Variable Selection for Individualized Treatment Rules with Discrete Outcomes

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Abstract

An individualized treatment rule (ITR) is a decision rule that aims to improve individual patients’ health outcomes by recommending optimal treatments according to patients’ specific information. In observational studies, collected data may contain many variables that are irrelevant for making treatment decisions. Including all available variables in the statistical model for the ITR could yield a loss of efficiency and an unnecessarily complicated treatment rule, which is difficult for physicians to interpret or implement. Thus, a data-driven approach to select important tailoring variables with the aim of improving the estimated decision rules is crucial. While there is a growing body of literature on selecting variables in ITRs with continuous outcomes, relatively few methods exist for discrete outcomes, which pose additional computational challenges even in the absence of variable selection. In this paper, we propose a variable selection method for ITRs with discrete outcomes. We show theoretically and empirically that our approach has the double robustness property, and that it compares favorably with other competing approaches. We illustrate the proposed method on data from a study of an adaptive web-based stress management tool to identify which variables are relevant for tailoring treatment.

Key Words: Double robustness; Individualized treatment rules; Penalization; Precision medicine; Variable selection; Weighted generalized linear model.
1 Introduction

In the precision medicine paradigm, treatment decisions are tailored to each individual rather than relying on a “one-size-fits-all” approach; this approach to treatment is beneficial in the presence of heterogeneous treatment effects. With the aim of improving individual patients’ health outcomes, individualized treatment rules (ITRs) (Chakraborty and Moodie, 2013; Kosorok and Moodie, 2015; Tsiatis et al., 2019) recommend effective treatments for each patient based on their specific characteristics. However, collected data often contain many variables that are irrelevant for tailoring treatment. Including all the variables as the tailoring variables in an analysis could reduce statistical efficiency (Hastie et al., 2009) due to the estimation of redundant variables that are not useful for tailoring treatment and yield an unnecessarily complicated treatment decision rule, which is difficult for physicians to interpret or implement. It is therefore important to develop variable selection methods with the objective of optimizing patients’ outcomes by identifying useful tailoring variables. Variable selection for ITRs has been studied in Bian et al. (2021); Jeng et al. (2018); Lu et al. (2013); Shi et al. (2018); all of these works focus on penalized regression-based estimation methods. Jeng et al. (2018) and Lu et al. (2013) only considered a singly robust method in which the propensity score must be correctly specified. Shi et al. (2018) used the Dantzig selector directly to penalize the A-learning (Murphy, 2003; Robins, 2004) estimating equation; Bian et al. (2021) used penalized dynamic weighted ordinary least squares regression to perform variable selection. Both methods considered in Bian et al. (2021) and Shi et al. (2018) are doubly robust, i.e., they can yield consistent estimators while only requiring one of two nuisance models to be correct.

All the methods described above focused solely on cases in which the outcome is continuous. Discrete outcomes introduce additional computational challenges to the estimation of ITR and the variable selection procedure, due to the use of the non-identity link function. Existing literature focusing on discrete outcomes ITR estimation includes Q-
learning (Chakraborty and Moodie, 2013; Linn et al., 2017), Bayesian additive regression trees (Logan et al., 2019), and A-learning (Robins et al., 1992; Tchetgen Tchetgen et al., 2010). However, none of these previous works have been extended to include variable selection. In this article, we focus on developing doubly robust ITR estimation with variable selection for discrete outcomes.

To provide robustness against model misspecification, ITRs are often estimated using estimating equations (Murphy, 2003; Robins, 2004). There are at least two ways to achieve sparsity in the use of estimating equations: via a Dantzig selector (Candes and Tao, 2007) or by a regularized estimating equation (REE). Denote by $U(\theta) \in \mathbb{R}^p$ an estimating equation, where $\theta \in \mathbb{R}^p$. The Dantzig estimator $\hat{\theta}_{dan}$ can be found by solving the constrained optimization problem: $\hat{\theta}_{dan} = \arg \min_{\theta} \|\theta\|_1$, subject to $\|U(\theta)\|_\infty \leq n\lambda$, where $\lambda$ is a tuning parameter used to control sparsity, and $n$ is the sample size. Another way to induce sparsity is to solve the REE: $U(\theta) = n\lambda q(|\theta|)$, where $q(|\cdot|)$ is the subgradient of a penalty function $\rho(|\cdot|)$, i.e., $q(|\cdot|) = \partial \rho(|\cdot|)$. For example, LASSO (Tibshirani, 1996) regression defined by $\min_\beta \{\|Y - X\theta\|^2 + n\lambda\|\theta\|_1\}$ is a special case of the REE $U(\theta) = n\lambda \partial \|\theta\|_1$, where $U(\theta) = X^T(Y - X\theta)$, $X \in \mathbb{R}^{n \times p}$ is the design matrix, and $Y \in \mathbb{R}^n$ is the response.

While the Dantzig selector and REE work well for continuous outcomes (Shi et al., 2018), their implementation in ITRs can be difficult for discrete outcomes, which are usually modelled with non-identity link functions. Indeed, the existing doubly robust estimating equations to estimate ITRs for discrete outcomes are non-linear (Robins et al., 1992; Tchetgen Tchetgen et al., 2010, see later in Section 2.2), and hence the Dantzig selector cannot be solved using linear programming (James and Radchenko, 2009). As for REE, it has been studied in Johnson et al. (2008) and Wang et al. (2012), where local quadratic approximation (Fan and Li, 2001) was used to solve the REE, which is computationally burdensome since it requires the calculation of the inverse of the Hessian matrix. Finally, even if the solution of the Dantzig selector or the REE can be found, it is challenging to
select the tuning parameter in an ITR context since interest lies in inference about treatment effects rather than just predictive performance. This means that we cannot simply select the tuning parameter that has the lowest prediction error as in the more classical prediction setting.

In this work, we propose two new doubly robust estimating functions to estimate the ITR for count and binary outcomes, respectively. The benefit of our proposed estimating function is that it can be easily generalized to a penalized framework, which permits estimating the optimal treatment regimes and selecting the important variables simultaneously. We show that with a suitable choice of weights, a simple penalized regression model for estimating an ITR enjoys the desired double robustness property, and yet is straightforward to implement. The advantage of the newly proposed approach compared to alternative regularized ITRs estimation methods lies in the fact that it can be viewed from a minimization perspective. Hence, the implementation is simple, various penalty functions can be used, and the solution can be found using existing computationally efficient tools in standard software. A tuning parameter selection procedure is proposed to select the tuning parameter that addresses the fact that the goal of an ITR analysis is estimation of a decision rule rather than prediction. To our knowledge, doubly robust variable selection in ITR estimation for discrete outcomes has not been studied in the existing literature.

