Constructing Stabilized Dynamic Treatment Regimes

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Abstract

We propose a new method termed stabilized O-learning for deriving stabilized dynamic treatment regimes, which are sequential decision rules for individual patients that not only adapt over the course of the disease progression but also remain consistent over time in format. The method provides a robust and efficient learning framework for constructing dynamic treatment regimes by directly optimizing a doubly robust estimator of the expected long-term outcome. It can accommodate various types of outcomes, including continuous, categorical and potentially censored survival outcomes. In addition, the method is flexible enough to incorporate clinical preferences into a qualitatively fixed rule, where the parameters indexing the decision rules that are shared across stages can be estimated simultaneously. We conducted extensive simulation studies, which demonstrated superior performance of the proposed method. We analyzed data from the prospective Canary Prostate Cancer Active Surveillance Study (PASS) using the proposed method.

Key words: Dynamic treatment regimes, Shared decision rule, Stabilization, Statistical learning, Double robustness
1 Introduction

Active surveillance is an increasingly popular strategy to address the overtreatment of disease. Such a strategy can delay intervention in patients who were diagnosed with a low-risk disease and treat only when a more severe malignancy is identified. In the prospective Canary Prostate Cancer Active Surveillance study (PASS), patients treated with active surveillance undergo serial monitoring with serum prostate specific antigen (PSA), clinical examinations and repeat biopsies (Newcomb et al., 2016). However, repeated biopsies could be burdensome and expensive for the patients. It is of great clinical importance to develop an active surveillance decision rule to identify patients at high risk of progression while sparing low-risk patients from the harm of biopsy at each clinical visit when a medical decision is made based on accumulated information.

Motivated by this problem, in this paper we propose a method from the perspective of dynamic treatment regimes (DTRs). Dynamic treatment regimes, also called adaptive treatment strategies (Murphy, 2003a, 2005), are sequential decision rules adapting over time to the time-varying characteristics of patients. It takes patient health histories as inputs and recommends the next treatment at each decision point. In our situation, to widely implement a rule on informing the necessities of biopsy in a patient population, it is desirable that such a rule be qualitatively fixed over time, which is also termed as a DTR with shared decision rules across stages.

Estimating an optimal DTR without shared decision rules has been widely studied in the past few years. Some methods first estimate the data generation process, e.g., using Monte Carlo simulation (Lavori and Dawson, 2004) or Bayesian models (Wathen and Thall, 2008), and then estimate the optimal DTRs based on the inferred data distributions. These approaches easily suffer from model misspecification and could be computationally intensive to implement. Machine learning approaches have become popular recently in the field. A Q-learning approach (Watkins, 1989; Nahum-Shani et al., 2012; Zhao et al., 2009; Laber et al., 2014; Goldberg and Kosorok, 2012) recursively estimates the conditional expecta-
tion of the outcomes given the current patient history, assuming that optimal decisions are achieved in the future. The foregoing conditional expectations are known as Q-functions. Murphy (2003b) proposed A-learning, which models the regret functions, representing the loss incurred by not following the optimal treatment regime at each stage. A-learning is shown to be a special case of a structural nested mean model (Robins, 2004; Moodie et al., 2007; Schulte et al., 2014). Other available methods include regret regression from Henderson et al. (2010) and weighted least squares from Wallace and Moodie (2015). Direct methods circumvent the need for conditional mean or regret modeling followed by inversion, and directly estimate the decision rule that maximizes the expected outcomes (Robins et al., 2008; Orellana et al., 2010; Zhang et al., 2013; Zhao et al., 2015; Zhu et al., 2017). See Chakraborty and Moodie (2013) and Kosorok and Moodie (2015) for detailed reviews of the current literature.

A setting where the decisions are shared throughout is analogous to stationary Markov decision processes with function approximations (Sutton and Barto, 1998a). Researchers proposed minimizing the squared Bellman error, though the nonsmooth maximization operation for defining the pseudo-outcomes imposes significant challenges for identifying the true solution (Antos et al., 2008). Chakraborty et al. (2016) proposed shared Q-learning to estimate the optimal shared-parameter DTR when it is believed that the decision rule at each stage is the same function of one or more time-varying covariates. In particular, they formulated the decision rules in terms of linear functions, and the parameters that appeared as coefficients of the linear combination determined the common decision rule over time to initiate or change treatment. Their proposal, however, requires correct model specifications of Q-functions. This is seldom true in the multistage setup since that the underlying data generating mechanism is usually complex. The simultaneous outcome weighted learning proposed in Zhao et al. (2015) estimates the optimal DTRs by casting the estimation problem as a single classification problem and could potentially handle the shared-parameter problem, but their procedure is based on the inverse probability weighted estimator of the expected
benefit. This introduces instabilities in their algorithm. In addition, directly applying the method proposed by Zhao et al. (2015) is not guaranteed to yield a shared decision rule. Simultaneous G-estimation (Robins, 2004) can in principle handle the shared-parameter problem. However, its empirical performance is largely unknown (Moodie and Richardson, 2010).

Furthermore, none of these methods for constructing a shared-parameter DTR can handle the time-to-event outcome, which is the outcome of interest in our case. In PASS, the outcome is time from diagnosis to reclassification, which is subject to censored at loss to followup or last study contact. In general, methods for accommodating time-to-event outcome has been limited in settings of DTRs. This is mainly due to two difficulties. First, the number of stages is not fixed, because the event times vary by individuals, and the treatment is usually stopped once the event happens. Subsequently, different patients may experience different numbers of treatments. Second, the treatment status of a subject may be unknown when censoring occurs (Goldberg and Kosorok, 2012).

We propose a method, termed as stabilized O-learning (abbreviated from “outcome weighted learning”), to construct the DTR with shared decision rules. First, we establish a general framework for constructing DTRs, when the decisions between different stages might be shared. The method is applicable to different types of outcomes, including continuous, discrete and time-to-event outcomes. Second, we develop the method based on an augmented inverse probability weighted estimator of the expected outcome that would be achieved under a particular decision rule. Hence, the proposed method is more efficient and robust to possible model misspecification compared to previous methods such as Zhao et al. (2015). Third, we propose a simultaneous concave relaxation of the estimator, and utilize the special shared decision rules structure to implement a computationally efficient algorithm. Finally, we incorporate variable selection aspects in the proposed procedure to further facilitate implementation of the constructed DTRs in practice. In summary, our work requires nontrivial theoretical and computational developments over the current literature.
to construct robust shared decision rules with a general outcome.

The remainder of the paper is organized as follows. In Section 2, we develop a general penalized framework for constructing sparse SDTRs based on an augmented inverse probability weighted estimator of the expected outcome of a decision rule. The framework can handle both non-censored and censored outcomes. We then introduce stabilized O-learning along with a computation algorithm. We also show that the method is Fisher consistent for the optimal DTR. We conduct numerical studies comparing the proposed methods with Q-learning and shared Q-learning in Section 4. Section 5 focuses on the application of the proposed method to the PASS data. Finally, we provide a discussion of open questions in Section 6. Technical details are given in the Appendix.

2 Methodology

2.1 Setup

Consider a multistage setup with a binary treatment assigned at each stage. We will first focus on non-censored outcomes, and discuss time-to-event outcomes that might be censored in Section 2.3. The information on each patient is represented by \((X_1, A_1, \ldots, X_T, A_T, Y)\), where \(X_1\) denotes initial information, \(X_j\) denotes intermediate information collected between stages \(j - 1\) and \(j\), \(A_j \in A_j = \{-1, 1\}\) denotes the treatment assigned at the \(j^{th}\) stage, for \(j = 1, \ldots, T\) and \(Y\) is the final outcome. We will use an overbar to denote the past information up to stage \(j\), e.g. the sequence of treatments \((a_1, a_2, \ldots, a_j)\) is represented by \(\bar{a}_j\), and underline to denote the future, e.g., \(\underline{a}_j = (a_j, a_{j+1}, \ldots, a_T)\). Let \(H_1 = X_1 \in H_1\) and \(H_j = (\bar{X}_j, \bar{A}_{j-1}) \in H_j\) denote the accrued information at each stage. Dynamic treatment regime is a sequence of deterministic decision rules, \(d = (d_1, \ldots, d_T)\), where \(d_j : H_j \mapsto A_j\) is a function mapping from the space of accrued information to the space of available treatments. Under \(d\), a patient presenting with \(H_j = h_j\) at time \(j\) is recommended to treatment \(d_j(h_j)\). We use \(D_T\) to denote the class of all possible treatment regimes.
The data consists of \( n \) independent and identically distributed samples, \((X_{i1}, A_{i1}, X_{i2}, A_{i2}, \ldots, X_{iT}, A_{iT}, Y_i), i = 1, \ldots, n\). Assume a larger response is more preferable. We aim to identify the optimal dynamic treatment regime, denoted by \( d^* \), which yields the largest average outcome if implemented to the whole population in the future. We formalize this concept through potential outcomes. Let \( X_k(\bar{a}_{j-1}) \) denote a person’s potential covariate status at the beginning of the \( j^{th} \) stage if a treatment sequence \( \bar{a}_{j-1} \) were received by that person, and \( Y(\bar{a}_T) \) denote the potential final outcome had s/he followed \( \bar{a}_T \). Let \( \bar{d}_j = (d_1, \ldots, d_j) \) be the first \( j \) decision rules, \( j = 1, \ldots, T \); then \( d = \bar{d}_T \). The potential outcomes associated with \( d \) for a patient presented with initial information \( H_1 = X_1 = x_1 \) are \( a_1 = d_1(x_1), x_2 = X_2(d_1) = X_2(a_1), h_2 = (\bar{x}_2, a_1), a_2 = d_2(h_2), x_3 = X_3(d_2) = X_3(\bar{a}_2), \ldots, a_{T-1} = d_{T-1}(h_{T-1}), x_T = X_T(\bar{d}_{T-1}) = X_T(\bar{a}_{T-1}), h_T = (\bar{x}_T, \bar{a}_{T-1}), a_T = d_T(h_T) \) and \( Y(d) = Y(\bar{a}_T) \).

Let \( G_d = \{X_1, X_2(d_1), \ldots, X_T(\bar{d}_{T-1}), Y(d)\} \) and \( \bar{X}_j(\bar{a}_{j-1}) = \{X_1, X_2(d_1), \ldots, X_j(\bar{d}_{j-1})\} \).

\( Y(d) \) is the final outcome that would be observed for the patient if s/he were to receive treatments according to that dictated by \( d \). The value function \( V(d) = E\{Y(d)\}, d \in D_T \), represents the expected long-term benefit if the population were to follow the regime \( d \). The optimal dynamic treatment regime, \( d^* \), is the regime leading to the value function with the highest value: namely, \( V(d) \leq V(d^*) \) for any \( d \in D_T \). Under the following conditions, which are assumed throughout in this paper, \( V(d) \) can be expressed in terms of the distribution from which the observed data are drawn:

(a) Sequential ignorability: \( A_j \) is independent of all potential values of the outcome and future variables conditional on \( H_j, j = 1, \ldots, T \);

(b) Positivity: with probability one, \( \pi_j(H_j) = P(A_j = 1|H_j) \in (c_0, c_1) \), where \( 0 < c_l < c_u < 1 \) are two constants, and \( \pi_j(H_j) \) denotes the propensity of receiving treatment 1 at stage \( j \);

(c) Consistency: the potential outcome of a treatment regime that would have been ob-
served equals to the actual outcome if assigned to that regime.

