1|H(\psi), X = x)] = \lambda_0 + H(\psi)x^T\lambda_1 + x^T\lambda_2.$$

Under the NUC assumption, the value of λ_1 should be zero. They estimated the value of ψ by fitting a logistic regression model and finding the value of ψ that resulted in a value of zero for $\hat{\lambda}_1$. When there is unmeasured confounding, the value of λ_1 is not zero and a sensitivity analysis can be conducted by changing the value of λ_1 and examining how it affects the estimated treatment regime.

Vancak and Sjölander also considered G-estimation to conduct sensitivity analysis [42]. They parameterized the mean of the counterfactual outcome with a single sensitivity parameter to capture the bias due to an invalid instrumental variable. In causal inference, instrumental variables are used to study treatment effects in the presence of unmeasured confounding. A valid instrumental variable is associated with the treatment and only influences the outcome through the treatment, avoiding any confounding with the outcome. On the other hand, an invalid instrumental variable directly affects the outcome apart from its impact on the treatment, which violates the assumption of NUC. Vancak and Sjölander performed a sensitivity analysis to assess the impact of an invalid instrumental variable by considering a reasonable range of values for the sensitivity parameter to determine the effect of the bias on the outcome [42].

Rose et al. proposed a MC sensitivity analysis to correct for bias in the estimation of DTRs in the presence of unmeasured confounders [33]. They captured the bias in the estimators by specifying the dependence of the unmeasured confounder on all other measured confounders and treatments.

Consider the following outcome model

$$E[Y|X = x, A = a, C = c; \beta, \psi, \beta_c] = x^T\beta + ax^T\psi + \beta_c c, \tag{2.2}$$

where β_c is the coefficient for the unmeasured confounder C. They performed a MC sensitivity analysis by specifying the mean of the unmeasured confounder conditional on the covariate X and treatment A, $E[C|X = x, A = a; \alpha]$ such that α denotes the parameters of the model as well as specifying a probability distribution for the parameter β_c. When C is continuous, α will be given by a linear regression model and if C is binary, α will be given by a logistic regression model.

They then sampled α and β_c from specified prior distributions, captured the bias by imputing the values of C, and finally, calculated the bias-adjusted estimation of ψ by using the dWOLS method $\psi^{\hat{adj}} = \hat{\psi} - \widehat{bias}(\hat{\psi})$ where $\hat{\psi}$ is the dWOLS estimates with imputed C and $\widehat{bias}(\hat{\psi}) = E(\hat{\psi}) - \psi$ using estimates for C and β_c. This analysis by Rose et al. [33] includes a complex method which requires considering the full distribution of $C|X, A$. It can also be difficult to implement in realistic settings.

We proposed a general yet simple method of sensitivity analysis inspired by Rose et al. In Chapter 3, we detail the proposed method which only relies on specifying the relationship between the unmeasured confounder and at least one other measured covariates. This simpler method may help to (partially) capture the bias in dWOLS estimators with unmeasured confounding by considering the distribution of $C|X$. We will explore this approach and assess whether this method can fully, or only partially, eliminate bias resulting from unmeasured confounding.

2.5 Summary

In this chapter, relevant background information was provided and a review of the literature on sensitivity analysis was given. More specifically, we have briefly introduced value search and regression-based approaches for DTRs. We then reviewed the notations and assumptions required in the dWOLS framework. A more detailed review of the dWOLS approach was provided, as this work focuses on this specific estimation technique.

We reviewed the literature on sensitivity analysis for assessing the impact of unmeasured confounding. We have described different methods of analyzing sensitivity such as E-values, Bayesian approaches, MC methods, and G-estimation. Borrowing from the MC approach considered in [33], in this work we propose a simpler sensitivity analysis method for dWOLS when the NUC assumption may be violated.

In the next chapter, we will describe how to execute the proposed sensitivity analysis approach to adapt the estimation of the optimal DTR in the dWOLS framework in the presence of unmeasured confounding. In Chapter 4, the proposed approach is evaluated in different simulation studies.

Chapter 3

Sensitivity Analysis of dWOLS Estimators

As mentioned in Chapter 2, a sensitivity analysis has been developed for unmeasured confounding in dynamic treatment regimes (DTRs) in [33]. This method, however, was fairly complex and required many assumptions, some of which would be difficult to meet in practice. In this chapter, we propose a simplification of the method considered in [33]. The proposed approach is a similar, yet simpler, way to adjust estimation by only specifying the relationship between unmeasured confounders and all other measured confounders. A new sensitivity analysis method was also introduced in [42] which was developed for invalid instrumental variables in the G-estimation framework. In this chapter, we show that the simplified approach of Rose et al. that we explore here is in fact a similar implementation to that of [33].

3.1 Proposed Approach

The main objective of this thesis is to characterize and reduce the bias of dWOLS estimators in the presence of unmeasured confounders. The directed acyclic graph (DAG) in Figure 3.1 illustrates a causal model including a treatment A and an outcome Y with an unmeasured confounder C and a measured covariate X. The arrows from C confirm that the model is affected by the unknown confounder.

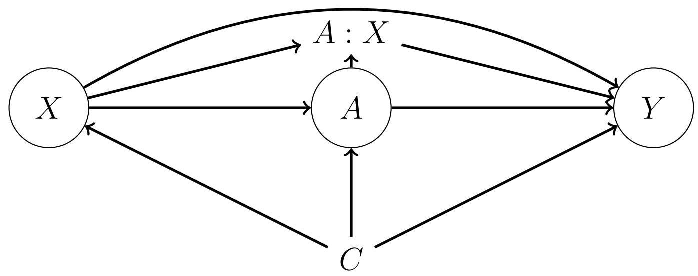

Figure 3.1: Causal diagram with interaction ($A : X$), where C is an unmeasured confounder.

Recall that in the dWOLS framework, the outcome model is represented as a function of the covariate X and the treatment variable A. Specifically, the outcome model can be expressed in terms of a treatment-free model, a blip function, and an error term, denoted as

$$\begin{aligned} Y(X, A = a; \beta, \psi) &= m(X; \beta) + \gamma(X, A = a; \psi) + \varepsilon \\ &= X^T\beta + aX^T\psi + \varepsilon. \end{aligned}$$

In the presence of an unmeasured confounder C, the outcome model is modified to include a confounder coefficient β_c, resulting in the expression

$$Y(X, C, A = a; \beta, \beta_c, \psi) = X^T\beta + \beta_c C + aX^T\psi + \varepsilon.$$

The causal parameters $\psi = (\psi_0, \psi_1)$ represent the average treatment effect, where ψ_0 is the coefficient of A and ψ_1 is the coefficient of the interaction term $A : X$. The mean causal effect can be expressed as

$$E[Y|X = x, C, A = a] - E[Y|X = x, C, A = 0] = a(\psi_0 + \psi_1 x),$$

which characterizes the difference in outcome means between treated and untreated subjects, after adjusting for the confounder C and the covariate X.

The true causal effect is thus obtained by adjusting for A, X, and C. Since we do not have any data on C, adjusting for C is ignored and the NUC assumption is violated. When the NUC assumption is violated and we only adjust for A and X in our model, there will then be an indirect relationship between A and Y through C that distorts the true causal relationship. The estimation of the true treatment effect will thus be biased due to not controlling for C.

To address this issue, we propose a method that approximates the true expectation of C given X and A with a linear function that depends only on X, i.e.,

$$E[C|A,X] \approx \eta_0 + \eta_1 X.$$

In fact, we use X as a surrogate for C and try to adjust for covariate X and unmeasured confounder C simultaneously by creating an offset. This offset would help us to adjust for the relationship between Y and X, as well as the relationship between Y and C.

If there is a linear relationship between X and C, we should be able to do a good job in approximating the estimation. However, if the dependency of C on X is not linear, the estimation may be less accurate, but it can still reduce the bias. Note that this linear relationship ignores the relationship between C and A, although we know there must be a relationship between C and A since C is a confounder.

We rewrite the expected outcome using the linear function of $E[C|A,X]$:

$$\begin{aligned}
E[Y|A,X] &= E_{C|A,X}(E[Y|A,X,C]) \\
&= \beta_0 + \psi_0 A + \beta_x X + \beta_c E[C|A,X] + \psi_1 AX \\
&\approx \beta_0 + \psi_0 A + \beta_x X + \beta_c(\eta_0 + \eta_1 X) + \psi_1 AX \\
&= (\beta_0 + \beta_c\eta_0) + \psi_0 A + \psi_1 AX + (\beta_x + \beta_c\eta_1)X \\
&= \alpha_0 + \psi_0 A + \psi_1 AX + \alpha^* X.
\end{aligned}$$

Therefore, $E[Y|A, X]$ is approximated by $\alpha_0 + \psi_0 A + \psi_1 AX + \alpha^* X$ where

$$\alpha^* = \beta_x + \beta_c \eta_1 \tag{3.1}$$
$$\alpha_0 = \beta_0 + \beta_c \eta_0.$$

We now propose to estimate the treatment effect ψ_0 and ψ_1 using the dWOLS method. We can obtain $\hat{\psi}_0$ and $\hat{\psi}_1$ by fitting a weighted ordinary regression model with A and AX in the model and an offset of αX, assuming that we know the true value of α denoted by α^*. Note that the function αX may not capture all of the effect of the unmeasured C, and we may still have some bias due to C left even after adjusting for αX.

In real data, we do not know the value of α^* and so we must find a plausible range of values. Based on the Formula 3.1, α must account for $E[C|X]$. We thus need to consider how strong the relationship between the unmeasured confounder C and covariate X is so that we can come up with a guess of a plausible range for α. We can either infer the relationship between C and X from outside data or may use the estimates from literature that propose a value or a range for α.

After finding a plausible $\alpha-$range, we carry out a sensitivity analysis to account for uncertainty in the value of α. The algorithm 2 shows the procedure to carry out a sensitivity analysis to find adjusted $\hat{\psi}_0$ and $\hat{\psi}_1$.

Algorithm 2 Proposed MC sensitivity analysis: one-stage example

```
1: Calculate the propensity score π = P(A = 1|X)
2: Calculate the weights ŵ
3: for α_j ∈ α−range do
4:     Estimate ψ̂_0^{adj−j} and ψ̂_1^{adj−j} by standard weighted ordinary least squares regression
   including A and AX in the outcome model and an offset of α_j X.
5: end for
```

Having described the details of the proposed method, in the next section, we provide demonstrations of the proposed method by presenting several examples, including a linear model that violates the assumption of NUC. These examples serve to illustrate how to determine the value of α^*.

3.2 Examples

To illustrate the implication of the nonzero value of α, we focus on a linear model with unmeasured confounder C. We assume the causal structure as illustrated in the DAG in Figure 3.1. We consider three one-stage examples with a single covariate (X), an unmeasured confounder (C), and a binary treatment (A). In all examples, Uni refers to a Uniform distribution, Ber is a Bernoulli distribution, N is a Normal distribution, and the expit function is defined as $\mathrm{expit}(u) = \frac{\exp(u)}{1+\exp(u)}$. In all of the examples, the mean outcome is given by $\beta_0 + \beta_x x + \beta_c c + a(\psi_0 + \psi_1 x)$ where the parameters of interest are ψ_0 and ψ_1.

As outlined in the previous section, to estimate the parameters of interest, we first need to find the value of α that accounts for $E[C|X]$. We begin by using Bayes' theorem to find the distribution of $C|X$. Then, we obtain the dWOLS estimators $\hat{\psi}_0$ and $\hat{\psi}_1$ by a weighted ordinary least squares regression including an offset αX. The following examples show the procedure to find the value of α.

Example 1: The first one-stage example's data generating mechanism (DGM) is as follows

$$\begin{aligned}
C &\sim \mathrm{Uni}(0,1) \\
X|C = c &\sim \mathrm{Ber}(c) \\
A|X = x, C = c &\sim \mathrm{Ber}(\mathrm{expit}(\gamma_0 + \gamma_x x + \gamma_c c)) \\
Y|C = c, X = x, A = a &\sim \mathrm{N}(\beta_0 + \beta_x x + \psi_0 a + \psi_1 a x + \beta_c c, 1).
\end{aligned}$$

We start the calculations by finding the distribution of $C|X$. Using Bayes' theorem

$$\begin{aligned}
f(C|X) &= \frac{f(X|C)f(C)}{\int_C f(X|C)f(C)dc} \\
&= \frac{c^x(1-c)^{(1-x)} \times 1}{\int c^x(1-c)^{(1-x)}dc} \\
&= 2c^x(1-c)^{(1-x)}.
\end{aligned}$$

Therefore, the distribution of $C|X$ is $\text{Beta}(X+1, 2-X)$ and $E[C|X] = \eta_0 + \eta_1 X = \frac{X+1}{3}$. Thus, $\eta_0 = \eta_1 = \frac{1}{3}$ and based on the Formula 3.1, $\alpha^* = \beta_x + \frac{1}{3}\beta_c$.

Note that we could also calculate the value of α numerically by MC averaging based on the Formula 3.1 equation and the fact that $C|X \sim Beta(1+X, 2-X)$. In this method, we draw $C' \sim \text{Beta}(1+x, 2-x)$ for a big sample size (e.g., $n = 1,000,000$) and compute the $f(X = x, C' = c') = \beta_x + \beta_c c'$. The average of the generated values of the function $f(X, C')$ is an estimate of α^*. This method can also be used to confirm that the value of α was calculated correctly.

Example 2: In this example, unmeasured confounder C and measured confounder X are from Bernoulli distributions. Let p is fixed, the DGM is as follows

$$
\begin{gathered}
C \sim \text{Ber}(p) \\
X|C = c \sim \text{Ber}(\xi_0 + \xi_1 c) \\
A|X = x, C = c \sim \text{Ber}(\text{expit}(\gamma_0 + \gamma_x x + \gamma_c c)) \\
Y|C = c, X = x, A = a \sim \text{N}(\beta_0 + \beta_x x + \psi_0 a + \psi_1 a x + \beta_c c, 1).
\end{gathered}
$$

We again need to find the distribution of $C|X$. Using Bayes' theorem

$$
\begin{aligned}
P(C = c|X = 0) &= \frac{P(X = 0|C = c)P(C = c)}{\sum_{C\in\{0,1\}} P(X = 0|C)P(C)} \\
&= \frac{(1-\xi_0-\xi_1 c)p^c(1-p)^{1-c}}{(1-\xi_0)(1-p) + (1-\xi_0-\xi_1)p} \\
&= \begin{cases} \frac{(1-\xi_0-\xi_1)p}{1-\xi_0-\xi_1 p}, & c = 1 \\ \frac{(1-\xi_0)(1-p)}{1-\xi_0-\xi_1 p}, & c = 0. \end{cases}
\end{aligned}
$$

Therefore, the distribution of $C|X = 0$ is $\text{Ber}(\frac{(1-\xi_0-\xi_1)p}{1-\xi_0-\xi_1 p})$.

Similarly, we find the distribution of $C|X=1$

$$
\begin{aligned}
P(C=c|X=1) &= \frac{P(X=1|C=c)P(C=c)}{\sum_{C\in\{0,1\}} P(X=1|C)P(C)} \\
&= \frac{(\xi_0+\xi_1 c)p^c(1-p)^{1-c}}{\xi_0(1-p)+(\xi_0+\xi_1)p} \\
&= \begin{cases} \frac{(\xi_0+\xi_1)p}{\xi_0+\xi_1 p}, & c=1 \\ \frac{\xi_0(1-p)}{\xi_0+\xi_1 p}, & c=0. \end{cases}
\end{aligned}
$$

Therefore, the distribution of $C|X=1$ is $\mathrm{Ber}(\frac{(\xi_0+\xi_1)p}{\xi_0+\xi_1 p})$. Thus, we have

$$
\begin{aligned}
E[C|X=1] &= \eta_0+\eta_1 = \frac{(\xi_0+\xi_1)p}{\xi_0+\xi_1 p}, \\
E[C|X=0] &= \eta_0 = \frac{(1-\xi_0-\xi_1)p}{1-\xi_0-\xi_1 p}.
\end{aligned}
$$

We can find the value of η_1 as follows:

$$
\begin{aligned}
\eta_1 &= E[C|X=1]-E[C|X=0] \\
&= \frac{(\xi_0+\xi_1)p}{\xi_0+\xi_1 p} - \frac{(1-\xi_0-\xi_1)p}{1-\xi_0-\xi_1 p} \\
&= \frac{\xi_1 p(1-p)}{(\xi_0+\xi_1 p)(1-\xi_0-\xi_1 p)}.
\end{aligned}
$$

Now we can obtain the value of α^* based on the Formula 3.1,

$$
\alpha^* = \beta_x + \beta_c \frac{\xi_1 p(1-p)}{(\xi_0+\xi_1 p)(1-\xi_0-\xi_1 p)}.
$$

Example 3: This example considers Normal distributions for unmeasured confounder C and measured confounder X. The DGM is as follows

$$
\begin{aligned}
C &\sim \mathrm{N}(0.5, 0.5) \\
X|C = c &\sim \mathrm{N}(c, 0.5) \\
A|X = x, C = c &\sim \mathrm{Ber}(\mathrm{expit}(\gamma_0 + \gamma_x x + \gamma_c c)) \\
Y|C = c, X = x, A = a &\sim \mathrm{N}(\beta_0 + \beta_x x + \psi_0 a + \psi_1 ax + \beta_c c, 1).
\end{aligned}
$$

We find the distribution of $C|X$ by Bayes' theorem

$$
\begin{aligned}
f(C|X) &\propto f(X|C)f(C) \\
&\propto \exp\{\frac{-1}{2} \times 2 \times (c^2 - c + \frac{1}{4} + x^2 - 2xc + c^2)\} \\
&\propto \exp\{\frac{-1}{2} \times 4 \times (c^2 - 2c(\frac{1+2x}{4}) + (\frac{1+2x}{4})^2\} \\
&\propto \exp\{\frac{-1}{2}\frac{(c - \frac{1+2x}{4})^2}{\frac{1}{4}}\}.
\end{aligned}
$$

Therefore, the distribution of $C|X$ is $\mathrm{N}(\frac{1+2x}{4}, \frac{1}{4})$ and $E[C|X] = \eta_0 + \eta_1 X = \frac{1+2x}{4}$. Thus, $\eta_0 = \frac{1}{4}$, $\eta_1 = \frac{1}{2}$, and based on the Formula 3.1, $\alpha^* = \beta_x + \frac{1}{2}\beta_c$.

These examples showed how we can find the value of α^*. As explained in the motivation for the approach, we propose approximating the true expectation of C given X and A with a linear function that depends only on X:

$$
E[C|A, X] \approx \eta_0 + \eta_1 X.
$$

In the examples here, we have focused only on the relationship between C and X, without regard for how it may be modified by A. This may be a reasonable approach in settings where the distributions of and the dependence between X and C are well-understood, but in practice these calculations are likely not feasible. In a real data analysis, it may be necessary to determine a plausible range of α from external data or subject-matter knowledge. After calculating the value of α or estimating its range, we can obtain estimators of interest using dWOLS with a weighted ordinary least squares regression including an offset αX.

3.3 Summary

In this chapter, we showed how a sensitivity analysis can be conducted by employing a single sensitivity parameter to construct adjusted dWOLS estimators of $\psi = (\psi_0, \psi_1)$ by offsetting the X effect according to α. For the linear causal model and a (measured) binary covariate X, we expressed $E[Y|X, A]$ as a function of the observed data by specifying the distribution of $C|X$. In more realistic settings where it is not possible to determine the value of sensitivity parameter α^*, we can consider a reasonable range of α. Finally, the parameter ψ is estimated for each value of α in the range.

In fact, since C also causally affects both treatment A and outcome Y, in order to consistently estimate ψ_0 and ψ_1, we would need to consider the dependency of C on X, A, and Y. This is the approach taken by Rose et al. [33]. However, this approach requires correctly specifying even more complex dependences, which is even less likely to be achieved in practice than the specification required in our proposal.

The proposed method aims to capture much of the confounding by a very straightforward analysis which only includes specifying the distribution of $C|X$. Thus, applying this simple method may help to eliminate much of the bias; the reason that all of the bias may not be captured is that the entire confounding relationship was not fully accounted for. In Section 4.2, the method has been applied to different scenarios and we examine its effectiveness in reducing bias.

Chapter 4

Simulations

In this chapter, the results from several simulation studies are provided. To demonstrate the impact of violating the NUC assumption, we focused on estimation of the optimal treatment rule using the dWOLS method in the first set of simulations. The second set of simulations consisted of a sensitivity analysis in the presence of unmeasured confounding. The following subsections detail the results and main findings from these analyses.

4.1 Impact of NUC Violations on dWOLS

The main goal of this study was to explore the impact of unmeasured baseline confounding on dWOLS estimators. Estimation was considered using two types of weights: absolute value weights and inverse probability of treatment weights. Several scenarios were explored in order to assess the impact of omitting certain confounders on the estimation, focusing on the case of two unmeasured confounders. We present a detailed outline of the simulation study plan, following the ADEMP guidelines [25, 46]. This plan includes key elements such as the data generating mechanism, simulation estimand, estimation method, and performance metrics. After providing this description, we present the study's results.

4.1.1 Data Generation

We focused on a two-stage example with a single covariate at stage one and stage two (X_1 and X_2, respectively), binary treatment at each stage (A_1 and A_2), and two potentially unmeasured confounders (C_1 and C_2). We assumed $X_1 \sim \mathrm{N}(0,1)$, $X_2 \sim \mathrm{N}(1.25X1, 1)$, $C_1 \sim \mathrm{Ber}(0.5)$, $C_2 \sim \mathrm{N}(-0.5, 0.5)$, and binary treatment $A_i \sim \mathrm{Ber}(\mathrm{expit}(X_i + C_1 + C_2))$ for $i = 1, 2$. We considered the following outcome model

$$Y = \exp(X_1) + X_1^3 + C_1 + C_2 - \mu_1 - \mu_2 + \varepsilon$$

where $\varepsilon \sim \mathrm{N}(0,1)$ and μ is the regret function defined as follows

$$\mu_1 = (A_1^{opt} - A_1)(1 + X_1)$$
$$\mu_2 = (A_2^{opt} - A_2)(1 + X_2).$$

4.1.2 Estimand, Methods, and Performance Metrics

In this example, the true data generating blip function is defined as $\gamma_1 = A_1(1 + X_1)$ and $\gamma_2 = A_2(1 + X_2)$ for stage 1 and 2, respectively. Thus, the blip parameters are given by $\psi_i = (\psi_{i0}, \psi_{i1})$ for each stage $i = 1, 2$. The true blip parameters are $\psi_{10} = \psi_{11} = \psi_{20} = \psi_{21} = 1$ and the two treatment rules are thus

$$A_1^{opt} = 1_{\psi_{10}+\psi_{11}X_1>0} = 1_{1+X_1>0} = 1_{X_1>-1}$$
$$A_2^{opt} = 1_{\psi_{20}+\psi_{21}X_2>0} = 1_{1+X_2>0} = 1_{X_2>-1}$$

where the function 1 is an indicator function, i.e., $1_{X>-1}$ is equal to 1 when $X > -1$, and it is equal to 0 otherwise.

For two different sample sizes of 1000 and 5000, we generated 500 datasets. In each iteration, we computed the dWOLS estimates using two weights: $w_1(a, x) = |a - P(A =$

$1|X = x)|$ and $w_2(a, x) = \frac{1}{P(A=a|X=x)}$; in what follows, we refer to these as the "absolute value" and "inverse" weights. The following three analyses were considered:

- Analysis 1: treatment model and treatment-free model are correctly specified
- Analysis 2: only treatment model is correctly specified
- Analysis 3: only treatment-free model is correctly specified

In Section 4.1.3, we discuss the results from two different set-ups in a two-stage setting, however, we first describe the estimand of interest and the performance metrics. Note that throughout, the same forms of model misspecification were considered at both stages.

Recall that the blip parameter estimators obtained from the dWOLS method are doubly-robust [45], i.e., the blip parameter estimators are consistent if at least one of the treatment or treatment-free models is correctly specified. This is precisely what we will demonstrate here, and then demonstrate the impact of misspecifications of the model including those that arise due to missing confounders.

In a regression-based framework, the outcome model $E[Y|X = x, A = a]$ can typically be parameterized as follows

$$E[Y|X = x, A = a] = m(x; \beta) + \gamma(x, a; \psi)$$

where $\gamma(x, a; \psi)$ and $m(x; \beta)$ are blip function and treatment-free models, respectively. In our simulation set-up, the outcome mean model is

$$\begin{aligned} E(Y|X_1, A_1, X_2, A_2, C_1, C_2) = {} & \exp(X_1) + X_1^3 + C_1 + C_2 - A_1^{opt}(1 + X_1) \\ & + A_1(1 + X_1) - A_2^{opt}(1 + X_2) + A_2(1 + X_2). \end{aligned}$$

We can express the mean outcome in terms of the second-stage treatment-free and blip models denoted by m_2 and γ_2, respectively, as follows

$$
\begin{aligned}
m_2(X_1, A_1, X_2, C_1, C_2) &= \exp(X_1) + X_1^3 + C_1 + C_2 - A_1^{opt}(1 + X_1) \\
&\quad + A_1(1 + X_1) - A_2^{opt}(1 + X_2) \\
\gamma_2(A_2, X_2, A_1, X_1, C_1, C_2) &= A_2(1 + X_2)
\end{aligned}
$$

Since $A_2^{opt} = 1_{1+X_2>0}$, the sign of $(1 + X_2)$ determines the optimal treatment at the second stage. For the first interval, we calculate the pseudo-outcome

$$
\begin{aligned}
\tilde{Y} = Y + \gamma_2(A_2^{opt}) - \gamma_2(A_2) &= \exp(X_1) + X_1^3 + C_1 + C_2 - A_1^{opt}(1 + X_1) + A_1(1 + X_1) \\
&\quad - A_2^{opt}(1 + X_2) + A_2(1 + X_2) + \varepsilon + A_2^{opt}(1 + X_2) - A_2(1 + X_2) \\
&= \exp(X_1) + X_1^3 + C_1 + C_2 - A_1^{opt}(1 + X_1) + A_1(1 + X_1) + \varepsilon.
\end{aligned}
$$

Thus, the conditional expectation $E[\tilde{Y}|X_1, A_1, C_1, C_2]$ is

$$
E[\tilde{Y}|X_1, A_1, X_2, A_2, C_1, C_2] = \exp(X_1) + X_1^3 + C_1 + C_2 - A_1^{opt}(1 + X_1) + A_1(1 + X_1)
$$

which has the following components

$$
\begin{aligned}
m_1(X_1, A_1, X_2, C_1, C_2) &= \exp(X_1) + X_1^3 + C_1 + C_2 - A_1^{opt}(1 + X_1) \\
\gamma_1(A_2, X_2, A_1, X_1, C_1, C_2) &= A_1(1 + X_1)
\end{aligned}
$$

where m_1 and γ_1 denote the first-stage treatment-free and blip models, respectively. So, the correct models are as follows

- Treatment model at stage one: $A_1 \sim X_1 + C_1 + C_2$
- Treatment-free model at stage one: $\sim \exp(X_1) + X_1^3 + C_1 + C_2 - A_1^{opt} - A_1^{opt} X_1$
- Treatment model at stage two: $A_2 \sim X_2 + C_1 + C_2$

- Treatment-free model at stage two: $\sim \exp(X_1)+X_1^3+C_1+C_2+A_1(1+X_1)-A_1^{opt}(1+X_1)-A_2^{opt}(1+X_2)$.