The rest of this article is organized as follows. In Section 2, we present some introductory concepts and review some existing doubly robust estimation methods for discrete outcomes. In Section 3, we introduce our proposed estimation methods, and we extend them to a penalized framework in Section 4, followed by statements of theoretical properties. A number of simulation studies are given in Section 5. Finally, we apply our method to data from an adaptive web-based stress management study in Section 6.
2 Background

2.1 Notations, Assumptions and Introductory Concepts

Throughout, we use upper case letters to denote random variables and lower case letters to denote observed values. We use non-bold letters to denote individual-level data and bold letters to denote all observations in the data, e.g., $X_i \in \mathbb{R}^p$ are the covariates for subject $i$, while $X \in \mathbb{R}^{n \times p}$ are covariates for all subjects. In a single stage ITR, $V_i = (X_i, A_i, Y_i)$ consists of the data for $i$th individual patient, where $X_i$ is the patient’s baseline covariates, $A_i$ is the binary treatment received, and $Y_i$ is the patient’s outcome. In the sequel, we will suppress subscript $i$ where it is clear. We denote the potential outcome (Rubin, 1978) under the treatment $a$ as $Y^a$. The potential outcome $Y^a$ of a subject is the outcome of the patient if treatment $a$ has been taken, which may be counter to fact. The objective of an ITR analysis is to find the optimal treatment $a_{opt}$ such that the expected potential outcome $E(Y^a)$ is maximized across the population of individuals. To estimate ITRs, we assume the following standard causal assumptions hold: (1) the stable unit treatment value assumption (SUTVA) (Rubin, 1980): a patient’s potential outcome is not affected by other patients’ treatment assignments; (2) consistency: $Y = AY^1 + (1 - A)Y^0$; (3) conditional exchangeability (Robins, 1997): $Y^a \perp \!\!\!\!\perp A | X = x$; and (4) positivity: $P(A = a | X = x) > 0$ almost surely for all $x$ and $a = 0, 1$.

Finally, we assume that the observations $V_i, i = 1, \ldots, n$ are independent and identically distributed with probability density $h(V)$ with respect to a measure $\nu$. Moreover, we assume the relationship between $Y$ and $(X, A)$ can be captured by a semi-parametric regression model: $g(E(Y^a | X = x)) = g(E(Y | X = x, A = a)) = f_0(x; \beta) + \gamma(x, a; \psi)$, where $g$ is a known link function, $f_0$ is an unknown baseline function, and $\gamma$ is a known function that satisfies $\gamma(x, 0; \psi) = 0$, which is referred to as the blip function (Robins, 2004). A blip function can be interpreted as the difference on the linear predictor scale of the transformed
mean potential outcomes

\[ \gamma(x, a) = g(E(Y^a | X = x)) - g(E(Y^0 | X = x)) \]

\[ = g(E(Y^a | X = x, A = a)) - g(E(Y^0 | X = x, A = a)). \]

In this model, \( f_0 \) is irrelevant for making treatment decisions (a nuisance model). Hence, our parameter of interest is \( \psi \), and the optimal ITR is given by

\[ a_{\text{opt}} = \arg \max_a E(Y^a) = \arg \max_a E_X \left[ g^{-1}(f_0(x; \beta) + \gamma(x, a; \psi)) \right] \]

\[ = E_X \left[ \arg \max_a g^{-1}(f_0(x; \beta) + \gamma(x, a; \psi)) \right] = \arg \max_a \gamma(x, a; \psi), \]

given an increasing link function. In the sequel, we only consider a log link for count outcomes and a logit link for binary outcomes.

### 2.2 Existing Estimation Methods for Discrete Outcomes

#### 2.2.1 A-learning for Count Outcomes

Denote by \( x^\psi \) the covariates in the blip model and by \( x^\beta \) the covariates in the baseline model; in what follows, the superscript is omitted if they are identical. Suppose that the blip function is known: \( \gamma(x^\psi, a; \psi) = a^\psi^T x^\psi \), and the link function is the log link. Then the A-learning estimating equation (Robins et al., 1992) for a count outcome is

\[ U_1(\psi) = \frac{1}{n} \sum_{i=1}^{n} x_i^\psi (a_i - \hat{\pi}_i) \exp\{-\gamma(x_i^\psi, a_i; \psi)\} \left( y_i - \exp(f(x_i^\beta; \hat{\beta}) + \gamma(x_i^\psi, a_i; \psi)) \right), \]

where \( f \) is the posited baseline model (not necessarily identical to \( f_0 \)), \( \hat{\beta} \) is a plug-in estimator, and \( \hat{\pi} \) is the estimated propensity score (Rosenbaum and Rubin, 1983). It can be shown that \( U_1(\psi) \) is an unbiased estimating equation (Robins et al., 1992), provided that at least one nuisance model (propensity score model or the baseline model) is correctly
2.2.2 A-learning for Binary Outcomes

Estimation is more complicated when the outcome is binary; the blip parameter is estimated by solving the following estimating equation when the link function is the logit link:

\[ U_2(\psi) = \frac{1}{n} \sum_{i=1}^{n} x_i^\psi (a_i - \hat{\pi}^*) \left( y_i - \expit(f(x_i^\beta; \tilde{\beta}) + \gamma(x_i^\psi, a_i; \psi)) \right), \]

where

\[ \hat{\pi}^* = \left( 1 + \frac{(1 - \expit(u(x; \hat{\tau})) \expit(f(x; \tilde{\beta}))}{\expit(u(x; \hat{\tau})) \expit(f(x; \tilde{\beta}) + \gamma(x, a; \psi))} \right)^{-1}, \]

\[ \expit(t) = \frac{\exp(t)}{1 + \exp(t)}, \]

and \( u(x; \tau) \) is the nuisance treatment model of \( \mathbb{E}(A|Y = 0, X) \). Tchetgen Tchetgen et al. (2010) showed that \( U_2(\psi) \) is an unbiased estimating equation when at least one of \( \mathbb{E}(Y|X, A = 0) \) or \( \mathbb{E}(A|X, Y = 0) \) is correctly specified. Note that for logit link, the quantity \( \mathbb{E}(A|Y = 0, X) \) is modeled instead of the propensity score to assure the double robustness property, because of the symmetry property of the odds ratio:

\[ e^{X^\top \psi} = \frac{P(Y = 1|A = 1, X)P(Y = 0|A = 0, X)}{P(Y = 0|A = 1, X)P(Y = 1|A = 0, X)} = \frac{P(A = 1|Y = 1, X)P(A = 0|Y = 0, X)}{P(A = 0|Y = 1, X)P(A = 1|Y = 0, X)}. \]

Chen (2007) showed that there are at least two ways to study the association parameter (in our case, the blip parameter): through the density of \( Y \) given \( X \) and \( A \) or through the density of \( A \) given \( X \) and \( Y \). This provides an intuitive explanation of why \( \mathbb{E}(Y|X, A = 0) \) and \( \mathbb{E}(A|X, Y = 0) \) are modeled to assure the double robustness property.