Given these assumptions are true, the value function associated with the dynamic treatment regime $d$ can be written as

$$V(d) = E \left[ \frac{YI\{\tilde{A}_T = d(H_T)\}}{P(\tilde{A}_T|H_T)} \right] .$$

(1)

where $I(\cdot)$ is the indicator function, $I\{\tilde{A}_T = d(H_T)\} = I\{A_1 = d_1(H_1), \ldots, A_T = d_T(H_T)\} = \prod_{j=1}^T I\{A_j = d_j(H_j)\}$, indicating $T$ received treatments coincide with that dictated by $d$ at all stages, and $P(\tilde{A}_T|H_T) = \prod_{j=1}^T P(A_j|H_j)$ is the conditional probability of receiving the sequence of treatments $\tilde{A}_T$ for patients with observed accrued information $H_j, j = 1, \ldots, T$ in the actual data.

Due to delayed effects, we need to consider the entire treatment sequence in order to optimize the long-term outcome. Dynamic programming shows that $d^*_T(h_T) = \arg \max_{a_T} Q_T(h_T, a_T)$ where $Q_T(h_T, a_T) = E(Y|H_T = h_T, A_T = a_T)$ and recursively $d^*_j(h_j) = \arg \max_{a_j} Q_j(h_j, a_j)$ where $Q_j(h_j, a_j) = E(\max_{a_{j+1}} Q_{j+1}(h_{j+1}, a_{j+1})|H_j = h_j, A_j = a_j)$ for $j = T - 1, \ldots, 1$ when the underlying generative distribution is known (Bellman, 1957; Sutton and Barto, 1998b).

Q-learning is an approximate dynamic programming algorithm that uses regression models to estimate the Q-functions $Q_j(h_j, a_j), j = 1, \ldots, T$ and then estimate $d^*_j(h_j)$ recursively.

Time varying covariates are usually collected in longitudinal studies. To facilitate the clinical implementation, it is plausible in practice to have a common decision rule in its functional form across multiple stages, where the decision rule in each stage is the same while allowing the covariate values to change over time. To handle the situation where there is a scientific and clinical interest in sharing of parameters, Chakraborty et al. (2016) proposed a shared Q-learning method, which is a simultaneous estimation method that directly accounts for the sharing of parameters. However, their method depends on the correct specification of regression model at each stage, which is hard to satisfy in practice. In the following, we will propose a general framework that finds the stabilized dynamic treatment regimes (SDTRs).
We will utilize the repeatedly measured covariate information, and construct a common stabilized decision that is flexible to account for shared covariates in certain or all stages by directly optimizing the overall benefit, hence more robust compared to Chakraborty et al. (2016).

2.2 Estimators for the value function

We first discuss the situation where the outcome is completely observed. In Section 2.3, we will focus on the time-to-event endpoint that could be censored. The data is comprised of \( n \) independent identically distributed subjects, \( \{X_{1i}, A_{1i}, \ldots, X_{Ti}, A_{Ti}, Y_i\}, i = 1, \ldots, n \).

Following Tsiatis (2006) and Zhang et al. (2013), we construct a group of estimators for the value functions. Let \( C_d \) be a variable taking values \( 1, \ldots, T, \infty \), reflecting the extent to which the received treatments are in accordance with those dictated by \( d \). In particular, for \( j = 1, \ldots, T \), if \( A_1 = d_1(H_1), \ldots, A_{j-1} = d_{j-1}(H_{j-1}) \) and \( A_j \neq d_j(H_j) \), then \( C_d = j \). In other words, \( I(C_d = j) = \prod_{k=1}^{j-1} I\{A_k = d_k(H_k)\} I\{A_j \neq d_j(H_j)\} \). Thus, the observed data are consistent with the rules in \( d \) up to stage \( j \), and ceased to be consistent at decision \( j \). When \( C_d = \infty \), the observed treatment sequence is consistent with the one dictated by \( d \) through all stages. Let \( P(C_d = j|C_d \geq j, G_d) \) be the probability that the observed treatments cease to be consistent with \( d \) at decision \( j \), given they are consistent with \( d \) prior to \( j \) and all potential outcomes. Under the previously assumed conditions (a) - (c), \( P(C_d = j|C_d \geq j, G_d) \) is a function of the observed data through \( j \). Denote this function as \( \lambda_{d,j}(H_j) \), and

\[
\lambda_{d,j}(H_j) = P(C_d = j|C_d \geq j, G_d) = P\{A_j \neq d_j(H_j)|\overline{X}_j, \overline{A}_{j-1} = \overline{d}_{j-1}(H_{j-1})\} \\
= \pi_j\{\overline{X}_j, \overline{d}_{j-1}(H_{j-1})\}^{-1} \times [1 - \pi_j\{\overline{X}_j, \overline{d}_{j-1}(H_{j-1})\}]^{-1}.
\]
The probabilities of being consistent with \( d \) through at least the first \( j \) stages given all potential outcomes can be written as

\[
P(C_d > j | G_d) = \prod_{k=1}^{j} P\{ A_k = d_k(H_k) | \bar{X}_k, \bar{A}_{k-1} = \bar{d}_{k-1}(H_{k-1}) \} = \prod_{k=1}^{j} (1 - \lambda_{d,k}(H_k)).
\]

According to Chapter 3 of Tsiatis (2006), under the correct specification of the propensity score models, all regular, asymptotically linear, consistent estimators for the regime \( d \) have the form

\[
\hat{V}(d) = \mathbb{P}_n \left( \frac{Y \mathcal{I}(C_d = \infty)}{\prod_{j=1}^{T} \{1 - \lambda_{d,j}(H_j)\}} + \sum_{j=1}^{T} \frac{I\{C_d = j\} - \lambda_{d,j}(H_j) I\{C_d \geq j\}}{\prod_{k=1}^{d} \{1 - \lambda_{d,k}(H_k)\}} L_j(H_j) \right), \tag{2}
\]

where \( \mathbb{P}_n \) is the empirical distribution and \( L_j(H_j) \) are arbitrary functions of \( H_j \).

One must specify \( \lambda_{d,j}(H_j) \) and \( L_j(H_j) \) to obtain \( \hat{V}(d) \). We can posit models for \( \pi_1(h_1) = \pi_1(x_1) \) as \( \pi_1(h_1; \gamma_1) \), \( \pi_j(h_j) = \pi_j(\bar{x}_j, \bar{a}_{j-1}) \) as \( \pi_j(h_j; \gamma_j) \) for \( j = 2, \ldots, T \), where \( \gamma_j \) is the parameter in the propensity score model at the \( j^{th} \) stage. We denote the estimator of \( \gamma_j \) as \( \hat{\gamma}_j \). Then \( \lambda_{d,j}(H_j) \) can be estimated by

\[
\lambda_{d,j}(H_j; \hat{\gamma}_j) = \pi_j\{ \bar{X}_j, \bar{d}_{j-1}(H_{j-1}); \hat{\gamma}_j \} I[\{d_j\{\bar{X}_j, \bar{d}_{j-1}(H_{j-1})\} = -1] \\
\times \{1 - \pi_j\{ \bar{X}_j, \bar{d}_{j-1}(H_{j-1}); \hat{\gamma}_j \}\} I[\{d_j\{\bar{X}_j, \bar{d}_{j-1}(H_{j-1})\} = 1].
\]

If we set \( L_j(H_j) \equiv 0 \), we obtain the inverse probability weighted estimator

\[
\hat{V}_{IPWE}(d) = \mathbb{P}_n \left( \frac{Y \mathcal{I}(C_d = \infty)}{\prod_{j=1}^{T} \{1 - \lambda_{d,j}(H_j; \hat{\gamma}_j)\}} \right).
\]

However, the inverse probability weighted estimator \( \hat{V}_{IPWE}(d) \) has potentially high vari-
ance because it only uses outcome information from subjects whose treatment assignments coincide with those dictated by \( d \) throughout. It has been shown in Tsiatis (2006) that we can improve efficiency by incorporating contributions from the subjects who did not receive the specified treatment assignments across all stages. Indeed, the optimal choice of \( L_j(H_j) \) in (2) that leads to the smallest asymptotic variance is \( L^*_d(h_j) = E\{Y(d)|\bar{X}_j(d_{j-1}) = \bar{x}_j\} \), and (2) is a consistent estimator for \( E\{Y(d)\} \) if either \( \lambda_{d,j}(H_j) \)'s are correctly specified or if \( L_j(H_j) \)'s are equal to \( L^*_d(H_j), j = 1, \ldots, T \) (Zhang et al., 2013). This is also known as the double robustness property.

Hence, we posit parametric models to approximate \( L^*_d(h_j) \), and then plug in the obtained parameter estimates. Particularly, at the final stage \( T \), we specify a model for \( \mu_{d_T}(h_T, a_T) = E(Y|H_T = h_T, A_T = a_T) \) as \( \mu_{d_T}(h_T, a_T; \theta_T) \), and estimate \( \theta_T \) by \( \hat{\theta}_T \). Define \( \eta_{d_T}(h_T) = \mu_{d_T}\{h_T, d_T(h_T)\} \). Next, we posit a model for \( \mu_{d_{T-1}}(h_{T-1}, a_{T-1}) = E\{\eta_{d_{T-1}}(h_{T-1})|H_{T-1} = h_{T-1}, A_{T-1} = a_{T-1}\} \) as \( \mu_{d_{T-1}}(h_{T-1}, a_{T-1}; \theta_{T-1}) \), and estimate \( \theta_{T-1} \) as \( \hat{\theta}_{T-1} \). Note that \( \eta_{d_{T-1}}(h_{T-1}; \hat{\theta}_{T-1}) = \mu_{d_{T-1}}\{h_{T-1}, d_{T-1}(h_{T-1})\} \) can be used in place of \( \eta_{d_{T-1}}(h_{T-1}) \) for estimating \( \theta_{T-1} \).

Define \( \eta_{d_{T-1}}(h_{T-1}) = \mu_{d_{T-1}}\{h_{T-1}, d_{T-1}(h_{T-1})\} \). We continue this process recursively for \( j = T - 2, \ldots, 1 \) and obtain a sequence of estimates \( \hat{\theta}_{T-1}, \ldots, \hat{\theta}_1 \), and subsequently, we obtain estimates for \( L^*_{d,j}(h_j), j = 1, \ldots, T \) as \( \mu_{d_j}\{h_j, d_j(h_j); \hat{\theta}_j\} \). We denote \( \hat{V}^{AIPWE}(d) \) as

\[
\hat{V}^{AIPWE}(d) = \mathbb{P}_n \left( \frac{YI(C_d = \infty)}{\prod_{j=1}^T \{1 - \lambda_{d,j}(H_j; \hat{\gamma}_j)\}} \right. \\
+ \sum_{j=1}^T \left. \frac{I\{C_d = j\} - \lambda_{d,j}(H_j)I\{C_d \geq j\}}{\prod_{k=1}^j \{1 - \lambda_{d,k}(H_k; \hat{\gamma}_k)\}} \mu_{d_j}\{h_j, d_j(h_j); \hat{\theta}_j\} \right).
\]

If either \( \pi_1(h_1; \gamma_1) \) and \( \pi_k(h_k; \gamma_k), (k = T, \ldots, 2) \) are correctly specified, or the \( \mu_{d_k}(h_k, a_k; \theta_k) \) are, \( \hat{V}^{AIPWE}(d) \) is a consistent estimator for \( V(d) \).
2.3 Time-to-event outcomes

In clinical studies, it is common that the primary endpoint is survival time that subjects to censoring. Let $\tilde{Y}$ denote survival time, and $\tau$ denote the end of the study. The outcome of interest is $Y = \min(\tilde{Y}, \tau)$ given that no information on survival is available beyond $\tau$. Let $C \in [0, \tau]$ denote the censoring time. Let $U = Y \land C$ and $\Delta$ be the censoring indicator, i.e., $\Delta = I(Y \leq C)$. If $U$ is not subject to censoring, we can observe a full trajectory of the sequence $\{X_1, A_1, \ldots, X_T, A_T, U\}$ with a fixed length $2T + 1$. However, in the context of time-to-event outcomes, if a failure event occurs before the final decision point $T$, the trajectory will not be of full length. In addition, the trajectories themselves may not be fully observed due to the censoring (Goldberg and Kosorok, 2012). We denote the stage in which $U$ occurs by the $\bar{T}^{th}$ stage, with $\bar{T} \leq T$, and $\bar{T}$ could vary by subject. Accordingly, we modify the definition of $C_d$. For the subject with the number of stages $\bar{T}$, $C_d$ takes value in $1, \ldots, \bar{T}, \infty$. When $C_d = \infty$, the observed treatment sequence is consistent with the one dictated by $d$ through all stages.