The model specifications considered in the three analyses are summarized in Table 4.1.

Table 4.1: Model specification for analysis 1, 2, and 3 (where the true models include the optimal treatment terms)

Analysis	Item-Stage	Model
1	treatment - stage 1	$A_1 \sim X_1 + C_1 + C_2$
	treatment-free - stage 1	$\sim \exp(X_1) + X_1^3 + C_1 + C_2 - A_1^{opt} - A_1^{opt} X_1$
	treatment - stage 2	$A_2 \sim X_2 + C_1 + C_2$
	treatment-free - stage 2	$\sim \exp(X_1) + X_1^3 + C_1 + C_2 + A_1(1+X_1)$ $-A_1^{opt}(1+X_1) - A_2^{opt}(1+X_2)$
2	treatment - stage 1	$A_1 \sim X_1 + C_1 + C_2$
	treatment-free - stage 1	$\sim X_1$
	treatment - stage 2	$A_2 \sim X_2 + C_1 + C_2$
	treatment-free - stage 2	$\sim X_1 + X_2$
3	treatment - stage 1	$A_1 \sim 1$
	treatment-free - stage 1	$\sim \exp(X_1) + X_1^3 + C_1 + C_2 - A_1^{opt} - A_1^{opt} X_1$
	treatment - stage 2	$A_2 \sim 1$
	treatment-free - stage 2	$\sim \exp(X_1) + X_1^3 + C_1 + C_2 + A_1(1+X_1)$ $-A_1^{opt}(1+X_1) - A_2^{opt}(1+X_2)$

Note that the correct specifications here are in fact impossible to fit in practice since they rely precisely on the primary targets of interest, namely A_1^{opt} and A_2^{opt}. Thus, we considered more realistic specifications that exclude these optimal terms. Note that this implies that the "true" treatment-free models will in fact be misspecified.

The primary goal of personalized medicine is to estimate the optimal DTR from the data, and the optimal DTR is that which yields the maximum possible outcome. A useful metric for evaluating the estimated optimal treatment rule is the value function, which is defined as $V^a = E[Y(A=a)]$. Amongst various estimated rules, the one with the largest value function is considered the best. It is observed that estimated rules with greater value functions exhibit less bias. Note that the greatest value for a value function is $V^{A^{opt}}$. Thus, along with reporting parameter estimates $\hat{\psi}_{10}$, $\hat{\psi}_{11}$, $\hat{\psi}_{20}$, and $\hat{\psi}_{21}$, the value function of the estimated rules ($V^{\hat{A}^{opt}}$) help us in comparing the dWOLS estimators. We used a large sample size $N = 10,000$ with fixed values of X_{1N}, X_{2N}, and ε_N (for the errors on Y) that are generated according to the known (true) DGM. We then allocated treatment according to the estimated optimal treatment for each of the replicates in the simulation and computed the value function under the estimated optimal treatment. We also computed the proportion of times that the estimated optimal decision rules agree with the true optimal decision rules. We reported the following three metrics as well as the value of V for each estimated rule:

- Prop.A_1: agreement of A_1 only
- Prop.A_2: agreement of A_2 only
- Prop.A_1 and A_2: agreement of A_1 and A_2.

The test set of data is generated using the same set-up previously described.

4.1.3 Results

Figure 4.1 and Table 4.2 illustrate the estimated blip parameters under the 3 analyses as shown in Table 4.1. Note that the y-axis scale varies in the individual plots. As one can see the dWOLS estimates are unbiased using these 3 analyses. In terms of weights, the estimates are unbiased using both weights, however, there is less variability with absolute value weights. The larger sample size results in less variability, as would be expected.

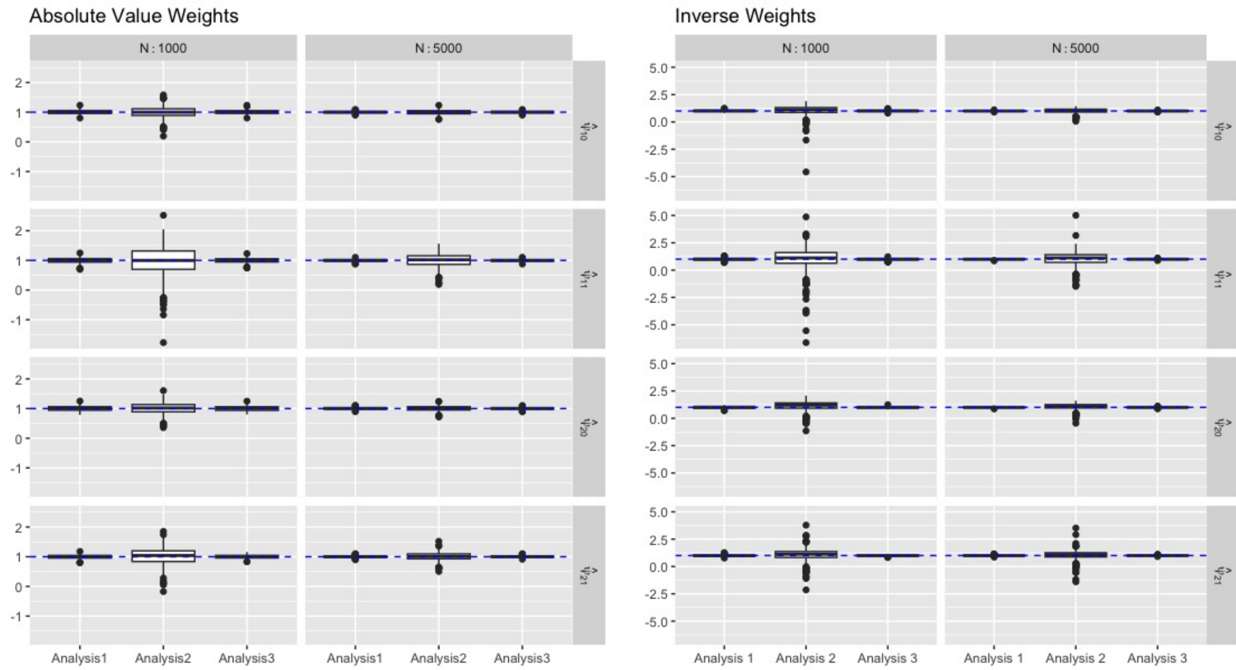

Figure 4.1: Empirical distribution of the estimated blip parameters over 500 simulated datasets for Analysis 1, 2, and 3. The true value of the parameters is indicated by a dashed horizontal line.

Table 4.2: Empirical mean and standard error (SE) of estimated blip parameters over 500 simulated datasets for Analysis 1, 2, and 3 where the true models include the optimal treatment terms and the true values are $\psi_{10} = \psi_{11} = \psi_{20} = \psi_{21} = 1$. This information is also presented in Figure 4.1.

	Weights	n	Analysis 1	Analysis 2	Analysis 3
$\hat{\psi}_{10}$ (SE)	absolute value	1000	1.00 (0.07)	0.99 (0.18)	1.00 (0.07)
$\hat{\psi}_{11}$ (SE)			1.00 (0.08)	1.01 (0.47)	1.00 (0.08)
$\hat{\psi}_{20}$ (SE)			1.00 (0.08)	1.01 (0.19)	1.00 (0.08)
$\hat{\psi}_{21}$ (SE)			1.01 (0.07)	1.01 (0.30)	1.01 (0.06)
$\hat{\psi}_{10}$ (SE)	inverse		1.00 (0.08)	1.04 (0.41)	1.00 (0.07)
$\hat{\psi}_{11}$ (SE)			1.01 (0.09)	1.05 (1.04)	1.00 (0.08)
$\hat{\psi}_{20}$ (SE)			1.00 (0.10)	1.10 (0.50)	1.00 (0.08)
$\hat{\psi}_{21}$ (SE)			1.00 (0.08)	1.05 (0.70)	1.01 (0.06)
$\hat{\psi}_{10}$ (SE)	absolute value	5000	1.00 (0.03)	1.01 (0.08)	1.00 (0.03)
$\hat{\psi}_{11}$ (SE)			1.00 (0.04)	1.00 (0.22)	1.00 (0.04)
$\hat{\psi}_{20}$ (SE)			1.00 (0.03)	1.01 (0.08)	1.00 (0.03)
$\hat{\psi}_{21}$ (SE)			1.00 (0.03)	1.01 (0.13)	1.00 (0.03)
$\hat{\psi}_{10}$ (SE)	inverse		1.00 (0.04)	1.02 (0.22)	1.00 (0.03)
$\hat{\psi}_{11}$ (SE)			1.00 (0.04)	1.02 (0.68)	1.00 (0.04)
$\hat{\psi}_{20}$ (SE)			1.00 (0.04)	1.04 (0.34)	1.00 (0.03)
$\hat{\psi}_{21}$ (SE)			1.00 (0.04)	1.07 (0.63)	1.00 (0.03)

By considering the true underlying data generating models, the results show that the estimated parameters are consistent if at least one of the treatment or treatment-free models is correctly specified. As noted above, these model specifications are idealized since in reality, we are not able to obtain the true optimal treatments (recall that the optimal treatment is a function of the true blip parameters, which we do not know). Since A_1^{opt} and A_2^{opt} are unknown, the model specifications cannot include these terms. A more realistic approach is then to consider a slightly misspecified treatment-free model for each stage which omits the terms involving the stage-specific optimal treatments. Table 4.3 details the model specifications considered for each stage in each of the three analyses.

Table 4.3: Model specifications for analysis 1, 2, and 3. The models do not include the optimal terms, and thus the treatment-free models are incorrectly specified for all three analyses, but Analyses 1 and 2 correctly specific the treatment models.

Analysis	Item-Stage	Model
1	treatment - stage 1	$A_1 \sim X_1 + C_1 + C_2$
	treatment-free - stage 1	$\sim X_1 + \exp(X_1) + X_1^3 + C_1 + C_2$
	treatment - stage 2	$A_2 \sim X_2 + C_1 + C_2$
	treatment-free - stage 2	$\sim X_1 + X_2 + \exp(X_1) + X_1^3 + C_1 + C_2 + A_1(1 + X_1)$
2	treatment - stage 1	$A_1 \sim X_1 + C_1 + C_2$
	treatment-free - stage 1	$\sim X_1$
	treatment - stage 2	$A_2 \sim X_2 + C_1 + C_2$
	treatment-free - stage 2	$\sim X_1 + X_2$
3	treatment - stage 1	$A_1 \sim 1$
	treatment-free - stage 1	$\sim X_1 + \exp(X_1) + X_1^3 + C_1 + C_2$
	treatment - stage 2	$A_2 \sim 1$
	treatment-free - stage 2	$\sim X_1 + X_2 + \exp(X_1) + X_1^3 + C_1 + C_2 + A_1(1 + X_1)$

Note that the data generating model can be either based on the blip function or based on the regret function; the latter is considered in this chapter. The data generating process can be devised such that the treatment-free models do not depend on the optimal terms (A^{opt}), however, these scenarios are often unrealistic. The following DGM is an example of one based on the blip function

$$
\begin{aligned}
X_1 &\sim \mathrm{N}(0,1)\\
A_1|X_1 = x_1 &\sim \mathrm{Ber}(\mathrm{expit}(-2 + 2x_1))\\
X_2|A_1 = a_1, X_1 = x_1 &\sim \mathrm{N}(0.5, 0.5)\\
A_2|A_1 = a_1, X_1 = x_1, X_2 = x_2 &\sim \mathrm{Ber}(\mathrm{expit}(-2 + 2x_1 + x_2 - a_1))\\
Y|A_1 = a_1, X_1 = x_1, X_2 = x_2, A_2 = a_2 &\sim \mathrm{N}(0.2 - a_1 + 2a_2 + 0.5x_1 + 0.2x_2, 1).
\end{aligned}
$$

The treatment-free models do not include the optimal treatment terms. However, for the parameters in the DGM to correspond to the true causal treatment effects, it is necessary for the stage-wise covariates, X_1 and X_2, to be independent. In reality, the independence of the covariates in each stage rarely happens.

In this thesis, we are interested in assessing how omitting a confounder affects the dWOLS estimators. Therefore, in this next set of simulations, we considered omitting one or both confounders from the model specifications. Note that in this setting, the treatment and treatment-free models are all misspecified by omitting confounder C_1 or C_2, or both (and also omitting the optimal treatment terms). Again, we considered the three analyses with different forms of model misspecification and explored the impact on the resulting dWOLS estimates.

The results, reported in Table 4.4, provide the mean and standard error (SE) for the blip parameter estimates, estimated value function, and estimates for the optimal stage-specific treatment A_{1N} and A_{2N}. Results are shown for a sample size of 1000 and 5000, each with 500 replicates. The box-plots in Figure 4.2 show the blip parameters for the 500 iterations of the simulation. Note that y-axes are variably scaled. In terms of the model performance, omitting both C_1 and C_2 introduces bias in the dWOLS estimates; the bias is smaller when only one of the confounders C_1 or C_2 is omitted. A similar trend is observed for both sample sizes, except, variability decreased when the sample size is larger. In this particular scenario, where the strength of confounding was the same for both C_1 and C_2, by omitting both confounders we faced more bias in comparison to the scenario where only one confounder is omitted. The value function and proportion of agreements are smaller when one of the confounders is omitted from the model. Recall that confounders C_1 and C_2 are different types of variables, and we considered binary (C_1) and continuous (C_2) confounders in our models. By disregarding the binary confounder C_1, the bias $\hat{\psi}_{10}$ and $\hat{\psi}_{20}$ is similar to the bias in the models omitting the continuous confounder C_2. Therefore, this bias did not seem to depend on the type of omitted confounder. However, we speculate that the strength of the confounding, rather than the variable type of the confounder, will affect bias. We therefore perform additional simulations to examine this possibility.

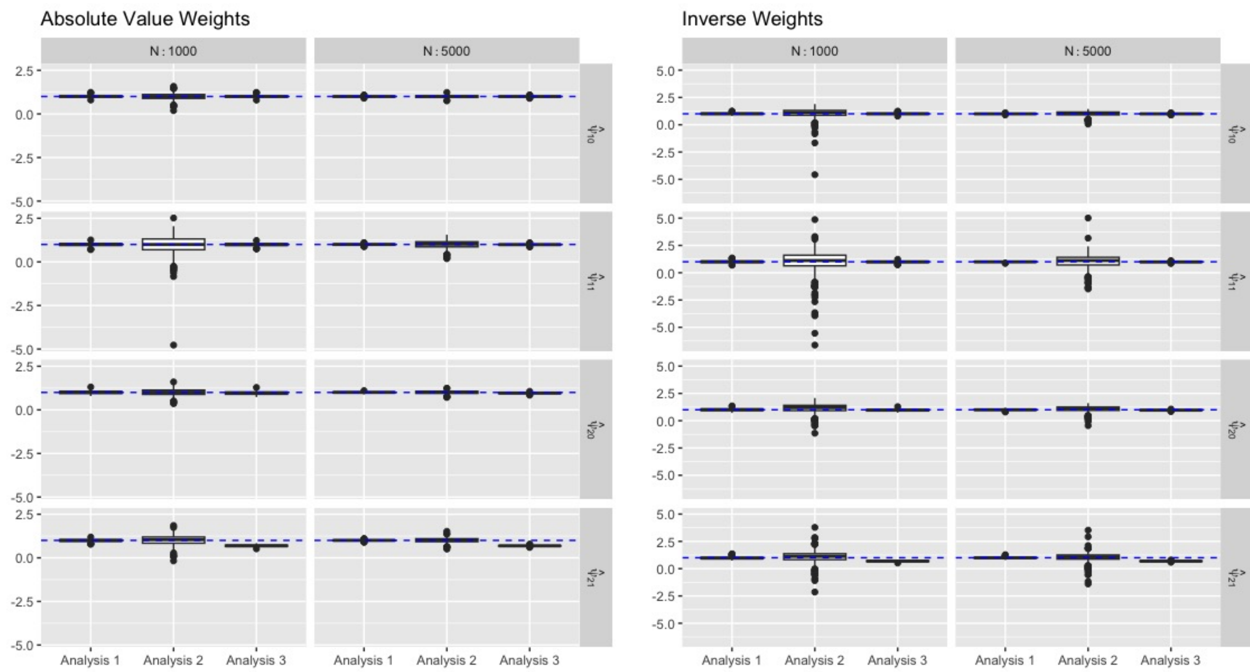

Figure 4.2: Estimated blip parameters when model specifications do not include the optimal terms but includes the confounders C_1 and C_2 for Analysis 1, 2, and 3, over 500 simulated datasets. The true value of the parameters is indicated by a dashed horizontal line.

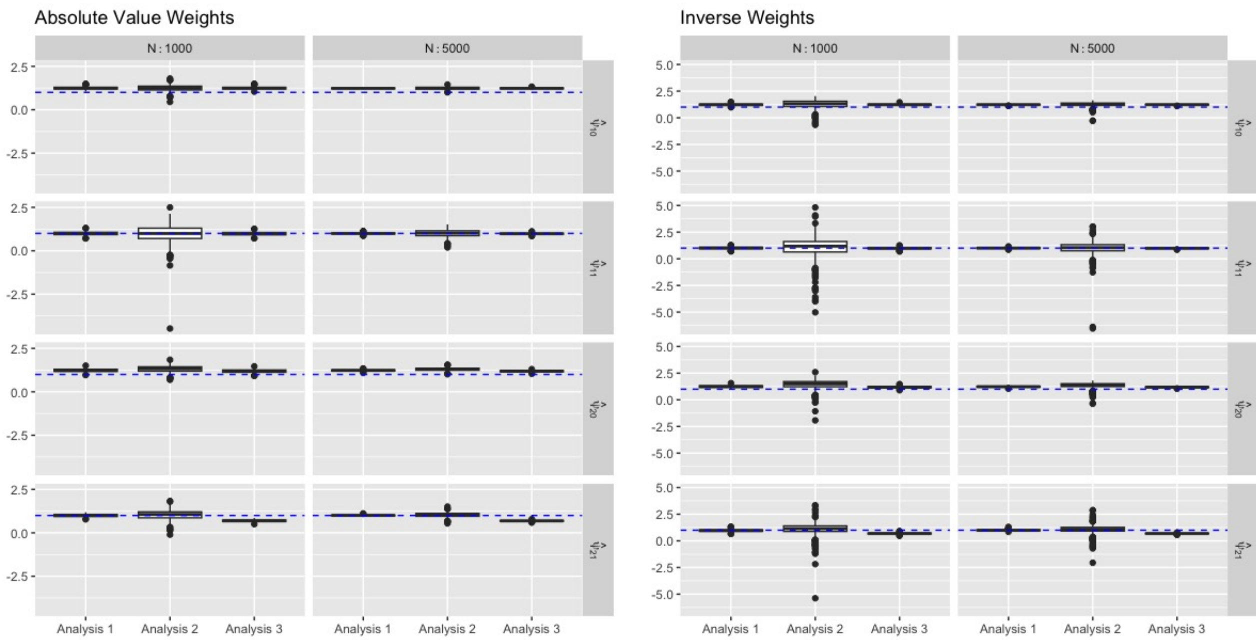

Figure 4.3: Estimated blip parameters when model specifications do not include the optimal terms and the confounder C_1 for Analysis 1, 2, and 3, over 500 simulated datasets. The true value of the parameters is indicated by a dashed horizontal line.

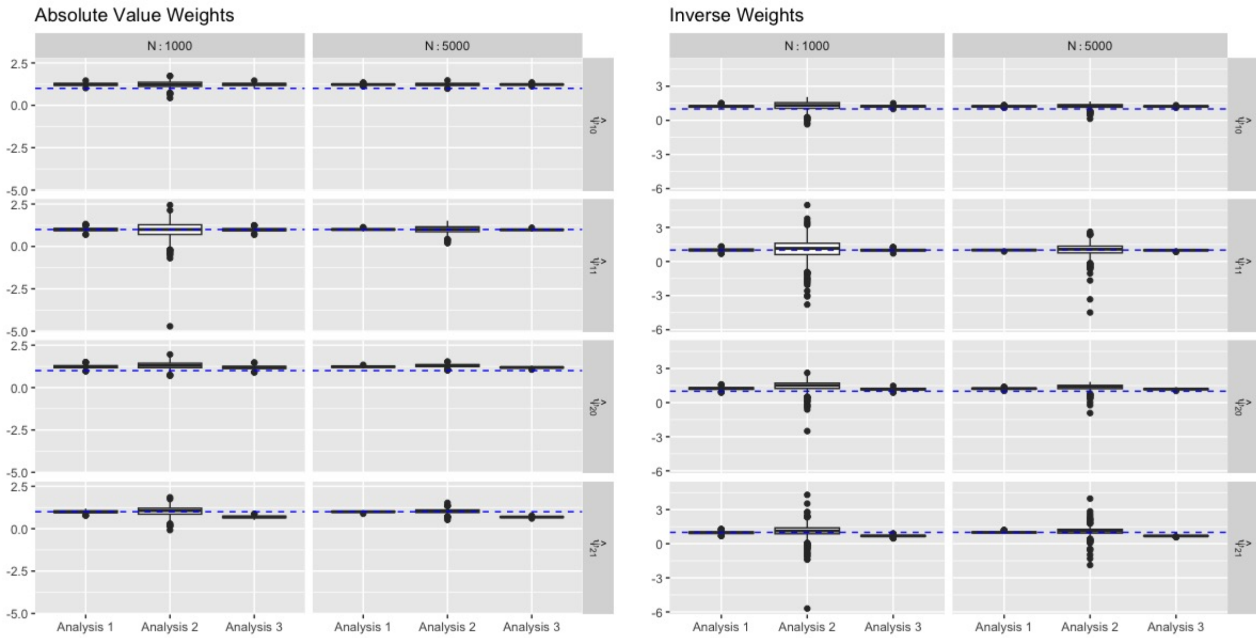

Figure 4.4: Estimated blip parameters when model specifications do not include the optimal terms and the confounder C_2 for Analysis 1, 2, and 3, over 500 simulated datasets. The true value of the parameters is indicated by a dashed horizontal line.

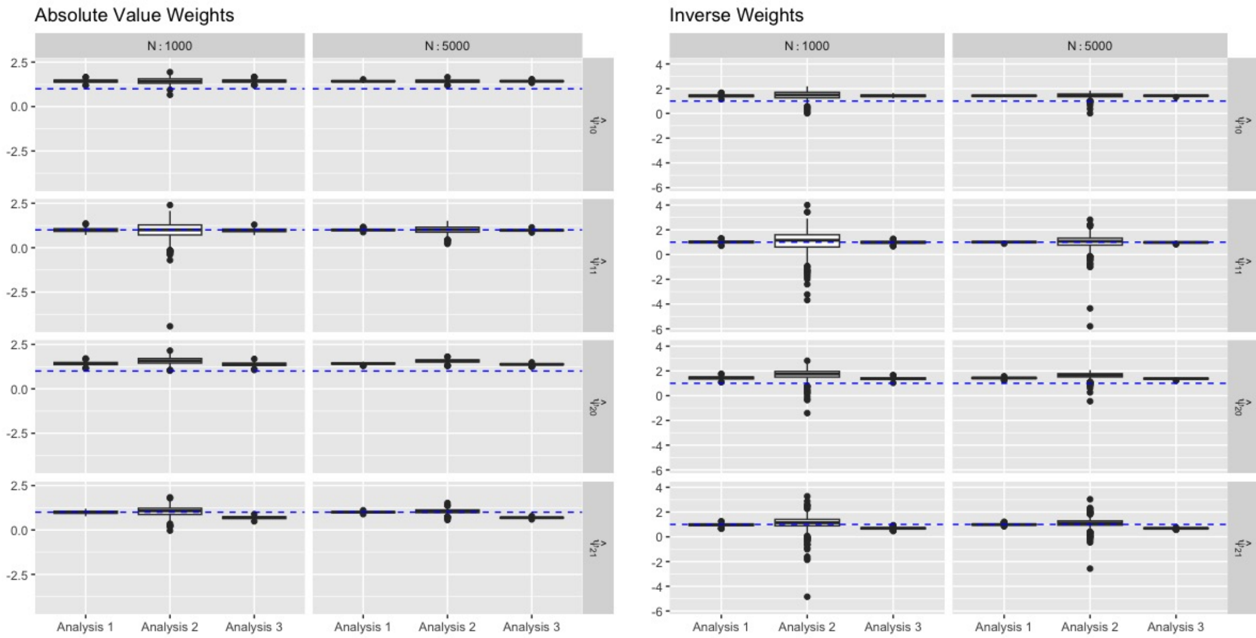

Figure 4.5: Estimated blip parameters when model specifications do not include the optimal terms and the confounders C_1 and C_2 for Analysis 1, 2, and 3, over 500 simulated datasets. The true value of the parameters is indicated by a dashed horizontal line.

