Independence weights for causal inference with continuous exposures

Jared D. Huling\textsuperscript{1}, Noah Greifer\textsuperscript{2}, Guanhua Chen\textsuperscript{3}\textdagger

\begin{itemize}
\item \textsuperscript{1}Division of Biostatistics, University of Minnesota
\item \textsuperscript{2}Department of Mental Health, Johns Hopkins Bloomberg School of Public Health
\item \textsuperscript{3}Department of Biostatistics and Medical Informatics, University of Wisconsin-Madison
\end{itemize}

Abstract

Studying causal effects of continuous exposures is important for gaining a deeper understanding of many interventions, policies, or medications, yet researchers are often left with observational studies for doing so. In the observational setting, confounding is a barrier to estimation of causal effects. Weighting approaches seek to control for confounding by reweighting samples so that confounders are comparable across different values of the exposure, yet for continuous exposures, weighting methods are highly sensitive to model misspecification. In this paper we elucidate the key property that makes weights effective in estimating causal quantities involving continuous exposures. We show that to eliminate confounding, weights should make exposure and confounders independent on the weighted scale. We develop a measure that characterizes the degree to which a set of weights induces such independence. Further, we propose a new model-free method for weight estimation by optimizing our measure. We study the theoretical properties of our measure and our weights, and prove that our weights can explicitly mitigate exposure-confounder dependence. The empirical effectiveness of our approach is demonstrated in a suite of challenging numerical experiments, where we find that our weights are quite robust and work well under a broad range of settings.

**Keywords** — Continuous treatments, Distance Covariance, Confounding, Covariate Balance, Balancing Weights

\textsuperscript{*}corresponding authors: huling@umn.edu
\textsuperscript{†}corresponding authors: gchen25@wisc.edu
1 Introduction

Confounding is a major barrier to studying causal effects of exposures from observational data, regardless of whether the exposure is binary, continuous, or otherwise. Considerable work has focused on the development of approaches for studying causal effects of binary or otherwise discrete-valued exposures from observational data. With continuous exposures, however, the choices of methods for confounding control are far more limited, and clear guidance that can help practitioners choose among the available methods is lacking. A common approach to reduce confounding by observed variables is using the propensity score, which was initially proposed for binary treatments Rosenbaum and Rubin (1983) and has been generalized to the setting of continuous treatments (Hirano and Imbens, 2004; Imai and Van Dyk, 2004; Zhu et al., 2015; Galvao and Wang, 2015). With binary treatments, the causal effect of interest is often the average treatment effect, which can be estimated as a difference in the weighted averages of the treatment group outcomes, where the weights are proportional to the inverse of the propensity score; this method is known as inverse probability weighting (IPW). With continuous treatments, the interest is often in estimation of the causal dose-response functionals (Robins et al., 2000; van der Laan and Robins, 2003) such as the the causal average dose-response function (ADRF), which can be estimated using a weighted regression of the outcome on the treatment, where the weights are proportional to the inverse of the conditional density of the treatment given the covariates, the generalized propensity score (GPS).

In the binary treatment setting, IPW estimators can be unstable due to extreme weights and susceptible to model misspecification (Kang and Schafer, 2007). These issues carry over to IPW estimators for continuous treatments and are substantially more challenging to address. The reason is that IPW estimation via the GPS requires inverse weighting by a conditional density estimate, not just a conditional probability. Even if the conditional mean of the treatment given covariates is correctly specified, GPS weights can fail to perform well if the distribution of the conditional density is misspecified (Naimi et al., 2014). The difficulty of correctly specifying or accurately estimating a full conditional distribution is exacerbated with increased dimension of the confounders. The tailored use of flexible machine learning estimation approaches such as that proposed in Zhu et al. (2015) can in many cases yield substantial improvements, however, as shown in our simulation studies and data analysis, they are not fully immune from the issues
of GPS weighting and can perform poorly and/or yield large weights in practice.

As misspecification of a conditional density model can be difficult to diagnose and assess, several works have focused on directly estimating weights through various optimization criteria with the goal of inducing a lack of correlation between marginal moments of confounders and the exposure. Approaches along this line of work include the generalized covariate balancing propensity score (CBPS) approach of Fong et al. (2018), covariate association eliminating weights (Yiu and Su, 2018), and entropy balancing weights (Tübbicke, 2020; Vegetabile et al., 2021). Because these approaches focus on estimation of weights directly as opposed to estimating a conditional density explicitly and inverting it, they tend to be more robust and effective empirically than direct modeling of the GPS. While intuitively appealing, these approaches require careful choices of which moments of both the confounders and the exposure to “decorrelate”. Yet, there is no guidance on how to specify the correct moments necessary to mitigate bias in estimation of the ADRF due to confounding. Missing important moments can leave substantial residual dependence between confounder and exposure, see e.g. Figure 1. In our simulations, we show that the choice of moments is indeed critically important in practice and that numerical instability can arise when too many moments are used. The tension between including enough moments to reduce bias and the instability of weights as more moments are included can make the use of these methods challenging in practice. Kernel Optimal Orthogonality Weighting (KOW) (Kallus and Santacatterina, 2019) and a generalization of KOW proposed in Martinet (2020), are kernel-based nonparametric extensions of direct weights estimation ideas. They focus on estimating weights to decorrelate over function spaces of exposure and confounders such that there is no need of choosing models or what moments to decorrelate. Yet, careful tuning is still required when flexible kernels are used, and, on the other hand, when inflexible kernels are used, there is no guarantee that the resulting weights fully mitigate confounding. Thus, the user is often left with a difficult choice of which kernel to use and unclear guidance on how to choose the kernel’s tuning parameters.

Our work aims to achieve several goals. First, we provide clarity on the role of weights in estimation of the ADRF. To do so, we provide a general decomposition of the error of a weighted nonparametric estimator of the ADRF and demonstrate that, under broad conditions, the ideal weights should induce independence between the treatment variable and confounders to guaran-
tee mitigation of confounding bias when estimating the ADRF. While this is already intuitively understood in the literature, our decomposition shows the precise form that dependence shows up in the error of an estimator. We also show that dependence plays a key role in other estimands, such as the causal quantile dose-response function. Second, we develop a measure based on energy statistics (Székely et al., 2007; Székely and Rizzo, 2013) that allows one to assess how well a set of weights is able to induce independence, where smaller values of our measure indicate the weights yield less treatment-confounder dependence and a value of zero indicates complete independence between the treatment and confounders in the weighted data. Our proposed measure can effectively characterize how well dependence is mitigated by a set of weights without the need for fine-tuning hyperparameters. Finally, we propose a new approach for estimating weights, which we call the distance covariance optimal weights (DCOWs), by optimizing our measure. Thus, the proposed weights directly aim to mitigate dependence, the key source of error in a weighted nonparametric estimate of the ADRF. Our weight construction approach does not require modeling a conditional density, careful tuning of hyperparameters, or choosing which moments of covariates and treatment to decorrelate, which means it can be readily and effectively used “out-of-the-box” by practitioners with varying degrees of statistical sophistication. Because our approach targets the key source of error in estimates of causal estimands involving continuous exposures, our weights yield estimators of the ADRF that are highly robust empirically and work well in a variety of settings, including when confounders are of moderate dimension. The key benefits of our approach are its ease of use, requiring minimal to no fine-tuning on the part of the user, and its ability to provide highly reliable estimates in many settings. As such, it has the potential for wide applicability in practice.