As noted above, the implementation of the Dantzig selector or the REE can be difficult for the A-learning estimating function. In the next section, we propose an alternative estimation method that is also doubly robust and, unlike A-learning, can easily accommodate variable selection.
3 Doubly Robust Weighted Generalized Linear Model

In this section, we propose two new estimating equations for count and binary outcomes, respectively, and we show that solving these two estimating equations can be reformulated as an iteratively reweighted generalized linear model (IRGLM). Moreover, the obtained estimators are doubly robust, and the newly proposed estimating equation can be easily generalized to a penalized framework for variable selection.

3.1 Count Outcomes

From now on, we posit a linear model for the baseline function, i.e., \( f(x; \beta) = x^T \beta \). For count outcomes, we present the following estimating function:

\[
U_3(\beta, \psi) = \sum_{i=1}^{n} \left( a_i x_i^\psi \frac{x_i}{x_i^\beta} \right) \left| x_i - \hat{\pi}_i \right| \exp\{-\gamma(x_i^\psi, a; \psi)\} \left( y_i - \exp(f(x_i^\beta; \beta) + \gamma(x_i^\psi, a; \psi))\right).
\]

This equation takes a similar form to \( U_1(\psi) \) with the leading term \( \exp\{-\gamma(x_i^\psi, a; \psi)\} \), and also shared a similar form to Wallace and Moodie (2015) using overlap weights, but is not identical to either.

**Assumption 1.** When at least one of the two nuisance models \( \pi \) or \( f \) is correctly specified, there exists a unique population parameter \( \theta^* = (\beta^*, \psi^*) \) such that \( E[U_3(\beta^*, \psi^*)] = 0 \).

**Theorem 1.** Assume that the SUTVA, ignorability, consistency, and positivity conditions described in the previous section and **Assumption 1** hold. If the posited baseline model satisfies \( x^\psi \subseteq x^\beta \), then \( \psi^* = \psi_0 \), where \( \psi_0 \) is the underlying true blip parameter.

Theorem 1 states that under standard causal assumptions, the population parameter \( \psi^* \) is equivalent to the true data-generating value of the blip (and corresponding ITR) parameter \( \psi_0 \) if one of two nuisance models \( \pi \) or \( f \) is correctly specified. This implies that the blip estimator \( \hat{\psi} \) obtained by solving \( U_3(\beta, \psi) \) is a doubly robust estimator.
Remark 1. The condition of the existence of a unique population parameter is similar to the condition of the existence of the quasi-maximum likelihood estimate when the likelihood is misspecified (White, 1982). The assumption that $x^{\psi} \subseteq x^{\beta}$ in the posited model is referred to as the strong heredity assumption (Chipman, 1996): the corresponding main effects of an interaction term must be included in the model.

Now we demonstrate that $U_3(\beta, \psi)$ can be specified as an IRGLM for which efficient computational solutions exist, and thus a penalized estimator can be constructed from the penalized generalized weighted linear model accordingly. We propose Algorithm 1 to solve $U_3(\beta, \psi)$. The key is to treat the $|a_i - \hat{\pi}_i| \exp\{-\gamma(x_i^{\psi}, a; \psi_t)\}$ term in $U_3(\beta, \psi)$ as a constant in each iteration $t$. In this way, Step 7 in Algorithm 1 is equivalent to a weighted generalized linear model with weights $|a_i - \hat{\pi}_i| \exp\{-\gamma(x_i^{\psi}, a; \hat{\psi}_t)\}$, where $\hat{\pi}$ is the estimated propensity score which does not change across iterations and $\hat{\psi}$ is the current value of the blip parameter estimate from the most recent iteration update. This can be solved efficiently using, for example, the glm function in R and specifying the weights argument.

Algorithm 1

1: function $(x_i, a_i, y_i, \hat{\pi}_i, \varepsilon)$
2: Set iteration counter $t \leftarrow 0$
3: Initialize $\hat{\psi}_0$
4: $w_{i0} \leftarrow |a_i - \hat{\pi}_i| \exp\{-\gamma(x_i^{\psi}, a; \hat{\psi}_0)\}$ for $i = 1, \ldots, n$
5: repeat
6: Solve $\beta_t$ and $\psi_t$ such that
7: $\sum_{i=1}^{n} \left(a_i x_i^{\psi} \frac{x_i^{\psi}}{x_i^{\beta}}\right) w_{it} \left(y_i - \exp(f(x_i^{\beta}; \beta_t) + \gamma(x_i^{\psi}, a_i; \psi_t))\right) = 0$
8: $\hat{\psi}_{t+1} \leftarrow \psi_t$
9: $w_{i(t+1)} \leftarrow |a_i - \hat{\pi}_i| \exp\{-\gamma(x_i^{\psi}, a_i; \hat{\psi}_{t+1})\}$
10: $t \leftarrow t + 1$
11: until $\|\psi_t - \psi_{t-1}\| < \varepsilon$
### 3.2 Binary Outcomes

A similar framework can be built for binary outcomes using the logit link function. We present estimating equation $U_4(\beta, \psi)$ for binary outcomes:

$$U_4(\beta, \psi) = \sum_{i=1}^{n} \left( a_i x_i^\psi \right) |a_i - \hat{\pi}_i^*| \left( y_i - \expit(f(x_i^\beta; \beta) + \gamma(x_i^\psi, a_i; \psi)) \right),$$

where

$$\hat{\pi}_i^* = \left( 1 + \frac{(1 - \expit(u(x; \xi)) \expit(f(x; \hat{\beta}^*))}{\expit(u(x; \xi)) \expit(f(x; \hat{\beta}^*) + \gamma(x; 1; \psi))} \right)^{-1},$$

and $u(x; \xi)$ is the nuisance treatment model for $E(A|Y = 0, X)$. Under mild conditions, the solution of $U_4(\beta, \psi)$ is a doubly robust estimator. Note that all theoretical properties for count outcomes can be applied equally to binary outcomes; for convenience and space, we include the results of binary outcomes in the Appendix. Algorithm 2 can be used to solve $U_4(\beta, \psi)$, once again treating the term $|a_i - \hat{\pi}_i^*|$ as a constant in each iteration.