We assume that $C$ and $Y$ are independent given $(X_1, A_1, \ldots, X_{\bar{T}}, A_{\bar{T}})$. Let $S_C(t|H_{\bar{T}}, A_{\bar{T}}) = P(C > t|H_{\bar{T}}, A_{\bar{T}})$ be the conditional survival function for the censoring time given history information up to stage $\bar{T}$ and treatment received at that stage. Then

$$E \left\{ \frac{U \Delta}{S_C(U|H_{\bar{T}}, A_{\bar{T}})} | H_{\bar{T}}, A_{\bar{T}} \right\} = E \left\{ \frac{\tilde{Y} I(\tilde{Y} < \tau) I(C > \tilde{Y})}{S_C(\tilde{Y}|H_{\bar{T}}, A_{\bar{T}})} + \frac{\tau I(\tilde{Y} \geq \tau) I(C > \tau)}{S_C(\tau|H_{\bar{T}}, A_{\bar{T}})} | H_{\bar{T}}, A_{\bar{T}} \right\}$$

$$= E \{\tilde{Y} I(\tilde{Y} < \tau) + \tau I(\tilde{Y} \geq \tau)|H_{\bar{T}}, A_{\bar{T}}\}$$

$$= E(Y|H_{\bar{T}}, A_{\bar{T}}).$$
Hence, we propose $\hat{V}_{AIPWE}(d)$ in the scenario with time-to-event outcomes as

$$\hat{V}_{AIPWE}(d) = \mathbb{P}_n \left( \frac{UI(C_d = \infty)}{\prod_{j=1}^T \{1 - \lambda_{d,j}(H_j; \hat{\gamma}_j)\}} \cdot \frac{\Delta}{\hat{S}_C(U|H_T, A_T)} \right) + \sum_{j=1}^T \frac{I\{C_d = j\} - \lambda_{d,j}(H_j)I\{C_d \geq j\}}{\prod_{k=1}^d \{1 - \lambda_{d,k}(H_k; \hat{\gamma}_k)\}} \mu_{d,j}(h_j, d_j(h_j); \hat{\theta}_j) \right),$$

where $\hat{S}_C(U|H_T, A_T)$ is an estimator for $S_C(U|H_T, A_T)$.

Recall that the most efficient choice in (2) is $L^*_d(h_j) = E\{Y(d)|\bar{X}_j(\bar{d}_j - 1) = \bar{x}_j\}$. Due to censoring, $Y$ is not fully observed. Consequently, the construction of $\mu_{d,j}(h_j, d_j(h_j); \hat{\theta}_j)$ needs to be modified. Let $\Delta_t$ be an indicator where $\Delta_t = 1$ if no censoring event happened before $(t + 1)^{th}$ stage. Hence, $\Delta_{t-1} = 0$ implies $\Delta_t = 0$. At the final stage $T$, we specify a model for $\mu_{d,T}(h_T, a_T) = E(Y|H_T = h_T, A_T = a_T)$ as $\mu_{d_T}(h_T, a_T; \theta_T)$. We estimate $\theta_T$ by weighted least squares,

$$\arg\min_{\theta_T} \mathbb{P}_n \left[ \{U - \mu_{d_T}(H_T, A_T; \theta_T)\}^2 \frac{\Delta_T}{\hat{S}_C(U|H_T, A_T)} \right].$$

Define $\eta_{d_T}(h_T; \hat{\theta}_T) = \mu_{d_T}(h_T, d_T(h_T); \hat{\theta}_T)$. Next, we posit a model for $\mu_{d_{T-1}}(h_{T-1}, a_{T-1}) = E\{\eta_{d_T}(h_T)|H_{T-1} = h_{T-1}, A_{T-1} = a_{T-1}\}$ and estimate $\theta_{T-1}$ by

$$\arg\min_{\theta_{T-1}} \mathbb{P}_n \left[ \{\eta_{d_T}(H_T; \hat{\theta}_T) - \mu_{d_{T-1}}(H_{T-1}, A_{T-1}; \theta_{T-1})\}^2 \frac{\Delta_{T-1}}{\hat{S}_C(U|H_{T-1}, A_{T-1})} \right].$$

We continue this process recursively for $j = T - 2, \ldots, 1$ and obtain a sequence of estimates $\hat{\theta}_{T-1}, \ldots, \hat{\theta}_1$. Subsequently, we obtain estimates for $L^*_{d,j}(h_j), j = 1, \ldots, T$ as $\mu_{d_T}(h_j, d_j(h_j); \hat{\theta}_T)$. 

\[11\]
2.4 A general framework for constructing dynamic treatment regimes

We now introduce our method on deriving the SDTR. For the outcomes without any censoring, $\hat{V}(d)$ can be reformulated as

$$
\hat{V}(d) = \mathbb{P}_n \left[ \sum_{a_1, \ldots, a_T} I\{a_1 = d_1(H_1), \ldots, a_T = d_T(H_T)\} W_a(Y, H_T; \lambda, L) \right],
$$

where

$$
W_a(Y, H_T; \lambda, L) = \frac{Y I(C_a = \infty)}{\prod_{j=1}^T (1 - \lambda_{a,j}(H_j))} + \sum_{j=1}^T \frac{I\{C_a = j\} - \lambda_{a,j}(H_j) I\{C_a \geq j\}}{\prod_{k=1}^j (1 - \lambda_{a,k}(H_k))} L_j(H_j),
$$

$C_a$ and $\lambda_{a,j}(H_j)$ are defined in the same fashion as $C_d$ and $\lambda_{d,j}(H_j)$ except that $d_j$ is set to be equal to $a_j, j = 1, \ldots, T$. Hence, $\hat{V}^{IPWE}(d)$ uses the weights $W_a\{Y, H_T; \lambda_a(\hat{\gamma}), 0\}$, and $\hat{V}^{AIPWE}(d)$ uses the weights $W_a\{Y, H_T; \lambda_a(\hat{\gamma}), \mu_a(\hat{\theta})\}$, where $\lambda_a(\hat{\gamma}) = \{\lambda_{a,1}(H_1; \hat{\gamma}_1), \ldots, \lambda_{a,T}(H_T; \hat{\gamma}_T)\}$ and $\mu_a(\hat{\theta}) = \{\mu_{a,1}(h_1, a_1; \hat{\theta}_1), \ldots, \mu_{a,T}(h_T, a_T; \hat{\theta}_T)\}$, and $\mu_{a,j}(h_j, a_j), j = 1, \ldots, T$ are defined iteratively in the same fashion as $\mu_{a,j}(h_j, a_j)$ with $d_j$ replaced by $a_j$. For the time-to-event outcomes, we can modify the weights as

$$
W_a(U, \Delta, H_T; \lambda, L, S_C) = \frac{U I(C_a = \infty)}{\prod_{j=1}^T (1 - \lambda_{a,j}(H_j))} \cdot \frac{\Delta}{S_C(U|H_T, A_T)}
$$

$$
+ \sum_{j=1}^T \frac{I\{C_a = j\} - \lambda_{a,j}(H_j) I\{C_a \geq j\}}{\prod_{k=1}^j (1 - \lambda_{a,k}(H_k))} L_j(H_j)
$$

to account for censoring. In the following, we will use outcomes without any censoring for illustration.

Let $\mathcal{M}$ be the class of measurable functions from $\mathbb{R}^p$ into $\mathbb{R}$. Any rule $d_j(h_j)$ can be written as $d_j(h_j) = \text{sgn}\{f_j(h_j)\}$ for some function $f_j \in \mathcal{M}$, where we define $\text{sgn}(0) = 1$. 

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Consequently, we maximize over \((f_1, \ldots, f_T)\)

\[
\hat{V}(f) = \mathbb{P}_n \left[ \sum_{a_1, \ldots, a_T} I\{a_1 f_1(H_1) \geq 0, \ldots, a_T f_T(H_T) \geq 0\} W_a(Y, H_T; \lambda, L) \right]
\]

\[
= \mathbb{P}_n \left[ \sum_{a_1, \ldots, a_T} I\left[ \min_{j=1, \ldots, T} \{a_j f_j(H_j)\} \geq 0 \right] W_a(Y, H_T; \lambda, L) \right].
\]

where we use \(\hat{V}(f)\) to denote \(\hat{V}\{\text{sgn}(f)\}\), and substitute \(I\{a_j = d_j(H_j)\}\) by \(I\{a_j f_j(H_j) \geq 0\}\).

A computationally efficient way to solve the above optimization problem is to replace a concave surrogate for the indicator, which will greatly alleviate the computational difficulties. This leads to an optimization problem of

\[
\max_{(f_1, \ldots, f_T)} \mathbb{P}_n \left( \sum_{a_1, \ldots, a_T} \psi \left[ \min_{j=1, \ldots, T} \{a_j f_j(H_j)\} \right] W_a(Y, H_T; \lambda, L) \right),
\]

where \(\psi\) is a concave function. In this paper, we will use \(\psi(t) = -\log(1 + e^{-t})\), which is an analog of the logistic loss in the machine learning literature. However, other choices of \(\psi(t)\) are available; for example, analogs of exponential loss, hinge loss and others can also be applied (Bartlett et al., 2006).

If there are outcomes with negative values, (4) becomes a nonconcave function. To fix the issue, we note that \(\hat{V}(f)\) is equivalent to

\[
\hat{V}(f) = \mathbb{P}_n \left( \sum_{a_1, \ldots, a_T} |W_a(Y, H_T; \lambda, L)| I \left[ \min_{j=1, \ldots, T} \{a_j f_j(H_j)\} > 0 \right] I(W_a(Y, H_T; \lambda, L) \geq 0) \right)
\]

\[
+ \mathbb{P}_n \left( \sum_{a_1, \ldots, a_T} -|W_a(Y, H_T; \lambda, L)| I \left[ \min_{j=1, \ldots, T} \{a_j f_j(H_j)\} > 0 \right] I(W_a(Y, H_T; \lambda, L) < 0) \right)
\]

\[
= \mathbb{P}_n \left( \sum_{a_1, \ldots, a_T} |W_a(Y, H_T; \lambda, L)| I \left[ \text{sgn}\{W_a(Y, H_T; \lambda, L)\} \min_{j=1, \ldots, T} \{a_j f_j(H_j)\} > 0 \right] \right)
\]

\[
- \mathbb{P}_n \left[ \sum_{a_1, \ldots, a_T} |W_a(Y, H_T; \lambda, L)| I \{W_a(Y, H_T; \lambda, L) < 0\} \right]
\]

\[
= (I) + (II).
\]
Since (II) does not depend on $f_j$, maximizing $\hat{V}(f)$ is effectively similar to maximize (I), where all the weights are nonnegative.