We provide some theoretical results for our proposal, showing that our weights indeed induce independence between treatment and covariates and that, with a small penalty on the variability of the weights, our proposal results in the same convergence rate as a nonparametric regression estimate of the ADRF in a scenario with no confounding. Although adding a penalty to reduce weight variability involves the inclusion of a tuning parameter, our proposed approach rarely results in weights with large variability even without penalization, so careful tuning of the parameter that controls weight variability is rarely necessary, as evidenced by our simulation studies, which investigate a wide variety of scenarios with strong and complex confounding and
scenarios with moderately high-dimensional confounding, in all of which we allow the tuning parameter to remain at its default value.

Our proposed weights can be used beyond simple weighted nonparametric estimators of the ADRF. Recently, Kennedy et al. (2017) and Díaz and van der Laan (2013) extended the idea of doubly robust estimation to continuous treatments, allowing for estimates that combine outcome regression models (Imbens, 2004; Hill, 2011) and the conditional density models. This allows for relaxed dependence on the correctness of the regression and conditional density models. However, doubly robust estimators are not immune to highly variable weights and their finite sample performance can suffer materially if the conditional density model is misspecified. We show that our weights can enhance doubly-robust estimators. In particular, our measure of dependence can provide a sharper bound on error for doubly robust estimators. This reveals that pairing of a reasonable outcome regression model with our weights in a doubly-robust fashion can be effective for estimating the ADRF. Our weight estimation procedure can also be modified to allow for exact decorrelation of chosen moments, allowing one to mitigate dependence while emphasizing decorrelation of certain features known to be important. This may improve performance in some settings.

The remainder of this paper is organized as follows. We investigate the role of dependence in weighted estimation of the ADRF in Section 2 and we develop a criterion that assesses how much dependence is mitigated by a set of weights, propose a new weight estimation strategy, and provide some corresponding theory in Section 3. We demonstrate the effectiveness of our approach in finite samples with a suite of challenging simulation studies in Section 4 and illustrate the use of our approach in a real-world study of EHR data in Section 5. We conclude the paper with some discussion.
2 Continuous Treatments and Confounding, Weighting and Dependence

2.1 Setup, notation, and assumptions

The observable quantities we consider consist of the random triplet \((X, A, Y)\), where \(X \in \mathcal{X} \subseteq \mathbb{R}^p\) is a vector of pre-treatment covariates, \(A \in \mathcal{A} \subseteq \mathbb{R}\) is a continuous-valued treatment variable indicating the assigned dose for a unit, and \(Y \in \mathcal{Y} \subseteq \mathbb{R}\) is an outcome of interest. The variate \((X, A, Y)\) has a joint distribution \(F_{X,A,Y}\) with respect to a dominating measure. We denote the marginal density of the treatment and covariates as \(f_A(a)\) and \(f_X(x)\), respectively, the conditional density of the treatment given \(X\) as \(f_A|X(a|x)\), and their joint density as \(f_{X,A}(a,x)\). Similarly, corresponding distribution functions are denoted \(F_A(a) = \mathbb{P}(A \leq a)\), \(F_X(x) = \mathbb{P}(X \leq x)\), \(F_A|X(a|x) = \mathbb{P}(A \leq a \mid X = x)\), and \(F_{X,A}(x,a) = \mathbb{P}(X \leq x, A \leq a)\). Our observed data consists of \(n\) i.i.d. samples \((X_i, A_i, Y_i)_{i=1}^n\) from \((X, A, Y)\). Note that we drop the subscripts on the density and cumulative distribution functions when there is no ambiguity.

To clarify the causal quantity of interest, we work under the potential outcomes framework, wherein the potential outcome function \(Y(a)\) for \(a \in \mathcal{A}\) is the outcome that would be observed if \(A\) were set to the value \(a\). The causal quantity of prime interest in this paper is the mean potential outcome function, also called the causal average dose-response function (ADRF), which is

\[
\mu(a) \equiv \mathbb{E}[Y(a)], \text{ for } a \in \mathcal{A}.
\]

The causal ADRF \(\mu(a)\) can be identified, or expressed in terms of observational data, under standard causal assumptions. These assumptions, which we employ throughout this paper are 1) consistency, which posits that \(A = a\) implies \(Y = Y(a)\), 2) positivity, which states that all values of the treatment as possible across the covariate space in that \(f(a|X = x) \geq \nu > 0\) for all \(x \in \mathcal{X}\) for some constant \(\nu\), and 3) ignorability of the assignment mechanism: \(Y(a) \perp \!\!\!\perp A \mid X\) for all \(a \in \mathcal{A}\), where \(\perp \!\!\!\perp\) denotes (conditional) independence (Dawid, 1979). Under assumptions 1)-3), the dose-response function is identified as

\[
\mu(a) = \mathbb{E}_X (\mathbb{E}[Y \mid X, A = a]) = \mathbb{E}_X [\mu(X, a)].
\]
Estimation of the dose-response function via regression-based estimation of the mean function \( \mu(X, a) \equiv \mathbb{E}[Y | X, A = a] \) can be highly challenging. Misspecification of the regression function can result in poor estimation of \( \mu(a) \), and nonparametric estimation of the regression function is also difficult, especially when \( X \) is not low dimensional. Instead, in this paper we focus on weighting-based estimators of \( \mu(a) \). A benefit of weighting estimators is that the dose-response function can be flexibly estimated by univariate (weighted) nonparametric regression, whereas with regression-based estimation, the need to incorporate confounders in a regression may make flexible estimation of the ADRF more difficult due to the additional dimensions. A conceptual benefit of weighting methods over regression-based approaches is that they provide a clear separation between the design phase and the analysis phase of a study. This separation is critical when substantial or iterative modeling effort is required to control for confounding.

The focus of this manuscript is in developing a criterion that can evaluate how effective a set of weights is in mitigating confounding and providing a new set of weights which is optimal under the criterion. We will demonstrate that this approach results in weights that yield robust control of the dependence between \( A \) and \( X \) and thus robust estimation of the ADRF.

### 2.2 Ignorability, independence, and the GPS

To reliably estimate the causal dose response function using observational data, sources of structural bias should be mitigated, among which the confounding bias is the most common. Consider the following DAG which illustrates our setting, where the covariate \( X \) is a confounder in studying the causal relationship between \( A \) and \( Y \). To mitigate the confounding, the backdoor path \( A \leftarrow X \rightarrow Y \) must be blocked. One way of blocking the backdoor path is by removing the arrow between \( A \) and \( X \) (i.e. making \( A \) independent of \( X \)). In a randomized trial, the independence between \( A \) and \( X \) holds due to randomization. This motivates us to create a pseudo-population mimicking the one we would observe under such a trial by reweighting the subjects in an observational study such that \( A \perp X | r(X) \). Together with the ignorability condition, if \( A \perp X | r(X) \), \( r(X) \) is also a balancing score such that weak unconfoundedness holds given the balancing score, i.e., for every \( a \), \( f_A(a | r(a, X), Y(a)) = f_A(a | r(a, X)) \) (Hirano and Imbens, 2004). The generalized propensity score \( f_A|X(A | X) \) (GPS) (Hirano and
Imbens, 2004) is such a balancing score and extends the pioneering work of Rosenbaum and Rubin (1983) proposed for binary treatments to continuous treatments.