#### Algorithm 2

1. function $(x_i, a_i, y_i, \hat{\pi}_i, \varepsilon)$
2. Set iteration counter $t \leftarrow 0$
3. Initialize: $\bar{\psi}_0$
4. $w_{i0} \leftarrow |a_i - \hat{\pi}_i(\bar{\psi}_0)|$ for $i = 1, \ldots, n$
5. repeat
6. Solve $\beta_t$ and $\psi_t$ such that
7. $$\sum_{i=1}^{n} \left( a_i x_i^\psi \right) w_{it} \left( y_i - \expit(f(x_i^\beta; \beta_t) + \gamma(x_i^\psi, a_i; \psi_t)) \right) = 0$$
8. $\bar{\psi}_{t+1} \leftarrow \psi_t$
9. $w_{i(t+1)} \leftarrow |a_i - \hat{\pi}_i^*(\bar{\psi}_{t+1})|$
10. $t \leftarrow t + 1$
11. until $\|\psi_t - \psi_{t-1}\| < \varepsilon$

### 4 Tailoring Variable Selection

In this section, we introduce sparsity to our proposed estimating function using the formulation of a REE, and show that this REE is asymptotically equivalent to a penalized
weighted generalized linear model given an appropriate initial estimator. Throughout, the main effect of the treatment \( A \) is not penalized as our goal is to select the important tailoring variables.

### 4.1 Penalized Doubly Robust Method

Due to the non-linear part (log or logit link) of the estimating equation for discrete outcomes, a Dantzig selector with A-learning estimating equation \( U_1(\psi) \) or \( U_2(\psi) \) cannot be solved using linear programming (James and Radchenko, 2009). Hence, we pursue an REE approach to introduce sparsity to the proposed estimating equations \( U_3(\beta, \psi) \) and \( U_4(\beta, \psi) \), and once again, reformulate the REE as a penalized weighted GLM. We call this approach the penalized doubly robust (PDR) method, as it will be shown later, the penalized estimator obtained by solving the ITR REE is a doubly robust estimator.

For count outcomes and binary outcomes, respectively, the ITR REE require finding the solution of

\[
\sum_{i=1} \left( \frac{a_i x_i^\psi}{x_i^\beta} \right) |a_i - \hat{\pi}_i| \exp\{-\gamma(x_i^\psi, a; \psi)\} \left( y_i - \exp(f(x_i^\beta; \beta) + \gamma(x_i^\psi, a; \psi)) \right) = n\lambda q(|\theta|),
\]

(1)

and

\[
\sum_{i=1} \left( \frac{a_i x_i^\psi}{x_i^\beta} \right) |a_i - \hat{\pi}_i^*| \left( y_i - \expit(f(x_i^\beta; \beta) + \gamma(x_i^\psi, a; \psi)) \right) = n\lambda q(|\theta|). \tag{2}
\]

To estimate the blip parameters \( \psi \) consistently, we require that the penalized model satisfies the following properties: (a) no false exclusion of tailoring variables, and (b) the selected model has the strong heredity property, i.e., \( \hat{\psi}_j \neq 0 \implies \hat{\beta}_j \neq 0 \) (without loss of generality, assume that \( x^\psi \) has the same “ordering” as \( x^\beta \)). Many penalty functions can yield a model
that has variable selection consistency, i.e., no false inclusion and no false exclusion, for example, LASSO (Tibshirani, 1996), SCAD (Fan and Li, 2001), and adaptive LASSO (Zou, 2006). However, these methods all fail to achieve the strong heredity property, thus, further work is required to implement them in this setting. Bian et al. (2021), borrowing on the work in Choi et al. (2010) and Bhatnagar et al. (2020) used the reparametrization to ensure strong heredity when using penalization in the context of ITR. Here, we modify the adaptive LASSO penalty, and show that by using these modified adaptive weights, not only can the blip parameters be unbiasedly estimated (asymptotically), but also the strong heredity constraint can be met.

We omit the subscript for the estimating functions $U_3(β, ψ)$ and $U_4(β, ψ)$ for now, as the properties for both count and binary outcomes can be developed using a general notation $U(β, ψ)$. Let $θ_0 = (β_0, ψ_0)$ denote the underlying true parameters and recall that $θ^* = (β^*, ψ^*)$ is the unique population parameter such that $E[U(β^*, ψ^*)] = 0$. Let $s$ be the number of non-zero components of $ψ_0$ (or equivalently, $ψ^*$) and denote by $S$ the set of indices of non-zero components for $ψ_0$. Denote by $S'$ the set of indices of non-zero components for $β^*$; in order to satisfy the strong heredity property, we want the estimated baseline model to satisfy $\hat{β}_S \neq 0$ as $n$ goes to infinity, where $\bar{S} = S \cup S'$ (as such, $S \subseteq \bar{S}$ and hence strong heredity holds). The goal is to obtain a targeted indices set $S^*$ such that $\hat{θ}_{S^*} \neq 0$ and $\hat{θ}_{S^*_c} = 0$ with probability tending to 1, where $S^*_c$ is the complement of $S^*$. We note that this targeted set $S^*$ can be written as $\boldsymbol{θ}^*_{S^*} = (β^*_{S}, ψ^*_{S})$.

Suppose that we have an initial estimator $\hat{θ}_{ini} = (\hat{β}_{ini}, \hat{ψ}_{ini})$ such that $\sqrt{n}\|\beta_{ini} - β^*\| = O_p(1)$ and $\sqrt{n}\|\psi_{ini} - ψ^*\| = O_p(1)$. Following the adaptive LASSO (Zou, 2006) principle, we construct our adaptive weights for the corresponding coefficients $β$ and $ψ$ as follows:

$$\hat{w}^β_j = \left\{ \max \left( |\hat{β}_{ini,j}|, |\hat{ψ}_{ini,j}| \right) \right\}^{-1} \text{ and } \hat{w}^ψ_j = |\hat{ψ}_{ini,j}|^{-1}. \quad (3)$$
We then use the penalty function $\rho(|\theta|) = \rho(|\beta|) + \rho(|\psi|)$, where

$$
\rho(|\beta|) = \sum_{j=1}^{p} \hat{w}_j \beta_j |\beta_j| \quad \text{and} \quad \rho(|\psi|) = \sum_{j=1}^{p} \hat{w}_j \psi_j |\psi_j|.
$$

In this way, for non-zero coefficients of blip variables, the associated weights and those of their corresponding main effects both converge to finite constants, and thus always remain in the model. We refer to our proposed weights in Expression (3) as modified adaptive weights, since these build on the adaptive LASSO framework but differ from it in the choice of $\hat{w}_j$.