Table 4.4: Estimated blip parameters, value function, and proportion of agreements with the same coefficients for C_1 and C_2 over 500 simulated datasets, ($\psi_{10} = \psi_{11} = \psi_{20} = \psi_{21} = 1$ and $V^{A^{opt}} = 1.67$).

		w_1			w_2	
	Analysis 1	Analysis 2	Analysis 3	Analysis 1	Analysis 2	Analysis 3
Included C_1 and C_2 - $n = 1000$						
$\hat{\psi}_{10}$ (SE)	1.00 (0.07)	0.99 (0.18)	1.00 (0.07)	1.00 (0.08)	1.04 (0.41)	1.00 (0.07)
$\hat{\psi}_{11}$ (SE)	1.00 (0.08)	1.01 (0.47)	1.00 (0.08)	1.01 (0.09)	1.05 (1.04)	1.00 (0.08)
$\hat{\psi}_{20}$ (SE)	1.00 (0.08)	1.01 (0.19)	0.95 (0.09)	1.00 (0.11)	1.10 (0.50)	0.95 (0.09)
$\hat{\psi}_{21}$(SE)	1.01 (0.07)	1.01 (0.30)	0.69 (0.06)	0.98 (0.10)	1.05 (0.70)	0.69 (0.06)
V(SE)	1.65 (0.00)	1.62 (0.06)	1.64 (0.01)	1.65 (0.00)	1.50 (0.34)	1.64 (0.01)
Prop. A_1	0.98	0.93	0.98	0.98	0.88	0.98
Prop. A_2	0.98	0.95	0.93	0.97	0.90	0.93
Prop. A_1 and A_2	0.96	0.89	0.91	0.95	0.80	0.91
Included C_1 and C_2 - $n = 5000$						
$\hat{\psi}_{10}$ (SE)	1.00 (0.03)	1.01 (0.08)	1.00 (0.03)	1.00 (0.04)	1.02 (0.22)	1.00 (0.03)
$\hat{\psi}_{11}$ (SE)	1.00 (0.04)	1.00 (0.22)	0.99 (0.04)	1.00 (0.05)	1.02 (0.68)	0.99 (0.04)
$\hat{\psi}_{20}$ (SE)	1.00 (0.04)	1.01 (0.08)	0.96 (0.04)	1.00 (0.05)	1.04 (0.34)	0.96 (0.04)
$\hat{\psi}_{21}$ (SE)	1.00 (0.03)	1.01 (0.13)	0.68 (0.03)	1.00 (0.05)	1.07 (0.63)	0.68 (0.03)
V(SE)	1.67 (0.00)	1.67 (0.01)	1.66 (0.00)	1.67 (0.00)	1.60 (0.22)	1.66 (0.00)
Prop. A_1	0.99	0.96	0.99	0.99	0.91	0.99
Prop. A_2	0.99	0.98	0.92	0.99	0.94	0.92
Prop. A_1 and A_2	0.98	0.94	0.92	0.97	0.86	0.92
Omitted C_2 - $n = 1000$						
$\hat{\psi}_{10}$ (SE)	1.23 (0.08)	1.22 (0.18)	1.23 (0.08)	1.23 (0.08)	1.26 (0.38)	1.23 (0.08)
$\hat{\psi}_{11}$ (SE)	1.00 (0.09)	1.01 (0.46)	0.99 (0.09)	1.01 (0.10)	1.04 (0.95)	0.99 (0.09)
$\hat{\psi}_{20}$ (SE)	1.22 (0.09)	1.29 (0.19)	1.18 (0.09)	1.23 (0.11)	1.39 (0.46)	1.18 (0.09)
$\hat{\psi}_{21}$ (SE)	1.00 (0.08)	1.03 (0.29)	0.69 (0.07)	0.98 (0.10)	1.07 (0.67)	0.69 (0.07)
V(SE)	1.64 (0.01)	1.61 (0.06)	1.60 (0.02)	1.64 (0.01)	1.50 (0.31)	1.60 (0.02)
Prop. A_1	0.95	0.93	0.95	0.95	0.89	0.95
Prop. A_2	0.96	0.93	0.88	0.95	0.89	0.88
Prop. A_1 and A_2	0.91	0.87	0.85	0.91	0.80	0.85
Omitted C_2 - $n = 5000$						
$\hat{\psi}_{10}$ (SE)	1.23 (0.04)	1.24 (0.08)	1.23 (0.04)	1.23 (0.04)	1.25 (0.20)	1.23 (0.04)
$\hat{\psi}_{11}$ (SE)	1.00 (0.04)	1.00 (0.21)	0.98 (0.04)	1.00 (0.04)	1.01 (0.63)	0.98 (0.04)
$\hat{\psi}_{20}$ (SE)	1.23 (0.04)	1.30 (0.08)	1.18 (0.04)	1.23 (0.05)	1.34 (0.28)	1.18 (0.04)
$\hat{\psi}_{21}$ (SE)	1.00 (0.04)	1.03 (0.12)	0.68 (0.03)	1.00 (0.05)	1.08 (0.49)	0.68 (0.03)
V(SE)	1.66 (0.00)	1.66 (0.02)	1.63 (0.01)	1.66 (0.00)	1.60 (0.16)	1.63 (0.01)
Prop. A_1	0.95	0.94	0.95	0.95	0.92	0.95
Prop. A_2	0.95	0.95	0.88	0.95	0.92	0.88
Prop. A_1 and A_2	0.91	0.90	0.84	0.91	0.85	0.84
Omitted C_1 - $n = 1000$						
$\hat{\psi}_{10}$ (SE)	1.23 (0.08)	1.23 (0.18)	1.23 (0.08)	1.23 (0.08)	1.27 (0.38)	1.23 (0.08)
$\hat{\psi}_{11}$ (SE)	1.01 (0.09)	1.01 (0.46)	0.99 (0.09)	1.01 (0.10)	1.06 (0.97)	0.99 (0.09)
$\hat{\psi}_{20}$ (SE)	1.23 (0.09)	1.31 (0.19)	1.18 (0.09)	1.23 (0.11)	1.40 (0.45)	1.18 (0.09)
$\hat{\psi}_{21}$ (SE)	1.00 (0.08)	1.03 (0.29)	0.69 (0.06)	0.98 (0.10)	1.07 (0.63)	0.69 (0.06)
V(SE)	1.64 (0.01)	1.61 (0.06)	1.60 (0.02)	1.64 (0.01)	1.52 (0.26)	1.60 (0.02)
Prop. A_1	0.95	0.93	0.95	0.95	0.89	0.95
Prop. A_2	0.95	0.93	0.88	0.95	0.89	0.88
Prop. A_1 and A_2	0.91	0.87	0.84	0.90	0.80	0.84
Omitted C_1 - $n = 5000$						
$\hat{\psi}_{10}$ (SE)	1.23 (0.04)	1.24 (0.08)	1.23 (0.04)	1.23 (0.04)	1.26 (0.19)	1.23 (0.04)
$\hat{\psi}_{11}$ (SE)	1.00 (0.04)	1.01 (0.21)	0.98 (0.04)	1.00 (0.05)	1.02 (0.60)	0.98 (0.04)
$\hat{\psi}_{20}$ (SE)	1.23 (0.04)	1.30 (0.08)	1.18 (0.04)	1.23 (0.05)	1.34 (0.31)	1.18 (0.04)
$\hat{\psi}_{21}$ (SE)	1.00 (0.03)	1.04 (0.12)	0.68 (0.03)	0.99 (0.05)	1.09 (0.57)	0.68 (0.03)
V(SE)	1.66 (0.00)	1.66 (0.02)	1.63 (0.01)	1.66 (0.00)	1.61 (0.16)	1.63 (0.01)
Prop. A_1	0.95	0.94	0.94	0.95	0.92	0.94
Prop. A_2	0.95	0.95	0.88	0.95	0.92	0.88
Prop. A_1 and A_2	0.91	0.90	0.84	0.91	0.85	0.84
Omitted C_1 and C_2 - $n = 1000$						
$\hat{\psi}_{10}$ (SE)	1.42 (0.08)	1.42 (0.18)	1.42 (0.08)	1.42 (0.09)	1.45 (0.37)	1.42 (0.08)
$\hat{\psi}_{11}$ (SE)	1.01 (0.09)	1.01 (0.45)	0.99 (0.09)	1.01 (0.10)	1.06 (0.91)	0.99 (0.09)
$\hat{\psi}_{20}$ (SE)	1.42 (0.09)	1.57 (0.19)	1.37 (0.10)	1.43 (0.11)	1.66 (0.42)	1.37 (0.10)
$\hat{\psi}_{21}$ (SE)	1.00 (0.08)	1.05 (0.29)	0.69 (0.07)	0.98 (0.10)	1.09 (0.60)	0.69 (0.07)
V(SE)	1.62 (0.01)	1.59 (0.06)	1.56 (0.03)	1.62 (0.02)	1.52 (0.23)	1.56 (0.03)
Prop. A_1	0.92	0.92	0.92	0.92	0.89	0.92
Prop. A_2	0.92	0.90	0.84	0.92	0.88	0.84
Prop. A_1 and A_2	0.86	0.84	0.79	0.85	0.80	0.79
Omitted C_1 and C_2 - $n = 5000$						
$\hat{\psi}_{10}$ (SE)	1.42 (0.04)	1.43 (0.07)	1.43 (0.04)	1.42 (0.04)	1.45 (0.17)	1.43 (0.04)
$\hat{\psi}_{11}$ (SE)	1.00 (0.04)	1.01 (0.21)	0.98 (0.04)	1.00 (0.05)	1.01 (0.54)	0.98 (0.04)
$\hat{\psi}_{20}$ (SE)	1.42 (0.04)	1.57 (0.08)	1.37 (0.04)	1.43 (0.05)	1.62 (0.25)	1.37 (0.04)
$\hat{\psi}_{21}$ (SE)	1.00 (0.04)	1.05 (0.12)	0.68 (0.03)	0.99 (0.05)	1.11 (0.44)	0.68 (0.03)
V(SE)	1.64 (0.01)	1.63 (0.02)	1.58 (0.01)	1.64 (0.01)	1.60 (0.13)	1.58 (0.01)
Prop. A_1	0.92	0.92	0.91	0.92	0.91	0.91
Prop. A_2	0.92	0.91	0.84	0.92	0.90	0.84
Prop. A_1 and A_2	0.85	0.85	0.79	0.85	0.83	0.79

In the previous set of simulations, where the confounders had the same strength in the outcome model, we saw similar results whether C_1 or C_2 was excluded from the model specifications. Next, we explored how the bias differed when the strength of the confounders are different. Specifically, we considered different coefficients for the confounders C_1 and C_2 and assessed the resulting dWOLS estimators when the confounders are omitted from our model specifications. We considered the same two-stage example with the same covariates and confounders, however, in these simulations we made C_2 a stronger confounder by generating data in which its impact on the outcome was greater and also made the effect of the confounder C_1 negative. The outcome model is defined as follows

$$Y = \exp(X_1) + X_1^3 - 0.5C_1 + 1.75C_2 - \mu_1 - \mu_2 + \varepsilon$$

where $\varepsilon \sim \mathrm{N}(0, 1)$ and μ is the regret function defined as before.

The box-plots shown in Figure 4.6 through 4.9 summarize the blip parameters for the 500 iterations of the simulation. Note that y-axes are variably scaled. Figure 4.6 shows the box-plots when C_1 and C_2 are included in the model specifications. Figure 4.7 shows the box-plots when C_1 is omitted from the model specifications while in Figure 4.8 only C_2 is omitted from the model specifications. Figure 4.9 includes the box-plots when C_1 and C_2 are both omitted from the model specifications.

As in the previous simulation, we explored the effects on the blip parameter estimates, the estimated value function, and the proportion of treatment agreement for the different forms of model misspecification. The results are summarized in Table 4.5. In all model specifications, the SEs are decreasing when the sample size is larger. Unlike the previous simulation, omitting both C_1 and C_2 did not introduce the most bias in the dWOLS estimates. The bias was greatest when only C_2 was omitted. One plausible explanation for this finding is that the coefficients of C_1 and C_2 had different signs, leading to a "cancelling out" of biases that were acting in different directions. The bias was smaller when only C_1 was omitted from model specification. Unsurprisingly, omitting the stronger confounder caused more bias, whereas disregarding the weaker confounder resulted in less bias. Therefore, omitting confounder C_2 caused more bias in comparison to the scenarios where only one confounder C_1 or both confounders were omitted. The value function was smaller than the estimated value function with C_1 or both C_1 and C_2 in the model. The proportion of agreements to treatments were also smaller. Thus, we see that the strength of confounder affected the bias.

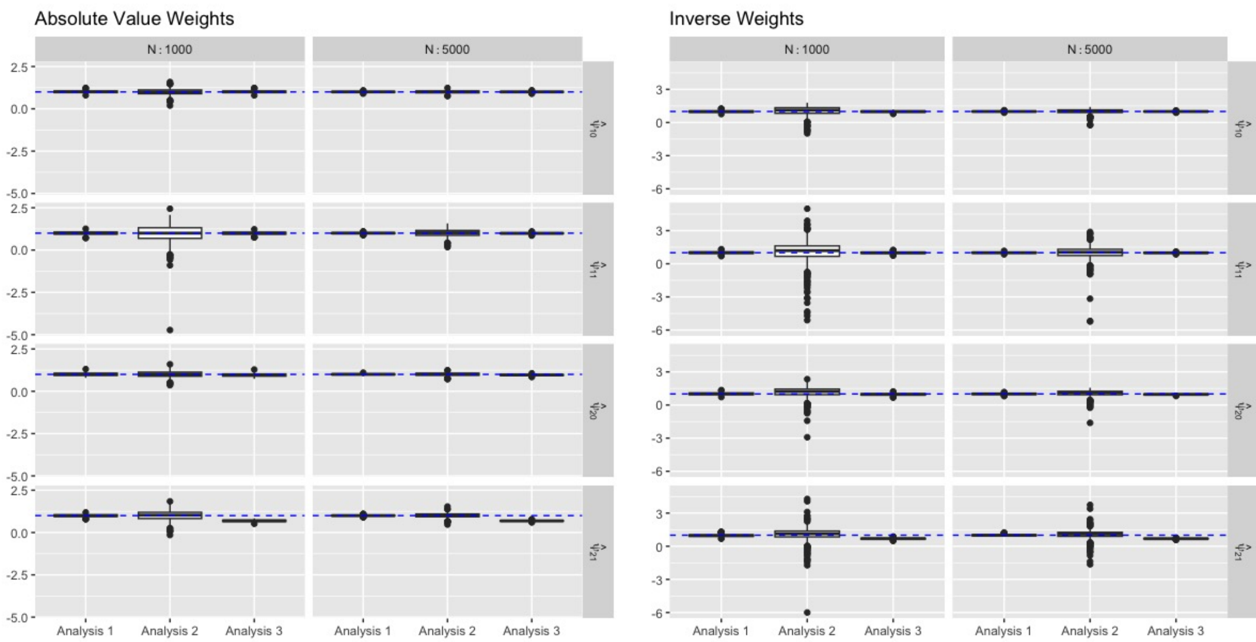

Figure 4.6: Estimated blip parameters when model specifications do not include the optimal terms but includes the confounders C_1 and C_2 for Analysis 1, 2, and 3, over 500 simulated datasets. The true value of the parameters is indicated by a dashed horizontal line.

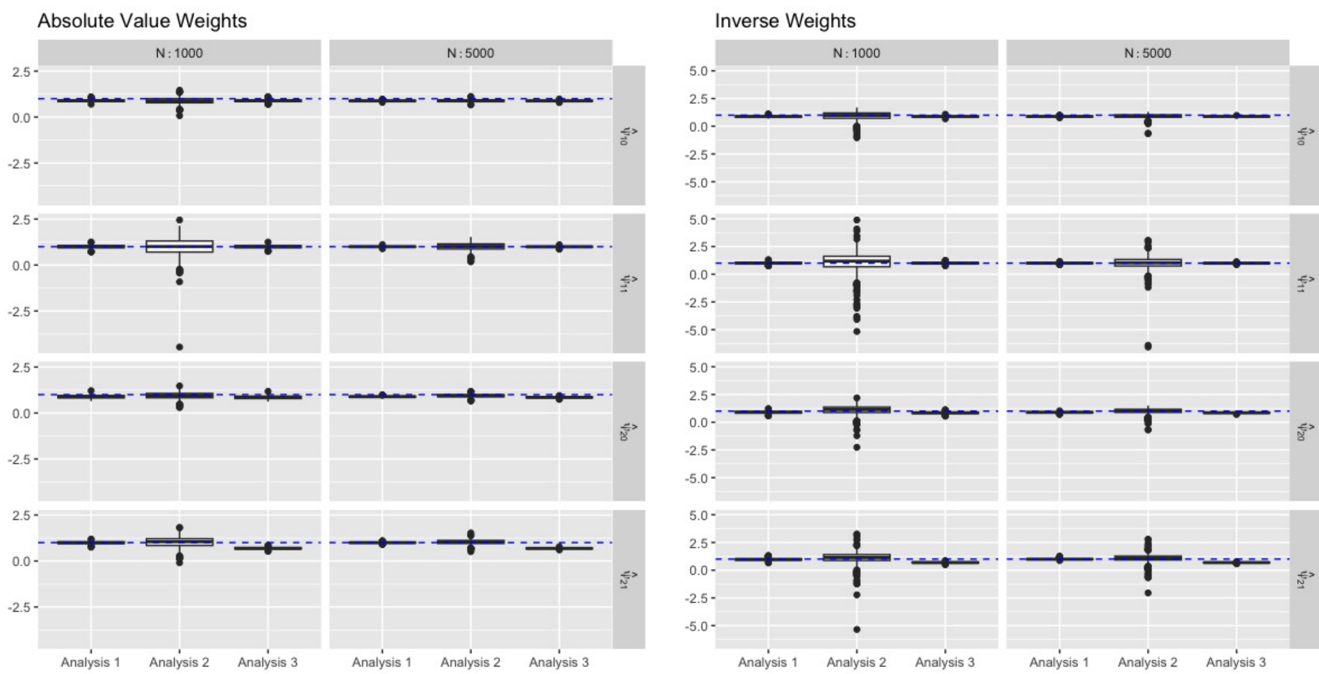

Figure 4.7: Estimated blip parameters when model specifications do not include the optimal terms and the confounder C_1 for Analysis 1, 2, and 3, over 500 simulated datasets. The true value of the parameters is indicated by a dashed horizontal line.

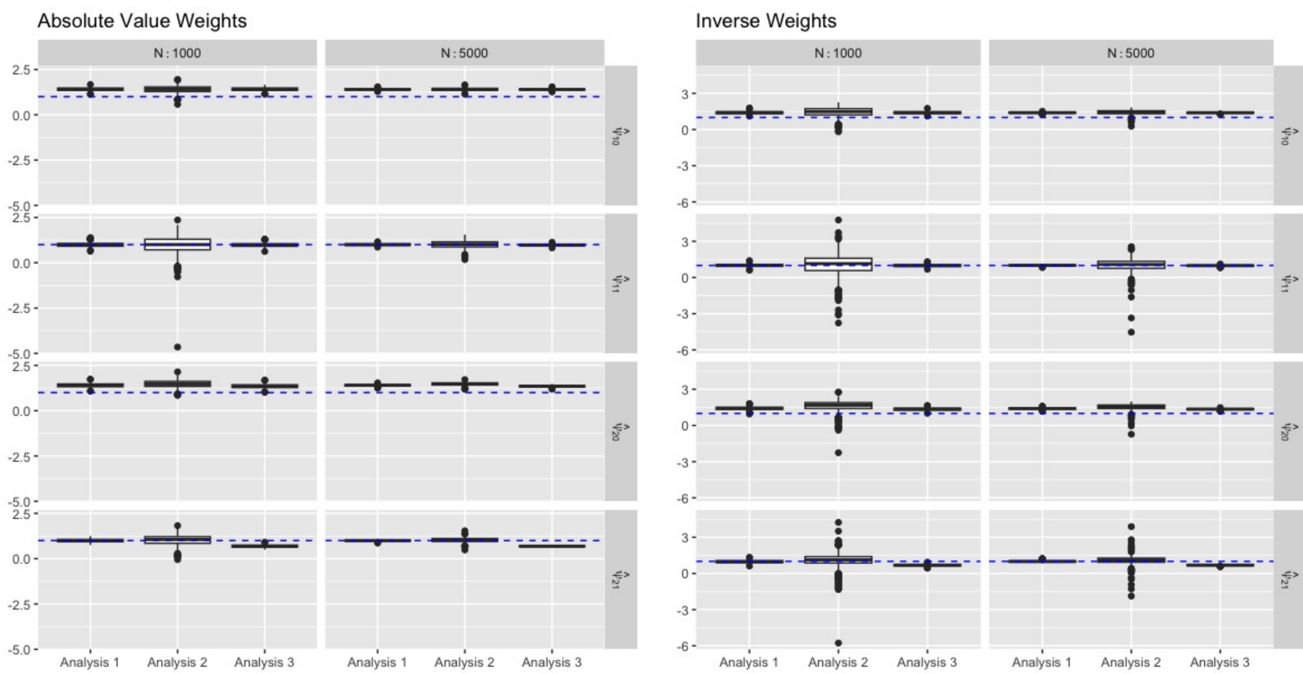

Figure 4.8: Estimated blip parameters when model specifications do not include the optimal terms and the confounder C_2 for Analysis 1, 2, and 3, over 500 simulated datasets. The true value of the parameters is indicated by a dashed horizontal line.

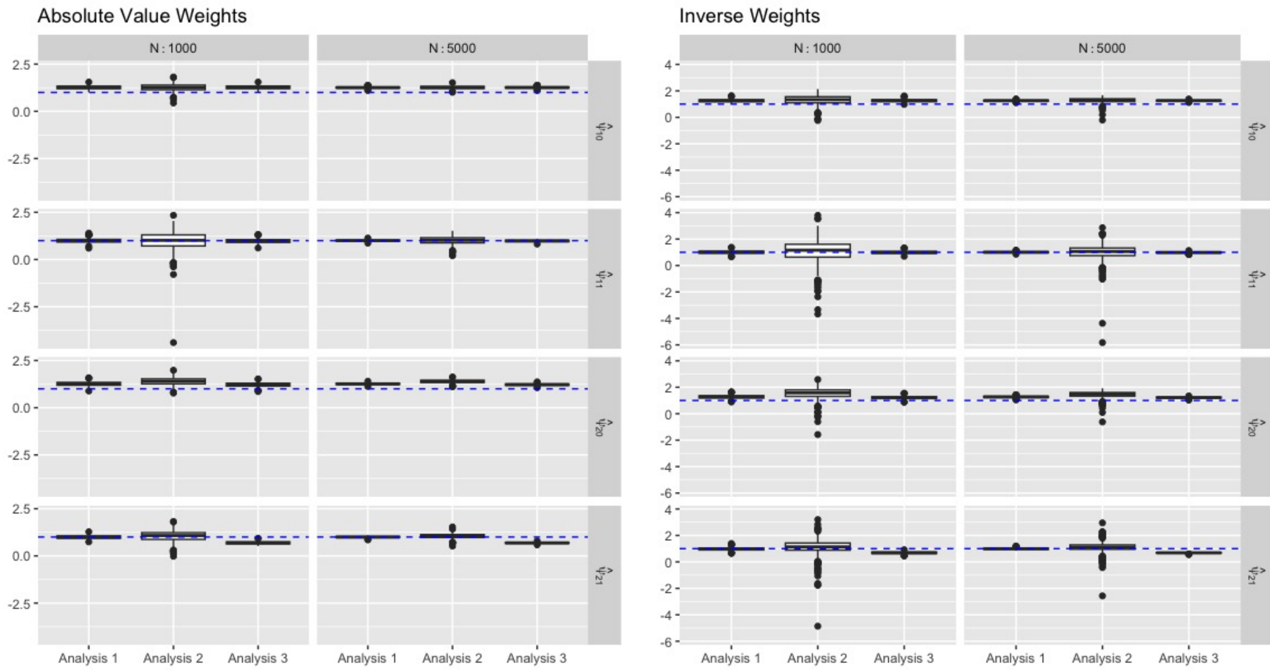

Figure 4.9: Estimated blip parameters when model specifications do not include the optimal terms and the confounders C_1 and C_2 for Analysis 1, 2, and 3, over 500 simulated datasets. The true value of the parameters is indicated by a dashed horizontal line.