For categorical treatments, weights for inducing independence between $A$ and $X$ are computed as $1/\mathbb{P}(A = a \mid X)$, with the variability-reducing stabilized weights computed as $\mathbb{P}(A = a)/\mathbb{P}(A = a \mid X)$. For continuous treatments, stabilized GPS weights are computed as $f_A(A)/f_{A\mid X}(A \mid X)$ (Robins et al., 2000), which naturally arise in estimating equations for the dose-response function via semiparametric theory (Kennedy et al., 2017). Estimating the weights requires correct specification not only of the mean of the conditional density of the treatment, but also of its shape. When either of these are misspecified, bias can result in estimates of the ADRF (Naimi et al., 2014; Zhu et al., 2015), indicating a particularly sensitive reliance on correct modeling of the full relationship between covariates and the conditional distribution of the treatment. Furthermore, similar to standard propensity score weights, GPS modeling can yield extreme weights, leading to unstable estimation. Weight trimming/capping may alleviate the problem of large weights but can be seen as ad hoc and may change the estimand (Crump et al., 2009): the estimated ADRF will correspond to the population represented by the newly weighted sample rather than to the original target population.

The stabilized GPS weights $f_A(A)/f_{A\mid X}(A \mid X)$ have several key properties that have motivated work to improve upon the GPS weights. Namely, when weighting by the GPS weights in the population sense, they 1) result in independence of $A$ and $X$, 2) preserve the marginal distributions of $X$ and $A$, and 3) have mean 1. These properties are listed more explicitly in Appendix A. Instead of indirectly estimating the weights by estimating the GPS, a nascent line of work has involved methods which directly estimate weights designed to satisfy the above three properties via balancing criteria. For example, work has focused on estimation of weights that induce zero marginal correlation between treatment and covariates subject to constraints that weighted marginal means of covariates and treatment are the same as the unweighted marginal means (Fong et al., 2018; Yiu and Su, 2018; Vegetabile et al., 2021). Although they are more robust than GPS weights, these approaches rely on both the correct choice of moments of the confounders and the choice of moments of the exposure variable to decorrelate. Yet, there is little guidance in deciding which set of moments in both confounders and exposure to focus on.

The aforementioned three properties of GPS weights are intuitively appealing, but it is not
immediately clear which of or in what manner these properties are important in mitigating bias in a weighted nonparametric estimator of the ADRF. To justify which properties are crucial in weights estimation, we derive the relationship between the properties of weighted dose-response function estimators using generic weights and the systematic source of error of the weighted estimator for the ADRF. We demonstrate that the ability of a set of weights to induce independence between $A$ and $X$ is critical for reducing the bias of a weighted estimator. Thus, we show that inducing independence should be the primary aim when estimating weights to study the causal effect of a continuous exposure, i.e. treatment.

2.3 A general error decomposition for weighted nonparametric estimators of the ADRF

In this section we aim to provide an explicit mechanistic connection between dependence and bias in weighted estimates of the ADRF. Although it is understood that using weights constructed from a well-estimated conditional density are consistent (Kennedy et al., 2017), it is unclear what role weights play more generally. It is not immediately clear what the connection is between the balance criteria that aim to “decorrelate” moments of covariates and moments of the treatment variable and the systematic bias in estimating the ADRF. We will investigate the precise source of the systematic bias of an estimator and illuminate the role of the weights in influencing the bias. Here, we focus on weighted Nadaraya-Watson estimators of the ADRF for clarity of presentation, though the key message applies to weighted local polynomial regression and other weighted nonparametric regression.

The response can be expressed as $Y_i = \mu(X_i, A_i) + \varepsilon_i$, where $\varepsilon_i \equiv Y_i(A_i) - \mu(X_i, A_i)$. By construction, $\varepsilon_i$ have mean zero but are not necessarily identically distributed. Given any set of weights $w = (w_1, \ldots, w_n)$ and a kernel $K_h(A_i - a_0) = K(A_i - a_0)/h$ centered at $A = a_0$ with bandwidth $h > 0$, the weighted Nadaraya-Watson estimator of the dose-response function at $A = a_0$ is

$$\mu_{NW}^w(a_0) = \frac{\sum_{i=1}^n Y_i w_i K_h(A_i - a_0)}{\sum_{i=1}^n K_h(A_i - a_0)}. \quad (1)$$
Given any \( w \), the error of (1) at \( A = a_0 \) can be decomposed as

\[
\hat{\mu}_w^{NW}(a_0) - \mu(a_0) = \int_X \int_A \mu(x, a_0) d \left[ F_{X,A,w}^n - F_{X,A}^n \right] (x, a) \\
+ \int_X \mu(x, a_0) d \left[ F_X^n - F_X^n \right] (x) + \left( \frac{f_A(a_0)}{\hat{f}_{A,h}^n(a_0)} - 1 \right) \int_X \int_A \mu(x, a_0) d \left[ F_{X,A,w}^n - F_{X,A}^n \right] (x, a) \\
+ \hat{f}_{A,h}^{n-1}(a_0) \int_X \int_A [\mu(x, a) K_h(a - a_0) - \mu(x, a_0) f_A(a_0)] dF_{X,A,w}^n(x, a) \\
+ \frac{1}{n} \sum_{i=1}^n \varepsilon_i w_i \hat{f}_{A,h}^{n-1}(a_0) K_h(A_i - a_0),
\]

where \( \hat{f}_{A,h}^n(a_0) = \int_A K_h(a - a_0) dF_A^n(a) \) is a kernel density estimate of \( f_A(a_0) \). We provide a derivation of this decomposition in the Supplementary Material. The second term on the right is due to sampling variability only and has mean zero and converges at rate \( n^{-1/2} \) if the sample is representative of the super-population. The expectations of the third, fourth, and fifth terms on the right above go to 0 when \( h \to 0 \) regardless of the weights \( w \). The last term has mean zero regardless of both the weights and the bandwidth, though its variability is impacted by the weights. A subtle point here is that the error decomposition above holds if \( F_{X,A}^n \) in (2) is replaced with any valid marginal distribution function of the treatment defined on \( \mathbb{R} \).