### 2.5 Stabilized O-learning

In this section, we focus on constructing SDTRs using stabilized O-learning. We formulate the decision rules in terms of linear functions of the present variables at each stage, and the coefficients in the linear combinations determine the decision rules. In most scenarios when a SDTR is preferred, the same decision rule is shared across a number of stages. However, in certain stages, for example, the first stage, the decision rule could be different since we have more covariates available or we want a specific rule to begin with. To unify the notations, we combine both situations and let $\beta_j = (\beta_j^{(u)}\top, \beta_j^{(s)}\top)\top$. Here, $\beta_j^{(u)}$ are the unshared parameters that are specific to stage $j$, and $\beta_j^{(s)}$ are the shared parameters across multiple stages. We also decompose $H_j$ into $H_j^{(s)}$ and $H_j^{(u)}$, which represent variables that are shared or specific in stage $j$. Either $H_j^{(s)}$ or $H_j^{(u)}$ could be an empty set. Then, we can write a restricted class of treatment regimes as $d_j(h_j) = \text{sgn}\{f_j(h_j)\}$, where $f_j(h_j) = h_j^{(s)}\beta_j^{(s)} + h_j^{(u)}\beta_j^{(u)}$, $j = 1, \ldots, T$. Combining with the previous arguments, we can maximize

$$\mathbb{P}_n \left( \sum_{a_1, \ldots, a_T} \psi \left[ \text{sgn}\{W_a(Y, H_T; \lambda, L)\} \min_{j=1, \ldots, T} \left\{ a_j \left( H_j^{(u)}\top \beta_j^{(u)} + H_j^{(s)}\top \beta_j^{(s)} \right) \right\} \right] |W_a(Y, H_T; \lambda, L)| \right).$$

The procedure based on $\hat{V}^{IPWE}(d)$ set $\lambda = \lambda_d(\hat{\gamma})$ and $L = 0$, and the procedure based on $\hat{V}^{AIPWE}(d)$ set $\lambda = \lambda_a(\hat{\gamma})$ and $L = \mu_a(\hat{\theta})$.

The above objective function is not differentiable in $\beta_j^{(u)}$ and $\beta^{(s)}$. To account for the non-differentiability of the minimum function, we instead consider a soft minimum function of $u$ and $v$, which equals to $-\log\{\exp(-uK) + \exp(-vK)\}/K$, with $K$ being a positive
constant. We maximize

\[ \Phi(\beta_j^{(u)}, \beta^{(s)}) = \mathbb{P}_n \left[ \sum_{a_1, \ldots, a_T} |W_a(Y, H_T; \lambda, L)| \log \left\{ 1 + K^{-\text{sgn}(W_n(Y, H_T; \lambda, L))} \right\} \right]. \]

In practice, interpretable and simple rules are preferable. Hence, we will apply the LASSO penalty for sparsity, where the coefficients for unimportant variables will shrink to zero. That is, we maximize

\[
\max_{\beta_j^{(u)}, \beta^{(s)}} \Phi(\beta_j^{(u)}, \beta^{(s)}) - \tau_n \left( \sum_j |\beta_j^{(u)}| + \sum_j |\beta^{(s)}| \right),
\]

where \(L_1\) penalties are imposed on \(\beta_j^{(u)}\) and \(\beta^{(s)}\) and \(\tau_n\) is a tuning parameter controlling the amount of penalization.

With the derivative derived, where details are shown in the appendix, we can employ the Orthant–Wise Limited-memory Quasi-Newton algorithm proposed by Andrew and Gao (2007) to solve the penalized optimization problem (5). The algorithm is essentially a Limited-memory Broyden-Fletcher-Goldfarb-Shanno algorithm that incorporates the \(\ell_1\) regulation. The method does not involve any \(\ell_1\)-regularized quadratic optimization subproblem, hence the non-differentiable penalty function does not play a role in the Hessian matrix approximation, making the algorithm particularly suited for large-scale problems (Gong and Ye, 2015). We also note that it is possible to write out the Hessian matrix for our proposed objective function; however, this turns out not benefiting the numerical performance since the second derivative calculation is a fairly complicated form to calculate and is less efficient than numerical approximation and updating using Sherman–Morrison, as implemented in Broyden-Fletcher-Goldfarb-Shanno algorithm.
3 Theoretical Results

In this section, we present the theoretical results for stabilized O-learning based on $\hat{V}^{AIPWE}(d)$, which uses the weights $W_a(Y, H_T; \lambda_a(\hat{\gamma}), \mu_a(\hat{\theta}))$, where $\lambda_a(\hat{\gamma}) = \{\lambda_{a,1}(H_1; \hat{\gamma}_1), \ldots, \lambda_{a,T}(H_T; \hat{\gamma}_T)\}$ and $\mu_a(\hat{\theta}) = \{\mu_{a,1}\{h_1, a_1; \hat{\theta}_1\}, \ldots, \mu_{a,T}\{h_T, a_T; \hat{\theta}_T\}\}$. Assume that $\gamma^m$ and $\theta^m$ are limits of $\hat{\gamma}$ and $\hat{\theta}$. Also, assume $Y$ are bounded, as well as $\mu_{a,j}(h_j, a_j)$ for all $(h_j, a_j), j = 1, \ldots, T$.

To establish the theoretical results for the proposed method, we need to investigate the properties of the new multi-dimensional surrogate function. We also should take advantage of the double robustness property of $\hat{V}^{AIPWE}(d)$. Furthermore, the theoretical results need to account for the fact that the best rule at the earlier stages will depend on the best rules at future stages. Define

$$V_\psi(f; \lambda, L) = E\left(\sum_{a_1, \ldots, a_T} \psi\left[\min_{j=1, \ldots, T} \{a_j f_j(H_j)\}\right] W_a(Y, H_T; \lambda, L)\right).$$

We will show in Proposition 3.1 that Fisher consistency is satisfied for the proposed general framework. Particularly, by replacing the 0-1 function with the concave $\psi$ function in $\hat{V}(f)$, and maximizing the surrogate objective (4), we obtain a sequence of decision rules that is equivalent to the optimal dynamic treatment regime if either the set of propensity score models or the set of outcome regression models are correctly specified. The proof is deferred to the Appendix.

**Proposition 3.1.** If either $\pi_k(h_k; \gamma_k), (k = 1, \ldots, T)$ are correctly specified, or the $\mu_{a_k}(h_k, a_k; \theta_k)$ are, and $(\tilde{f}_1, \ldots, \tilde{f}_T)$ maximize $V_\psi(f; \lambda_a(\gamma^m), \mu_a(\theta^m))$ over $\mathcal{M} \times \ldots, \times \mathcal{M}$, then for $h_j \in \mathcal{H}_j$, $d^*_j(h_j) = \text{sgn}\{\tilde{f}_j(h_j)\}$, $j = 1, \ldots, T$.

In addition, we show in Theorem 3.2 that the difference between the value for $(f_1, \ldots, f_T)$ and the optimal value function with 0-1 rewards is can be bounded the difference under the surrogate reward function $\psi$ scaled by a constant. Hence, if we can show that the estimated rule is consistent under the surrogate function, the consistency under the value function is also guaranteed.
Theorem 3.2. Let \( \phi(\theta) = (1 + \theta) \log(1 + \theta)/2 + (1 - \theta) \log(1 - \theta)/2 \). If either \( \pi_1(h_1; \gamma_1) \) and \( \pi_k(h_k; \gamma_k), (k = T, \ldots, 2) \) are correctly specified, or the \( \mu_{a_k}(h_k, a_k; \theta_k) \) are, for any \( f_j \in \mathcal{M}, j = 1, \ldots, T, \) we have

\[
\phi^{-1}\left[ \max_f V_\psi(f; \lambda_a(\gamma^m), \mu_a(\theta^m)) - V_\psi(f; \lambda_a(\gamma^m), \mu_a(\theta^m)) \right] / K_1 \geq K_2 \{ V(f^*) - V(f) \},
\]

where \( K_1 \) and \( K_2 \) are constants depending the number of stages, \( (f_1^*, \ldots, f_T^*) \) maximizes \( V(f) \) over \( \mathcal{M} \times \ldots \times \mathcal{M} \).

We next show that the proposed procedure consistently estimate the optimal SDTR provided that the the optimal DTR is indeed of the imposed stabilized form, and is included in the sequence of function spaces.

Theorem 3.3. Assume that the sequence \( \tau_n \) satisfies \( \tau_n \to 0 \) and \( n\tau_n^2 \to \infty \). Assume also that \((\hat{f}_1, \ldots, \hat{f}_T)\) is obtained by maximizing (5), and that \((f_1^*, \ldots, f_T^*)\) has the form of \( f_j^*(h_j) = h_j^{(s)}(s) + h_j^{(u)}(u) \). If either \( \pi_1(h_1; \gamma_1) \) and \( \pi_k(h_k; \gamma_k), (k = T, \ldots, 2) \) are correctly specified, or the \( \mu_{a_k}(h_k, a_k; \theta_k) \) are, then for all distributions \( P \), we have that

\[
\lim_{n \to \infty} V(\hat{f}) = V(f^*)
\]

in probability.

4 Simulation Studies

We conducted extensive simulation studies to evaluate the performances of the proposed method, where each scenario involved 500 Monte Carlo data sets. In the first scenario, we considered a four-stage study. Baseline covariates \( X_1, \ldots, X_1,p \) were generated from the standard normal distribution, where \( p \) took values in 5 or 50. Covariates in stages \( j, j = 2, \ldots, 4 \), were generated according to \( X_j \sim N(X_{j-1,k}, 0.25), k = 1, \ldots, p \), where \( N(\mu, \sigma^2) \) denotes a normal distribution with mean \( \mu \) and variance \( \sigma^2 \). Treatments \( A_j, j = 1, \ldots, 4 \)
were simulated from \{-1, 1\} with \(P(A_j = 1|X) = \{1 + \exp(X_{j,1} + X_{j,3} - 0.5)\}^{-1}\). The final outcomes were generated as

\[
Y = 10 + 1.6X_{1,1}X_{1,2} + X_{1,3} - \sum_{j=1}^{4} |X_{j,1} - 1|\{I(A_j > 0) - I(X_{j,1} - 1 > 0)\}^2 + \epsilon,
\]

where \(\epsilon\) was a standard normal random variate. It was straightforward to deduce that the optimal regime at each stage was a linear function of \(X_2\), which was shared across stages. In the second scenario, 30 baseline covariates \(X_{1,1}, \ldots, X_{1,30}\) were generated from \(N(0, 1)\). In addition, \(p\) time-varying variables were simulated, where \(X_{1,31}, \ldots, X_{1,p+30}\) were simulated according to \(N(0, 1)\), and \(X_{j,31}, \ldots, X_{j,p+30}\) were further simulated via \(X_{j,k} \sim N(X_{j-1,k}, 0.25)\), \(k = 1, \ldots, p\). Treatments at each stage were simulated similarly as they were done in Scenarios 1 and 2. And the outcome model was

\[
Y \sim 10 + 1.6X_{1,1}X_{1,2} + X_{1,3} - |X_{1,1} + X_{1,2} - 2|\{I(A_j > 0) - I(X_{1,1} + X_{1,2} - 2 > 0)\}^2 \\
- \sum_{j=2}^{4} |X_{j,1} - 1|\{I(A_j > 0) - I(X_{j,1} - 1 > 0)\}^2 + N(0, 1).
\]