Theorem 2 establishes the existence of a $\sqrt{n}$-consistent solution to the ITR REE (1) and (2).

**Theorem 2 (Existence and Selection Consistency).** Assume that conditions in Theorem 1 hold, penalty functions are constructed using the modified adaptive weights described in Expression (3), and the tuning parameter satisfies $\sqrt{n}\lambda = o(1)$ and $n\lambda \to \infty$, then there exists a $\sqrt{n}$-consistent solution $\hat{\theta} = (\hat{\beta}, \hat{\psi})$ of the ITR REE such that $\hat{\psi}_S \neq 0$ and $\hat{\psi}_{Sc} = 0$.

By Lemma 1 in the Appendix, to establish the existence of the REE solution, it suffices to show that for sufficiently large $n$, there exists a constant $r$ such that on the boundary of a ball around $\theta^*$ with radius $n^{-1/2}r$, the variational inequality holds for function $U(\theta) - n\lambda q(|\theta|)$ with high probability; that is, for any $\varepsilon > 0$,

$$
P\left(\inf_{\|\theta - \theta^*\|=n^{-1/2}r} (\theta - \theta^*)^T [U(\theta) - n\lambda q(|\theta|)] > 0\right) > 1 - \varepsilon.
$$

This technique has been adopted in Portnoy (1984) and Wang (2011) to prove the existence of the $M$-estimator and GEE estimator when the number of predictors is large. Theorem 3 establishes the asymptotic normality of the ITR REE estimators under standard regularity conditions (see Appendix for the details).
Theorem 3 (Asymptotic Normality). For any $\sqrt{n}$-consistent solution $\hat{\theta}$ of ITR REE,

$$\sqrt{n}J(\psi^*_S)\{\hat{\psi}_S - \psi^*_S + J(\psi^*_S)^{-1}\lambda q(|\psi^*_S|)\} \overset{d}{\to} N(0, I(\psi^*_S)),$$

where $I(\theta)$ is the variance of the estimating equation $U(V, \theta)$, $J(\theta)$ is the quantity $E_{\theta}\left[-\frac{\partial U_3(V, \theta)}{\partial \theta}\right]$, and $I(\psi^*_S)$ and $J(\psi^*_S)$ are the corresponding $s \times s$ sub-matrices of $I$ and $J$ evaluated at the truth.

A detailed proof of Theorem 2 and Theorem 3 can be found in the Appendix. In order to illustrate the double robustness property of our proposed estimators, we borrow the idea of the oracle estimator (Fan and Li, 2001). Define the oracle estimator $\hat{\psi}_{ora} \in \mathbb{R}^s$ as the solution of $U(\beta, \psi)$ using $f(x\bar{z})$ and $\gamma(x, a)$ (i.e., assume that the zero and non-zero of the coefficients are known in advance). Since we do not know the truly important variables in the application, the oracle estimator is just a conceptual idea to help us establish the theoretical properties in variable selection. Due to the double robustness of $U(\beta, \psi)$, $\hat{\psi}_{ora}$ is a consistent asymptotically normal estimator of $\psi^*_S$ under standard regularity conditions (see Appendix for the details) for $M$-estimators. The properties of $\hat{\psi}$ in Theorems 2 and 3 are referred to as the oracle property (Fan and Li, 2001), i.e., $\hat{\psi}$ performs as well as the oracle estimator $\hat{\psi}_{ora}$.

Corollary (Double Robustness). It can be seen that the oracle estimator $\hat{\psi}_{ora}$ constructed above is a doubly robust estimator of $\psi_0$. Since the resulting estimator $\hat{\psi}$ mimics the oracle estimator $\hat{\psi}_{ora}$, $\hat{\psi}$ is also a doubly robust estimator. That is to say, the resulting estimator $\hat{\psi}$ is a consistent estimator of $\psi_0$ if either one of two nuisance models is correct.

4.2 A One-step Estimator

In the setting where the number of variables $p$ is fixed, we present an approximation to solve the ITR REE (1) in one-step. Suppose that we can find an initial estimator $\hat{\psi}_{ini}$ of the blip parameter, such that $\sqrt{n}\|\hat{\psi}_{ini} - \psi^*\|_2 = O_p(1)$. Then we could plug in $\hat{\psi}_{ini}$ to the weight
term of Expression (1) and solve it directly, which is equivalent to maximizing a weighted penalized likelihood. Taking the count outcomes for example, we could use the solution of the unpenalized estimating equation $U_1(\theta)$ or $U_3(\beta, \theta)$ as the initial estimator. Then under mild conditions, using $\hat{\psi}_{ini}$ as a plug-in estimator will have a negligible effect on the resulting estimator $\hat{\psi}$. That is, the solution of

$$
\sum_{i=1} a_i x_i^\psi \left| a_i - \hat{\pi}_i \right| \exp \{-\gamma(x_i^\psi, a_i; \hat{\psi}_{ini})\} \left( y_i - \exp(f(x_i^\beta; \beta) + \gamma(x_i^\psi, a_i; \psi)) \right) = n\lambda \partial \rho(|\theta|)
$$

is asymptotically equivalent to the solution of (1). In the high dimensional setting where an unpenalized initial estimator cannot easily be computed, the ridge penalty can be used to obtain the initial estimator.

### 4.3 Tuning Parameter Selection

The choice of the tuning parameter $\lambda$ in Expressions (1) and (2) plays an important role in the performance of the REE: an inappropriately large or small value of $\lambda$ will greatly weaken the performance of the resulting estimator with respect to the estimation error and variable selection results. In penalized likelihood, where the goal is prediction, the optimal $\lambda$ is often chosen in a way such that the corresponding model has the lowest information criterion, usually estimated by a measure of model fit (e.g., negative log-likelihood) with an extra penalty term, eg., the Akaike information criterion (AIC) (Akaike, 1974) or the Bayesian information criterion (BIC) (Schwarz, 1978). However, using AIC or BIC to select the tuning parameter would fail if the likelihood is misspecified (i.e., outcome model is misspecified). An alternative approach is to replace the negative log-likelihood part in the information criterion with the negative estimated value function (Qian and Murphy, 2011;
Shi et al., 2021; Zhao et al., 2012):

\[-\frac{1}{n} \sum_{i=1}^{n} Y_i I(A_i = \hat{a}_i^{opt}) \frac{A_i\hat{\pi}_i + (1 - A_i)(1 \hat{\pi}_i)}{A_i\hat{\pi}_i + (1 - A_i)(1 \hat{\pi}_i)},\]

where \(I(\cdot)\) is the indicator function; note that the term value function refers to the marginal or population average outcome under a particular treatment strategy—in this case, under the strategy defined by the estimated optimal ITR, \(\hat{a}^{opt}\). However, this requires that the propensity score model is correctly specified. Here we propose an approach to select the tuning parameter while only requiring one of the nuisance models to be correctly specified. We refer to this approach as being a doubly robust criterion.