On the other hand, the first term (2) on the right above is the source of systematic bias of the weighted estimator unrelated to kernel smoothing. In other words, taking limits of the bandwidth of the kernel to 0 and sample size to infinity does not make (2) vanish. This term also provides insight into why using the weights we propose later perform well in finite sample settings when used in treatment effect estimators, as targeting this term specifically can help decrease the magnitude of the systematic component of the finite sample error of an estimator. If a given set of weights induces finite-sample independence of \( X \) and \( A \) in the sense that \( F_{X,A,w}^n(x, a) = F_X^n(x) F_A^n(a) \) for all \( x \in \mathcal{X}, a \in \mathcal{A} \), then the systematic source of error of \( \hat{\mu}_w(a_0) \) will be zero. The mean-squared error of the estimator will, however, depend primarily on both the bias term (2) and the variance of (3). Mitigating the variance of (3) merely amounts to controlling the squares of the weights; however, providing a measure that can characterize (2) is non-trivial and none exists in the literature. The systematic component (2) of the finite sample error is bounded by the distance between \( F_{X,A,w}^n(x, a) \) and \( F_X^n(x) F_A^n(a) \) provided that \( \mu(x, a_0) \)
is bounded. The mean function $\mu(x, a_0)$ is unknowable, so without modeling the response function, constructing a measure that bounds (2) is critical for assessing a set of weights.

In practice, the estimator $\hat{\mu}_{NW}^w(a_0)$ in (1) may be unstable, as the weights only appear in the numerator, so the estimated ADRF may lie outside the range of the observed values of the response. Instead, a more stable estimator is the following weighted average of the responses

$$\mu_{NW}^w(a_0) = \frac{\sum_{i=1}^{n} Y_i w_i K_h(A_i - a_0)}{\sum_{i=1}^{n} w_i K_h(A_i - a_0)},$$

which can be viewed as the minimizer of a weighted least squares problem where the $i$th weight is $w_i K_h(A_i - a_0)$. The estimator (4) is also a valid estimator of the ADRF as long as the denominator is a consistent estimator of $f_A(a_0)$; in this case the key source of systematic bias still depends on the term (2).

### 2.4 Error decompositions for estimands beyond the ADRF

Although we do not present a general theory, we emphasize that the role of weights in their ability to induce independence between treatment and covariates is not unique to estimation of the ADRF and applies to a wide variety of estimands. Consider estimation of the causal dose-response quantile function $q_Y(a_0)(\alpha) = \inf\{y : F_Y(a_0)(y) \leq \alpha\}$, where $F_Y(a_0)(y) = \mathbb{P}(Y(a_0) \leq y) = \mathbb{E}_X \{\mathbb{P}(Y \leq y|X, A = a_0)\} = \mathbb{E}_X \{F_{Y|X,A}(y|X, A = a_0)\}$.

The weighted nonparametric estimator of the CDF of $Y(a_0)$ is

$$\hat{F}_{Y(a_0)}^w(y) = \frac{\sum_{i=1}^{n} I(Y_i \leq y) w_i K_h(A_i - a_0)}{\sum_{i=1}^{n} K_h(A_i - a_0)}$$

and the resulting kernel quantile estimator of $q_Y(a_0)(\alpha) = \inf\{y : \alpha \leq F_Y(a_0)(y)\}$ at quantile $\alpha$ when $A = a_0$ is $\hat{q}_{Y(a_0)}^w(\alpha) = \inf\{y : \alpha \leq \hat{F}_{Y(a_0)}^w(y)\}$.

The error of (5) at $A = a_0$ can be decomposed as

$$\hat{F}_{Y(a_0)}^w(y) - F_Y(a_0)(y) = \int_{\chi} F(y|x, a_0) \int_{A} \left[ F_{X,A}^n(a) - F_{X}^n(a) \right] (x, a)$$

$$+ R_n(a_0) + R_{n,h}(a_0) + R_{1n,h,w}(a_0) + R_{2n,h,w}(a_0)$$

$$+ \frac{1}{n} \sum_{i=1}^{n} e_i(y) w_i \hat{F}_{n,h}^{-1}(a_0) K_h(A_i - a_0),$$

where $e_i(y) = I(Y_i \leq y) - \mathbb{P}(Y \leq y|X_i, A_i)$ where by construction, $\mathbb{E}[e_i(y)] = 0$, and $R_n(a_0)$, $R_{n,h}(a_0)$, $R_{1n,h,w}(a_0)$, and $R_{2n,h,w}(a_0)$ behave similarly to the second through fifth terms in
the decomposition (2) with their consistency for zero only depending on either the sample size and/or bandwidth $h$ and not the weights. Thus, just as in estimation of the ADRF, the key source of systematic bias in causal quantile function estimation can be mitigated by the use of weights that make the covariates and treatment independent.

3 Measuring and Controlling Weighted Dependence with Energy Statistics

3.1 A criterion to evaluate the quality of a set of weights

Having established the relationship between the dependence of $A$ and $X$ and the error in a weighted nonparametric estimate of the ADRF, we now construct a criterion that can assess how well a given set of weights induces independence on the weighted scale, i.e., we aim to characterize and bound the distance between $F^n_{X,A,w}$ and $F^n_X F^n_A$. We do so by building on the ideas of distance covariance (Székely et al., 2007), which is a measure of dependence between two random vectors of arbitrary dimension. The population distance covariance is zero if and only if the vectors are independent. Hence, a weighted distance covariance will be a useful component for our measure. Let $w = (w_1, \ldots, w_n)$ and define the weighted distance covariance to be

$$V^2_{n,w}(X, A) = \frac{1}{n^2} \sum_{k,\ell=1}^n w_k w_\ell C_{k\ell} D_{k\ell},$$

where

$$c_{k\ell} = \|X_k - X_\ell\|_2, \quad c_k. = \frac{1}{n} \sum_{\ell=1}^n c_{k\ell}, \quad c_.\ell = \frac{1}{n} \sum_{k=1}^n c_{k\ell},$$

$$\bar{c}. = \frac{1}{n^2} \sum_{k,\ell=1}^n c_{k\ell}, \quad C_{k\ell} = c_{k\ell} - c_k. - c_.\ell + \bar{c}..,$$

for $k, \ell = 1, \ldots, n$. Similarly define $d_{k\ell} = |A_k - A_\ell|$, $\bar{d}_k. = \frac{1}{n} \sum_{\ell=1}^n d_{k\ell}$, $\bar{d}.\ell = \frac{1}{n} \sum_{k=1}^n d_{k\ell}$, and $D_{k\ell} = d_{k\ell} - \bar{d}_k. - \bar{d}.\ell + \bar{d}..$. The quantity (6) simplifies to the original distance covariance when weights are all 1. Since the original distance covariance is always non-zero, (6) is also always non-zero if the weights are positive. We now provide further insight and motivation of the form of $V^2_{n,w}(X, A)$ and its interpretation in terms of weighted distributions.
Letting \( i = \sqrt{-1} \), we define the (weighted) empirical characteristic functions as \( \varphi_{X,A,w}^n(t, s) = \frac{1}{n} \sum_{i=1}^{n} w_i \exp\{i(t, X_i) + isA_i\} \), \( \varphi_{X,w}^n(t) = \frac{1}{n} \sum_{i=1}^{n} w_i \exp\{i(t, X_i)\} \), \( \varphi_{A,w}^n(s) = \frac{1}{n} \sum_{i=1}^{n} w_i \exp\{isA_i\} \), and unweighted empirical characteristic functions \( \varphi_{X,A}^n(t, s) \), \( \varphi_{X}^n(t) \) and \( \varphi_{A}^n(s) \) are defined accordingly.