In these settings the optimal regimes from stage 2 to 4 were the same, though the optimal regime in the first stage was different. The third scenario was a time-to-event outcome setting. The survival time \(T\) was the minimum of \(\tau = 15\) and \(\tilde{Y}\), where \(\tilde{Y}\) was generated from a Cox model,

\[
\lambda_{\tilde{Y}}(t|H_T, A_T) = \lambda_{\tilde{Y}_0}(t) \exp[-2 + 1.6X_{1,1}^2 + X_{1,3} \\
+ \sum_{j=1}^{4} |X_{j,1} - 1|\{I(A_1 > 0) - (X_{j,1} - X_{j,2} - 0.5 > 0)\}^2].
\]

We let censoring time \(C\) be generated from an accelerated failure time model with \(\log(C) = -0.5 + 0.5 X_{1,1} + X_{1,3} + \epsilon\), where \(\epsilon\) is generated from \(N(0, 1)\). The censoring percentage was around 41%.
In each scenario, we generated a large validation data set of size 10000. Using a training set out of 500 replicates, we constructed SDTRs using different methods for the purpose of comparison. We then calculated the mean response had the whole population followed the estimated rule, where we obtained the outcome under the estimated dynamic treatment regimes for each subject in the validation data set and then averaged the outcomes over 10000 subjects. Specifically, for each simulated data set, we implemented the proposed method, and the competitors, including the Q-learning and shared Q-learning. In order to carry out Q-learning, we considered a linear working model for the Q-function of the form
\[ Q_j(H_j, a_j; \alpha_j, \gamma_j) = \alpha_j^\top H_j + \gamma_j^\top H_j A_j, j = 1, \ldots, T. \]
Accordingly, \( d_j(h_j) = \arg \max_{a_j} Q_j(h_j, a_j; \alpha_j, \gamma_j) = \text{sgn}(\gamma_j^\top H_j). \) At each stage, parameters were estimated via least squares. The Q-functions were correctly specified in the final stage but incorrectly specified in other stages due to the maximization operator. Furthermore, Q-learning did not account for the shared structure in the decision rule. The shared Q-learning assumed the decision rule parameters are shared across stages, i.e., \( \gamma_1 = \ldots = \gamma_T = \gamma, \) but the nuisance parameters \( \alpha_j \)s are left unshared.

Let \( Y_j(\theta_{j+1}) = \alpha_{j+1}^\top H_j + |\gamma_{j+1}^\top H_{j+1}|, Y^*(\theta) = (Y_1^\top, Y_{T-1}^\top, \ldots, Y_1(\theta_2)^\top)^\top, \theta_j^\top = (\alpha_j^\top, \gamma^\top), \) and \( \theta^\top = (\alpha_T^\top, \ldots, \alpha_1^\top, \gamma^\top). \) It iteratively solved an estimating equation involving the Bellman residual, \( Y^*(\theta) - Z\theta, \) where \( Z \) was a design matrix combining the data from all \( T \) stages and partitioned according to the partition of \( \theta. \)

We applied the proposed stabilized O-learning methods. In the following, we call the stabilized O-learning method based on \( \hat{V}^{IPWE}(d) \) and \( \hat{V}^{AIPWE}(d) \) SOL-IPW and SOL-AIPW respectively. We considered the case with \( \lambda_{d_j}(H_j) = \lambda_{d,j}(H_j; \hat{\gamma}_j) \) and \( L_j(H_j) \equiv 0 \) that result in the estimator \( \hat{V}^{IPWE}(d), \) and \( \lambda_{d,j}(H_j) = \lambda_{d,j}(H_j; \hat{\gamma}_j) \) and \( L_j(H_j) = \eta_{d,j}(H_j; \hat{\theta}_j) \) that result in \( \hat{V}^{AIPWE}(d). \) We considered both situations where the propensity scores could be incorrectly or correctly modeled. We posited correct models for the propensity scores at each stage as \( \pi_j(h_j) = \exp(\gamma_{0j} + \gamma_j^\top x_j)/\{1 + \exp(\gamma_{0j} + \gamma_j^\top x_j)\}, \) and incorrect models as \( \pi_j(h_j) = \exp(\gamma_{0j})/\{1 + \exp(\gamma_{0j})\}. \) We modeled the Q-functions similarly as above in Q-learning, where \( Q_j(H_j, a_j; \alpha_j, \gamma_j) = \alpha_j^\top H_j + \gamma_j^\top H_j A_j, j = 1, \ldots, T. \) In Scenario 3 with censored
observations, we used the Cox proportional hazards model to estimate $S_C(U|H_T, A_T)$. Let $Z$ denote the regressors in the Cox models, and $\lambda_{C_i}(t)$ denote the hazard functions of censoring times for subject $i$. Then, $\lambda_{C_i}(t) = \lambda_{C0}(t) \exp(\beta_C^T Z_{C_i})$, where $\lambda_{C0}(t)$ was the baseline hazard functions for censoring time. The estimator for $\beta_C$, say $\hat{\beta}_C$, maximized the partial likelihood

$$\prod_{i=1}^{n} \left\{ \frac{\exp(\beta_C^T Z_{C_i})}{\sum_{U_j \leq U_i} \exp(\beta_C^T Z_{C_j})} \right\}^{1-\Delta_i}.$$

We used the Breslow estimator for the cumulative baseline hazard function $\Lambda_{C0}(t)$. An estimator of $S_C(t|H_{T,i}, A_{T,i})$ for subject $i$ was $\hat{S}_C(t|H_{T,i}, A_{T,i}) = \exp\{-\hat{\Lambda}_{C0}(t)\}\exp(\hat{\beta}_C^T Z_{C_i})$, where $\hat{\Lambda}_{C0}(t)$ is the estimator for $\Lambda_{C0}(t)$.

We applied 3-fold cross validation to select tuning parameters $(K, \tau_n)$ by grid search over the parameter for soft minimum function $K = 0.1, 1$ and the parameter for penalization $\tau_n = 2^{-15}, 2^{-13}, \ldots, 2^3$. The data was partitioned into 3: each time 2 subsets of data were used as the training data for constructing the SDTR while the remaining set was used as the validation data for calculating the value of the estimated rule. The value of the estimated rule can be estimated via an inverse probability weighted estimator. For each pair of tuning parameters, the process was repeated 3 times and the values calculated on validation sets were averaged; then we chose $(K, \tau_n)$ that maximized the averaged values.

The means and the standard errors of the 500 values of the estimated rules on the validation set for each scenario were presented in Table 1. We also presented the allocation matching rates at all stages for different methods in Table 2. Since regression models were misspecified in Q-learning, and the shared parameter setup was not taken into consideration, it was expected that Q-learning would yield biased results in general. The shared Q-learning had a comparatively better performance, given that it imposed the shared decision rule structure. Scenario 2 involved more covariates, and the decision rules were shared among stages 2 to 4, but not in stage 1. Again, the performances of Q-learning based methods were not satisfactory. In contrast, the SOL-AIPW method showed superior performance.
throughout. It yielded estimated regimes that were close to the optimal value, especially when the sample size was large. SOL-IPW was not robust to model misspecification in propensity scores, but the performance was improved with a correct model. Evidently, augmentation in SOL-AIPW using even incorrect models for Q-functions led to considerable gains over SOL-IPW regardless of whether the propensity model was correct or not.

Table 1: Mean values (s.e.) under the estimated optimal treatment rules; ‘Opt’ indicates the optimal value.

| n   | p   | PS Model Incorrect | PS Model Correct |
|-----|-----|--------------------|-----------------|
|     |     | SOL-IPW            | SOL-AIPW        | SOL-IPW         | SOL-AIPW | QL    | Shared QL | Opt   |
| 1   | 300 | 5 9.13 (0.10)      | 9.46 (0.33)     | 9.65 (0.36)     | 9.80 (0.16) | 8.90 (0.44) | 9.55 (0.23) | 10    |
| 1   | 300 | 20 9.11 (0.09)     | 9.41 (0.39)     | 9.59 (0.33)     | 9.70 (0.22) | 8.53 (0.33) | 9.23 (0.29) | 10    |
| 1   | 600 | 5 9.13 (0.07)      | 9.51 (0.39)     | 9.78 (0.28)     | 9.83 (0.16) | 9.06 (0.34) | 9.63 (0.15) | 10    |
| 1   | 600 | 20 9.12 (0.06)     | 9.54 (0.24)     | 9.75 (0.28)     | 9.78 (0.16) | 8.78 (0.28) | 9.45 (0.16) | 10    |
| 2   | 300 | 5 8.78 (0.10)      | 9.03 (0.44)     | 9.05 (0.50)     | 9.39 (0.33) | 8.45 (0.37) | 8.61 (0.24) | 10    |
| 2   | 300 | 20 8.75 (0.12)     | 8.94 (0.51)     | 8.90 (0.39)     | 9.24 (0.39) | 8.14 (0.30) | 8.39 (0.20) | 10    |
| 2   | 600 | 5 8.83 (0.08)      | 9.18 (0.23)     | 9.24 (0.35)     | 9.57 (0.20) | 8.64 (0.32) | 8.65 (0.18) | 10    |
| 2   | 600 | 20 8.80 (0.07)     | 9.09 (0.34)     | 9.14 (0.33)     | 9.50 (0.26) | 8.38 (0.28) | 8.54 (0.12) | 10    |
| 3   | 300 | 5 0.52 (0.09)      | 0.57 (0.05)     | 0.63 (0.03)     | 0.62 (0.05) | 0.38 (0.07) | 0.54 (0.07) | 0.68  |
| 3   | 300 | 20 0.49 (0.07)     | 0.55 (0.05)     | 0.59 (0.05)     | 0.58 (0.06) | 0.31 (0.03) | 0.46 (0.06) | 0.68  |
| 3   | 600 | 5 0.55 (0.06)      | 0.58 (0.04)     | 0.65 (0.02)     | 0.64 (0.03) | 0.43 (0.07) | 0.57 (0.06) | 0.68  |
| 3   | 600 | 20 0.52 (0.06)     | 0.57 (0.04)     | 0.63 (0.02)     | 0.61 (0.04) | 0.34 (0.03) | 0.50 (0.05) | 0.68  |