Recall that our proposed method can be viewed from a minimization perspective, i.e., \(\hat{\theta} = \arg\min_{\theta} \{L_n(\theta; y) + n\lambda \rho(|\theta|)\}\). Following the idea used in classical information criteria (Akaike, 1974; Nishii, 1984; Schwarz, 1978), we propose to select the tuning parameter by choosing the model that has the smallest value of \(n^{-1}[D_\lambda(\hat{\theta}; y) + \kappa_n s_\lambda]\), where \(D_\lambda(\hat{\theta}; y) = 2[L_n^{sat}(\hat{\theta}; y) - L_n(\hat{\theta}; y)]\) is the quasi-deviance, \(L_n^{sat}\) is the quasi-log-likelihood of the saturated model, \(\kappa_n\) is some positive sequence, and \(s_\lambda\) is the number of non-zero components in the model, for a given \(\lambda\). We suggest to set \(\kappa_n\) as \(\log(\log n) \log p\) following (Fan and Tang, 2013), as this can achieve model selection consistency in a penalized likelihood setting. In practice, we could also use cross-validation to choose the tuning parameter that corresponds to the lowest average loss \(L_n^{cv}(\hat{\theta}; y)\).

5 Numerical Studies

In this section, we first illustrate the double robustness of our proposed method as well as how the choice of the initial estimator can impact the resulting estimators, in the presence of a small number of predictors; then we demonstrate the proposed method in a large dimension setting.
5.1 Experiments Examining the Double Robustness Property in Low Dimension

Recall that in Section 4.2, the initial estimator can be obtained from A-learning or our proposed IRGLM. We now evaluate the performance of our proposed PDR method using two different initial estimators, with respect to the variable selection rate, and the resulting error rate in the estimated treatment decision as well as the value function (expected outcome) of the estimated decision rules. The error rates and the average value function were calculated over a testing set of size 10,000.

The data generation procedure for count outcomes is as follows: Step 1: Generate 15 independent multivariate normal covariates \((X_1, \ldots, X_{15})\) with mean equal to 0.5 and unit variance. Step 2: Generate treatment such that \(P(A = 1|x_1, x_2) = \expit(-0.2 + \sum_{j=1}^{2} x_j)\).

Step 3: Set the blip function as \(\gamma(x, a; \psi) = a(\psi_0 + \psi_1 x_1)\) for \(\psi_0 = 1\) and \(\psi_1 = -2\).

Step 4: Set the baseline model to \(f(x; \beta) = \exp(-x_1^2 - x_2^2 + x_3 - x_4) + x_1 - 0.2 x_2\).

Step 5: Generate the outcome \(Y \sim \text{Poisson}(\exp(f(x; \beta) + \gamma(x, a; \psi)))\). Under this data generation procedure, the optimal treatment is \(I(1 - 2x_1 > 0)\) which corresponds to treatment \(A = 1\) for about 50% of subjects; and the marginal mean of the outcome under observed (rather than optimal) treatment is 1.21.

The data generation procedure for binary outcomes is the same for steps 1-3 above, except now we set the nuisance treatment model as \(E(A|Y = 0, X = x) = \exp(-x_1^2 - x_2^2 + x_3 - x_4) + x_1 - 0.2 x_2\), and marginalize the conditional expectation over the distribution of \(Y\) to obtain the propensity score model \(E(A|X = x)\). Generate the outcome \(Y \sim \text{Bernoulli}(\expit(f(x; \beta) + \gamma(x, a; \psi)))\). Under this data generation procedure, the optimal treatment corresponds to treatment \(A = 1\) for about 50% of subjects; and the marginal mean of the outcome under observed (rather than optimal) treatment is 0.47.

For both count outcomes and binary outcomes, we consider three scenarios with two sample sizes (500 and 1000), where the baseline model is misspecified in scenario 1, and the
treatment model is misspecified in scenario 2. In scenario 3, both models are correctly specified. As the number of predictors is small in this experiment, we compare our proposed PDR with unpenalized doubly robust A-learning. For PDR, we consider two alternative initial estimators: in the first case, referred to as PDR1, it is obtained from A-learning; and in the second, PDR2, from our proposed IRGLM approach. The \texttt{R} package \texttt{drgee} (Zetterqvist and Sjölander, 2015) is implemented to obtain the A-learning estimates.

Tables 1 and 2 present the error rate (proportion of times the estimated optimal ITR fails to coincide with the true optimal ITR), value, false negative rate (i.e., setting a tailoring variable’s coefficient to 0 when it should be non-zero), false positive rate (i.e., selecting a tailoring variable, when the coefficient should be in fact be zero), mean absolute error (MAE): $\|\psi_0 - \hat{\psi}\|_1$ and mean squared error (MSE): $\|\psi_0 - \hat{\psi}\|_2$ of the blip parameter estimates of the three methods for binary and count outcomes respectively. In summary, all three methods have good performance (as they are all doubly robust methods), however, our proposed PDR1 and PDR2 outperform the unpenalized method with respect to the error rate, value, and estimation error for both types of outcomes in all three scenarios regardless of the sample size. No obvious difference in the error rate, value, and variable selection performance were observed between PDR1 and PDR2 in the simulations. Nonetheless, in scenario 2 for binary outcomes, the estimation error (MAE and MSE) is slightly smaller for PDR1 than PDR2, but this difference in estimation error does not translate into a noticeable difference with respect to the error rate or the value function.
Table 1: Error rate (ER), value, false negative (FN) rate, and false positive (FP) rate of variable selection results, mean absolute error (MAE) and mean squared error (MSE) using unpenalized estimation (UE) and penalized doubly robust methods (PDR1 and PDR2), with \( n = 500 \) and \( 1000 \), for 400 simulations and a test size 10,000 in three scenarios for a count outcome. For comparison, the value function of the true optimal regime, and the strategies of always treat and never treat are 3.36, 1.82, and 2.08, respectively.