**Theorem 3.1.** Let \( w = (w_1, \ldots, w_n) \) be a vector of weights such that \( \sum_{i=1}^{n} w_i = n \) and \( w_i \geq 0 \) for all \( i = 1, \ldots, n \). Then \( \mathcal{V}_{n,w}^2(X, A) \geq 0 \) and

\[
\mathcal{V}_{n,w}^2(X, A) = \int_{\mathbb{R}^{p+1}} |\varphi_{X,A,w}^n(t, s) - \varphi_{X,w}^n(t)\varphi_{A,w}^n(s) + (\varphi_{X,w}^n(t) - \varphi_{X}^n(t))(\varphi_{A,w}^n(s) - \varphi_{A}^n(s))|^2 \omega(t, s) dt \, ds
\]

where \( \omega(t, s) = (c_p c_1 \|t\|_2^{1+p} \|s\|^2)^{-1} \) with \( c_d = \frac{\pi^{(1+d)/2}}{\Gamma((1+d)/2)} \), and \( \Gamma(\cdot) \) is the complete gamma function.

Based on (7), it is clear that if \( F_{X,A,w}^n = F_X^n F_A^n \), then \( \mathcal{V}_{n,w}^2(X, A) = 0 \). However, the converse is not necessarily true. Yet, if the weights preserve the marginal distribution of treatment and covariates, i.e. \( F_{X,w}^n = F_X^n \) and \( F_{A,w}^n = F_A^n \), then \( \mathcal{V}_{n,w}^2(X, A) = 0 \) implies that \( F_{X,A,w}^n = F_X^n F_A^n \).

In other words, if one can add additional terms to (6) that also measure the distance between \( F_{X,w}^n \) and \( F_X^n \) along with that between \( F_{A,w}^n \) and \( F_A^n \), then (6) can be utilized to construct a measure that determines the distance between \( F_{X,A,w}^n \) and \( F_X^n F_A^n \), i.e., a measure for the weighted dependence between \( X \) and \( A \). In line with our use of the distance covariance, we leverage the weighted energy distance proposed in Huling and Mak (2020) to help construct such a measure.

Applied to our setting, the weighted energy distance between \( F_{X,w}^n \) and \( F_X^n \) is

\[
\mathcal{E}(F_{X,w}^n, F_X^n) = \frac{2}{n^2} \sum_{i=1}^{n} \sum_{j=1}^{n} w_i \|X_i - X_j\|_2^2 - \frac{1}{n^2} \sum_{i=1}^{n} \sum_{j=1}^{n} w_i w_j \|X_i - X_j\|_2^2 - \frac{1}{n^2} \sum_{i=1}^{n} \sum_{j=1}^{n} \|X_i - X_j\|_2^2.
\]

Due to Proposition 1 of Huling and Mak (2020), it can be shown that \( \mathcal{E}(F_{X,w}^n, F_X^n) = \int_{\mathbb{R}^{p}} |\varphi_{X,w}^n(t) - \varphi_{X}^n(t)|^2 \omega(t) dt \), where \( \omega(t) = 1/(C_p \|t\|_2^{1+p}) \), \( C_p = \pi^{(1+p)/2}/\Gamma((1 + p)/2) \) is a constant. The weighted energy distance \( \mathcal{E}(F_{A,w}^n, F_A^n) \) between \( F_{A,w}^n \) and \( F_A^n \) can be similarly defined.

Our proposed measure of the level of independence induced by a set of weights is defined as

\[
\mathcal{D}(w) = \mathcal{V}_{n,w}^2(X, A) + \mathcal{E}(F_{X,w}^n, F_X^n) + \mathcal{E}(F_{A,w}^n, F_A^n).
\]

The following result demonstrates that \( \mathcal{D}(w) \) indeed achieves its stated goal.
Theorem 3.2. Let \( w = (w_1, \ldots, w_n) \) be a vector of weights with \( w_i > 0 \) and \( \sum_{i=1}^{n} w_i = n \). Then \( D(w) \geq 0 \) with equality to zero if and only if \( \varphi_{X,A,w}^n(t,s) = \varphi_X^n(t)\varphi_A^n(s) \), \( \varphi_{X,w}^n(t) = \varphi_X^n(t) \), and \( \varphi_{A,w}^n(s) = \varphi_A^n(s) \) for all \( (t,s) \in \mathbb{R}^{p+1} \). Further, \( \int |\varphi_{X,A,w}^n(t,s) - \varphi_X^n(t)\varphi_A^n(s)|^2 \omega(t,s)dt\,ds \leq 3D(w) \).

Thus, smaller values of \( D(w) \) indicate weaker dependence between \( X \) and \( A \) after weighting and better preservation of the marginal distributions and larger values implying the opposite. \( D(w) = 0 \) implies the weights induce complete independence between \( A \) and \( X \) and that the marginal distributions of \( X \) and \( A \) are exactly preserved.

We also have the following result, which shows how the proposed distance acts as a bound on integration errors over a class of functions.

Lemma 3.3. Let \( H \) be the native space induced by the radial kernel \( \Phi(\cdot,\cdot) = -\|\cdot\|_2 \times -|\cdot| \) on \( X \times A \), and let \( g(\cdot,\cdot) \) be any function where \( g(\cdot,\cdot) \in H \). Then, for any weights \( w \) satisfying \( \sum_{i=1}^{n} w_i = n, w_i \geq 0 \), we have

\[
\left[ \int_{X} \int_{A} g(x,a) d \left[ F_{X,A,w}^n - F_X^n F_A^n \right] (x,a) \right]^2 \leq C_g D(w),
\]

(9)

where \( C_g = 3\|g\|_H^2 \geq 0 \) is a constant depending on only \( g \).

For any \( a \in A \) if \( \mu(\cdot,a) \in H \), we can see that \( D(w) \), modulo a constant, acts as a bound on the systematic bias term (2) as long as \( \mu(\cdot,a) \) is sufficiently smooth. Thus, if \( \mu(x,a) \) is contained in \( H \), then we can expect weights with smaller \( D(w) \) to lead to smaller systematic bias. The space \( H \) is a reasonably broad class of functions as it contains the Sobolev space of functions with square-integrable functions with \( r < [ (p + 1)/2 ] \)-th differentials (Mak and Joseph, 2018; Huling and Mak, 2020). Our goal for the next section is to define weights that are optimal in terms of our criterion. The weights that minimize \( D(w) \) will result in mitigation of the dependence of \( A \) and \( X \) induced by nonrandom selection into treatment.

It is natural to wonder whether it would instead be more appropriate to simply define a distance as \( \int |\varphi_{X,A,w}^n(t,s) - \varphi_X^n(t)\varphi_A^n(s)|^2 \omega(t,s)dt\,ds \) and construct a relationship between this distance and Euclidean norms computable from data. However, we have found that the resulting quantity can be empirically problematic and unreliable. Further, we have found that optimization of such a quantity cannot be achieved reliably by existing algorithms and is thus not suitable for the proactive construction of weights. Our proposed quantity, while more
complicated, does not exhibit any of these issues in the sense that it reliably measures dependence, and, as we will demonstrate, it is straightforward to optimize with existing quadratic programming software.