5 Data Application

The prospective PASS cohort was established in 2008 enrolling patients with clinically localized prostate cancer and who chose to manage the disease using active surveillance. They were followed with serum PSA measurements every 3 months, clinical and digital rectal examination every 6 months, and repeat prostate biopsy 6 to 12, 24, 48 and 72 months after diagnosis. A primary analysis of PASS shows that active surveillance delays or avoids primary therapy, and may potentially mitigate the overtreatment issue for low-risk prostate cancer (Newcomb et al., 2016). However, a biopsy is invasive and expensive. We utilized
Table 2: All stage allocation matching rates (s.e.) under the estimated optimal treatment rules

| n  | p  | PS Model Incorrect SOL-IPW | PS Model Incorrect SOL-AIPW | PS Model Correct SOL-IPW | PS Model Correct SOL-AIPW | QL | Shared QL |
|----|----|-----------------------------|-----------------------------|--------------------------|--------------------------|----|-----------|
| 1  | 300| 0.50 (0.02)                 | 0.55 (0.11)                 | 0.66 (0.12)              | 0.73 (0.07)              | 0.31 (0.14) | 0.62 (0.07) |
| 1  | 300| 0.49 (0.02)                 | 0.55 (0.11)                 | 0.63 (0.11)              | 0.69 (0.08)              | 0.22 (0.08) | 0.54 (0.06) |
| 1  | 600| 0.50 (0.01)                 | 0.56 (0.11)                 | 0.71 (0.10)              | 0.74 (0.06)              | 0.36 (0.12) | 0.64 (0.05) |
| 1  | 600| 0.49 (0.01)                 | 0.57 (0.09)                 | 0.70 (0.11)              | 0.71 (0.07)              | 0.28 (0.09) | 0.58 (0.04) |
| 2  | 300| 0.42 (0.02)                 | 0.42 (0.13)                 | 0.45 (0.11)              | 0.57 (0.12)              | 0.28 (0.08) | 0.34 (0.05) |
| 2  | 300| 0.41 (0.02)                 | 0.39 (0.15)                 | 0.42 (0.12)              | 0.52 (0.13)              | 0.21 (0.06) | 0.30 (0.03) |
| 2  | 600| 0.43 (0.02)                 | 0.46 (0.07)                 | 0.50 (0.09)              | 0.64 (0.09)              | 0.32 (0.07) | 0.34 (0.05) |
| 2  | 600| 0.43 (0.01)                 | 0.43 (0.10)                 | 0.48 (0.09)              | 0.61 (0.11)              | 0.27 (0.06) | 0.32 (0.02) |
| 3  | 300| 0.53 (0.12)                 | 0.59 (0.08)                 | 0.70 (0.06)              | 0.68 (0.09)              | 0.19 (0.10) | 0.53 (0.11) |
| 3  | 300| 0.47 (0.10)                 | 0.56 (0.07)                 | 0.61 (0.08)              | 0.61 (0.09)              | 0.10 (0.04) | 0.41 (0.08) |
| 3  | 600| 0.56 (0.09)                 | 0.60 (0.06)                 | 0.74 (0.05)              | 0.72 (0.07)              | 0.25 (0.11) | 0.58 (0.10) |
| 3  | 600| 0.52 (0.08)                 | 0.58 (0.05)                 | 0.67 (0.04)              | 0.66 (0.07)              | 0.14 (0.05) | 0.46 (0.07) |

the PASS data to derive a decision rule that informs a patient whether a subsequent biopsy should be performed at each decision point. The goal of such a rule is to spare biopsies for low-risk patients without missing many adverse events.

The PASS data we used for analysis included 848 low-grade prostate cancer patients from the cohort with a Gleason score of 3+3. The primary outcome was whether the patient had a grade reclassification by the 5th year, whereas the grade reclassification is defined as an increase in cancer grade (Gleason score) in a subsequent biopsy. For those subjects who did not have a reclassification event, they were censored at the last contact date, or the treatment date, whichever comes first. We treated each time for biopsy as a decision point, where every patient underwent an initial biopsy at baseline. Given the current available data, we considered three decision points after the baseline. Patients who had biopsies at the decision point $j$ were coded as $A_j = 1$, and those who did not were coded as $A_j = 0$. The covariates included baseline PSA level, baseline prostate volume on log scale, age at baseline, body mass index (BMI) at baseline, family history, smoking status, the most current PSA level, the maximum ratio of biopsy cores containing cancer to total cores from previous biopsies and the Gleason score from last biopsy. For those patients with missing values
in the time-varying variables at later stages, we used last observation carried forward for imputation.

Our goal is to construct SDTRs to inform whether a subsequent biopsy is necessary. In other words, those who are recommended with a biopsy should indeed be more likely to be reclassified during surveillance. We conducted both SOL-IPW and SOL-AIPW for the analysis. The probability of patients taking a biopsy at each time point was modeled using the present PSA level, the maximum ratio of biopsy cores containing cancer to total cores from previous biopsies and the Gleason score from last biopsy. The Q-function at each time point was modeled using all the available historical information. The probability of a patient being censored was modeled using Cox regression, where baseline covariates were included in the model. The tuning parameters were selected via cross validation such that the reclassification rate was maximized under the selected sets of tuning parameters. The coefficients in the treatment decision rules constructed by SOL-IPW and SOL-AIPW are presented in Table 3. Figure 1 shows the Kaplan–Meier curves of time to first reclassification for patients recommended with biopsy versus those who were not, for rules derived from both methods and at the first and subsequent time points. Each of the methods yielded a rule that kept a few patients from biopsies, whereas the current protocol recommends every patient go through biopsy. In particular, SOL-IPW kept 80, 68 and 59 patients, SOL-AIPW kept 4, 6 and 5 patients from biopsy at each stage respectively. The rule by SOL-AIPW is more conservative as it did not miss any reclassification events among individuals who were not recommend biopsy at all three decision times (Figure 1(a) and Figure 1(d)). In contrast, the rule for recommending biopsy based on SOL-IPW lead to many reclassification events being missed among patients without a biopsy recommendation, in particularly at the first biopsy (1(b)), although less so at the later time (Figure 1(c)). The recommendations from the SOL-AIPW, in particular for the first biopsy, might be preferred by clinicians. Such a rule is also consistent with the current clinical consensus to have the first active surveillance biopsy performed on all patients. For subsequent biopsy decisions, clinicians may opt to
adopt either rule based on his/her belief regarding the benefit of sparing biopsy versus the potential harm of missing just a few reclassification events. Overall, our proposed procedures were useful in identifying patients with different clinical outcomes and providing them with more personalized biopsy decision.

Table 3: Coefficients of the constructed SDTRs (covariates were standardized; PSA & max core ratio were on log scale.)

|                  | SOL-IPW | SOL-AIPW |
|------------------|---------|----------|
| Intercept        | 0.148   | 0.372    |
| Present PSA      | 0.078   | 0.062    |
| Max core ratio   | 0.012   | 0.084    |
| Prostate volume  | 0.010   | 0.053    |
| Age              | −0.087  | −0.016   |
| BMI              | −0.018  | −0.000   |
| Family history   | −0.019  | −0.008   |
| Smoking status   | 0.011   | 0.021    |

6 Discussion

Developing dynamic decision rules for a future outcome based on the longitudinal information has becomes a popular area of research in recent years. The developed method has mainly been within the framework of regression modeling, either based on the joint modeling of disease process and longitudinal information (Rizopoulos, 2011; Taylor et al., 2013), or a direct modeling of residual time partly conditioning on covariate history at landmark times (Zheng and Heagerty, 2005; van Houwelingen, 2007; Maziarz et al., 2017). Decision rules are then formed by thresholding the estimated risks from the regression model. When underlying model is misspecified, the approach may yield suboptimal decision rules. We proposed a new method for constructing the SDTR, which is a fixed function of time-varying covariates overtime and are adaptive to various types of outcomes. Such a rule yields a cost-effective monitoring strategy for surveillance and can be easily implemented in practice. We
Figure 1: Kaplan-Meier Curves of Reclassification-free Probability
show that the proposed method enjoys nice theoretical properties and provides an efficient computing algorithm to obtain the solution. It is worthwhile to generalize the proposed method for developing decision rules informing the optimal intervals between biopsies for each patient. Our method for decision rule is based on a linear combination of updated covariate information. It is also of interest to develop a more robust tree structured decision rule without the assumption of linearity, which has the additional advantage of ease of interpretation and dissemination.

**Appendix**

**Derivatives of the objective function** $\Phi(\beta^{(u)}_j, \beta^{(s)})$.

The derivative with respect to unshared parameters $\beta^{(u)}_j$ can be written as

$$\frac{\partial \Phi}{\partial \beta^{(u)}_j} = \mathbb{P}_n \left( \sum_{a_1, \ldots, a_T} |W_a| \cdot \frac{1}{1 + K \cdot \text{sgn}(W_a) \left[ \sum \exp\{-Ka_j(H_j^{(u)} \beta^{(u)}_j + H_j^{(s)} \beta^{(s)})\} \text{sgn}(W_a) \right]} \cdot \right.$$

$$\left. K^{-\text{sgn}(W_a)} \cdot \text{sgn}(W_a) \cdot \sum_{j=1}^T \exp\{-Ka_j(H_j^{(u)} \beta^{(u)}_j + H_j^{(s)} \beta^{(s)})\} \cdot \sum_{j=1}^T \exp\{-Ka_j(H_j^{(u)} \beta^{(u)}_j + H_j^{(s)} \beta^{(s)})\} \cdot (-Ka_j H_j^{(u)}) \right).$$

Similarly, we obtain the derivative with respect to shared parameters $\beta^{(s)}$,

$$\frac{\partial \Phi}{\partial \beta^{(s)}} = \mathbb{P}_n \left( \sum_{a_1, \ldots, a_T} |W_a| \cdot \frac{1}{1 + K \cdot \text{sgn}(W_a) \left[ \sum \exp\{-Ka_j(H_j^{(u)} \beta^{(u)}_j + H_j^{(s)} \beta^{(s)})\} \text{sgn}(W_a) \right]} \cdot \right.$$

$$\left. K^{-\text{sgn}(W_a)} \cdot \text{sgn}(W_a) \cdot \sum_{j=1}^T \exp\{-Ka_j(H_j^{(u)} \beta^{(u)}_j + H_j^{(s)} \beta^{(s)})\} \cdot \sum_{j=1}^T \exp\{-Ka_j(H_j^{(u)} \beta^{(u)}_j + H_j^{(s)} \beta^{(s)})\} \cdot (-Ka_j H_j^{(s)}) \right).$$
Proof of Proposition 3.1.

Without loss of generality, we consider $T = 2$. We need to show that the obtained $(\tilde{f}_1, \tilde{f}_2)$ by maximizing the objective $V_\psi(f; \lambda(\gamma^m), \mu(\theta^m))$ over all measurable functions satisfies, for particular $h_1$, $d_1^*(h_1) = \text{sgn}\{\tilde{f}_1(h_1)\}$ and for particular $h_2$, $d_2^*(h_2) = \text{sgn}\{\tilde{f}_2(h_2)\}$, where $d_1^*(h_1) = \text{argmax}_{a_1 \in \{-1, 1\}} E(Y | A_2 = d_2^*(H_2) / \{1 - \lambda_{\{a_1, a_2\}, 2}(H_2)\} | H_1 = h_1, A_1 = a_1)$, and $d_2^*(h_2) = \text{argmax}_{a_2 \in \{-1, 1\}} E(Y | H_2 = h_2, A_2 = a_2)$. For each $h_2$, $A_1 = a_1$ and $H_1 = h_1$ are fixed constants, given that $H_2$ contains all prior information. Then,

$$ E\left( \sum_{a_1, a_2} W_a(Y, H_T; \lambda(\gamma^m), \mu(\theta^m)) \psi[\min\{a_1 f_1(H_1), a_2 \tilde{f}_2(H_2)\}] | H_2 = h_2 \right) $$

$$ = E\left( \sum_{a_2} W_a(Y, H_T; \lambda(\gamma^m), \mu(\theta^m)) \psi[\min\{a_1 f_1(h_1), a_2 \tilde{f}_2(H_2)\}] | H_2 = h_2 \right). $$

According to Lemma 1, the above quantity is maximized at

$$ \tilde{f}_2(h_2) = \min \left\{ a_1 f_1(h_1), \log \frac{W_{a_1, 1}(Y, H_2; \lambda(\gamma^m), \mu(\theta^m))}{W_{a_1, -1}(Y, H_2; \lambda(\gamma^m), \mu(\theta^m))} \right\}. $$

$$ = \min \left\{ a_1 f_1(h_1), \log \frac{W_{a_1, 1}(Y, H_2; \lambda(\gamma^m), \mu(\theta^m))}{W_{a_1, -1}(Y, H_2; \lambda(\gamma^m), \mu(\theta^m))} \right\}. $$

$$ = \min \left\{ a_1 f_1(h_1), \log \frac{W_{a_1, 1}(Y, H_2; \lambda(\gamma^m), \mu(\theta^m))}{W_{a_1, -1}(Y, H_2; \lambda(\gamma^m), \mu(\theta^m))} \right\}. $$

$$ = \min \left\{ a_1 f_1(h_1), \log \frac{W_{a_1, 1}(Y, H_2; \lambda(\gamma^m), \mu(\theta^m))}{W_{a_1, -1}(Y, H_2; \lambda(\gamma^m), \mu(\theta^m))} \right\}. $$

which has the same sign as $d_2^*(h_2)$ if either the propensity score model or the outcome regression model is correctly specified. Particularly, $(f_1, f_2)$ achieves the maxima where $f_2 = \tilde{f}_2$. 