Table 4.5: Estimated blip parameters, value function, and proportion of agreements with different coefficients for C_1 and C_2 over 500 simulated datasets, ($\psi_{10} = \psi_{11} = \psi_{20} = \psi_{21} = 1$ and $V^{A^{opt}} = 0.55$).

	w_1			w_2		
	Analysis 1	Analysis 2	Analysis 3	Analysis 1	Analysis 2	Analysis 3
Included C_1 and C_2 - $n = 1000$						
$\hat{\psi}_{10}$ (SE)	1.00 (0.07)	0.99 (0.18)	1.00 (0.07)	1.00 (0.08)	1.04 (0.40)	1.00 (0.07)
$\hat{\psi}_{11}$ (SE)	1.00 (0.08)	1.00 (0.48)	1.00 (0.08)	1.01 (0.09)	1.04 (1.04)	1.00 (0.08)
$\hat{\psi}_{20}$ (SE)	1.00 (0.08)	1.01 (0.19)	0.95 (0.09)	1.00 (0.11)	1.10 (0.50)	0.95 (0.09)
$\hat{\psi}_{21}$ (SE)	1.01 (0.07)	1.01 (0.30)	0.69 (0.06)	0.98 (0.10)	1.05 (0.70)	0.69 (0.06)
V(SE)	0.54 (0.00)	0.50 (0.07)	0.53 (0.01)	0.54 (0.00)	0.38 (0.34)	0.53 (0.01)
Prop. A_1	0.98	0.93	0.98	0.98	0.88	0.98
Prop. A_2	0.98	0.95	0.93	0.97	0.90	0.93
Prop. A_1 and A_2	0.96	0.89	0.91	0.95	0.80	0.91
Included C_1 and C_2 - $n = 5000$						
$\hat{\psi}_{10}$ (SE)	1.00 (0.03)	1.01 (0.08)	1.00 (0.03)	1.00 (0.04)	1.02 (0.22)	1.00 (0.03)
$\hat{\psi}_{11}$ (SE)	1.00 (0.04)	1.00 (0.22)	0.99 (0.04)	1.00 (0.05)	1.02 (0.68)	0.99 (0.04)
$\hat{\psi}_{20}$ (SE)	1.00 (0.04)	1.01 (0.08)	0.96 (0.04)	1.00 (0.05)	1.04 (0.34)	0.96 (0.04)
$\hat{\psi}_{21}$ (SE)	1.00 (0.03)	1.01 (0.13)	0.68 (0.03)	1.00 (0.05)	1.07 (0.63)	0.68 (0.03)
V(SE)	0.55 (0.00)	0.54 (0.01)	0.53 (0.00)	0.55 (0.00)	0.47 (0.22)	0.53 (0.00)
Prop. A_1	0.99	0.96	0.99	0.99	0.91	0.99
Prop. A_2	0.99	0.98	0.92	0.99	0.94	0.92
Prop. A_1 and A_2	0.98	0.94	0.92	0.97	0.86	0.92
Omitted C_2 - $n = 1000$						
$\hat{\psi}_{10}$ (SE)	1.40 (0.09)	1.39 (0.19)	1.40 (0.09)	1.40 (0.10)	1.43 (0.39)	1.40 (0.09)
$\hat{\psi}_{11}$ (SE)	1.00 (0.10)	1.00 (0.47)	0.99 (0.10)	1.01 (0.11)	1.04 (0.95)	0.99 (0.10)
$\hat{\psi}_{20}$ (SE)	1.39 (0.11)	1.47 (0.20)	1.34 (0.11)	1.40 (0.13)	1.56 (0.46)	1.34 (0.11)
$\hat{\psi}_{21}$ (SE)	1.00 (0.09)	1.03 (0.29)	0.69 (0.08)	0.98 (0.11)	1.07 (0.67)	0.69 (0.08)
V(SE)	0.51 (0.02)	0.48 (0.06)	0.46 (0.03)	0.51 (0.02)	0.39 (0.28)	0.46 (0.03)
Prop. A_1	0.93	0.92	0.92	0.93	0.89	0.92
Prop. A_2	0.93	0.91	0.85	0.92	0.88	0.85
Prop. A_1 and A_2	0.86	0.84	0.80	0.86	0.79	0.80
Omitted C_2 - $n = 5000$						
$\hat{\psi}_{10}$ (SE)	1.40 (0.04)	1.41 (0.08)	1.40 (0.04)	1.40 (0.05)	1.42 (0.20)	1.40 (0.04)
$\hat{\psi}_{11}$ (SE)	1.00 (0.05)	1.00 (0.21)	0.98 (0.05)	1.00 (0.05)	1.01 (0.62)	0.98 (0.05)
$\hat{\psi}_{20}$ (SE)	1.40 (0.04)	1.48 (0.09)	1.35 (0.05)	1.40 (0.06)	1.52 (0.28)	1.35 (0.05)
$\hat{\psi}_{21}$ (SE)	1.00 (0.04)	1.04 (0.12)	0.68 (0.03)	1.00 (0.06)	1.08 (0.49)	0.68 (0.03)
V(SE)	0.52 (0.01)	0.51 (0.02)	0.46 (0.01)	0.52 (0.01)	0.47 (0.14)	0.46 (0.01)
Prop. A_1	0.92	0.92	0.92	0.92	0.91	0.92
Prop. A_2	0.93	0.92	0.84	0.92	0.90	0.84
Prop. A_1 and A_2	0.86	0.85	0.79	0.86	0.83	0.79
Omitted C_1 - $n = 1000$						
$\hat{\psi}_{10}$ (SE)	0.88 (0.07)	0.88 (0.18)	0.89 (0.07)	0.89 (0.08)	0.93 (0.38)	0.89 (0.07)
$\hat{\psi}_{11}$ (SE)	1.00 (0.08)	1.00 (0.47)	1.00 (0.08)	1.01 (0.09)	1.06 (0.98)	1.00 (0.08)
$\hat{\psi}_{20}$ (SE)	0.88 (0.08)	0.94 (0.18)	0.84 (0.09)	0.89 (0.10)	1.04 (0.45)	0.84 (0.09)
$\hat{\psi}_{21}$ (SE)	1.00 (0.07)	1.03 (0.29)	0.69 (0.06)	0.98 (0.09)	1.08 (0.63)	0.69 (0.06)
V(SE)	0.54 (0.00)	0.51 (0.07)	0.53 (0.01)	0.54 (0.01)	0.40 (0.32)	0.53 (0.01)
Prop. A_1	0.97	0.92	0.97	0.97	0.87	0.97
Prop. A_2	0.97	0.95	0.96	0.97	0.91	0.96
Prop. A_1 and A_2	0.94	0.88	0.93	0.94	0.80	0.93
Omitted C_1 - $n = 5000$						
$\hat{\psi}_{10}$ (SE)	0.88 (0.03)	0.89 (0.08)	0.89 (0.03)	0.88 (0.03)	0.92 (0.19)	0.89 (0.03)
$\hat{\psi}_{11}$ (SE)	1.00 (0.04)	1.01 (0.21)	0.99 (0.04)	1.00 (0.04)	1.02 (0.61)	0.99 (0.04)
$\hat{\psi}_{20}$ (SE)	0.89 (0.03)	0.94 (0.08)	0.85 (0.04)	0.89 (0.05)	0.98 (0.31)	0.85 (0.04)
$\hat{\psi}_{21}$ (SE)	1.00 (0.03)	1.04 (0.13)	0.68 (0.03)	0.99 (0.05)	1.09 (0.57)	0.68 (0.03)
V(SE)	0.54 (0.00)	0.54 (0.01)	0.54 (0.00)	0.54 (0.00)	0.48 (0.19)	0.54 (0.00)
Prop. A_1	0.97	0.96	0.97	0.97	0.91	0.97
Prop. A_2	0.97	0.97	0.95	0.97	0.95	0.95
Prop. A_1 and A_2	0.95	0.93	0.93	0.95	0.87	0.93
Omitted C_1 and C_2 - $n = 1000$						
$\hat{\psi}_{10}$ (SE)	1.26 (0.09)	1.25 (0.18)	1.26 (0.09)	1.26 (0.10)	1.29 (0.37)	1.26 (0.09)
$\hat{\psi}_{11}$ (SE)	1.00 (0.11)	1.00 (0.46)	0.99 (0.10)	1.01 (0.11)	1.06 (0.91)	0.99 (0.10)
$\hat{\psi}_{20}$ (SE)	1.25 (0.10)	1.39 (0.19)	1.21 (0.11)	1.26 (0.12)	1.49 (0.42)	1.21 (0.11)
$\hat{\psi}_{21}$ (SE)	1.00 (0.10)	1.05 (0.29)	0.69 (0.08)	0.98 (0.11)	1.09 (0.60)	0.69 (0.08)
V(SE)	0.52 (0.01)	0.49 (0.06)	0.48 (0.03)	0.52 (0.01)	0.41 (0.26)	0.48 (0.03)
Agreement to A_1	0.95	0.93	0.94	0.95	0.89	0.94
Agreement to A_2	0.95	0.92	0.87	0.94	0.89	0.87
Agreement to A_1 and A_2	0.90	0.86	0.83	0.90	0.81	0.83
Omitted C_1 and C_2 - $n = 5000$						
$\hat{\psi}_{10}$ (SE)	1.26 (0.04)	1.27 (0.08)	1.26 (0.04)	1.26 (0.05)	1.29 (0.17)	1.26 (0.04)
$\hat{\psi}_{11}$ (SE)	1.00 (0.05)	1.01 (0.21)	0.98 (0.05)	1.00 (0.05)	1.01 (0.54)	0.98 (0.05)
$\hat{\psi}_{20}$ (SE)	1.26 (0.04)	1.39 (0.08)	1.22 (0.05)	1.27 (0.06)	1.45 (0.25)	1.22 (0.05)
$\hat{\psi}_{21}$ (SE)	1.00 (0.04)	1.06 (0.12)	0.68 (0.03)	1.00 (0.06)	1.11 (0.44)	0.68 (0.03)
V(SE)	0.53 (0.00)	0.52 (0.02)	0.49 (0.01)	0.53 (0.01)	0.48 (0.13)	0.49 (0.01)
Agreement to A_1	0.94	0.94	0.94	0.94	0.92	0.94
Agreement to A_2	0.95	0.94	0.87	0.95	0.92	0.87
Agreement to A_1 and A_2	0.90	0.88	0.83	0.90	0.85	0.83

Based on our simulations, we can conclude that any violation of the assumption of NUC will yield biased blip parameter estimators, and this bias is affected by the strength of the omitted confounder, however, the bias was similar regardless of the type of the confounder. In the next section, we explore a sensitivity analysis to attempt to compensate for the bias due to unmeasured confounding in the dWOLS framework.

4.2 Sensitivity Analysis

In this section, we explored a sensitivity analysis approach through several simulations to assess the bias of the blip parameter using dWOLS. The main goal of this study is to demonstrate the sensitivity analysis method and assess whether it can reduce or even eliminate bias resulting from unmeasured confounding. We implemented our proposed sensitivity analysis method which involves a single sensitivity parameter, α^*, that captures the impact of the violation of the NUC assumption as discussed in Chapter 3.

For the set-up considered here, after determining the true value of the sensitivity parameter, we considered a range of α based on the true value of α^*. In a real data example, it would not be possible to determine the true value of the sensitivity parameter without auxiliary data and so a plausible range of values would be used. For varying values of α in a specified range, dWOLS estimates were obtained by including an offset that is a function of α and the measured confounder X which is correlated with its unmeasured counterpart. Again, we considered dWOLS estimation using both the absolute value weights and the inverse probability of treatment weights.

4.2.1 Data Generation

We considered an one-stage example with a single covariate (X), an unmeasured confounder (C), and a binary treatment (A). We assumed the following DGM

$$
\begin{aligned}
C &\sim \mathrm{Uni}(0,1)\\
X|C=c &\sim \mathrm{Ber}(c)\\
A|X=x, C=c &\sim \mathrm{Ber}(\mathrm{expit}(\eta_0+\eta_x x+\eta_c c))\\
Y|C=c, X=x, A=a &\sim \mathrm{N}(\beta_0+\beta_x x+\psi_0 a+\psi_1 ax+\beta_c c, \sigma_y^2)
\end{aligned}
\tag{4.1}
$$

where $\eta = (\eta_0, \eta_x, \eta_c) = (0, -1, 0.5)$, $\sigma_y^2 = 1$, and we considered different values for $\beta = (\beta_0, \psi_0, \beta_x, \psi_1, \beta_c)$. The parameters of interest are ψ_0 and ψ_1.

Note that additional simulations were also conducted for the following scenarios with different values for the parameters of the treatment-free model:

- scenario 1

$$
\begin{aligned}
C &\sim \mathrm{Ber}(0.55)\\
X|C=c &\sim \mathrm{Ber}(0.25+0.75c)\\
A|X=x, C=c &\sim \mathrm{Ber}(\mathrm{expit}(-x+0.5c))\\
Y|C=c, X=x, A=a &\sim \mathrm{N}(\beta_0+\psi_0 a+\beta_x x+\psi_1 ax+\beta_c c, 1)
\end{aligned}
$$

- scenario 2

$$
\begin{aligned}
C &\sim \mathrm{N}(0.5, 0.5)\\
X|C=c &\sim \mathrm{N}(2.2c, 0.5)\\
A|X=x, C=c &\sim \mathrm{Ber}(\mathrm{expit}(-x+0.5c))\\
Y|C=c, X=x, A=a &\sim \mathrm{N}(\beta_0++\psi_0 a+\beta_x x+\psi_1 ax+\beta_c c, 1).
\end{aligned}
$$

The results can be found in Appendix A.

4.2.2 Estimands, Methods, and Performance Metrics

As in the previous simulations, we considered two different sample sizes of 1000 and 5000 and 500 replications in each scenario. We focused on a case where there is no interaction between treatment and covariate ($\psi_1 = 0$), then we considered an outcome model with an interaction between treatment and covariate ($\psi_1 \neq 0$). The mean (SE) of the resulting dWOLS estimates are summarized in tables and box-plots for each of the two cases. The estimand and methods are the parameters of the blip model, $\psi = (\psi_0, \psi_1)$, and the dWOLS estimator based on a model that includes the αX offset. The performance metrics, as in Section 4.1, are the mean (SE) of the estimators, the value function, and the proportion of agreement of the estimated optimal rule with the true optimal rule. As before, for every value of α in the specified range, estimation was carried out via dWOLS using both the absolute value weights and the inverse probability of treatment weights. The resulting estimates were then compared with the true value of $\psi = (\psi_0, \psi_1)$ which is $(1, 0)$ for the case where there is no interaction between treatment and covariate and $(1, 1)$ for the case with an interaction between treatment and covariate.

In a first simulation set-up, the ψ_1 is zero in DGM 4.1. We considered different values for $\beta = (\beta_0, \psi_0, \beta_x, \psi_1, \beta_c)$, and calculated the value of α^* using Formula 3.1, which we reproduce here for convenience:

$$\alpha^* = \beta_x + \beta_c \eta_1.$$

The MC Averaging Method was also used to calculate the α^*. As we showed in Section 3.2, we drew $C' \sim \mathrm{Beta}(1+x, 2-x)$ from a big sample size of $n = 1,000,000$ and computed the average of the function $f(x, c')$.

Considering the DGM 4.1, the function $f(X, C')$ was defined as

$$f(x,c') = (\beta_0 + \beta_x x + \beta_c c')(1 - \text{expit}(\eta_0 + \eta_x x + \eta_c c'))$$
$$+ (\beta_0 + \beta_x x + \psi_0 + \beta_c c' - \psi_0)\text{expit}(\eta_0 + \eta_x x + \eta_c c'),$$

and the value of α^* was then calculated by $\alpha^* = \bar{f}_{1,c'} - \bar{f}_{0,c''}$ where $c' \sim \text{Beta}(2,1)$ and $c'' \sim \text{Beta}(1,2)$.

The different sets of values for the parameter β led to different values for α^*, which are summarized in Table 4.6. For each of the three DGMs 1, 2, and 3 listed in Table 4.6, we considered a reasonable range of plausible α values to include in the outcome model within the dWOLS framework.

Table 4.6: α^* and α-range when there is NO interaction between treatment and covariate.

	$\beta = (\beta_0, \psi_0, \beta_x, \psi_1, \beta_c)$	α^*_{MC}	$\alpha^* = \beta_x + \frac{\beta_c}{3}$	α-range
DGM 1	(1, 1, -1.5, 0, 2)	-0.83	-0.83	(-1, -0.5)
DGM 2	(1, 1, 1.7, 0, 2.6)	2.57	2.56	(2.25, 2.75)
DGM 3	(1, 1, -2.5, 0, -2.6)	-3.37	-3.36	(-3.5, -3)

4.2.3 Results

The results of the three scenarios with sample sizes of 1000 and 5000 and 500 replications are summarized in Table 4.7. The results show that the dWOLS approach performs quite well, and the resulting $\hat{\psi}_0$ shows little or no bias. Using the absolute value weights and the inverse probability of treatment weight, the dWOLS estimators change very slightly for each value of α, whereas in the unweighted ordinary least squares approach, the estimates vary considerably with the value of α. This suggests that, for these DGMs, simply including X in the dWOLS analysis largely accounts for the effect of the unmeasured, but correlated, variable C such that there is relatively little impact of the NUC violation. The sensitivity analysis therefore has little effect on the dWOLS estimators.

The chosen α-range contains the true value of α^* that reduces bias. As the sample size increased the variability decreased for all dWOLS estimators. Using unweighted regression, the bias decreased as the sample size increases, whereas the bias does not change when the sample size is bigger by using absolute value and inverse weightings. As discussed in Chapter 3, we did not capture the entire bias by this proposed method. Here, we have observed that we could improve the estimations by a simple method that only requires specifying the relationship between the unmeasured confounder and all other measured confounders (covariates). To eliminate all bias we needed to consider the full distribution of $C|X, A$ rather than the distribution of $C|X$, however, the former is more complex and even less likely to be well-specified or understood in realistic settings. Figure 4.10 shows the average of estimator ($\hat{\psi}_0$) based on the value of α for the three DGMs and sample sizes of 1000 and 5000.

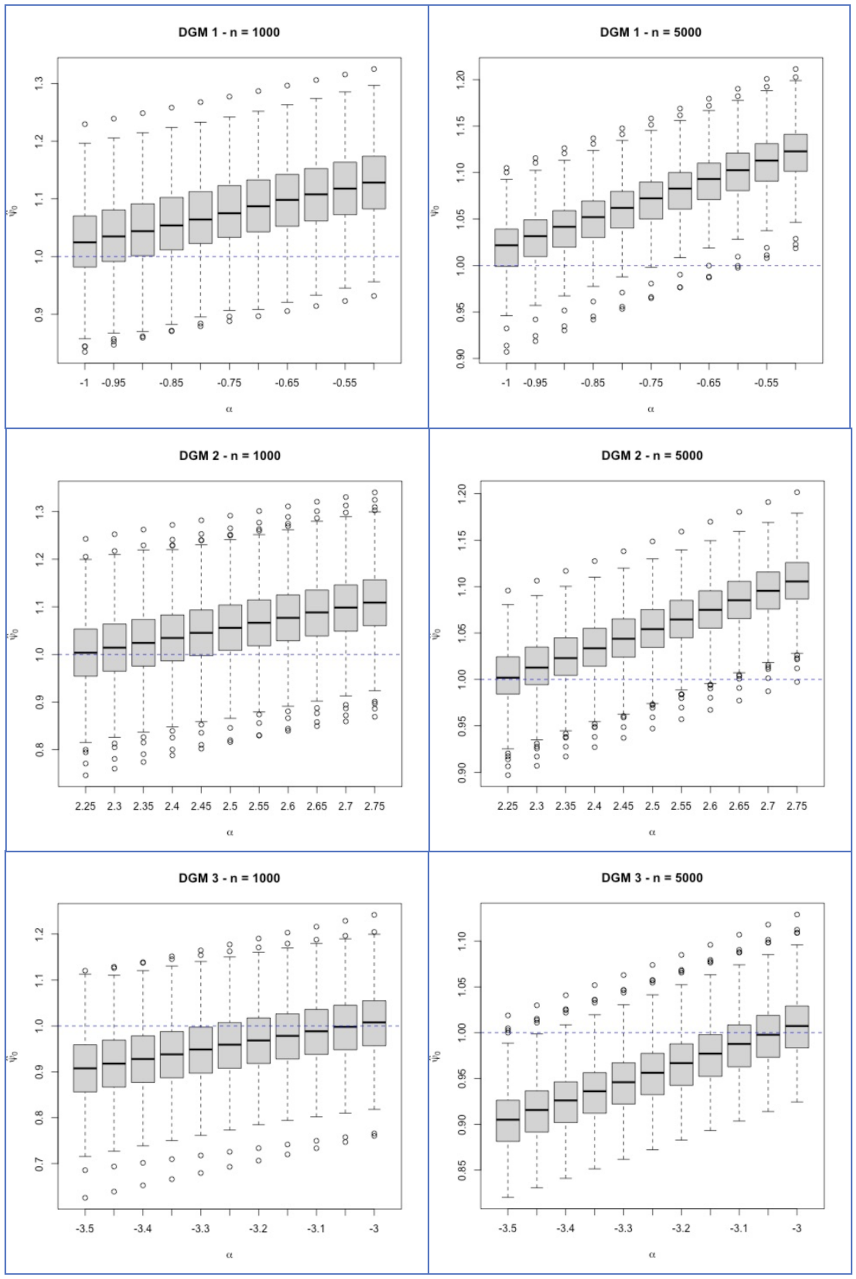

Figure 4.10: Box-plots of empirical distribution of the unweighted dWOLS estimator $\hat{\psi}_0$ of the true causal parameter $\psi_0 = 1$ (marked via a horizontal dashed line) in a linear causal model as a function of the sensitivity parameter α when there is no interaction between the treatment and covariate. The true values of α are $\alpha^*_{DGM1} = -0.83$, $\alpha^*_{DGM2} = 2.56$, and $\alpha^*_{DGM3} = -3.36$.

Table 4.7: Mean (SE) of $\hat{\psi}_0$, where true value is $\psi_0 = 1$ in a linear causal model as a function of the sensitivity parameter α when there is no interaction between treatment and covariate. The true values of α are $\alpha^*_{DGM1} = -0.83$, $\alpha^*_{DGM2} = 2.56$, and $\alpha^*_{DGM3} = -3.36$.

			$n = 1000$			$n = 5000$	
DGM	α	$\hat{\psi}_0$ (SE)	$\hat{\psi}_{0-w_1}$ (SE)	$\hat{\psi}_{0-w_2}$ (SE)	$\hat{\psi}_0$ (SE)	$\hat{\psi}_{0-w_1}$ (SE)	$\hat{\psi}_{0-w_2}$ (SE)
DGM 1	-1	1.03 (0.07)	1.06 (0.07)	1.06 (0.07)	1.02 (0.03)	1.06 (0.03)	1.06 (0.03)
	-0.95	1.04 (0.07)	1.06 (0.07)	1.06 (0.07)	1.03 (0.03)	1.06 (0.03)	1.06 (0.03)
	-0.9	1.05 (0.07)	1.06 (0.07)	1.06 (0.07)	1.04 (0.03)	1.06 (0.03)	1.06 (0.03)
	-0.85	1.06 (0.07)	1.06 (0.07)	1.06 (0.07)	1.05 (0.03)	1.06 (0.03)	1.06 (0.03)
	-0.8	1.07 (0.07)	1.06 (0.07)	1.06 (0.07)	1.06 (0.03)	1.06 (0.03)	1.06 (0.03)
	-0.75	1.08 (0.07)	1.06 (0.07)	1.06 (0.07)	1.07 (0.03)	1.06 (0.03)	1.06 (0.03)
	-0.7	1.09 (0.07)	1.06 (0.07)	1.06 (0.07)	1.08 (0.03)	1.06 (0.03)	1.06 (0.03)
	-0.65	1.10 (0.07)	1.06 (0.07)	1.06 (0.07)	1.09 (0.03)	1.06 (0.03)	1.06 (0.03)
	-0.6	1.11 (0.07)	1.06 (0.07)	1.06 (0.07)	1.10 (0.03)	1.06 (0.03)	1.06 (0.03)
	-0.55	1.12 (0.07)	1.06 (0.07)	1.06 (0.07)	1.11 (0.03)	1.06 (0.03)	1.06 (0.03)
	-0.5	1.13 (0.07)	1.06 (0.07)	1.06 (0.07)	1.12 (0.03)	1.06 (0.03)	1.06 (0.03)
DGM 2	2.25	1.00 (0.08)	1.07 (0.08)	1.07 (0.08)	1.00 (0.03)	1.07 (0.03)	1.07 (0.03)
	2.3	1.01 (0.08)	1.07 (0.08)	1.07 (0.08)	1.01 (0.03)	1.07 (0.03)	1.07 (0.03)
	2.35	1.02 (0.07)	1.07 (0.08)	1.07 (0.08)	1.02 (0.03)	1.07 (0.03)	1.07 (0.03)
	2.4	1.03 (0.07)	1.07 (0.08)	1.07 (0.08)	1.03 (0.03)	1.07 (0.03)	1.07 (0.03)
	2.45	1.05 (0.07)	1.07 (0.08)	1.07 (0.08)	1.04 (0.03)	1.07 (0.03)	1.07 (0.03)
	2.5	1.06 (0.07)	1.07 (0.08)	1.07 (0.08)	1.05 (0.03)	1.07 (0.03)	1.07 (0.03)
	2.55	1.07 (0.07)	1.07 (0.08)	1.07 (0.08)	1.07 (0.03)	1.07 (0.03)	1.07 (0.03)
	2.6	1.08 (0.07)	1.07 (0.08)	1.07 (0.08)	1.08 (0.03)	1.07 (0.03)	1.07 (0.03)
	2.65	1.09 (0.07)	1.07 (0.08)	1.07 (0.08)	1.09 (0.03)	1.07 (0.03)	1.07 (0.03)
	2.7	1.10 (0.07)	1.07 (0.08)	1.07 (0.08)	1.10 (0.03)	1.07 (0.03)	1.07 (0.03)
	2.75	1.11 (0.07)	1.07 (0.08)	1.07 (0.08)	1.11 (0.03)	1.07 (0.03)	1.07 (0.03)
DGM 3	-3.5	0.91 (0.07)	0.93 (0.08)	0.93 (0.08)	0.90 (0.03)	0.93 (0.03)	0.93 (0.03)
	-3.45	0.92 (0.07)	0.93 (0.08)	0.93 (0.08)	0.91 (0.03)	0.93 (0.03)	0.93 (0.03)
	-3.4	0.93 (0.07)	0.93 (0.08)	0.93 (0.08)	0.92 (0.03)	0.93 (0.03)	0.93 (0.03)
	-3.35	0.94 (0.07)	0.93 (0.08)	0.93 (0.08)	0.94 (0.03)	0.93 (0.03)	0.93 (0.03)
	-3.3	0.95 (0.07)	0.93 (0.08)	0.93 (0.08)	0.95 (0.03)	0.93 (0.03)	0.93 (0.03)
	-3.25	0.96 (0.07)	0.93 (0.08)	0.93 (0.08)	0.96 (0.03)	0.93 (0.03)	0.93 (0.03)
	-3.2	0.97 (0.07)	0.93 (0.08)	0.93 (0.08)	0.97 (0.03)	0.93 (0.03)	0.93 (0.03)
	-3.15	0.98 (0.07)	0.93 (0.08)	0.93 (0.08)	0.98 (0.03)	0.93 (0.03)	0.93 (0.03)
	-3.1	0.99 (0.07)	0.93 (0.08)	0.93 (0.08)	0.99 (0.03)	0.93 (0.03)	0.93 (0.03)
	-3.05	1.00 (0.07)	0.93 (0.08)	0.93 (0.08)	1.00 (0.03)	0.93 (0.03)	0.93 (0.03)
	-3	1.01 (0.07)	0.93 (0.08)	0.93 (0.08)	1.01 (0.03)	0.93 (0.03)	0.93 (0.03)

Next, we considered an interaction in the outcome model, i.e., $\psi_1 \neq 0$, in DGM 4.1. Considering different sets of the parameters for the treatment-free model, the value of α^* was calculated based on Formula 3.1. As described in the previous section, the MC Averaging Method was also used to confirm that the value of α^* is calculated correctly. Considering different DGMs, the value of α^* and the α-range are summarized in Table 4.8.

Table 4.8: α^* and α-range when there is interaction between the treatment and covariate.