3.2 A new proposal: optimal independence weights

We define the distance covariance optimal weights (DCOWs) to be

$$ w^d_n \in \arg\min_{w=(w_1, \ldots, w_n)} D(w) \text{ such that } \sum_{i=1}^n w_i = n, \text{ and } w_i \geq 0 \text{ for } i = 1, \ldots, n. $$

Due to Theorem 3.2, the distance covariance optimal weights $w^d_n$ are designed to minimize dependence between $X$ and $A$ on the weighted scale while keeping the weighted marginal distributions of $X$ and $A$ close to those of the unweighted data. The constraint $\sum_{i=1}^n w_i = n$ ensures that $F_{X,A,w^d_n}^n$ is a valid distribution function. Since $D(w)$ tracks with the dependence induced by a set of weights, the DCOWs can be thought of as optimal independence weights.

Although, as we will show later, the DCOWs result in consistent weighted dose-response estimators due to their explicit targeting of the source of systematic error, without additional constraints they may not guarantee optimal convergence rates. Instead, a small change to our criterion to allow for penalization of the squares of the weights allows for us to control the variability of the weights without sacrificing their bias-reduction property. This additional penalty is akin to focusing more directly on mean squared error instead of bias and can be interpreted as discouraging the effective sample size (ESS) of the weights from being too small. In particular, the ESS is typically approximated as $\left(\sum_i w_i\right)^2/\sum_i w_i^2$ (Kish, 1965), which, due to our constraints, is $4n^2/\sum_i w_i^2$ and is precisely the inverse of our proposed penalty. Further, combining a “balance” criterion with a means of weight variability mitigation is in line with the recommendations of Chattopadhyay et al. (2020).

We now define the penalized distance covariance optimal weights (PDCOWs) to be

$$ w^{pd}_n \in \arg\min_{w=(w_1, \ldots, w_n)} D(w) + \lambda \frac{1}{n^2} \sum_{i=1}^n w_i^2 \text{ such that } \sum_{i=1}^n w_i = n, w_i \geq 0 \text{ for } 0 < \lambda < \infty, i = 1, \ldots, n. $$

Here, the tuning parameter $\lambda$ is any positive constant and can be chosen by the user to achieve
a desired ESS. A lemma provided in the Supplement similar to Lemma 3.3 shows that the penalized version of our criterion acts as a bound on the term in the left hand side of (9) plus the squares of the weights, which is more akin to a bound on the root mean squared error than bias as in Lemma 3.3. Although additional penalty terms are necessary for convergence rate guarantees, in practice we have found that only very minimal or even no penalization at all works well because the unpenalized weights, the DCOWs, tend to be quite stable. In all analyses described later, we use only the DCOWs with no penalization of the weights. Alternatively, one can simply choose $\lambda$ so that a desired effective sample size is achieved.

Both the DCOWs and PDCOWs can be used in a wide variety of estimators for various causal estimands involving continuous treatments, not just Nadaraya-Watson-based estimators and not just estimators of the ADRF. The weights can be used either in a simple weighted nonparametric estimator of the dose-response function or to supplement any doubly-robust estimator of such. For the former, our weights provide a completely nonparametric and empirically robust estimation approach that requires only mild moment conditions on the covariates and treatment for estimation consistency. For the latter, such an estimator using our weights is guaranteed to be consistent regardless of the correctness of the outcome model, while it still enjoys efficiency gains if the outcome model is well-specified.

In a later section, we provide more formal statements on the consistency of dose-response function estimators that use our proposed distance covariance optimal weights.

### 3.3 Doubly robust estimation with optimal independence weights

Another class of estimators for causal ADRFs are doubly-robust estimators such as in Kennedy et al. (2017) and Colangelo and Lee (2020), which combine sample weights and an outcome model $\hat{\mu}(x, a_0)$, ideally a consistent estimator of $\mu(x, a_0)$. Though the term “doubly-robust” is reflective of the property that if either the weights or outcome model is correctly specified, the estimator will be consistent, a more consequential property of doubly-robust estimators is that the error rates of each model are multiplied. Loosely-speaking, this implies that reasonable estimation of one model can alleviate the strain on the other. However, the variance of such estimators tends to be more significantly impacted by variable or poor estimation of the weights, indicating potentially an outsize impact of poor estimation of the weights in practice relative
Although in the next section we reveal that the use of the DCOWs alone results in the ideal convergence rate for the ADRF, our view is that DCOWs can be enhanced by using doubly-robust estimators, or more provocatively, that the use of DCOWs can significantly enhance doubly-robust estimators. The DCOWs provide grounding and confidence to the analyst that the estimator will converge at the right rate without the need for careful modeling, but the use of a reasonably well-specified outcome model provides an opportunity to fine-tune performance, resulting in an estimator that works well empirically. Unlike in Colangelo and Lee (2020), we do not require the use of flexible machine learning methods to guarantee consistency due to the independence-inducing property of our weights.

Here, for simplicity of presentation, we focus on the following Nadaraya-Watson-based doubly-robust estimator based on any estimator \( \hat{\mu}(x, a_0) \) of \( \mu(x, a_0) \) as

\[
\mu_{NW}^{w,DR}(a_0) = \frac{1}{n} \sum_{i=1}^{n} \hat{\mu}(X_i, a_0) + \frac{\sum_{i=1}^{n} (Y_i - \hat{\mu}(X_i, a_0)) w_i K_h(A_i - a_0)}{\sum_{i=1}^{n} K_h(A_i - a_0)}.
\]

In the Appendix we derive a decomposition of the error \( \mu_{NW}^{w,DR}(a_0) - \mu(a_0) \) and show that the systematic bias term not related to smoothing is

\[
\int_X \{\mu(x, a_0) - \hat{\mu}(x, a_0)\} \int_A d\left[F_{X,A}^{n} - F_{X}^{n} F_{A}^{n}\right](x, a).
\]

(12)

Lemma 3.3 implies that (12) is less than or equal to \( 3\|g\|_{\mathcal{H}} \mathcal{D}(w) \) provided that \( \mu(\cdot, a_0) - \hat{\mu}(\cdot, a_0) \in \mathcal{H} \). With the DCOWs, we provide a set of weights \( w^d \) that makes \( \mathcal{D}(w) \) as small as possible, though it may not be exactly zero for a finite sample.

Lemma 3.3 and our error decomposition for doubly-robust estimators illustrate that a reasonable but imperfect model can help mitigate leftover bias due to residual dependence, i.e. locations where \( F_{X,A,w^d}^{n} - F_{X}^{n} F_{A}^{n} \) differs significantly from zero. For a doubly-robust estimator with a well-specified outcome model, the constant \( 3\|g\|_{\mathcal{H}} \) in the bound of Lemma 3.3 can be smaller than for a non-doubly robust estimator. As a result, using a doubly-robust estimator with the weights \( w^d \) and a reasonably well-specified outcome model results in a tighter bound on the systematic bias term. Further, the additional terms in the error decomposition for \( \mu_{NW}^{w,DR}(a_0) \) that involve \( \hat{\mu}(x, a_0) \) are likely to be made smaller as long as \( \mu(x, a_0) \approx \hat{\mu}(x, a_0) \). Given this, it is clear that using a doubly-robust estimator with the PDCOWs is a well-motivated strategy to improve performance for a given dataset. Although this exploration focuses on a Nadaraya-
Watson estimator, the same message applies to the local linear doubly-robust estimator of Kennedy et al. (2017).