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Furthermore, for each $h_1 \in \mathcal{H}_1$, to find $\tilde{f}_1 \in \mathcal{M}_1$, we maximize

$$
E\left( \sum_{a_1, a_2} W_a(Y, H_2; \lambda_a(\gamma^m), \mu_a(\theta^m)) \psi[\min\{a_1 f_1(H_1), a_2 \tilde{f}_2(H_2)\}] | H_1 = h_1 \right)
$$

$$
= E\left( \sum_{a_1, a_2} W_a(Y, H_2; \lambda_a(\gamma^m), \mu_a(\theta^m)) \psi[\min\{a_1 f_1(H_1), a_2 \tilde{f}_2(H_2)\}] I\{a_2 = \text{sgn}(\tilde{f}_2(H_2))\} | H_1 = h_1 \right)
$$

$$
+ E\left( \sum_{a_1, a_2} W_a(Y, H_2; \lambda_a(\gamma^m), \mu_a(\theta^m)) \psi[\min\{a_1 f_1(H_1), a_2 \tilde{f}_2(H_2)\}] I\{a_2 \neq \text{sgn}(\tilde{f}_2(H_2))\} | H_1 = h_1 \right),
$$

(6)

over all measurable functions. If $a_2 \neq \text{sgn}(\tilde{f}_2(H_2))$, $a_2 \tilde{f}_2(H_2) = -\min\{|a_1 f_1(H_1)|, |G|\}$, where $G = \log\{W_{a,1}(Y, H_2; \lambda_a(\gamma^m), \mu_a(\theta^m))/W_{a,-1}(Y, H_2; \lambda_a(\gamma^m), \mu_a(\theta^m))\}$. Thus the second term in (6) equals

$$
E\left[ \sum_{a_1, a_2} W_a(Y, H_2; \lambda_a(\gamma^m), \mu_a(\theta^m)) \psi\{a_2 \tilde{f}_2(H_2)\} I\{a_2 \neq \text{sgn}(\tilde{f}_2(H_2))\} | H_1 = h_1 \right]
$$

$$
+ E\left[ \sum_{a_1, a_2} W_a(Y, H_2; \lambda_a(\gamma^m), \mu_a(\theta^m)) [\psi\{a_1 f_1(h_1)\} - \psi(-|G|)] I\{a_1 f_1(h_1) \leq -|G|\} \right]
$$

$$
\cdot I\{a_2 \neq \text{sgn}(\tilde{f}_2(H_2))\} | H_1 = h_1 \right].
$$

(7)

Conversely, if $a_2 = \text{sgn}(\tilde{f}_2(H_2))$, then $a_2 = d^*_2(H_2)$ and $a_2 \tilde{f}_2(H_2) = \min\{|a_1 f_1(H_1)|, |G|\}$. The first term in (6) equals

$$
E\left[ \sum_{a_1, a_2} W_a(Y, H_2; \lambda_a(\gamma^m), \mu_a(\theta^m)) \psi\{a_1 f_1(h_1)\} I\{a_2 = \text{sgn}(\tilde{f}_2(H_2))\} | H_1 = h_1 \right]
$$

$$
+ E\left[ \sum_{a_1, a_2} W_a(Y, H_2; \lambda_a(\gamma^m), \mu_a(\theta^m)) [\psi\{|G|\} - \psi(a_1 f_1(h_1)) I\{a_1 f_1(h_1) \geq |G|\} \right]
$$

$$
\cdot I\{a_2 = \text{sgn}(\tilde{f}_2(H_2))\} | H_1 = h_1 \right].
$$

(8)

The first item in (7) does not play a role in determining $\tilde{f}_1$. If $|f_1| \geq |G|$, (7) takes its maximum value at $|f_1| = |G|$ when $a_1 \neq \text{sgn}\{f_1(h_1)\}$, i.e., $a_1 f_1(h_1) = -|G|$; and (8) equals

$$
E\left[ \sum_{a_1, a_2} W_a(Y, H_2; \lambda_a(\gamma^m), \mu_a(\theta^m)) \psi\{|G|\} I\{a_2 = \text{sgn}(\tilde{f}_2(H_2))\} | H_1 = h_1 \right]
$$

regardless of the
$f_1$ value. Hence, the maximum of (6) is taken at $|f_1| = |G|$ when $|f_1| \geq |G|$. Subsequently, the maximum of (6) should be taken when $|f_1| \leq |G|$. According to (7) and (8), if $|f_1| \leq |G|$, (6) equals to

$$\sum_{a_1,a_2} E \left[ W_a(Y, H_2; \lambda_a(\gamma^m), \mu_a(\theta^m)) \psi\{a_1 f_1(h_1)\} I\{a_2 = \text{sgn}(\tilde{f}_2(H_2))\} | H_1 = h_1 \right]$$

$$= E \left( \sum_{a_1} \psi\{a_1 f_1(h_1)\} \frac{I(A_1 = a_1)}{1 - \lambda_{a_1, a_2}(h_1)} E \left[ \frac{Y I(A_2 = \tilde{d}_2(H_2))}{1 - \lambda_{a_1, a_2}(H_2)} \frac{I(A_2 \neq \tilde{d}_2(H_2)) - \lambda_{a_1, a_2}(H_2)}{\mu_{a_1}(H_2)} \frac{I(A_1 = \tilde{d}_2(H_2)) - \lambda_{a_1, a_2}(H_2)}{\mu_{a_1}(H_2)} | H_1 = h_1 \right] \right).$$

Take derivative with respect to $f_1$. (6) is maximized at $\tilde{f}_1(h_1)$, with

$$\tilde{f}_1(h_1) = \log \frac{E([E\{Y | A_2 = \tilde{d}_2(H_2)\}] | H_1 = h_1, A_1 = 1)}{E([E\{Y | A_2 = \tilde{d}_2(H_2)\}] | H_1 = h_1, A_1 = -1)},$$

and the conclusion of $d_1^*(h_1) = \text{sgn}(\tilde{f}_1(h_1))$ follows. $\square$

**Proof of Theorem 3.2.**

We prove the results for $T = 2$ while the results for $T > 2$ can be obtained by induction. We assume that $W_a(Y, H_T; \lambda_a(\gamma^m), \mu_a(\theta^m))$ are nonnegative. Otherwise, we can add a large constant such that $W_a(Y, H_T; \lambda_a(\gamma^m), \mu_a(\theta^m))$ are nonnegative. Let $\tilde{f} = (\tilde{f}_1, \ldots, \tilde{f}_T)$ maximize $V_\psi(f; \lambda_a(\gamma^m), \mu_a(\theta^m))$, i.e., $V_\psi(\tilde{f}; \lambda_a(\gamma^m), \mu_a(\theta^m)) = \max_f V_\psi(f; \lambda_a(\gamma^m), \mu_a(\theta^m))$. If either $\pi_1(h_1; \gamma_1)$ and $\pi_k(h_k; \gamma_k), (k = T, \ldots, 2)$ are correctly specified, or the $\mu_k(h_k, a_k; \theta_k)$ are, then

$$V(f) = E \left[ \sum_{a_1,a_2} W_a(Y, H_T; \lambda_a(\gamma^m), \mu_a(\theta^m)) I(a_1 f_1 > 0, a_2 f_2 > 0) \right].$$
Also, according to Proposition 3.1,

\[ V(f^*) = E \left[ \sum_{a_1,a_2} W_a \{ Y, H_T; \lambda_a(\gamma^m), \mu_a(\theta^m) \} I(a_1 \tilde{f}_1 > 0, a_2 \tilde{f}_2 > 0) \right]. \]

We first show that

\[
V(f^*) - V(f) = V(\tilde{f}) - V(f_1, \tilde{f}_2) + V(f_1, \tilde{f}_2) - V(f)
\]

\[
= E \left( \sum_{a_1,a_2} W_a \{ Y, H_T; \lambda_a(\gamma^m), \mu_a(\theta^m) \} \right) I(a_2 \tilde{f}_2 > 0) \left[ I(a_1 \tilde{f}_1 > 0) - I(a_1 f_1 > 0) \right] \]

\[
+ E \left( \sum_{a_1,a_2} W_a \{ Y, H_T; \lambda_a(\gamma^m), \mu_a(\theta^m) \} \right) I(a_1 f_1 > 0) \left[ I(a_2 \tilde{f}_2 > 0) - I(a_2 f_2 > 0) \right] \]

\[
= E \left( \sum_{a_1,a_2} W_a \{ Y, H_T; \lambda_a(\gamma^m), \mu_a(\theta^m) \} \right) I(a_2 \tilde{f}_2 > 0) \left[ I(a_1 \tilde{f}_1 > 0) - I(a_1 f_1 > 0) \right] \]

\[
+ E \left( I(a_1 f_1 > 0) E \left[ \sum_{a_1,a_2} W_a \{ Y, H_T; \lambda_a(\gamma^m), \mu_a(\theta^m) \} \left( I(a_2 \tilde{f}_2 > 0) - I(a_2 f_2 > 0) \right) \right] \right) H_2 \right] \right). \]

(9)