	$\beta = (\beta_0, \psi_0, \beta_x, \psi_1, \beta_c)$	α^*_{MC}	$\alpha^* = \beta_x + \frac{\beta_c}{3}$	α-range
DGM 1	(1, 1, -1.5, 1, 2)	-0.83	-0.83	(-1, -0.5)
DGM 2	(1, 1, 1.7, 1, 2.6)	2.57	2.56	(2.25, 2.75)
DGM 3	(1, 1, -2.5, 1, -2.6)	-3.37	-3.36	(-3.5, -3)

Table 4.9 shows the mean (SE) of $\hat{\psi}_0$ for two different sample sizes of 1000 and 5000 over 500 replications. The average (SE) of $\hat{\psi}_1$ for two sample sizes of 1000 and 5000, and iteration of 500 datasets are summarized in Table 4.10. We can see the bias of the dWOLS estimators as a function of α in this table. Figure 4.11 also shows the average of estimators of $\hat{\psi}_0$ and $\hat{\psi}_1$ for DGM 1 when $n = 1000$. DGM 2, and 3 exhibited the same pattern as DGM 1. The results for DGM 1, 2, and 3 for $n = 5000$ can be found in Appendix B.

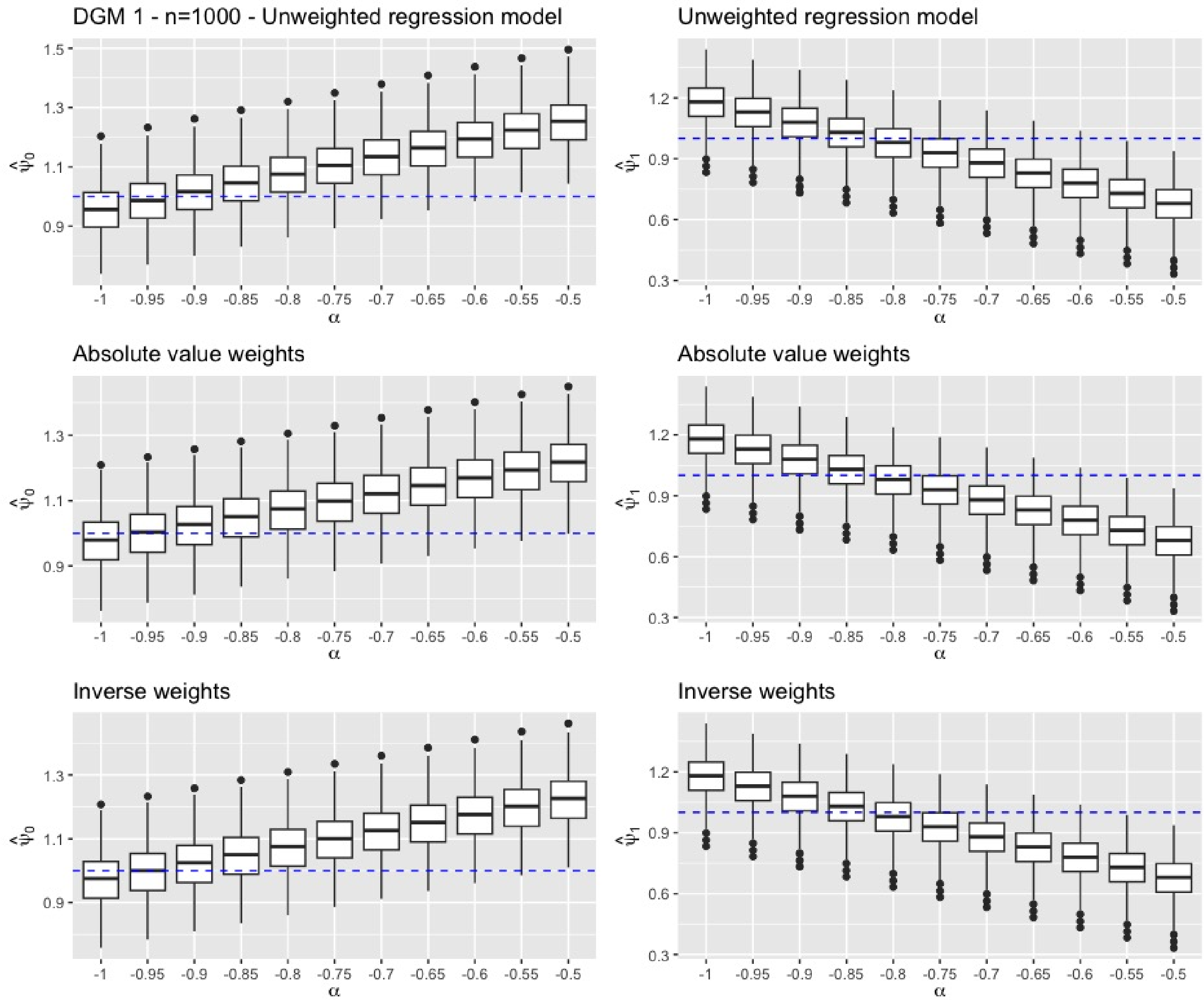

Figure 4.11: Box-plots of empirical distribution of $\hat{\psi}_0$ and $\hat{\psi}_1$ of the true causal parameter $\psi_0 = \psi_1 = 1$ (marked via a horizontal dashed line) as a function of the sensitivity parameter α when there is an interaction between the treatment and covariate in DGM 1 when $n = 1000$.

Table 4.9: Mean (SE) of blip parameter $\hat{\psi}_0$, where true value is $\psi_0 = 1$ as a function of the sensitivity parameter α when there is interaction between treatment and covariate. The true value of α are $\alpha^*_{DGM1} = -0.83$, $\alpha^*_{DGM2} = 2.56$, and $\alpha^*_{DGM3} = -3.36$.

			$n = 1000$			$n = 5000$	
DGM	α	$\hat{\psi}_0$ (SE)	$\hat{\psi}_{0-w_1}$ (SE)	$\hat{\psi}_{0-w_2}$ (SE)	$\hat{\psi}_0$ (SE)	$\hat{\psi}_{0-w_1}$ (SE)	$\hat{\psi}_{0-w_2}$ (SE)
DGM 1	-1	0.96 (0.08)	0.98 (0.08)	0.97 (0.08)	0.95 (0.04)	0.97 (0.04)	0.97 (0.04)
	-0.95	0.99 (0.08)	1.00 (0.08)	1.00 (0.08)	0.98 (0.04)	0.99 (0.04)	0.99 (0.04)
	-0.9	1.02 (0.08)	1.03 (0.08)	1.02 (0.08)	1.01 (0.04)	1.02 (0.04)	1.02 (0.04)
	-0.85	1.05 (0.08)	1.05 (0.08)	1.05 (0.08)	1.04 (0.04)	1.04 (0.04)	1.04 (0.04)
	-0.8	1.08 (0.08)	1.07 (0.08)	1.07 (0.08)	1.07 (0.04)	1.07 (0.04)	1.07 (0.04)
	-0.75	1.11 (0.08)	1.10 (0.08)	1.10 (0.08)	1.10 (0.04)	1.09 (0.04)	1.09 (0.04)
	-0.7	1.14 (0.08)	1.12 (0.08)	1.12 (0.08)	1.13 (0.04)	1.11 (0.04)	1.12 (0.04)
	-0.65	1.16 (0.08)	1.14 (0.08)	1.15 (0.08)	1.16 (0.04)	1.14 (0.04)	1.14 (0.04)
	-0.6	1.19 (0.08)	1.17 (0.08)	1.17 (0.08)	1.19 (0.04)	1.16 (0.04)	1.17 (0.04)
	-0.55	1.22 (0.08)	1.19 (0.08)	1.20 (0.08)	1.22 (0.04)	1.18 (0.04)	1.19 (0.04)
	-0.5	1.25 (0.08)	1.22 (0.08)	1.22 (0.08)	1.25 (0.04)	1.21 (0.04)	1.22 (0.04)
DGM 2	2.25	0.87 (0.09)	0.91 (0.09)	0.90 (0.09)	0.88 (0.04)	0.92 (0.04)	0.91 (0.04)
	2.3	0.90 (0.09)	0.93 (0.09)	0.93 (0.09)	0.91 (0.04)	0.94 (0.04)	0.93 (0.04)
	2.35	0.93 (0.09)	0.96 (0.09)	0.95 (0.09)	0.94 (0.04)	0.96 (0.04)	0.96 (0.04)
	2.4	0.96 (0.09)	0.98 (0.09)	0.98 (0.09)	0.97 (0.04)	0.99 (0.04)	0.98 (0.04)
	2.45	0.99 (0.09)	1.01 (0.09)	1.00 (0.09)	1.00 (0.04)	1.01 (0.04)	1.01 (0.04)
	2.5	1.02 (0.09)	1.03 (0.09)	1.03 (0.09)	1.03 (0.04)	1.04 (0.04)	1.03 (0.04)
	2.55	1.05 (0.09)	1.05 (0.09)	1.05 (0.09)	1.06 (0.04)	1.06 (0.04)	1.06 (0.04)
	2.6	1.08 (0.09)	1.08 (0.09)	1.08 (0.09)	1.08 (0.04)	1.08 (0.04)	1.08 (0.04)
	2.65	1.11 (0.09)	1.10 (0.09)	1.10 (0.09)	1.11 (0.04)	1.11 (0.04)	1.11 (0.04)
	2.7	1.14 (0.09)	1.12 (0.09)	1.13 (0.09)	1.14 (0.04)	1.13 (0.04)	1.13 (0.04)
	2.75	1.17 (0.09)	1.15 (0.09)	1.15 (0.09)	1.17 (0.04)	1.15 (0.04)	1.16 (0.04)
DGM 3	-3.5	0.85 (0.08)	0.87 (0.09)	0.86 (0.09)	0.86 (0.04)	0.87 (0.04)	0.87 (0.04)
	-3.45	0.88 (0.08)	0.89 (0.09)	0.89 (0.09)	0.89 (0.04)	0.90 (0.04)	0.90 (0.04)
	-3.4	0.91 (0.08)	0.91 (0.09)	0.91 (0.09)	0.92 (0.04)	0.92 (0.04)	0.92 (0.04)
	-3.35	0.94 (0.08)	0.94 (0.09)	0.94 (0.09)	0.95 (0.04)	0.94 (0.04)	0.95 (0.04)
	-3.3	0.97 (0.08)	0.96 (0.09)	0.96 (0.09)	0.98 (0.04)	0.97 (0.04)	0.97 (0.04)
	-3.25	1.00 (0.08)	0.98 (0.09)	0.99 (0.09)	1.01 (0.04)	0.99 (0.04)	1.00 (0.04)
	-3.2	1.03 (0.08)	1.01 (0.09)	1.01 (0.09)	1.04 (0.04)	1.02 (0.04)	1.02 (0.04)
	-3.15	1.06 (0.08)	1.03 (0.09)	1.04 (0.09)	1.07 (0.04)	1.04 (0.04)	1.05 (0.04)
	-3.1	1.09 (0.08)	1.06 (0.09)	1.06 (0.09)	1.10 (0.04)	1.06 (0.04)	1.07 (0.04)
	-3.05	1.12 (0.08)	1.08 (0.09)	1.09 (0.09)	1.12 (0.04)	1.09 (0.04)	1.10 (0.04)
	-3	1.15 (0.08)	1.10 (0.09)	1.11 (0.09)	1.15 (0.04)	1.11 (0.04)	1.12 (0.04)

Table 4.10: Mean (SE) of blip parameter $\hat{\psi}_1$, where true value is $\psi_1 = 1$ as a function of the sensitivity parameter α when there is interaction between treatment and covariate. The true values of α are α^*_{DGM1} =-0.83, α^*_{DGM2} =2.56, and $\alpha^*_{DGM3} = -3.36$.

			$n = 1000$			$n = 5000$	
DGM	α	$\hat{\psi}_1$ (SE)	$\hat{\psi}_{1-w_1}$ (SE)	$\hat{\psi}_{1-w_2}$ (SE)	$\hat{\psi}_1$ (SE)	$\hat{\psi}_{1-w_1}$ (SE)	$\hat{\psi}_{1-w_2}$ (SE)
DGM 1	-1	1.18 (0.10)	1.18 (0.10)	1.18 (0.10)	1.18 (0.05)	1.18 (0.05)	1.18 (0.05)
	-0.95	1.13 (0.10)	1.13 (0.10)	1.13 (0.10)	1.13 (0.05)	1.13 (0.05)	1.13 (0.05)
	-0.9	1.08 (0.10)	1.08 (0.10)	1.08 (0.10)	1.08 (0.05)	1.08 (0.05)	1.08 (0.05)
	-0.85	1.03 (0.10)	1.03 (0.10)	1.03 (0.10)	1.03 (0.05)	1.03 (0.05)	1.03 (0.05)
	-0.8	0.98 (0.10)	0.98 (0.10)	0.98 (0.10)	0.98 (0.05)	0.98 (0.05)	0.98 (0.05)
	-0.75	0.93 (0.10)	0.93 (0.10)	0.93 (0.10)	0.93 (0.05)	0.93 (0.05)	0.93 (0.05)
	-0.7	0.88 (0.10)	0.88 (0.10)	0.88 (0.10)	0.88 (0.05)	0.88 (0.05)	0.88 (0.05)
	-0.65	0.83 (0.10)	0.83 (0.10)	0.83 (0.10)	0.83 (0.05)	0.83 (0.05)	0.83 (0.05)
	-0.6	0.78 (0.10)	0.78 (0.10)	0.78 (0.10)	0.78 (0.05)	0.78 (0.05)	0.78 (0.05)
	-0.55	0.73 (0.10)	0.73 (0.10)	0.73 (0.10)	0.73 (0.05)	0.73 (0.05)	0.73 (0.05)
	-0.5	0.68 (0.10)	0.68 (0.10)	0.68 (0.10)	0.68 (0.05)	0.68 (0.05)	0.68 (0.05)
DGM 2	2.25	1.33 (0.12)	1.33 (0.12)	1.33 (0.12)	1.33 (0.05)	1.33 (0.05)	1.33 (0.05)
	2.3	1.28 (0.12)	1.28 (0.12)	1.28 (0.12)	1.28 (0.05)	1.28 (0.05)	1.28 (0.05)
	2.35	1.23 (0.12)	1.23 (0.12)	1.23 (0.12)	1.23 (0.05)	1.23 (0.05)	1.23 (0.05)
	2.4	1.18 (0.12)	1.18 (0.12)	1.18 (0.12)	1.18 (0.05)	1.18 (0.05)	1.18 (0.05)
	2.45	1.13 (0.12)	1.13 (0.12)	1.13 (0.12)	1.13 (0.05)	1.13 (0.05)	1.13 (0.05)
	2.5	1.08 (0.12)	1.08 (0.12)	1.08 (0.12)	1.08 (0.05)	1.08 (0.05)	1.08 (0.05)
	2.55	1.03 (0.12)	1.03 (0.12)	1.03 (0.12)	1.03 (0.05)	1.03 (0.05)	1.03 (0.05)
	2.6	0.98 (0.12)	0.98 (0.12)	0.98 (0.12)	0.98 (0.05)	0.98 (0.05)	0.98 (0.05)
	2.65	0.93 (0.12)	0.93 (0.12)	0.93 (0.12)	0.93 (0.05)	0.93 (0.05)	0.93 (0.05)
	2.7	0.88 (0.12)	0.88 (0.12)	0.88 (0.12)	0.88 (0.05)	0.88 (0.05)	0.88 (0.05)
	2.75	0.83 (0.12)	0.83 (0.12)	0.83 (0.12)	0.83 (0.05)	0.83 (0.05)	0.83 (0.05)
DGM 3	-3.5	1.12 (0.11)	1.12 (0.11)	1.12 (0.11)	1.12 (0.05)	1.12 (0.05)	1.12 (0.05)
	-3.45	1.07 (0.11)	1.07 (0.11)	1.07 (0.11)	1.07 (0.05)	1.07 (0.05)	1.07 (0.05)
	-3.4	1.02 (0.11)	1.02 (0.11)	1.02 (0.11)	1.02 (0.05)	1.02 (0.05)	1.02 (0.05)
	-3.35	0.97 (0.11)	0.97 (0.11)	0.97 (0.11)	0.97 (0.05)	0.97 (0.05)	0.97 (0.05)
	-3.3	0.92 (0.11)	0.92 (0.11)	0.92 (0.11)	0.92 (0.05)	0.92 (0.05)	0.92 (0.05)
	-3.25	0.87 (0.11)	0.87 (0.11)	0.87 (0.11)	0.87 (0.05)	0.87 (0.05)	0.87 (0.05)
	-3.2	0.82 (0.11)	0.82 (0.11)	0.82 (0.11)	0.82 (0.05)	0.82 (0.05)	0.82 (0.05)
	-3.15	0.77 (0.11)	0.77 (0.11)	0.77 (0.11)	0.77 (0.05)	0.77 (0.05)	0.77 (0.05)
	-3.1	0.72 (0.11)	0.72 (0.11)	0.72 (0.11)	0.72 (0.05)	0.72 (0.05)	0.72 (0.05)
	-3.05	0.67 (0.11)	0.67 (0.11)	0.67 (0.11)	0.67 (0.05)	0.67 (0.05)	0.67 (0.05)
	-3	0.62 (0.11)	0.62 (0.11)	0.62 (0.11)	0.62 (0.05)	0.62 (0.05)	0.62 (0.05)

As we saw in Section 4.1, the dWOLS estimators are biased when the NUC assumption is violated. The bias is affected by the strength of confounding. In this section, we explored a sensitivity analysis approach wherein a single sensitivity parameter adjusts for the effect of the unmeasured confounder.

The proposed approach reduced the bias in the estimators by considering the dependency of C only on X; this procedure is simpler and more straightforward than a previous proposal by Rose et al [33] that relies on specifying the dependence of C on X and A. We captured much of the bias and the α-range includes the true value of α^* that led to an improved estimator of $\psi = (\psi_0, \psi_1)$ in all scenarios.

As one can see from Tables 4.9 and 4.10, larger sample size can provide lower variance for all unweighted, absolute weights, and inverse weights dWOLS estimators, although the bias is not reduced – rather a more precise but biased estimate is found as sample size increases.

4.3 Summary

In this chapter, we conducted several simulation studies with different settings and investigated a novel proposal for a sensitivity analysis method. The approach is illustrated through several simulations, which highlights the importance of sensitivity analysis and provides general points for conducting such analyses.

A comprehensive sensitivity analysis has been done in [33] that includes a complex method; we proposed a simpler method to capture the bias in dWOLS estimators with unmeasured confounding in the model. Our method only relied on determining the relationship between unmeasured confounders and measured covariates. The result showed that we could improve the estimations but we could not eliminate all of the bias since we were not fully accounting for confounding. In next chapter, we implement the proposed method of sensitivity analysis in a real-world data example.

Chapter 5

Application: Analysis of the NHANES Data

Chapter 3 introduced a straightforward sensitivity analysis method aimed at quantifying the possible extent of the bias in estimators when the assumption of NUC is violated. The previous chapter conducted simulations using known DGMs to evaluate the effectiveness of the proposed sensitivity analysis approach. In this chapter, we apply the proposed method to real-world data obtained from the United States' National Health and Nutrition Examination Survey (NHANES) with the objective of assessing the impact of a potential unmeasured confounder on an analysis that seeks to determine whether physical activity recommendations should be tailored to an individual's socioeconomic status.

5.1 Background

Maintaining a healthy body mass index (BMI) is widely recognized as beneficial for overall human health. Various factors have been shown to affect an individual's BMI, including physical activity, dietary habits, and genetics. Studies have shown that socioeconomic factors such as educational level and economic status are also associated (not necessarily causally) with BMI [9,10]. In developed countries, lower wealth levels have been linked to higher BMI [9] due to limited access to healthy food options and reliance on high-calorie processed foods. Additionally, educational level has been found to affect BMI [8], potentially due to greater knowledge about healthy eating and regular exercise or through mechanisms such as higher education increasing income, which in turn is associated with lower BMI in developed nations. Therefore, when examining the causal impact of physical activity on BMI (which may be heterogeneous across covariates), it is crucial to consider the influence of educational level and wealth status, as these may act as important confounders that can introduce bias if adjustment is inadequate or not possible. Further, physical activity requirements may be greater for lower income individuals to compensate for structural and environmental inequities such living in a food desert (low access to high quality nutrition) or being in a less walkable neighbourhood [18, 21].

To address this, our analysis aims to estimate an individual treatment rule (ITR) for physical activity tailored to wealth levels with the objective of optimizing BMI. In this analysis, we consider educational level as an unmeasured confounder. To evaluate the sensitivity of the estimated physical activity recommendation to the unmeasured educational level, we apply the proposed sensitivity analysis procedure.

5.2 Methods

This section provides an overview of the NHANES data and outlines the variables used in the analysis including physical activity, BMI, educational levels, and wealth status.

NHANES data

The NHANES program assesses the health and nutritional well-being of individuals, both children and adults, residing in the United States. The survey, initiated in 1999, has been conducted continuously and releases data publicly in 2-year cycles. It is carried out by the National Center for Health Statistics (NCHS) within the Centers for Disease Control and Prevention (CDC) by collecting data through interviews and physical examinations. The data are accessible through the CDC's NCHS official website [www.cdc.gov/nchs/nhanes].

The NHANES data provide invaluable insights for understanding population health and public health policies in the United States. It employs a diverse range of data collection methods, including clinical examinations, selected medical and laboratory tests, and in-depth interviews. Data is collected through the use of laptops, personal interviews, and computer-assisted self-interviewing. The survey consists of two parts: the initial part involves computer-assisted personal interviewing, conducted by mobile exam center interviewers, the second part is administered through an audio computer-assisted self-interviewing system.

NHANES starts data collection by contacting selected households and obtaining basic demographic information such as age, race, and gender for all household members. Through a random selection process, certain household members are then chosen for further, more detailed data collection.

For the analysis in this chapter, we focus on several specific variables of the NHANES data relevant to our motivating question: BMI, physical activity, wealth status, educational level, age, and diabetes. The outcome of interest in our analysis is BMI, which is calculated as the weight in kilograms divided by the height in meters squared. It provides a measurement allowing the classification of individuals into different ranges. The commonly used ranges based on BMI are classified as follows [2].

Table 5.1: Common BMI classification system.

Classification	BMI
Underweight	≤ 18.5
Normal weight	$18.6 - 24.9$
Overweight	$25 - 29.9$
Obesity	≥ 30

We use BMI as a continuous variable in our analysis, and mentioned these thresholds merely for context. The physical activity variable is categorized as either Yes or No, with participants considered physically active if they engage in moderate or vigorous-intensity sports, fitness, or recreational activities. This variable is derived from a comprehensive survey consisting of 21 questions aimed at assessing the individual's activity level. These questions cover various aspects of (in)activity, including the frequency of being active for at least one hour in the past 7 days, the average hours spent watching TV, using a computer, and playing video games in the past 30 days, the nature and extent of physical activity involved in the person's work, the frequency of walking or cycling for at least 10 minutes in a typical week, engagement in moderate-intensity or vigorous-intensity sports or recreational activities, and the number of hours spent sitting in a typical day. The responses to these questions collectively determine the assignment of the physical activity variable.

The wealth level is determined as a ratio of family income to wealth guidelines, where smaller numbers indicate greater poverty. The educational level is recorded as 8^{th} grade, $9^{th} - 11^{th}$ grade, high school, some college, or college graduate. Table 5.2 shows the summary statistics for the variables for the years $2009 - 2010$ and $2011 - 2012$. For continuous variables, the mean and standard deviation (SD) are provided. The categorical variables are represented by the percentage for each category. Note that missing data are excluded from the dataset. Table 5.3 presents the summary statistics for the two subgroups defined by the physical activity variable.

Table 5.2: Summary of NHANES data for $2009-2012$, excluding missing data.

Variable	**2009-2010** (N=3303)	**2011-2012** (N=3329)
BMI (mean (SD))	28.9 (6.9)	28.7 (6.4)
Wealth Level (mean (SD))	2.9 (1.6)	2.9 (1.7)
Age (mean (SD))	46.8 (16.8)	47.2 (16.9)
Physical Activity (N (%))		
Yes	1719 (52%)	1832 (55%)
No	1584 (48%)	1497 (45%)
Diabetes (N (%))		
Yes	337 (10%)	334 (10%)
No	2966 (90%)	2995 (90%)
Educational Level (N (%))		
8^{th} grade	201 (6%)	181 (5%)
$9^{th}-11^{th}$ grade	435 (13%)	354 (11%)
High school	754 (23%)	629 (19%)
Some college	1014 (31%)	1075 (32%)
College graduate	899 (27%)	1090 (33%)

Table 5.3: Summary of NHANES data ($2009-2012$) for each category of physical activity, excluding missing data.

Variable	**2009-2010**		**2011-2012**	
Physical Activity	**No** (N=1584)	**Yes** (N=1719)	**No** (N=1497)	**Yes** (N=1832)
BMI (mean (SD))	30.0 (7.5)	27.9 (6.1)	29.7 (6.8)	27.9 (6.0)
Wealth Level (mean (SD))	2.6 (1.6)	3.3 (1.6)	2.5 (1.6)	3.2 (1.7)
Age (mean (SD))	49.4 (17.4)	44.4 (15.8)	51.1 (16.7)	44.1 (16.3)
Diabetes (N (%))				
Yes	215 (14%)	122 (7%)	209 (14%)	125 (7%)
No	1369 (86%)	1597 (93%)	1288 (86%)	1707 (93%)
Educational Level (N (%))				
8^{th} grade	141 (9%)	60 (3%)	141 (9%)	40 (2%)
$9^{th}-11^{th}$ grade	297 (19%)	138 (8%)	239 (16%)	115 (6%)
High school	464 (29%)	290 (17%)	333 (22%)	296 (16%)
Some college	459 (29%)	555 (33%)	500 (34%)	575 (32%)
College graduate	223 (14%)	676 (39%)	284 (19%)	806 (44%)

Analysis

In our analysis, the objective is to determine the optimal ITR for recommending physical activity, and then to use the proposed sensitivity analysis to demonstrate the potential impact of violating the assumption of NUC in a real-world setting. We also investigate whether physical activity recommendations should be tailored to the individual's wealth level.

We use NHANES data collected during the years $2009-2010$ to examine the impact of physical activity on individual's BMI and estimate an ITR to optimize BMI while adjusting for wealth level. We assume that educational level acts as an unmeasured confounder. The initial sample size consisted of 5000 participants, from which we removed 1352 participants below the age of 20 years. We further removed 345 data points with missing values in any of the variables used in our analysis. Out of all participants, 61 individuals were classified as underweight (BMI$<$ 18.5) and were excluded from the sample, resulting in a final sample size of 3242 non-underweight adult participants aged 20 years or above with complete data. Among these participants, 1684 (52.0%) individuals were physically active, while 1558 (48%) have the physical activity variable coded as "No".