3.4 Asymptotic properties

We first show that the distance covariance optimal weights do indeed induce independence asymptotically. Throughout this section we define \( w(x, a) = \frac{f_A(a)}{f_A|X(a|X = x)} \) to be the “true” normalized density weights.

**Theorem 3.4.** Let \( w_n^d \) be the distance covariance optimal weights defined in (10). Then if \( E\|X\|_2 < \infty \) and \( E|A| < \infty \) we have

\[
\lim_{n \to \infty} F_{X,A,w_n^d}(x, a) = F_X(x) F_A(a) \tag{13}
\]

almost surely for every continuity point \((x, a) \in \mathbb{R}^{p+1}\). If, additionally \( Ew^2(X, A) < \infty \) holds, then

\[
\lim_{n \to \infty} F_{X,A,w_n^{pd}}(x, a) = F_X(x) F_A(a) \tag{14}
\]

almost surely for every continuity point \((x, a) \in \mathbb{R}^{p+1}\).

Theorem 3.4 is in some sense the most important property of the DCOWs, as it demonstrates the feasibility of using these weights not just in dose-response function estimation, but also in the estimation of any causal estimand that requires independence.

We now show that for the particular task of estimating the ADRF, using the DCOWs in a weighted Nadaraya-Watson estimator results in consistent estimation of the dose-response function.

**Theorem 3.5.** Assume that the kernel \( K(\cdot) \) is symmetric, second order, i.e. it meets the conditions that \( \int uK(u)du = 0, \int K(u)du = 1, \) and \( 0 < \int u^2K(u)du < \infty \), and is bounded differentiable. Further, assume that the moment conditions required in Theorem 3.4 hold and that \( \mu(x, a_0) \) and is bounded and continuous on \( \mathcal{X} \times \mathcal{A} \) and has second order derivatives, \( f_A(a_0) \) is bounded and has second order derivatives, \( 1/f_A(a_0) \) is uniformly bounded. Then for \( w = w^d \) and \( w = w^{pd} \)

\[
\lim_{n \to 0, nh \to \infty} \mu_{NW}^w(a_0) = \mu(a_0) \tag{15}
\]

in probability for all continuity points \( a_0 \in \mathcal{A} \).
Thus, both the DCOWs and PDCOWs result in consistent estimation of the causal average dose-response function. Since $\mu_{NW}(a_0)$ can be viewed as a special case of the double-robust estimator with a misspecified outcome model, it can also be straightforwardly shown that $\mu_{NW}^{DR}(a_0)$ is also consistent even if $\hat{\mu}(x, a_0)$ is inconsistent for $\mu(x, a_0)$ as long as the outcome model does not diverge.

The following result shows the rate of convergence of $D(w^d)$ and $D(w^{pd})$ to zero and also shows that the squares of the PDCOWs are controlled asymptotically under certain moment conditions.

**Lemma 3.6.** Assume the moment conditions (A1) and (A2) listed in Appendix B hold, then $D(w^d) = O_p(1/n)$. If in addition we have $\mathbb{E}w^2(X, A) < \infty$, then $D(w^{pd}) = O_p(1/n)$ and $\frac{1}{n^2} \sum_{i=1}^{n} w_{pd,i}^2 = O_p(1/n)$.

Lemma 3.6 implies the rate of convergence of $\int |\phi_{X,A,w}^n(t, s) - \phi_{X}^n(t)\phi_{A}^n(s)|^2 \omega(t, s) dt ds$ to zero for both $w^d$ and $w^{pd}$, indicating they result in independence of the treatment and covariates at a parametric rate. It also implies that the variability of $w^{pd}$ is not a rate-limiting factor in nonparametric estimates of the ADRF.

The following shows the convergence rate of the penalized distance covariance optimal weights under additional mild moment conditions on the covariates, treatment, and $w(X, A)$.

**Theorem 3.7.** Assume the conditions required in Theorem 3.5 hold. Additionally assume the moment conditions required in Lemma 3.6 hold and that $\mathbb{E}[Y^2 | X = x, A = a] < c$ for some $c$ uniformly over $x \in X$. Then

$$\mu_{NW}^{pd}(a_0) - \mu(a_0) = O_p(1/\sqrt{nh + h^2}). \quad (16)$$

As long as the outcome model does not diverge, a result similar to Theorem 3.7 holds for the doubly-robust estimator $\mu_{NW}^{DR}(a_0)$. This convergence rate is the standard rate for unweighted Nadaraya-Watson estimators of a univariate regression function; thus, the convergence rate of the weighted estimator based on our proposed weights is unaffected by the nonparametric nature of the estimation of $w^{pd}$. 


3.5 Computation

The optimization problems (10) and (11) can be formulated as quadratic programming problems with linear constraints, making them straightforward to implement with commercial and open-source solvers such as OSQP (Stellato et al., 2020) or CCCP (Andersen et al., 2011). We will show how the (P)DCOW optimization problem can be represented as a generic quadratic program

$$\min_w w^T P w + q^T w \quad \text{s.t.} \quad A^T w \leq c.$$ 

The (P)DCOW optimization criterion takes $P = P_{DCOW} + P_{EB(A)} + P_{EB(X)} + P_\lambda$, $q^T = q_{EB(A)}^T + q_{EB(X)}^T$, where $P_{DCOW} = \frac{1}{n^2} C \circ D$, $P_{EB(A)} = -\frac{1}{n^2} Q_A$, $P_{EB(X)} = -\frac{1}{n^2} Q_X$, $P_\lambda = \lambda \frac{1}{n^2} I_n$, $q_{EB(A)}^T = \frac{2}{n^2} 1^T Q_A$, and $q_{EB(X)}^T = \frac{2}{n^2} 1^T Q_X$. The terms $C = (C_{kl})$ and $D = (D_{kl})$ are as defined in (6), $\circ$ is the elementwise product, and $Q_A$ and $Q_X$ are the Euclidean distance matrices of $A$ and $X$, respectively. From this formulation, we have $V_{n,w}(X, A) = w^T P_{DCOW} w$, $E(F_{n,w}(X, A), w, F_{n,w}(X, A)) = w^T P_{EB(A)} w + q_{EB(A)}^T w + c_A$, $E(F_{n,w}(X, A)) = w^T P_{EB(X)} w + q_{EB(X)}^T w + c_X$, and $\lambda \frac{1}{n^2} \sum_{i=1}^n w_i^2 = w^T P_{\lambda} w$, where $c_A$ and $c_X$ are constants, so minimizing $w^T P w + q^T w$ amounts to minimizing $D(w) + \lambda \frac{1}{n^2} \sum_{i=1}^n w_i^2$, the solution to which are the PDCOWs (or the DCOWs when $\lambda = 0$). The constraints $A^T$ and $c$ can be specified as $A^T = (-I_n, 1, -1)^T$ and $c = (0^T, n, -n)^T$ so that $A^T w \leq c$ implies $w_i \geq 0$ for all $i$ and $\sum_i w_i = n$. Although the optimization problem has the form of a linearly constrained quadratic program, the problem is not convex because $P$ is not positive semi-definite. Despite this, algorithms such as OSQP or CCCP can reliably provide high quality solutions to the optimization problem.