On the other hand, since \( V_\psi(\tilde{f}; \lambda_a(\gamma^m), \mu_a(\theta^m)) - V_\psi(f; \lambda_a(\gamma^m), \mu_a(\theta^m)) \geq 0 \), we have

\[
V_\psi(\tilde{f}; \lambda_a(\gamma^m), \mu_a(\theta^m)) - V_\psi(f; \lambda_a(\gamma^m), \mu_a(\theta^m))
\]

\[
= E \left( \sum_{a_1,a_2} W_a \{ Y, H_T; \lambda_a(\gamma^m), \mu_a(\theta^m) \} \left[ \psi \{ \min(a_1 \tilde{f}_1, a_2 \tilde{f}_2) \} - \psi \{ \min(a_1 f_1, a_2 f_2) \} \right] \right) \]

\[
\geq E \left( \sum_{a_1,a_2} W_a \{ Y, H_T; \lambda_a(\gamma^m), \mu_a(\theta^m) \} I(a_2 \tilde{f}_2 > 0) \left[ \psi \{ \min(a_1 \tilde{f}_1, a_2 \tilde{f}_2) \} - \psi \{ \min(a_1 f_1, a_2 f_2) \} \right] \right) \]

\[
\geq E \left( \sum_{a_1,a_2} W_a \{ Y, H_T; \lambda_a(\gamma^m), \mu_a(\theta^m) \} I(a_2 \tilde{f}_2 > 0) \left( \psi(a_1 \tilde{f}_1) - \psi(a_1 f_1) \right) \right). \]
The second inequality follows since \( \min(a_1 \tilde{f}_1, a_2 \tilde{f}_2) = a_1 \tilde{f}_1 \) if \( a_2 \tilde{f}_2 > 0 \), which has been shown in the proof of Proposition 3.1, and \( a_1 f_1 \geq \min(a_1 f_1, a_2 f_2) \). Moreover,

\[
\sum_{a_1, a_2} E \left[ W_a(Y, H_T; \lambda_a(\gamma^m), \mu_a(\theta^m)) I(a_2 \tilde{f}_2 > 0) \mid H_1 = h_1 \right] = E \left( \sum_{a_1} \frac{I(A_1 = a_1)}{1 - \lambda_{d_1} (h_1; \gamma_1^m)} \right) \]

\[
E \left[ \frac{Y I(A_2 = \tilde{d}_2(H_2))}{1 - \lambda_{d_2} (H_2; \gamma_2^m)} + \frac{I(A_2 \neq \tilde{d}_2(H_2)) - \lambda_{d_2} (H_2; \gamma_2^m)}{1 - \lambda_{d_2} (H_2; \gamma_2^m)} \mu_{\tilde{d}_2}(H_2, \tilde{d}_2; \theta_2^m) \mid H_1 = h_1 \right]
\]

\[
+ \frac{I(A_1 \neq a_1) - \lambda_{d_1} (h_1; \gamma_1^m)}{1 - \lambda_{d_1} (h_1; \gamma_1^m)} \mu_{\tilde{d}_1}(h_1, a_1; \theta_1^m) \mid H_1 = h_1 \}
\]

The second equality follows if either \( \mu_{\tilde{d}_2}(H_2, \tilde{d}_2; \theta_2^m) \) or \( \lambda_{d_2}(H_2; \gamma_2^m) \) is correctly specified. Hence, \( d^*(H_1) = \text{sgn}\{f_1^*(H_1)\} \) maximizes both \( E\{\sum_{a_1, a_2} W_a I(a_2 \tilde{f}_2 > 0) \psi(a_1 f_1)\} \) and \( E\{\sum_{a_1, a_2} W_a I(a_2 \tilde{f}_2 > 0) I(a_1 f_1 > 0)\} \) if either \( \mu_{\tilde{d}_1}(H_1, a_1; \theta_1^m) \) or \( \lambda_{d_1}(H_1; \gamma_1^m) \) is correctly specified. The function \( \phi \) is invertible on \([0, 1]\), and its inverse is monotone non-decreasing.

By Proposition 3.1 in (Zhao et al., 2018),

\[
\phi^{-1} \left[ \frac{V_\psi(\tilde{f}) - V_\psi(f)}{c_0} \right] \geq \phi^{-1} \left\{ E \left( \sum_{a_1, a_2} W_a I(a_2 \tilde{f}_2 > 0) \{ \psi(a_1 \tilde{f}_1) - \psi(a_1 f_1) \} \right) / c_0 \right\} \]

\[
\geq E \left( \sum_{a_1, a_2} W_a I(a_2 \tilde{f}_2 > 0) [I(a_1 \tilde{f}_1 > 0) - I(a_1 f_1 > 0)] \right) / c_1. \quad (10)
\]
Also,

\[ V_{\psi}(\tilde{f}; \lambda_a(\gamma^m), \mu_a(\theta^m)) - V_{\psi}(f; \lambda_a(\gamma^m), \mu_a(\theta^m)) = E\left( \sum_{a_1, a_2} W_a(Y, H_T; \lambda_a(\gamma^m), \mu_a(\theta^m)) \{ \psi\{ \min(a_1 \tilde{f}_1, a_2 \tilde{f}_2) \} - \psi\{ \min(a_1 f_1, a_2 f_2) \} \} \right) \]

\[ \geq E\left( \sum_{a_1, a_2} W_a(Y, H_T; \lambda_a(\gamma^m), \mu_a(\theta^m)) I(a_2 \tilde{f}_2 < 0) \{ \psi\{ \min(a_1 \tilde{f}_1, a_2 \tilde{f}_2) \} - \psi\{ \min(a_1 f_1, a_2 f_2) \} \} \right) \]

\[ = E\left( E\left[ \sum_{a_1, a_2} W_a(Y, H_T; \lambda_a(\gamma^m), \mu_a(\theta^m)) P(a_2 \tilde{f}_2 < 0) \{ \psi(a_2 \tilde{f}_2) - \psi(a_2 f_2) \} \bigg| H_2 \right] \right) \]

\[ \geq c_1 E\left( E\left[ \sum_{a_1, a_2} W_a \{ \psi(a_2 \tilde{f}_2) - \psi(a_2 f_2) \} \bigg| H_2 \right] \right) . \]

The first inequality follows since \( a_2 f_2 \geq \min(a_1 f_1, a_2 f_2) \), and \( a_2 \tilde{f}_2 \leq a_1 \tilde{f}_1 \) if \( a_2 \tilde{f}_2 < 0 \). The second inequality is a direct consequence from Assumption (b). Conditional on \( H_2 \), \( \text{sgn}\{f_2(H_2)\} \) maximizes both \( E[\sum_{a_1, a_2} W_a(Y, H_T; \lambda_a(\gamma^m), \mu_a(\theta^m)) \psi(a_2 f_2) \big| H_2] \) and \( E[\sum_{a_1, a_2} W_a(Y, H_T; \lambda_a(\gamma^m), \mu_a(\theta^m)) I(a_2 f_2 > 0) \big| H_2) \) if either \( \mu_2(h_2, a_2; \theta_2) \) or \( \lambda_{a_2}(h_2; \gamma_2) \) is correctly specified. Therefore, by the established results in (Zhao et al., 2018),

\[ \phi^{-1}\left[ \{ V_{\psi}(\tilde{f}; \lambda_a(\gamma^m), \mu_a(\theta^m)) - V_{\psi}(f; \lambda_a(\gamma^m), \mu_a(\theta^m)) \} / (c_0 c_1) \right] \]

\[ \geq \phi^{-1}\left\{ E\left[ E\left[ \sum_{a_1, a_2} W_a(Y, H_T; \lambda_a(\gamma^m), \mu_a(\theta^m)) \{ \psi(a_2 \tilde{f}_2) - \psi(a_2 f_2) \} \bigg| H_2 \right] \right] \bigg| c_0 \right\} \]

\[ \geq E\left[ E\left[ \sum_{a_1, a_2} W_a(Y, H_T; \lambda_a(\gamma^m), \mu_a(\theta^m)) \{ I(a_2 \tilde{f}_2 > 0) - I(a_2 f_2 > 0) \} \bigg| H_2 \right] \right] / c_1 \]

\[ \geq E\left( I(a_1 f_1 > 0) E\left[ \sum_{a_1, a_2} W_a(Y, H_T; \lambda_a(\gamma^m), \mu_a(\theta^m)) \{ I(a_2 \tilde{f}_2 > 0) - I(a_2 f_2 > 0) \} \bigg| H_2 \right] \right) / c_1 . \]

(11)

We obtain the desired relationship by combining the results from (9), (10) and (11). □

**Proof of Theorem 3.3.**

The proof of this theorem follows along the lines of the proofs of Theorem 3.3 in Zhao et al. (2012). We consider the case when \( T = 2 \). Results for \( T > 2 \) can be obtained similarly.
Consider \((f_1, f_2)\) when maximizing (5), which has as an upper bound

\[
|f_1| + |f_2| \leq -\frac{2}{n\tau_n c_0} \sum_{i=1}^{n} \sum_{a_1, a_2} W_a(Y_i, H_{T_i}; \lambda_a(\gamma), \mu_a(\hat{\theta})) \psi(0, 0) \leq \frac{4K_1}{\tau_n},
\]

where \(K_1\) is a constant depending on the bound of \(W_a\). Hence, \(\tau_n\{f_1(H_1) + f_2(H_2)\}\) is bounded by \(K_1\), and the class \(\{\tau_n(f_1 + f_2) : \tau_n(|f_1| + f_2) \leq K_1\}\) is contained in a Donsker class.

The surrogate function used in \(V_{\psi}(f; \lambda_a(\gamma^m), \mu_a(\theta^m))\) with \(T = 2\), is a two-dimensional concave function, denoted as

\[
L_{\psi}(f; \lambda_a(\gamma^m), \mu_a(\theta^m)) = \sum_{a_1, a_2} W_a\{Y, H_T; \lambda_a(\gamma^m), \mu_a(\theta^m)\} \psi\{\min(a_1 f_1, a_2 f_2)\}.
\]

Thus \(V_{\psi}(f; \lambda_a(\gamma^m), \mu_a(\theta^m)) = E(L_{\psi}(f; \lambda_a(\gamma^m), \mu_a(\theta^m)))\). Particularly, note that the function of \(\psi\) and \(\min(t, c)\) are both Lipschitz continuous in \(t\) for any constant \(c\). Since for any \(t_1, t'_1 \in \mathbb{R}\) and \(t_2, t'_2 \in \mathbb{R}\),

\[
\psi\{\min(t_1, t_2)\} - \psi\{\min(t'_1, t'_2)\} \leq K\{\min(t_1, t_2) - \min(t'_1, t'_2)\} \leq K(|t_1 - t'_1| + |t_2 - t'_2|).
\]

The Lipschitz continuity of \(L_{\psi}(f; \lambda_a(\gamma^m), \mu_a(\theta^m))\) with respect to \((f_1, f_2)\) follows consequently. In addition, \(L_{\psi}(f; \lambda_a(\gamma^m), \mu_a(\theta^m))\) is concave.

Consider the class of functions

\[
\mathcal{W}_a = \{W(Y, H_2; \lambda_a(\gamma), \mu(\theta)) : ||\gamma - \gamma^m|| < \delta_0, ||\theta - \theta^m|| < \delta_0\},
\]

where \(\delta_0\) is a small constant. We can obtain that \(\{\tau_n L_{\psi}(f; \lambda_a(\gamma), \mu_a(\theta)), \tau_n(|f_1| + |f_2|) \leq K_1, W_a \in \mathcal{W}_a\}\) is P-Donsker. Using empirical process techniques, we can show \(P_n\{L_{\psi}(\hat{f}; \lambda_a(\hat{\gamma}), \mu_a(\hat{\theta}))\} \rightarrow E\{L_{\psi}(\hat{f}; \lambda_a(\hat{\gamma}), \mu_a(\hat{\theta}))\}\) in probability if \(n\tau_n^2 \rightarrow \infty\). Subsequently, \(P_n\{L_{\psi}(\hat{f}; \lambda_a(\hat{\gamma}), \mu_a(\hat{\theta}))\} \rightarrow \inf_{f_1, f_2} E\{L_{\psi}(f; \lambda_a(\gamma^m), \mu_a(\theta^m))\}\) in probability. Combined with Theorem 3.2, the desired...
result follows. □

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