In our model, the outcome variable of interest is BMI, where higher BMI values are indicative of being considered overweight. To align with the dWOLS method, which typically is implemented so as to maximize the outcome, we transform the outcome as the negative value of the BMI measure, i.e., in our analysis, Y represents negative BMI. Physical activity serves as the "treatment" variable, denoted as A. We define $A = 1$ if a participant engaged in moderate or vigorous-intensity sports, fitness, or recreational activities; otherwise, $A = 0$ is assigned.

In addition to physical activity, we include the wealth variable X as a covariate, which is derived from reported wealth levels; we let X serve as both a tailoring variable and as a potential confounder. The wealth level X measured as a continuous positive number between 0 and 5. Educational level is represented by variable C, reflecting the number of years of schooling. We recode the five educational levels (8^{th} grade, $9^{th} - 11^{th}$ grade, high school, some college, or college grad) as 8, 10, 12, 14, and 16 years, respectively, and treat these as continuous since they represent (approximately) the number of years of formal schooling of the participant. Note that treating the educational level variable as a continuous variable helps us to obtain a smoother relationship between wealth status and educational level variables. We could then fit a straight line through the relationship. We are thus able to approximate the expectation of educational level variable given wealth status and physical activity with a linear function.

We also include age and diabetes status as covariates in our model. By including these variables as predictors of the outcome, we aim to reduce variability and control for potential distortions in the relationship between physical activity and BMI. Note that the diabetes variable is either "Yes" or "No", which we recode as 1 ("Yes") and as 0 ("No") for convenience.

In order to illustrate the concepts explored in the simulation, we utilize both tailored and non-tailored models in the data analysis. This approach aims to enhance our understanding of whether such tailoring would be beneficial for individuals from economically disadvantaged backgrounds. Specifically, we consider the two following outcome models

Model 1: $E[Y|X, A, C; \psi, \beta] = \beta_0 + \beta_1 \text{age} + \beta_2 \text{diabetes} + \beta_x X + \beta_c C + \psi_0 A,$

Model 2: $E[Y|X, A, C; \psi, \beta] = \beta_0 + \beta_1 \text{age} + \beta_2 \text{diabetes} + \beta_x X + \beta_c C + A(\psi_0 + \psi_1 X).$

We use dWOLS to estimate $\hat{\psi}_{model1} = \hat{\psi}_0$ and $\hat{\psi}_{model2} = (\hat{\psi}_0, \hat{\psi}_1)$. Estimation is performed using two types of weights: absolute value weights (w_1) and inverse probability of treatment weights (w_2). Table 5.4 shows the dWOLS estimations for model 1 and 2 when the educational level is measured.

Table 5.4: dWOLS estimations of parameters using NHANES data for $2009-2010$ when educational level is included in the regression model.

	Model 1		Model 2	
	w_1	w_2	w_1	w_2
$\hat{\beta}_0$ (SE)	-31.24 (0.76)	-31.19 (0.75)	-30.74 (0.81)	-30.73 (0.79)
$\hat{\beta}_1$ (SE)	0.00 (0.01)	0.01 (0.01)	0.00 (0.00)	0.01 (0.01)
$\hat{\beta}_2$ (SE)	-3.75 (0.41)	-3.51 (0.39)	-3.76 (0.40)	-3.52 (0.39)
$\hat{\beta}_x$ (SE)	0.08 (0.08)	0.08 (0.08)	-0.06 (0.10)	-0.04 (0.11)
$\hat{\beta}_c$ (SE)	0.08 (0.06)	0.07 (0.05)	0.07 (0.05)	0.07 (0.05)
$\hat{\psi}_0$ (SE)	1.71 (0.23)	1.73 (0.23)	0.91 (0.47)	1.02 (0.47)
$\hat{\psi}_1$ (SE)	NA	NA	0.27 (0.14)	0.24 (0.14)

In the first model, there is only a main treatment effect, so physical activity is the optimal recommendation if $\hat{\psi}_0 > 0$. In the second model, where the treatment effect is tailored to wealth status, the optimal ITR is to recommend physical activity if $\hat{\psi}_0 + \hat{\psi}_1 X > 0$. Equivalently, we can see that this means that physical activity is recommended if $X > -\hat{\psi}_0/\hat{\psi}_1$, assuming $\hat{\psi}_1$ is positive (the recommendation for physical activity is otherwise given if $X < -\hat{\psi}_0/\hat{\psi}_1$).

These results in Table 5.4 indicate that "everyone should engage in moderate or vigorous-intensity sports, fitness, or recreational activities", since the corresponding thresholds are both negative (-3.37 and -4.25), and the tailoring variable wealth is strictly positive hence always greater than these thresholds. The estimated optimal recommendation aligns with current recommendations on the benefits of physical activity for adults. Thus, there is no apparent benefit to tailoring the recommendations based on wealth status.

Next, we assume that educational level is unavailable and estimate an ITR to optimize BMI without adjusting for educational level in the analysis. We apply the proposed sensitivity analysis method to assess the impact of omitting the educational level from the model. We compare the results from this analysis to that obtained when educational level is measured, taking the estimate based on the absolute value weights as the gold standard since that choice of weights was found to provide a more accurate estimator in our simulations.

To conduct the sensitivity analysis, we first determine the value of α^* using Formula 3.1, which we reproduce here for convenience: $\alpha^* = \beta_x + \beta_c \eta_1$. In this formula, η_1 represents the coefficient of X in the model $E[C|X]$, while β_x and β_c are the coefficients of X and C, respectively. To obtain these parameters, we utilize NHANES data from the years $2011 - 2012$ as a secondary data source and estimate these key sensitivity parameters needed to posit a realistic range for α^* using linear regression models. The estimate of these parameters are shown in Table 5.5.

Table 5.5: Estimations of parameters using NHANES data for $2011 - 2012$.

	Model 1	Model 2
$\hat{\eta}_1$	0.67	0.67
$\hat{\beta}_c$	0.05	0.05
$\hat{\beta}_x$	0.13	0.08
α^*	0.16	0.11

Having posited the value of α^*, we follow the procedure outlined in Algorithm 2. We consider $(0.01, 0.21)$ as the plausible range of α (a range around α^*) and estimate $\hat{\psi}_{model1}$ and $\hat{\psi}_{model2}$ using dWOLS including the treatment with an offset of αX. In the next section, we present the results of the estimated values in the models which omit the educational level.

5.3 Results

This section presents the estimates of $\hat{\psi}_{model1}$ and $\hat{\psi}_{model2}$ for each α value within the specified range, considering models where educational level is unmeasured. Table 5.6 provides the estimates of $\hat{\psi}_{model1}$ and $\hat{\psi}_{model2}$ based on the absolute value weights and inverse probability of treatment weights denoted by w_1 and w_2, respectively. Note that the estimates using w_1 exhibit slight changes however this is not evident from the table as the results are rounded to two decimal places.

Table 5.6: Estimates of the treatment decision rule parameter $\hat{\psi}_{model1}$ (average treatment effect with no tailoring) and $\hat{\psi}_{model2}$ (parameters of a tailored decision rule) as a function of the sensitivity parameter α. The estimated values for $\hat{\psi}_{model1} = \hat{\psi}_0$, when the educational level is measured using weights w_1 and w_2, are 1.71 and 1.73, respectively. The estimated values for $\hat{\psi}_{model2} = (\hat{\psi}_0, \hat{\psi}_1)$, when the educational level is measured using weights w_1 and w_2, are $(0.91, 0.27)$ and $(1.02, 0.24)$, respectively.

α	$\hat{\hat{\psi}}_{0-w_1}$ (SE)	$\hat{\hat{\psi}}_{0-w_2}$ (SE)	$\hat{\psi}_{0-w_1}$ (SE)	$\hat{\psi}_{1-w_1}$ (SE)	$\hat{\psi}_{0-w_2}$ (SE)	$\hat{\psi}_{1-w_2}$ (SE)
0.01	1.71 (0.23)	1.72 (0.23)	0.97 (0.37)	0.25 (0.10)	1.01 (0.36)	0.24 (0.09)
0.02	1.71 (0.23)	1.72 (0.23)	1.00 (0.37)	0.24 (0.10)	1.04 (0.36)	0.23 (0.09)
0.03	1.71 (0.23)	1.72 (0.23)	1.03 (0.37)	0.23 (0.10)	1.07 (0.36)	0.22 (0.09)
0.04	1.71 (0.23)	1.73 (0.23)	1.06 (0.37)	0.22 (0.10)	1.10 (0.36)	0.21 (0.09)
0.05	1.71 (0.23)	1.73 (0.23)	1.09 (0.37)	0.21 (0.10)	1.13 (0.36)	0.20 (0.09)
0.06	1.71 (0.23)	1.73 (0.23)	1.12 (0.37)	0.20 (0.10)	1.16 (0.36)	0.19 (0.09)
0.07	1.71 (0.23)	1.73 (0.23)	1.15 (0.37)	0.19 (0.10)	1.19 (0.36)	0.18 (0.09)
0.08	1.71 (0.23)	1.73 (0.23)	1.17 (0.37)	0.18 (0.10)	1.22 (0.36)	0.17 (0.09)
0.09	1.71 (0.23)	1.73 (0.23)	1.20 (0.37)	0.17 (0.10)	1.25 (0.36)	0.17 (0.09)
0.10	1.71 (0.23)	1.73 (0.23)	1.23 (0.37)	0.16 (0.10)	1.28 (0.36)	0.16 (0.09)
0.11	1.71 (0.23)	1.73 (0.23)	1.26 (0.37)	0.15 (0.10)	1.31 (0.36)	0.15 (0.09)
0.12	1.71 (0.23)	1.73 (0.23)	1.29 (0.37)	0.14 (0.10)	1.34 (0.36)	0.14 (0.09)
0.13	1.71 (0.23)	1.73 (0.23)	1.32 (0.37)	0.13 (0.10)	1.36 (0.36)	0.13 (0.09)
0.14	1.71 (0.23)	1.73 (0.23)	1.35 (0.37)	0.12 (0.10)	1.39 (0.36)	0.12 (0.09)
0.15	1.71 (0.23)	1.73 (0.23)	1.38 (0.37)	0.11 (0.10)	1.42 (0.36)	0.11 (0.09)
0.16	1.71 (0.23)	1.73 (0.23)	1.40 (0.37)	0.10 (0.10)	1.45 (0.36)	0.10 (0.09)
0.17	1.71 (0.23)	1.73 (0.23)	1.43 (0.37)	0.09 (0.10)	1.48 (0.36)	0.09 (0.09)
0.18	1.71 (0.23)	1.73 (0.23)	1.46 (0.37)	0.08 (0.10)	1.51 (0.36)	0.08 (0.09)
0.19	1.71 (0.23)	1.73 (0.23)	1.49 (0.37)	0.07 (0.10)	1.54 (0.36)	0.07 (0.09)
0.20	1.71 (0.23)	1.73 (0.23)	1.52 (0.37)	0.06 (0.10)	1.57 (0.36)	0.06 (0.09)
0.21	1.71 (0.23)	1.73 (0.23)	1.55 (0.37)	0.06 (0.10)	1.60 (0.36)	0.05 (0.09)

Furthermore, Figure 5.1 displays the estimates of $\hat{\psi}_{model1}$ while Figure 5.2 shows the estimates of $\hat{\psi}_{model2}$ as α varies. As we saw in Section 4.2.3, both the estimates obtained with absolute value weights and inverse weights are consistent and the estimates derived from the absolute value weights display lower variability. Therefore, as noted above, we consider the estimates obtained with absolute value weights as a baseline representation

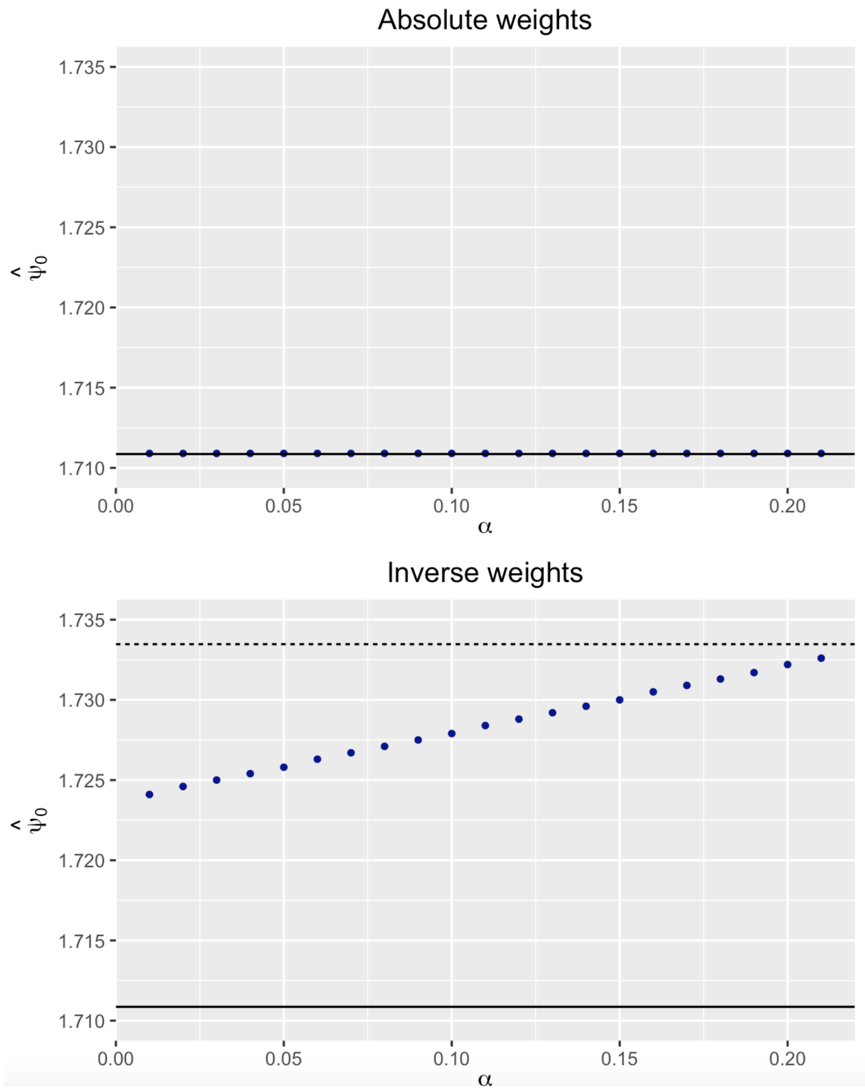

Figure 5.1: Estimates of the treatment decision rule parameter $\hat{\psi}_{model1}$ as a function of the sensitivity parameter α. The estimated parameters using absolute value weights (w_1) when educational level is included are shown by solid lines. The dashed line indicates the estimated parameters when adjusting for the educational level using inverse probability of treatment weights (w_2).

(i.e., our best guess at the truth) in both figures. The solid lines represent the estimated parameters for weight w_1 when the educational level is included. The dashed lines indicate the estimated parameters when adjusting for the educational level using weight w_2.

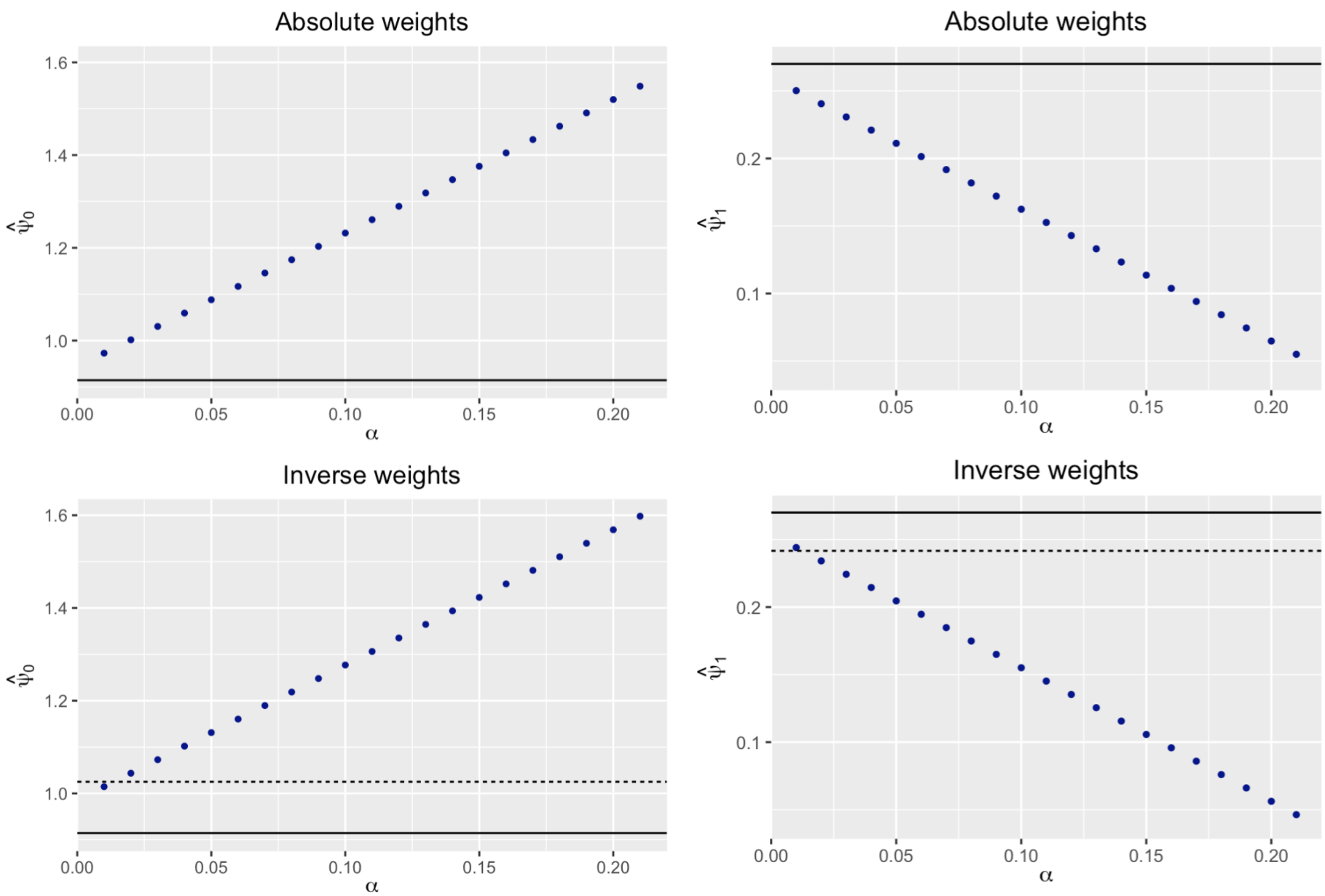

Figure 5.2: Estimates of the treatment decision rule parameter $\hat{\psi}_{model2}$ as a function of the sensitivity parameter α. The estimated parameters using absolute value weights (w_1) when educational level is included are shown by solid lines. The dashed lines indicate the estimated parameters when adjusting for the educational level using inverse probability of treatment weights (w_2).

Overall, the estimated optimal ITRs, regardless of whether they are tailored or not, support the conventional belief that adults should engage in moderate or vigorous-intensity sports, fitness, or recreational activities. In this particular analysis, the presence of an unmeasured confounder does not reverse this recommendation.

5.4 Summary

In this chapter, we applied the proposed sensitivity analysis method to a real dataset, aiming to examine how the optimal treatment regime changes in the presence of an unmeasured confounder. Specifically, we utilized NHANES data from the years $2009 - 2010$ to analyze the association between BMI and physical activity, tailored to the wealth level. We assumed that educational level is unknown and, therefore, not adjusted for. To estimate the value of the sensitivity parameter α, we employed a secondary dataset obtained from NHANES for the years $2011 - 2012$.

We conducted two analyses to explore the impact of a potential unmeasured confounder on the outcome model. One of the analyses was tailored to an individual's wealth status, while the other was conducted without tailoring. The estimated optimal ITRs from both analyses support each other, leading to the conclusion that physical activity should always be recommended to reduce BMI.

The analysis had limitations related to measurement error, missing data, and assumptions about the relationship between measured and unmeasured factors. In the next chapter, we will further discuss these limitations. By assessing the impact of the limitations, we can gain a better understanding of the strengths and weaknesses of our analysis.

Chapter 6

Discussion and Conclusion

This chapter provides additional discussions about the proposed approach, as well as the data analysis. The approach explored in this thesis consists of a straightforward sensitivity analysis method, specifically designed to address potential bias arising from unmeasured confounding when estimating DTRs. The proposed sensitivity analysis approach considered in this work incorporates a sensitivity parameter, which accounts for the posited impact of the unmeasured confounder on the outcome. This impact is captured by the correlation between an unmeasured confounder and a measured confounder, providing a means to adjust for potential confounding effects that may have been omitted in a standard dWOLS analysis. This method is simple and applicable to various types of unmeasured confounders, although the development is motivated by and analytically most obvious in the case where both the measured and unmeasured confounders are continuous and are linearly related both to one another and to the outcome.

It is important to note that implementing this method requires the specification of a parametric model to capture the relationship between the unmeasured confounder and the measured confounder. This model serves as a crucial component for determining the appropriate offset to adjust for the unmeasured confounder in the outcome model. Finding an appropriate model for the conditional mean of the unmeasured confounder(s) given the measured covariates may be a challenging task, particularly in the absence of external data or domain expertise.

As previously mentioned, the proposed sensitivity analysis approach provides a tool for reducing the bias in the blip parameters due to unmeasured confounding and leads to more accurate estimators of treatment effects. However, it is important to note that the approach cannot completely eliminate all of the bias since the issue of confounding is not fully resolved. Note that we could not eliminate all of the bias since we were not fully accounting for confounding: the method accounts for the relationship between the unmeasured confounder at the outcome, but not for its relationship with the treatment.

The approach was shown to perform well with simulated data and also appears to perform reasonably well for a real-world application. In simulated scenarios, where the true values of the underlying treatment rule parameters are known, the approach confirms the doubly-robustness property of the dWOLS blip parameter estimators and examines the impact of omitting either one or two confounders during estimation. While evaluating the approach's performance in real data scenarios poses challenges due to the absence of known true values, it shows reasonable performance based on available data.

The proposed approach has limitations and restrictions that need to be considered. The sensitivity analysis proposed and studied in this thesis may fail to reduce the bias of the estimators in scenarios where there is only a weak (or no) association between the unmeasured confounder(s) and the measured confounder(s) or when this relationship is not (approximately) linear. Additionally, the performance of the method has not been investigated in settings where other assumptions required for unbiasedness, such as positivity, are violated.

It is crucial to recognize that the analysis conducted in Chapter 5 was subject to some assumptions and limitations that could impact the findings. Our analysis relied on certain assumptions regarding the relationship between measured and unmeasured factors. Specifically, we made the assumption of a linear relationship between wealth status and educational level, despite the possibility that the actual relationship could be more complex. However, as we had access to data on both these variables, we were in fact able to assess this relationship and observed it to be at least approximately linear (results not shown). Of course, such an assessment would not typically be possible in settings where the unmeasured confounder was entirely unavailable even in an external or validation dataset. A limitation of the analysis is that we only considered a single-stage setting. It is also important to acknowledge that the confounding in the data was found to be weak. It typically leads to less bias in the results when confounding is weak. Furthermore, the strength of the correlation between measured and unmeasured confounders was not very strong in this analysis. Thus, the measured confounders do not strongly represent the influence of the unmeasured confounders.

The analysis also had limitations related to measurement error and missing data. Measurement error was introduced, for example, when we converted the categorical educational levels into a continuous variable, where midpoint values were assigned to each level. While this conversion introduced some degree of measurement error, we expect the impact to be small given the narrow range of each category, typically spanning only two years. Missing data posed another issue in our analysis. There were instances where certain variables or observations were not available. In the NHANES analysis in this thesis, missing data were simply removed. A more sophisticated approach might incorporate inverse probability weighting for missingness, or use multiple imputation. However, the combined use of these methods with the sensitivity analysis has not been explored either theoretically or in simulation. This would be an interesting avenue of future work.

Based on the limitations discussed here, there are several areas for future research that could improve the use of the proposed method. One possible direction is to adapt the method for situations where there are multiple stages involved. This is particularly important for real-world applications, which often involve complex multi-stage processes. Another area for future research is to explore other regression-based methods for estimating DTRs. While the thesis focused on dWOLS for estimating treatment regimes, this approach can be extended to other regression-based estimation methods aimed at either

DTRs or simpler estimands such as an average treatment effect, or a conditional average treatment effect.

Appendix A

Sensitivity Analysis for Other DGMs When There Is No Interaction Between the Treatment and Covariate

Scenario 1

Table A.1 shows the mean and standard error of $\hat{\psi}_0$ for the following DGMs. The true value of ψ_0 in a linear causal model as a function of the sensitivity parameter α is 1 and there is no interaction between treatment and covariate. Figure A.1 also includes the boxplots of empirical distribution of the estimator ψ_0. The DGM is as follows

$$C \sim \mathrm{Ber}(0.55)$$

$$X|C = c \sim \mathrm{Ber}(0.25 + 0.75c)$$

$$A|X = x, C = c \sim \mathrm{Ber}(\mathrm{expit}(-x + 0.5c))$$

$$Y|C = c, X = x, A = a \sim \mathrm{N}(\beta_0 + \beta_a a + \beta_x x + \beta_{ax} ax + \beta_c c, 1)$$

where the value of $\beta = (\beta_0, \beta_a, \beta_x, \beta_{ax}, \beta_c)$ for each DGM is

- DGM 1: $\beta = (1, 1, -1.5, 0, 2)$
- DGM 2: $\beta = (1, 1, 1.7, 0, 2.6)$
- DGM 3: $\beta = (1, 1, -2.5, 0, -2.6)$.

Table A.1: Mean (SE) of blip parameter $\hat{\psi}_0$ as a function of the sensitivity parameter α for the case that distribution of the unmeasured confounder is $\mathrm{Ber}(0.55)$. The true value is $\psi_0 = 1$ and there is interaction between treatment and covariate. The true value of α are $\alpha^*_{DGM1} = 0.16$, $\alpha^*_{DGM2} = 3.85$, and $\alpha^*_{DGM3} = -4.26$.