| Scenario 1 | Scenario 2 | Scenario 3 |
|------------|------------|------------|
| UE | PDR1 | PDR2 | UE | PDR1 | PDR2 | UE | PDR1 | PDR2 |
| \( n = 500 \) | | | | | | | | |
| ER | 0.13 | 0.07 | 0.08 | 0.09 | 0.03 | 0.03 | 0.12 | 0.07 | 0.07 |
| Value | 3.28 | 3.34 | 3.33 | 3.33 | 3.36 | 3.36 | 3.29 | 3.34 | 3.34 |
| FN | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| FP | 1.00 | 0.16 | 0.19 | 1.00 | 0.04 | 0.01 | 1.00 | 0.19 | 0.18 |
| MAE | 3.60 | 1.50 | 1.50 | 2.40 | 0.30 | 0.30 | 3.30 | 1.35 | 1.35 |
| MSE | 1.80 | 0.75 | 0.75 | 0.75 | 0.06 | 0.06 | 1.35 | 0.75 | 0.60 |
| \( n = 1000 \) | | | | | | | | |
| ER | 0.09 | 0.04 | 0.04 | 0.06 | 0.03 | 0.03 | 0.08 | 0.04 | 0.04 |
| Value | 3.33 | 3.36 | 3.35 | 3.35 | 3.36 | 3.36 | 3.33 | 3.35 | 3.35 |
| FN | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| FP | 1.00 | 0.07 | 0.08 | 1.00 | 0.01 | 0.00 | 1.00 | 0.13 | 0.13 |
| MAE | 2.54 | 0.82 | 0.85 | 1.66 | 0.18 | 0.18 | 2.32 | 0.91 | 0.89 |
| MSE | 0.91 | 0.39 | 0.39 | 0.33 | 0.03 | 0.03 | 0.70 | 0.35 | 0.33 |
Table 2: Error rate (ER), value, false negative (FN) rate, and false positive (FP) rate of variable selection results, mean absolute error (MAE) and mean squared error (MSE) using unpenalized estimation (UE) and penalized doubly robust methods (PDR1 and PDR2), with $n = 500$ and 1000, for 400 simulations and a test size 10,000 in three scenarios for a binary outcome. For comparison, the value function of the true optimal regime, and the strategies of always treat and never treat are 0.64, 0.48, and 0.48, respectively.

| Scenario 1 | Scenario 2 | Scenario 3 |
|------------|------------|------------|
|            | UE | PDR1 | PDR2 | UE | PDR1 | PDR2 | UE | PDR1 | PDR2 |
| $n=500$    |    |      |      |    |      |      |    |      |      |
| ER         | 0.18 | 0.07 | 0.07 | 0.18 | 0.07 | 0.08 | 0.18 | 0.07 | 0.07 |
| Value      | 0.61 | 0.64 | 0.64 | 0.61 | 0.64 | 0.64 | 0.61 | 0.64 | 0.64 |
| FN         | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| FP         | 1.00 | 0.05 | 0.05 | 1.00 | 0.04 | 0.08 | 1.00 | 0.06 | 0.06 |
| MAE        | 6.09 | 1.07 | 1.10 | 6.00 | 0.86 | 1.31 | 6.29 | 1.14 | 1.15 |
| MSE        | 4.20 | 0.66 | 0.69 | 3.97 | 0.41 | 0.81 | 4.43 | 0.69 | 0.69 |
| $n=1000$   |    |      |      |    |      |      |    |      |      |
| ER         | 0.13 | 0.05 | 0.05 | 0.13 | 0.04 | 0.05 | 0.13 | 0.04 | 0.04 |
| Value      | 0.63 | 0.64 | 0.64 | 0.63 | 0.64 | 0.64 | 0.63 | 0.64 | 0.64 |
| FN         | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| FP         | 1.00 | 0.03 | 0.02 | 1.00 | 0.03 | 0.05 | 1.00 | 0.03 | 0.03 |
| MAE        | 3.81 | 0.67 | 0.66 | 3.85 | 0.56 | 0.76 | 3.89 | 0.66 | 0.67 |
| MSE        | 1.59 | 0.28 | 0.29 | 1.61 | 0.19 | 0.31 | 1.65 | 0.27 | 0.27 |

5.2 Large Dimension Setting

In this section, we decrease the sample size to $n = 300$ and increase the number of covariates $p$ to 30, 60, and 100 (note that the dimension of the model is $2p + 2$, since $\beta$ and $\psi$ are estimated simultaneously in the model). Since the number of predictors is now large, we compare our doubly robust method with outcome regression using the LASSO (Tibshirani, 1996) penalty. The LASSO is implemented using the R package glmnet (Friedman et al., 2007), with the tuning parameter is selected using the information criterion discussed in Section 4.3. Finally, we obtain our initial estimator using the ridge penalty; see Algorithm A1 in the Appendix for implementation details.

The data generation procedures for both types of outcomes are similar to the previous low
dimensional setting, except for some changes in the values of the parameters (see Appendix for more details). For both count and binary outcomes, we consider the challenging scenario in which the baseline model is misspecified and the treatment model is correctly specified. Tables 3 and 4 present the error rate, value, false negative rate, false positive rate, MAE, and MSE of the two methods for the count and binary outcomes, respectively. Our proposed penalized doubly robust method (using the ridge estimator as the initial estimate) outperforms the LASSO with respect to the error rate, value, and MSE for both types of outcomes, regardless of the number of predictors. However, for binary outcomes, the MAE is slightly smaller for LASSO than PDR.

Table 3: Error rate (ER), value, false negative (FN) rate, and false positive (FP) rate of variable selection results, mean absolute error (MAE) and mean squared error (MSE) using LASSO and PDR with \( n = 300 \), for 400 simulations and a test size 10,000 for count outcome. For comparison, the value function of the true optimal regime, and the strategies of always treat and never treat are 2.01, 0.79, and 1.36, respectively.

|       | \( p = 30 \) | \( p = 60 \) | \( p = 100 \) |
|-------|--------------|--------------|--------------|
|       | LASSO | PDR | LASSO | PDR | LASSO | PDR |
| ER    | 0.15    | 0.09 | 0.17  | 0.11 | 0.18  | 0.11 |
| Value | 1.98    | 2.00 | 1.97  | 1.99 | 1.95  | 1.99 |
| FN    | 0.06    | 0.00 | 0.07  | 0.01 | 0.06  | 0.00 |
| FP    | 0.23    | 0.18 | 0.11  | 0.10 | 0.07  | 0.07 |
| MAE   | 3.04    | 2.09 | 3.46  | 2.42 | 3.67  | 2.58 |
| MSE   | 2.62    | 0.94 | 3.32  | 1.39 | 3.73  | 1.49 |
Table 4: Error rate (ER), value, false negative (FN) rate, and false positive (FP) rate of variable selection results, mean absolute error (MAE) and mean squared error (MSE) using LASSO and PDR with $n = 300$, for 400 simulations and a test size 10,000 for binary outcome. For comparison, the value function of the true optimal regime, and the strategies of always treat and never treat are 0.57, 0.42, and 0.29, respectively.