			$n = 1000$			$n = 5000$	
DGM	α	$\hat{\psi}_0$ (SE)	$\hat{\psi}_{0-w_1}$ (SE)	$\hat{\psi}_{0-w_2}$ (SE)	$\hat{\psi}_0$ (SE)	$\hat{\psi}_{0-w_1}$ (SE)	$\hat{\psi}_{0-w_2}$ (SE)
DGM 1	-0.25	1.03 (0.07)	1.09 (0.07)	1.09 (0.07)	1.03 (0.04)	1.08 (0.03)	1.09 (0.04)
	-0.2	1.04 (0.07)	1.09 (0.07)	1.09 (0.07)	1.04 (0.04)	1.08 (0.03)	1.09 (0.04)
	-0.15	1.05 (0.07)	1.09 (0.07)	1.09 (0.07)	1.04 (0.03)	1.08 (0.03)	1.09 (0.04)
	-0.1	1.05 (0.07)	1.09 (0.07)	1.09 (0.07)	1.05 (0.03)	1.08 (0.03)	1.09 (0.04)
	-0.05	1.06 (0.07)	1.09 (0.07)	1.09 (0.07)	1.05 (0.03)	1.08 (0.03)	1.09 (0.04)
	0	1.06 (0.07)	1.09 (0.07)	1.09 (0.07)	1.06 (0.03)	1.08 (0.03)	1.09 (0.04)
	0.05	1.07 (0.07)	1.09 (0.07)	1.09 (0.07)	1.07 (0.03)	1.08 (0.03)	1.09 (0.04)
	0.1	1.08 (0.07)	1.09 (0.07)	1.09 (0.07)	1.07 (0.03)	1.08 (0.03)	1.09 (0.04)
	0.15	1.08 (0.07)	1.09 (0.07)	1.09 (0.07)	1.08 (0.03)	1.08 (0.03)	1.09 (0.04)
	0.2	1.09 (0.07)	1.09 (0.07)	1.09 (0.07)	1.09 (0.03)	1.08 (0.03)	1.09 (0.04)
	0.25	1.10 (0.07)	1.09 (0.07)	1.09 (0.07)	1.09 (0.03)	1.08 (0.03)	1.09 (0.04)
DGM 2	3.5	1.07 (0.08)	1.11 (0.08)	1.12 (0.08)	1.06 (0.04)	1.11 (0.04)	1.11 (0.04)
	3.55	1.07 (0.08)	1.11 (0.08)	1.12 (0.08)	1.07 (0.04)	1.11 (0.04)	1.11 (0.04)
	3.6	1.08 (0.08)	1.11 (0.08)	1.12 (0.08)	1.07 (0.04)	1.11 (0.04)	1.11 (0.04)
	3.65	1.08 (0.08)	1.11 (0.08)	1.12 (0.08)	1.08 (0.04)	1.11 (0.04)	1.11 (0.04)
	3.7	1.09 (0.08)	1.11 (0.08)	1.12 (0.08)	1.09 (0.04)	1.11 (0.04)	1.11 (0.04)
	3.75	1.10 (0.08)	1.11 (0.08)	1.12 (0.08)	1.09 (0.04)	1.11 (0.04)	1.11 (0.04)
	3.8	1.10 (0.08)	1.11 (0.08)	1.12 (0.08)	1.10 (0.04)	1.11 (0.04)	1.11 (0.04)
	3.85	1.11 (0.08)	1.11 (0.08)	1.12 (0.08)	1.11 (0.04)	1.11 (0.04)	1.11 (0.04)
	3.9	1.12 (0.08)	1.11 (0.08)	1.12 (0.08)	1.11 (0.04)	1.11 (0.04)	1.11 (0.04)
	3.95	1.12 (0.08)	1.11 (0.08)	1.12 (0.08)	1.12 (0.04)	1.11 (0.04)	1.11 (0.04)
	4	1.13 (0.08)	1.11 (0.08)	1.12 (0.08)	1.13 (0.04)	1.11 (0.04)	1.11 (0.04)
DGM 3	-4.5	0.91 (0.08)	0.89 (0.08)	0.89 (0.08)	0.91 (0.04)	0.89 (0.04)	0.88 (0.04)
	-4.45	0.92 (0.08)	0.89 (0.08)	0.89 (0.08)	0.92 (0.04)	0.89 (0.04)	0.88 (0.04)
	-4.4	0.93 (0.08)	0.89 (0.08)	0.89 (0.08)	0.92 (0.04)	0.89 (0.04)	0.88 (0.04)
	-4.35	0.93 (0.08)	0.89 (0.08)	0.89 (0.08)	0.93 (0.04)	0.89 (0.04)	0.88 (0.04)
	-4.3	0.94 (0.08)	0.89 (0.08)	0.89 (0.08)	0.94 (0.04)	0.89 (0.04)	0.88 (0.04)
	-4.25	0.95 (0.08)	0.89 (0.08)	0.89 (0.08)	0.94 (0.04)	0.89 (0.04)	0.88 (0.04)
	-4.2	0.95 (0.08)	0.89 (0.08)	0.89 (0.08)	0.95 (0.04)	0.89 (0.04)	0.88 (0.04)
	-4.15	0.96 (0.08)	0.89 (0.08)	0.89 (0.08)	0.96 (0.04)	0.89 (0.04)	0.88 (0.04)
	-4.1	0.97 (0.08)	0.89 (0.08)	0.89 (0.08)	0.96 (0.04)	0.89 (0.04)	0.88 (0.04)
	-4.05	0.97 (0.08)	0.89 (0.08)	0.89 (0.08)	0.97 (0.04)	0.89 (0.04)	0.88 (0.04)
	-4	0.98 (0.08)	0.89 (0.08)	0.89 (0.08)	0.97 (0.04)	0.89 (0.04)	0.88 (0.04)

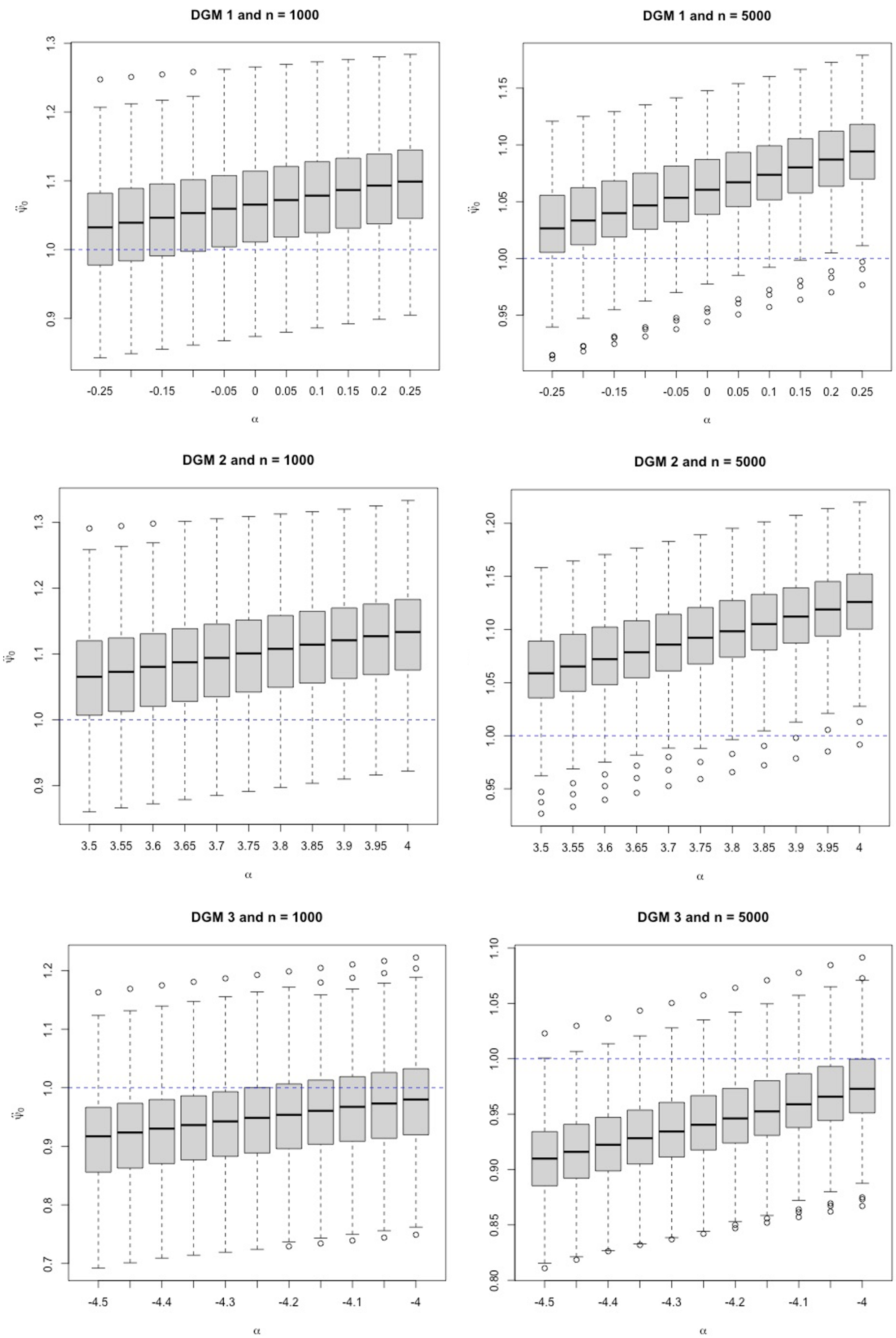

Figure A.1: Box-plots of empirical distribution of the estimator $\hat{\psi}_0$ of the true causal parameter $\psi_0 = 1$ (marked via a horizontal dashed line) in a linear causal model as a function of the sensitivity parameter α when there is no interaction between the treatment and covariate.

Scenario 2

Table A.2 shows the mean and standard error of $\hat{\psi}_0$ for the following DGMs. The true value of ψ_0 in a linear causal model as a function of the sensitivity parameter α is 1 and there is no interaction between treatment and covariate. Figure A.2 also includes the box-plots of empirical distribution of the estimator ψ_0. The DGM is as follows

$$\begin{aligned}
C &\sim \mathrm{N}(0.5, 0.5) \\
X|C = c &\sim \mathrm{N}(2.2c, 0.5) \\
A|X = x, C = c &\sim \mathrm{Ber}(\mathrm{expit}(-x + 0.5c)) \\
Y|C = c, X = x, A = a &\sim \mathrm{N}(\beta_0 + \beta_a a + \beta_x x + \beta_{ax} ax + \beta_c c, 1).
\end{aligned}$$

where the value of $\beta = (\beta_0, \beta_a, \beta_x, \beta_{ax}, \beta_c)$ for each DGM is

- DGM 1: $\beta = (1, 1, -1.5, 0, 2)$
- DGM 2: $\beta = (1, 1, 1.7, 0, 2.6)$
- DGM 3: $\beta = (1, 1, -2.5, 0, -2.6)$.

Table A.2: Mean (SE) of blip parameter $\hat{\psi}_0$ as a function of the sensitivity parameter α for the case that distribution of the unmeasured confounder is $\mathrm{N}(0.5, 0.5)$. The true value is $\psi_0 = 1$ and there is interaction between treatment and covariate. The true value of α are $\alpha^*_{DGM1} = -0.82$, $\alpha^*_{DGM2} = 2.94$, and $\alpha^*_{DGM3} = -3.83$.

			$n = 1000$			$n = 5000$	
DGM	α	$\hat{\psi}_0$ (SE)	$\hat{\psi}_{0-w_1}$ (SE)	$\hat{\psi}_{0-w_2}$ (SE)	$\hat{\psi}_0$ (SE)	$\hat{\psi}_{0-w_1}$ (SE)	$\hat{\psi}_{0-w_2}$ (SE)
DGM 1	-1	0.79 (0.08)	1.04 (0.08)	1.04 (0.09)	0.78 (0.03)	1.04 (0.03)	1.04 (0.04)
	-0.95	0.84 (0.08)	1.04 (0.08)	1.04 (0.09)	0.83 (0.03)	1.04 (0.03)	1.04 (0.04)
	-0.9	0.88 (0.08)	1.04 (0.08)	1.04 (0.09)	0.88 (0.03)	1.04 (0.03)	1.04 (0.04)
	-0.85	0.93 (0.08)	1.04 (0.08)	1.04 (0.09)	0.93 (0.03)	1.04 (0.03)	1.04 (0.04)
	-0.8	0.98 (0.07)	1.04 (0.08)	1.04 (0.09)	0.98 (0.03)	1.04 (0.03)	1.04 (0.04)
	-0.75	1.03 (0.07)	1.04 (0.08)	1.04 (0.09)	1.03 (0.03)	1.04 (0.03)	1.04 (0.04)
	-0.7	1.08 (0.07)	1.04 (0.08)	1.04 (0.09)	1.08 (0.03)	1.04 (0.03)	1.04 (0.04)
	-0.65	1.13 (0.08)	1.04 (0.08)	1.04 (0.09)	1.13 (0.03)	1.04 (0.03)	1.04 (0.04)
	-0.6	1.18 (0.08)	1.04 (0.08)	1.04 (0.09)	1.18 (0.03)	1.04 (0.03)	1.04 (0.04)
	-0.55	1.23 (0.08)	1.04 (0.08)	1.04 (0.09)	1.23 (0.03)	1.04 (0.03)	1.04 (0.04)
	-0.5	1.28 (0.08)	1.04 (0.08)	1.04 (0.09)	1.28 (0.03)	1.04 (0.03)	1.04 (0.04)
DGM 2	2.5	0.87 (0.08)	1.05 (0.08)	1.05 (0.10)	0.87 (0.03)	1.05 (0.03)	1.05 (0.04)
	2.55	0.92 (0.08)	1.05 (0.08)	1.05 (0.09)	0.92 (0.03)	1.05 (0.03)	1.05 (0.04)
	2.6	0.97 (0.08)	1.05 (0.08)	1.05 (0.09)	0.97 (0.03)	1.05 (0.03)	1.05 (0.04)
	2.65	1.02 (0.08)	1.05 (0.08)	1.05 (0.09)	1.02 (0.03)	1.05 (0.03)	1.05 (0.04)
	2.7	1.07 (0.08)	1.05 (0.08)	1.05 (0.09)	1.07 (0.03)	1.05 (0.03)	1.05 (0.04)
	2.75	1.12 (0.08)	1.05 (0.08)	1.05 (0.09)	1.12 (0.03)	1.05 (0.03)	1.05 (0.04)
	2.8	1.17 (0.08)	1.05 (0.08)	1.05 (0.09)	1.17 (0.03)	1.05 (0.03)	1.05 (0.04)
	2.85	1.22 (0.08)	1.05 (0.08)	1.05 (0.10)	1.22 (0.03)	1.05 (0.03)	1.05 (0.04)
	2.9	1.27 (0.08)	1.05 (0.08)	1.05 (0.10)	1.27 (0.03)	1.05 (0.03)	1.06 (0.04)
	2.95	1.31 (0.08)	1.05 (0.08)	1.05 (0.10)	1.32 (0.03)	1.05 (0.03)	1.06 (0.04)
	3	1.36 (0.08)	1.05 (0.08)	1.05 (0.10)	1.37 (0.03)	1.05 (0.03)	1.06 (0.04)
DGM 3	-3.85	0.59 (0.08)	0.95 (0.08)	0.95 (0.10)	0.58 (0.03)	0.94 (0.04)	0.94 (0.04)
	-3.8	0.64 (0.08)	0.95 (0.08)	0.95 (0.10)	0.63 (0.03)	0.94 (0.04)	0.94 (0.04)
	-3.75	0.69 (0.08)	0.95 (0.08)	0.95 (0.09)	0.68 (0.03)	0.94 (0.04)	0.94 (0.04)
	-3.7	0.74 (0.08)	0.95 (0.08)	0.95 (0.09)	0.73 (0.03)	0.94 (0.04)	0.94 (0.04)
	-3.65	0.79 (0.08)	0.95 (0.08)	0.95 (0.09)	0.78 (0.03)	0.94 (0.04)	0.94 (0.04)
	-3.6	0.84 (0.08)	0.95 (0.08)	0.95 (0.09)	0.83 (0.03)	0.94 (0.04)	0.94 (0.04)
	-3.55	0.89 (0.08)	0.95 (0.08)	0.95 (0.09)	0.88 (0.03)	0.94 (0.04)	0.94 (0.04)
	-3.5	0.94 (0.08)	0.95 (0.08)	0.95 (0.09)	0.93 (0.03)	0.94 (0.04)	0.94 (0.04)
	-3.45	0.99 (0.08)	0.95 (0.08)	0.95 (0.09)	0.98 (0.03)	0.94 (0.04)	0.94 (0.04)
	-3.4	1.04 (0.08)	0.95 (0.08)	0.95 (0.09)	1.03 (0.03)	0.94 (0.04)	0.94 (0.04)
	-3.35	1.09 (0.08)	0.95 (0.08)	0.95 (0.09)	1.08 (0.03)	0.94 (0.04)	0.94 (0.04)

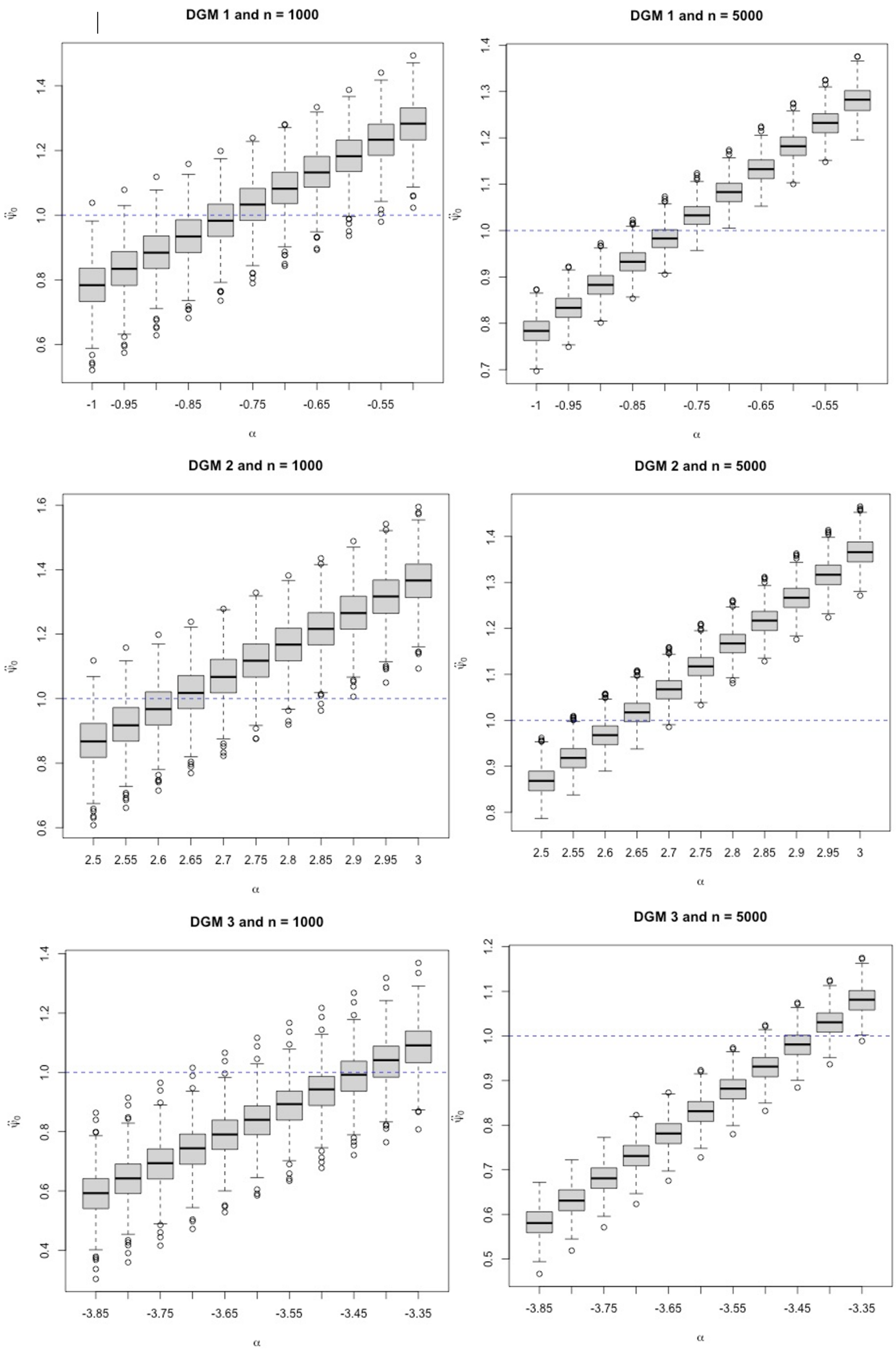

Figure A.2: Box-plots of empirical distribution of the estimator $\hat{\psi}_0$ of the true causal parameter $\psi_0 = 1$ (marked via a horizontal dashed line) in a linear causal model as a function of the sensitivity parameter α when there is no interaction between the treatment and covariate.

Appendix B

Sensitivity Analysis When There Is Interaction Between the Treatment and Covariate

Considering the following DGM

$$
\begin{aligned}
C &\sim \mathrm{Uni}(0,1) \\
X|C=c &\sim \mathrm{Ber}(c) \\
A|X=x, C=c &\sim \mathrm{Ber}(\mathrm{expit}(-x+0.5c)) \\
Y|C=c, X=x, A=a &\sim \mathrm{N}(\beta_0+\beta_x x+\beta_a a+\beta_{ax} ax+\beta_c c, 1)
\end{aligned}
$$

where the value of $\beta = (\beta_0, \beta_a, \beta_x, \beta_{ax}, \beta_c)$ for each DGM is as follows

- DGM 1: $\beta = (1, 1, -1.5, 1, 2)$
- DGM 2: $\beta = (1, 1, 1.7, 1, 2.6)$
- DGM 3: $\beta = (1, 1, -2.5, 1, -2.6)$,

Figure B.1 shows the average of estimators of ψ_0 and ψ_1 for DGM 1 when $n = 5000$. Figure B.2 also shows the average of estimators of ψ_0 and ψ_1 for DGM 2 when $n = 1000$, Figure B.3 shows the average of estimators of ψ_0 and ψ_1 for DGM 2 when $n = 5000$, Figure B.4 shows the average of estimators of ψ_0 and ψ_1 for DGM 3 when $n = 1000$, and Figure B.5 shows the average of estimators of ψ_0 and ψ_1 for DGM 3 when $n = 5000$.

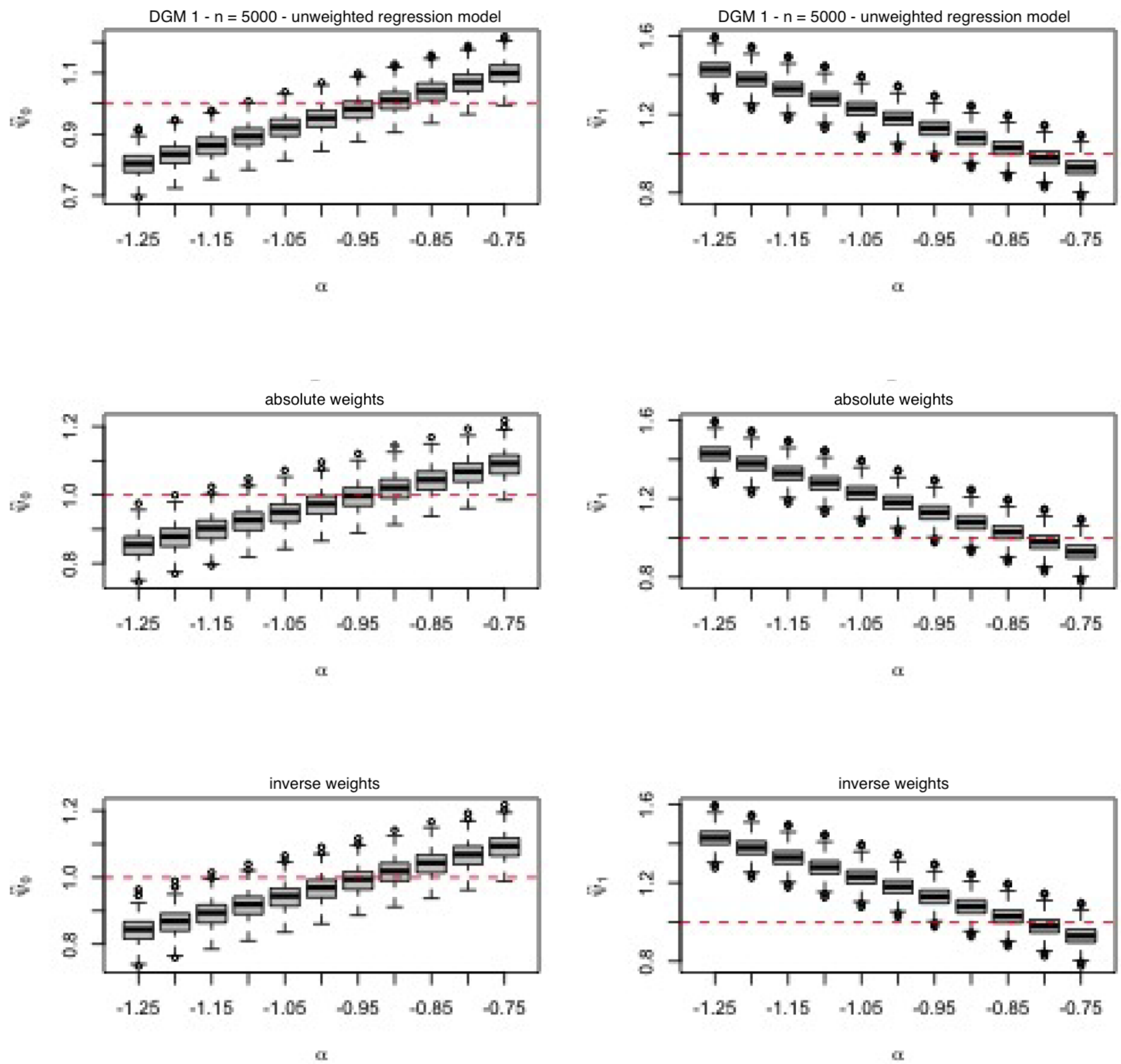

Figure B.1: Box-plots of empirical distribution of the estimator $\hat{\psi}_0$ and $\hat{\psi}_1$ for DGM 1 when $n = 5000$. The true causal parameters are $\psi_0 = \psi_1 = 1$ (marked via a horizontal dashed line) in a linear causal model as a function of the sensitivity parameter α when there is interaction between the treatment and covariate.

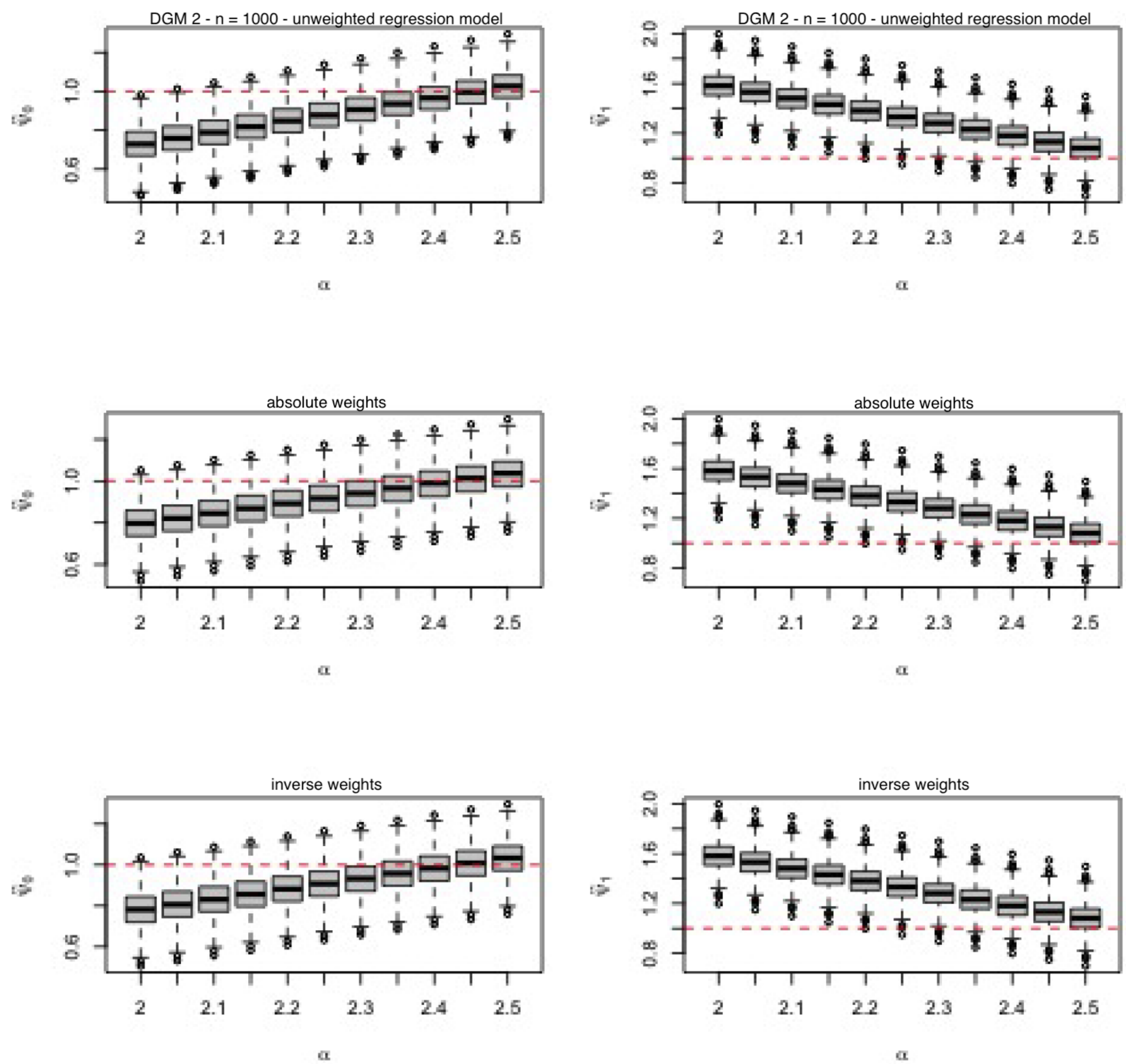

Figure B.2: Box-plots of empirical distribution of the estimator $\hat{\psi}_0$ and $\hat{\psi}_1$ for DGM 2 when $n = 1000$. The true causal parameters are $\psi_0 = \psi_1 = 1$ (marked via a horizontal dashed line) in a linear causal model as a function of the sensitivity parameter α when there is interaction between the treatment and covariate.

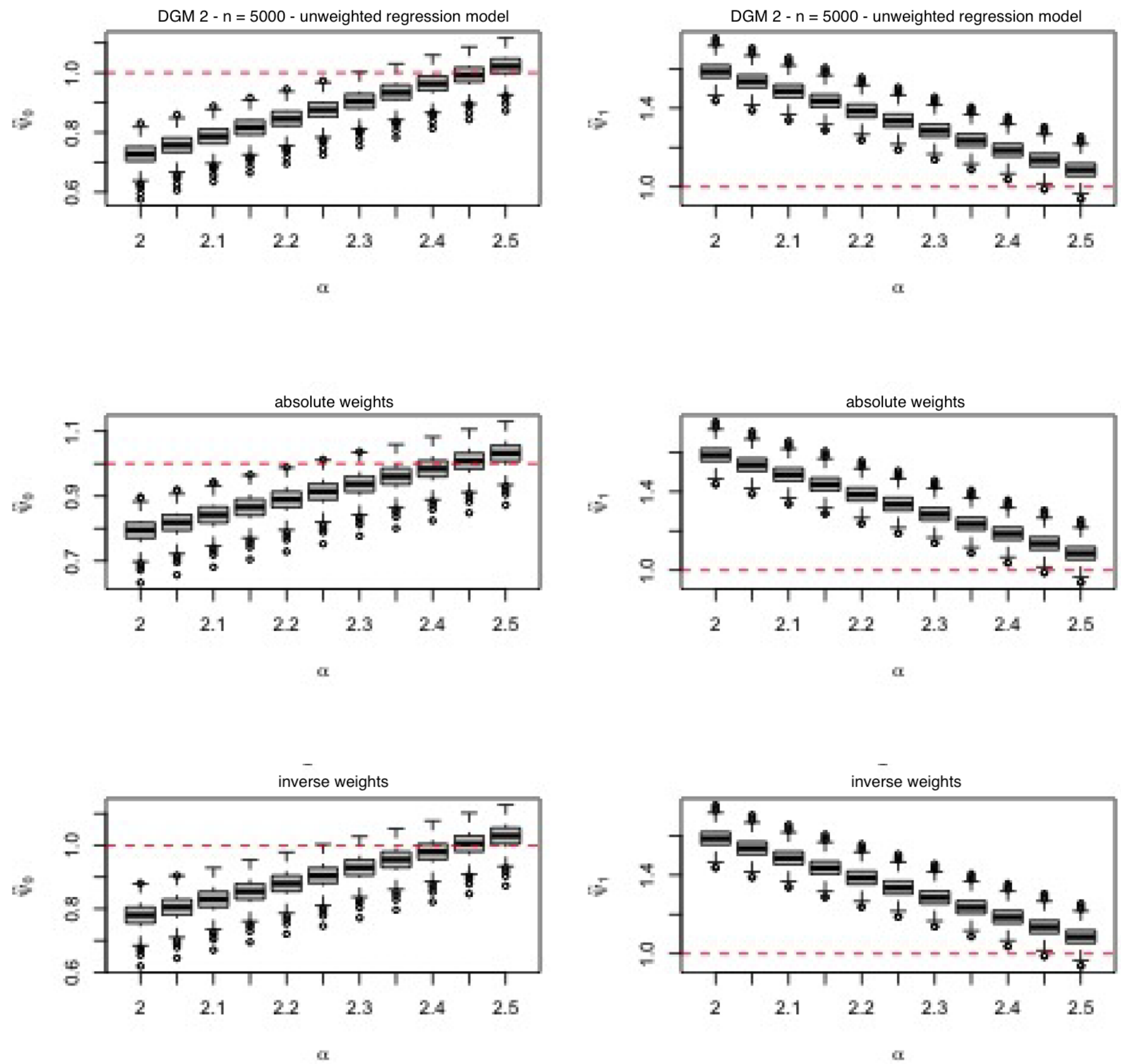

Figure B.3: Box-plots of empirical distribution of the estimator $\hat{\psi}_0$ and $\hat{\psi}_1$ for DGM 2 when $n = 5000$. The true causal parameters are $\psi_0 = \psi_1 = 1$ (marked via a horizontal dashed line) in a linear causal model as a function of the sensitivity parameter α when there is interaction between the treatment and covariate.

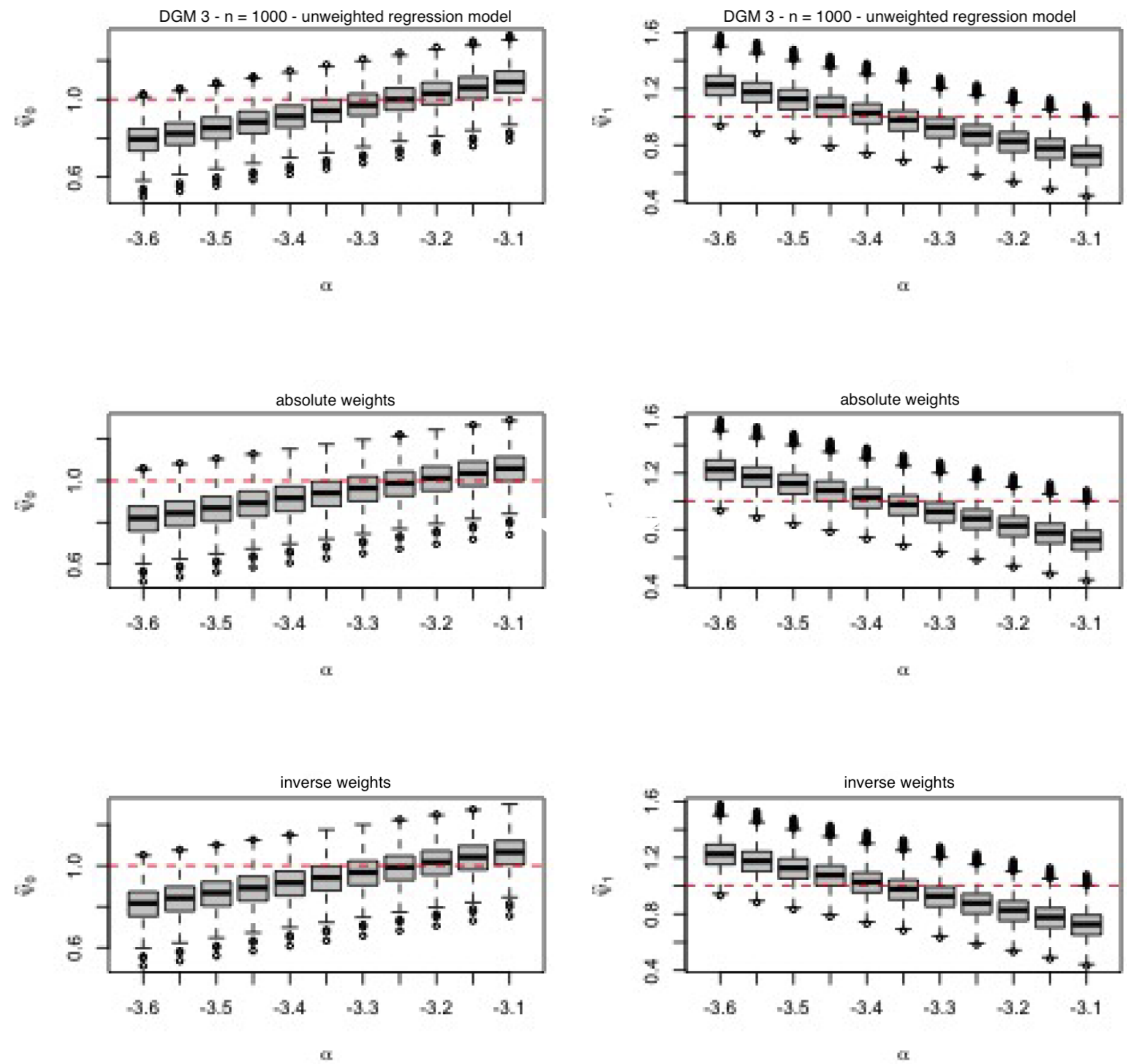

Figure B.4: Box-plots of empirical distribution of the estimator $\hat{\psi}_0$ and $\hat{\psi}_1$ for DGM 3 when $n = 1000$. The true causal parameters are $\psi_0 = \psi_1 = 1$ (marked via a horizontal dashed line) in a linear causal model as a function of the sensitivity parameter α when there is interaction between the treatment and covariate.

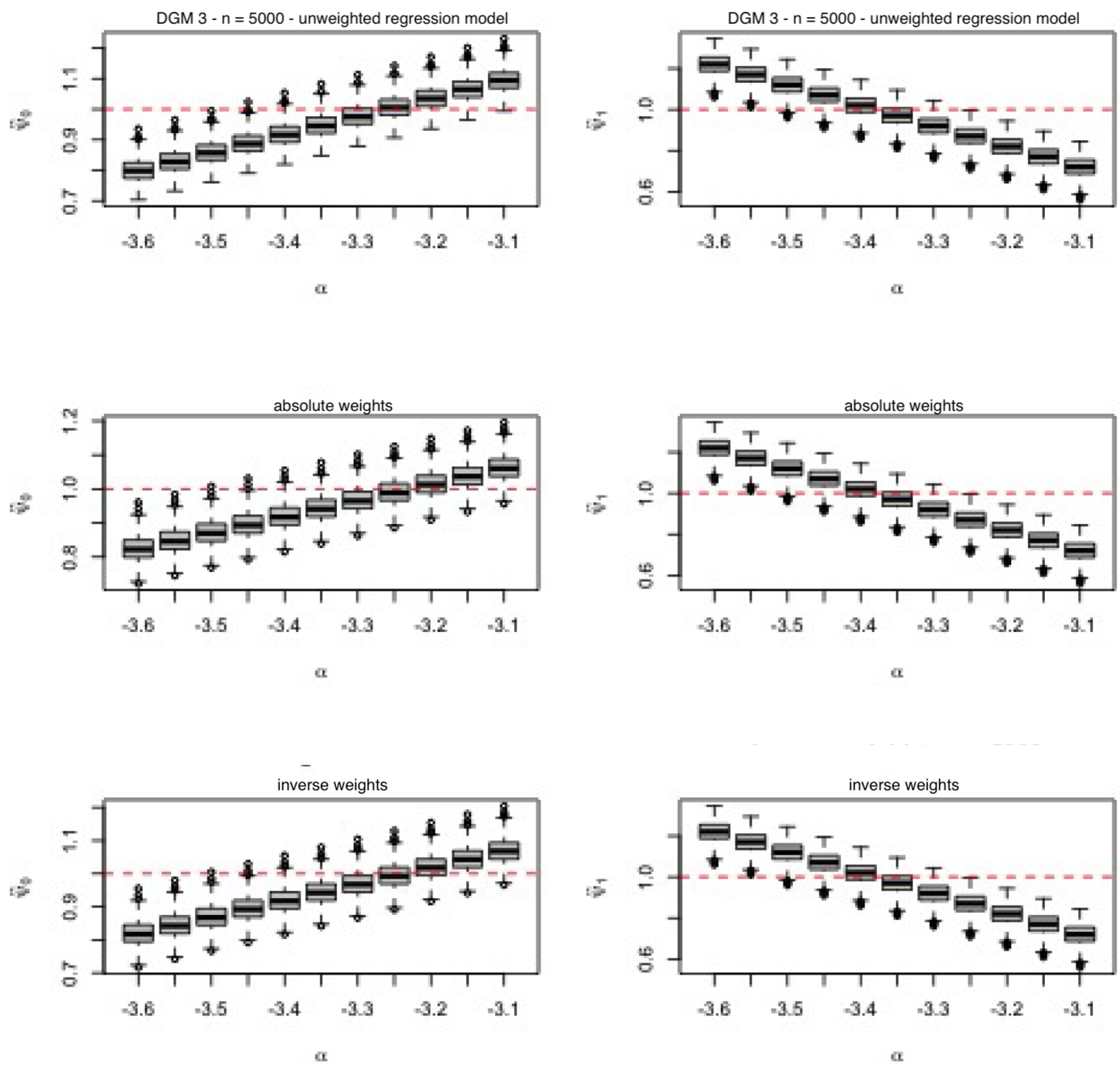

Figure B.5: Box-plots of empirical distribution of the estimator $\hat{\psi}_0$ and $\hat{\psi}_1$ for DGM 3 when $n = 5000$. The true causal parameters are $\psi_0 = \psi_1 = 1$ (marked via a horizontal dashed line) in a linear causal model as a function of the sensitivity parameter α when there is interaction between the treatment and covariate.

Bibliography

[1] Almustafa, K. M. Prediction of heart disease and classifiers' sensitivity analysis. *BMC Bioinformatics 21*, 278 (2020).

[2] Ardern, C. I., Janssen, I., Ross, R., and Katzmarzyk, P. T. Development of health-related waist circumference thresholds within BMI categories. *Obesity Research 12*, 7 (2004), 1094–1103.

[3] Bian, Z., Moodie, E. E. M., Shortreed, S. M., Lambert, S. D., and Bhatnagar, S. Variable selection for individualized treatment rules with discrete outcomes. *arXiv preprint arXiv:2205.13609* (2022).

[4] Chakraborty, B., and Moodie, E. E. M. *Statistical Methods for Dynamic Treatment Regimes: Reinforcement Learning, Causal Inference, and Personalized Medicine*. Springer, New York, NY, 2013.

[5] Cornfield, J., Haenszel, W., Hammond, E. C., Lilienfeld, A. M., Shimkin, M. B., and Wynder, E. L. Smoking and lung cancer: recent evidence and a discussion of some questions. *Journal of the National Cancer Institute 22*, 1 (1959), 173–203.

[6] de Haan, J., and Siermann, C. L. J. A sensitivity analysis of the impact of democracy on economic growth. *Empirical Economics 20*, 2 (1995), 197–215.

[7] Ding, P., and VanderWeele, T. J. Sensitivity analysis without assumptions. *Epidemiology 27*, 3 (2016), 368–377.

[8] Dinsa, G. D., Goryakin, Y., Fumagalli, E., and Suhrcke, M. Obesity and socioeconomic status in developing countries: A systematic review. *Obesity Reviews 13*, 11 (2012), 1067–1079.

[9] Dogbe, W. Can poverty status explain obesity in developing countries? evidence from Ghana. *Agribusiness 37*, 2 (2021), 409–421.

[10] Echeverría, S. E., Vélez-Valle, E., Janevic, T., and Prystowsky, A. The role of poverty status and obesity on school attendance in the United States. *Journal of Adolescent Health 55*, 3 (2014), 402–407.

[11] Greenland, S., and Robins, J. M. Identifiability, exchangeability and confounding revisited. *Epidemiologic Perspectives & Innovations 6*, 1 (2009), 1–9.

[12] Hernán, M. A., and Robins, J. M. *Causal Inference: What If*. Boca Raton: Chapman & Hall/CRC, 2020.

[13] Imai, K., and Yamamoto, T. Causal inference with differential measurement error: Nonparametric identification and sensitivity analysis. *American Journal of Political Science 54*, 2 (2010), 543–560.

[14] Ioannidis, J. P., Tan, Y. J., and Blum, M. R. Limitations and misinterpretations of E-values for sensitivity analyses of observational studies. *Annals of Internal Medicine 170*, 2 (2019), 108–111.

[15] Jiang, C., Wallace, M. P., and Thompson, M. E. Dynamic treatment regimes with interference. *Canadian Journal of Statistics 51*, 2 (2023), 469–502.

[16] Kalincik, T., and Butzkueven, H. Observational data: understanding the real MS world. *Multiple Sclerosis Journal 22*, 13 (2016), 1642–1648.

[17] Kosorok, M. R., and Moodie, E. E. M. *Adaptive Treatment Strategies in Practice*. Society for Industrial and Applied Mathematics, Philadelphia, PA, 2015.

[18] Levine, Y. T., McCrady-Spitzer, S. K., and Levine, J. A. Walk score and poverty in American cities. *Medical Research Archives 4*, 7 (2016).

[19] Linden, A., Mathur, M. B., and VanderWeele, T. J. Conducting sensitivity analysis for unmeasured confounding in observational studies using E-values: The evalue package. *Stata Journal 20*, 1 (2020), 162–175.

[20] Liu, H., Chen, W., and Sudjianto, A. Relative entropy based method for probabilistic sensitivity analysis in engineering design. *Journal of Mechanical Design 128*, 2 (2006), 326–336.

[21] Mamiya, H., Moodie, E. E. M., and Buckeridge, D. L. A novel application of point-of-sales grocery transaction data to enhance community nutrition monitoring. *AMIA Annual Symposium Proceedings 2017* (2018), 1253–1261.

[22] Mathur, M. B., Smith, L. H., Yoshida, K., Ding, P., and VanderWeele, T. J. E-values for effect heterogeneity and approximations for causal interaction. *International Journal of Epidemiology 51*, 4 (2022), 1268–1275.

[23] McCandless, L. C., Gustafson, P., and Levy, A. Bayesian sensitivity analysis for unmeasured confounding in observational studies. *Statistics in Medicine 26*, 11 (2007), 2331–2347.

[24] Morio, J. Global and local sensitivity analysis methods for a physical system. *European Journal of Physics 32*, 6 (2011), 1577–1584.

[25] Morris, T. P., White, I. R., and Crowther, M. J. Using simulation studies to evaluate statistical methods. *Statistics in Medicine 38*, 11 (2019), 2074–2102.

[26] Murphy, S. A. Optimal dynamic treatment regimes. *Journal of the Royal Statistical Society: Series B 65*, 2 (2003), 331–355.

[27] MURPHY, S. A., VAN DER LAAN, M. J., AND ROBINS, J. M. Marginal mean models for dynamic regimes. *Journal of the American Statistical Association 96*, 456 (2001), 1410–1423.

[28] ORSINI, N., BELLOCCO, R., BOTTAI, M., WOLK, A., AND GREENLAND, S. A tool for deterministic and probabilistic sensitivity analysis of epidemiologic studies. *Stata Journal 8*, 1 (2008), 29–48.

[29] PHAM, B. T., NGUYEN, M. D., DAO, D. V., PRAKASH, I., LY, H.-B., LE, T.-T., HO, L. S., NGUYEN, K. T., NGO, T. Q., HOANG, V., SON, L. H., NGO, H. T. T., TRAN, H. T., DO, N. M., VAN LE, H., HO, H. L., AND TIEN BUI, D. Development of artificial intelligence models for the prediction of compression coefficient of soil: An application of Monte Carlo sensitivity analysis. *Science of The Total Environment 679* (2019), 172–184.

[30] ROBINS, J. M. Causal inference from complex longitudinal data. In *Latent Variable Modeling and Applications to Causality*, M. Berkane, Ed. Springer, 1997, pp. 69–117.

[31] ROBINS, J. M. Optimal structural nested models for optimal sequential decisions. In *Proceedings of the Second Seattle Symposium in Biostatistics*, D. Y. Lin and P. J. Heagerty, Eds., vol. 179. Springer, New York, NY, 2004, pp. 189–326.

[32] ROBINS, J. M., HERNÁN, M. A., AND BRUMBACK, B. Marginal structural models and causal inference in epidemiology. *Epidemiology 11*, 5 (2000), 550–560.

[33] ROSE, E. J., MOODIE, E. E. M., AND SHORTREED, S. M. Monte Carlo sensitivity analysis for unmeasured confounding in dynamic treatment regimes. *Biometrical Journal* (2023), [Online early access]. doi:10.1002/bimj.202100359.

[34] ROSENBAUM, P. R., AND RUBIN, D. B. Assessing sensitivity to an unobserved binary covariate in an observational study with binary outcome. *Journal of the Royal Statistical Society: Series B 45*, 2 (1983), 212–218.

[35] Rosenbaum, P. R., and Rubin, D. B. The central role of the propensity score in observational studies for causal effects. *Biometrika 70*, 1 (1983), 41–55.

[36] Rubin, D. B. Bayesian inference for causal effects: The role of randomization. *The Annals of Statistics 6*, 1 (1978), 34–58.

[37] Schulz, J., and Moodie, E. E. M. Doubly robust estimation of optimal dosing strategies. *Journal of the American Statistical Association 116*, 533 (2021), 256–268.

[38] Simoneau, G., Moodie, E. E. M., Nijjar, J. S., and Platt, R. W. Estimating optimal dynamic treatment regimes with survival outcomes. *Journal of the American Statistical Association 115*, 531 (2020), 1531–1539.

[39] Steenland, K., and Greenland, S. Monte Carlo sensitivity analysis and Bayesian analysis of smoking as an unmeasured confounder in a study of silica and lung cancer. *American Journal of Epidemiology 160*, 4 (2004), 384–392.

[40] Sutton, R. S., and Barto, A. G. *Reinforcement learning: An introduction*. The MIT Press, 2018.

[41] Tsiatis, A. A., Davidian, M., Holloway, S. T., and Laber, E. B. *Dynamic treatment regimes: Statistical methods for precision medicine*. Chapman & Hall/CRC, 2019.

[42] Vancak, V., and Sjölander, A. Sensitivity analysis of G-estimators to invalid instrumental variables. *arXiv preprint arXiv:2208.05854* (2022).

[43] VanderWeele, T. J., and Ding, P. Sensitivity analysis in observational research: introducing the E-value. *Annals of Internal Medicine 167*, 4 (2017), 268–274.

[44] VanderWeele, T. J., Ding, P., and Mathur, M. Technical considerations in the use of the E-value. *Journal of Causal Inference 7*, 2 (2019).

[45] Wallace, M. P., and Moodie, E. E. M. Doubly-robust dynamic treatment regimen estimation via weighted least squares. *Biometrics 71*, 3 (2015), 636–644.

[46] WALLACE, M. P., MOODIE, E. E. M., AND STEPHENS, D. A. Dynamic treatment regimen estimation via regression-based techniques: Introducing R package DTRreg. *Journal of Statistical Software 80*, 2 (2017), 1–20.

[47] WATKINS, C. J. C. H. *Learning from Delayed Rewards*. PhD thesis, King's College, Oxford, 1989.

[48] ZHANG, B., TSIATIS, A. A., LABER, E. B., AND DAVIDIAN, M. A robust method for estimating optimal treatment regimes. *Biometrics 68*, 4 (2012), 1010–1018.