|       | $p = 30$ |       | $p = 60$ |       | $p = 100$ |
|-------|---------|-------|---------|-------|----------|
|       | LASSO   | PDR   | LASSO   | PDR   | LASSO    | PDR    |
| ER    | 0.30    | 0.21  | 0.34    | 0.23  | 0.37     | 0.27   |
| Value | 0.47    | 0.52  | 0.44    | 0.50  | 0.43     | 0.48   |
| FN    | 0.34    | 0.07  | 0.47    | 0.09  | 0.51     | 0.12   |
| FP    | 0.02    | 0.21  | 0.00    | 0.12  | 0.00     | 0.09   |
| MAE   | 8.33    | 8.73  | 8.79    | 9.70  | 8.85     | 12.41  |
| MSE   | 27.55   | 16.98 | 30.82   | 19.92 | 31.36    | 29.42  |

6 Application to an Adaptive Web-based Stress Management Study

We illustrate the newly proposed approach on a dataset from a two-stage pilot sequential multiple assignment randomized trial (Lambert et al., 2021) that aimed to assess a web-based, stress management intervention adapted across time using a stepped-care approach for people with cardiovascular disease (CVD). We focus our analysis on the first stage only, where 50 participants were randomized into two treatment groups each with probability 0.5, stratified by recruitment sources and stress level. The two treatment groups are the website only group ($A = 0$) and the website plus weekly telephone coaching group ($A = 1$).

The primary outcome in this analysis was the stress subscale from the Depression Anxiety Stress Scales (DASS) (Lovibond and Lovibond, 1996), which is a count outcome measured at 6 weeks after stage 1 randomized allocation. As a lower DASS-stress subscale score suggests the presence of fewer symptoms of stress, the optimal treatment decision is made such that one minimizes the DASS-stress subscale score. The aims of our analysis are to determine the tailoring variables related to the decision rule and to obtain the estimated individualized
treatment rule for CVD patients. We restrict our analysis to eight variables: mental component score (MCS), age, DASS-stress subscale score at baseline, sex, marital status, stomach condition, physical component score (PCS), and vision, as they were previously found to be useful for tailoring treatment using Bian et al. (2021).

A logistic regression model is posited to estimate the propensity score adjusted for the recruitment source and stress level. We apply PDR to this study with A-learning as the initial estimator (this approach was referred to as PDR1 in Section 5); both the baseline model and the blip model are posited to be linear. We found that five variables are relevant for tailoring treatment: DASS at baseline, sex, marital status, stomach condition, and vision. The estimated treatment rule is

\[
\hat{a}^{opt} = \mathbb{I}\{-0.78 + 0.09 \mathbb{I}(\text{male}) + 0.45 \mathbb{I}(\text{unmarried}) + 0.01 \text{DASS} + 0.45 \mathbb{I}(\text{stomach=yes}) - 0.08 \mathbb{I}(\text{vision=yes}) < 0\}.
\]

For example, a married woman who does not have either a vision problem nor a stomach ailment, and who has a DASS greater than 13, would be recommended for website plus weekly telephone coaching \((A = 1)\). We compared our estimated treatment rule with the results using the approach in Bian et al. (2021), wherein the DASS was treated as a continuous measure, and we found that 74% of the subjects’ recommended treatments were the same under the two strategies. Moreover, all five non-zero estimated blip parameters had the same signs as the estimated blip parameters using Bian et al. (2021).

We also considered, for illustrative purposes, an analysis dichotomizes the outcome \(Y\) by its median, and used our proposed binary outcome approach. However, due to the small sample size, neither A-learning nor a standard logistic regression yielded a solution due to lack of convergence.

Finally, we illustrate our newly proposed approach on data from the sequenced treatment
alternatives to relieve depression (STAR*D) (Fava et al., 2003). The STAR*D data are considered a benchmark dataset for ITR analyses and have been analyzed in Bian et al. (2021); Chakraborty et al. (2013); Shi et al. (2018); Wallace et al. (2019b), among others. While these data are less novel, we considered the comparison relevant and provide results in the Appendix. In summary, the findings in the current analysis using the methods proposed here for both count and binary outcomes align well with the results found in Bian et al. (2021); Chakraborty et al. (2013); Wallace et al. (2019b).

7 Discussion

In this article, we propose new doubly robust estimating functions to determine an individualized treatment rule when the outcome is discrete and the log or logit link functions are used to model the outcome. The newly proposed approach can be solved using a weighted GLM iteratively given a suitable choice of observational weights. The benefit of our proposed estimating function is that it can be easily generalized to a penalized framework, which permits estimating a parsimonious ITR and selecting the important tailoring variables simultaneously. Based on this, we also present a doubly robust criterion to select the tuning parameter. Numerical studies indicated that the newly proposed penalized doubly robust method compares favorably with other competing approaches in the context of ITRs. To our knowledge, doubly robust variable selection approach for ITRs has not previously been studied.

To obtain a doubly robust estimator, we need a well-behaved initial estimator, which can be found using an unpenalized doubly robust approach. In the setting where the number of predictors is larger than the sample size, we recommend using the ridge estimator to acquire the initial estimate. In future work, we could also build on idea in Huang et al. (2008), who used the marginal regression approach to obtain the initial estimator for the adaptive LASSO, i.e, the outcome is regressed separately on each variable. However, this technique is more chal-
lenging in our setting, as it violates the assumption that the blip model is correctly specified. This is a partial identification problem, and it has been studied in Van der Laan and Robins (2003), which may be able to shed some light on how to use marginal regression to obtain a valid initial estimator. It also may be of interest, in future work, to investigate the algorithm to directly solve the REE instead of using the approximation. As this alternative does not require an initial estimator, it might perform better in a large $p$, small $n$ scenario.

The extension of the single stage estimation approach to a multi-stage setting also requires further investigation. In a multi-stage setting, the estimation procedure is conducted recursively using backward induction, and the “outcome” at each stage is set to be a predicted or estimated optimal response. For discrete outcomes, the optimal outcome is usually modeled by multiplicative effects, e.g., the optimal outcome at the $(k-1)$th stage for a count outcome is computed by $\hat{\gamma}_{k-1}^{\text{opt}} = y \times \prod_{k}^{K} \exp\{\gamma_k(x_k, a_k^{\text{opt}}, \psi_k) - \gamma_k(x_k, a_k, \psi_k)\}$, where $K$ is the total number of stages. A challenge under the multi-stage scenario is that the estimated optimal outcome at any stage for subjects with zero-valued outcome will always remain zero, unless adjustments are made (Wallace et al., 2019a), which may lead to a loss of efficiency.

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