3.6 Extensions and implementation considerations

If in practice additional emphasis on correlations of particular moments of covariates and the treatment is of importance, the optimization criterion in (10) can be straightforwardly modified to optimize $D(w)$ subject to the constraints

$$\sum_{i=1}^n w_i \{m_X(X_i) - \overline{m}_X(X_i)\} \{m_A(A_i) - \overline{m}_A(A_i)\}^T = 0,$$

where $m_X$ is a vector of moments of $X$, $\overline{m}_X$ is the average of the moments over the sample, $m_A$ is a vector of moments of $A$, and similarly $\overline{m}_A$ is their sample average. These constraints allow for
the user to construct weights that minimize dependence between $X$ and $A$ while emphasizing decorrelation of desired moments. If exactly zero correlation is infeasible, a constraint that the marginal correlations are less than a threshold can be used instead, similar to Zubizarreta (2015). Additional emphasis on marginal correlation may improve finite sample performance if known moments are especially imbalanced or highly related to outcomes. These exact or inexact constraints can be straightforwardly incorporated into the quadratic programming problem described above.

When the dimension of $X$ is high, the relative emphasis of the energy distance terms for $A$ and $X$ in $D(w)$ can be imbalanced, with less emphasis on the individual components of $X$ relative to $A$. To help mitigate this issue, one can instead use a version of $D(w)$ that aims to re-balance the terms to be more comparable on a per-unit basis like the following:

$$D_c(w) = V_{n,w}(X, A) + c_X \mathcal{E}(F^n_{X, w}, F^n_X) + c_A \mathcal{E}(F^n_{A, w}, F^n_A),$$

where $c_X + c_A = 1$ and $c_X/c_A = \sqrt{p}$. This modification has no meaningful impact on the theoretical properties of $D_c(w)$, as our proof of Theorem 3.2 applies to this modified distance.

## 4 Numerical experiments

### 4.1 Comparator methods

We use the following methods to estimate weights. We use a naïve method which uses weights equal to identity (unweighted). We use stabilized GPS weights computed four ways: a linear regression model for estimating $\mathbb{E}(A|X)$ (i.e., the conditional mean of dose given covariates) and a normal conditional density ("GPS normal"); a gamma regression model for estimating $\mathbb{E}(A|X)$ and a gamma conditional density ("GPS gamma"); a generalized boosted model for estimating $\mathbb{E}(A|X)$, where the number of trees was chosen to minimize the weighted average absolute correlation between the treatment and covariates as in Zhu et al. (2015), and a normal conditional density ("GBM"); and a Bayesian Additive Regression Trees model for estimating $\mathbb{E}(A|X)$ and a normal conditional density ("BART"). For methods that estimate weights by directly inducing a lack of correlation between moments of the treatment and covariates, we use the covariate balancing generalized propensity score of Fong et al. (2018) and the entropy balancing approach of Tübbicke (2020); Vegetabile et al. (2021). Among this class of meth-
ods, we only consider these two as other approaches to estimating weights that decorrelate pre-specified moments behave largely similarly to each other (Tübbicke, 2020; Vegetabile et al., 2021). We use the exactly-identified version of the covariate balancing generalized propensity score (“CBPS”). We use versions of the entropy balancing approach that decorrelate either all first order moments (“Entropy (1)”), all first order moments and squared terms in continuous covariates (“Entropy (2)”), or all first order moments, pairwise interactions, and squared terms in continuous covariates (“Entropy (int)”). Any resulting weights greater than 500 when standardized to sum to \( n \) are truncated at 500. We use our proposed DCOWs (“DCOW”) and the proposed DCOWS where we further induce exact decorrelation of first order moments as discussed in Section 3.6 (“DCOW (dm)”), both using the dimension adjustment described in Section 3.5. For each method, the weights are used in a weighted local linear regression used to estimate the ADRF. For the GPS (normal), GPS (gamma), DCOW, and DCOW (dm) methods, we also use the doubly-robust estimator of Kennedy et al. (2017) with a an outcome model that is linear in the covariates with additive first order terms; the methods are labeled as “GPS (normal,DR)”, “GPS (gamma,DR)”, “DCOW (DR)”, and “DCOW (dm,DR)”, respectively.

4.2 Simulation using National Medical Expenditure Survey Data

The National Medical Expenditure Survey (NMES) relates medical expenditures with degree of smoking among U.S. citizens (Johnson et al., 2003). The NMES dataset contains information on 9708 individuals. The outcome variable is the total medical expenditures in dollars and the treatment \( A \in [0.05, 216] \) is the amount of smoking in pack years. We limit the data to those with \( A \leq 80 \) (i.e. \( A = [0.05, 80] \)), leaving 9368 units. Two of the covariates are continuous (\( X_1: \) age started to smoke and \( X_2: \) age last smoked) and the remaining 7 are discrete (\( X_{3k}: \) gender (male, female); \( X_{4k}: \) race (African American, other); \( X_{5k}: \) seat belt use, (low, medium, high); \( X_{6k}: \) education (< high school, high school, 1 – 3 years of college, 4+ years of college); \( X_{6k}: \) marital status (never married, widowed/divorced, married); \( X_{7k}: \) census region (Northeast, Midwest, South, West); \( X_{8k}: \) poverty status (poor, near poor, low income, middle income, high income), with anywhere from \( \ell_k = 2 \) to 5 levels. The overall covariate vector thus has dimension 18. In our simulation, we leave the treatment level (pack years) and covariates intact.
and simulate outcomes for each unit from the following model.

\[
Y = \gamma_1 b_1 X_1 + \gamma_2 b_2 \bar{X}_1^2 + \gamma_3 b_3 \bar{X}_1^3 + \gamma_4 b_4 X_2 + \gamma_5 b_5 \bar{X}_2^2 + \gamma_6 b_6 \bar{X}_2^3 \\
+ \sum_{j=3}^{8} \sum_{k=1}^{s} \left\{ \alpha_{jk} b_{1jk} + \eta_{1jk} b_{2jk} X_1 + \eta_{2jk} b_{3jk} \bar{X}_1^2 + \eta_{3jk} b_{4jk} X_2 + \eta_{4jk} b_{5jk} \bar{X}_2^2 \right\} I(X_j = k) \\
- \overline{m}(X) + f(A)(1 + \delta(X))) + \varepsilon,
\]

where \( \tilde{X}_j = X_j - \overline{X}_j \), \( \gamma_1, \gamma_3, \eta_{1jk}, \eta_{3jk} \sim \text{Unif}(-0.5, 0.5) \), \( \gamma_2, \gamma_4, \eta_{2jk}, \eta_{4jk} \sim \text{Unif}(-0.1, 0.1) \), \( \gamma_5, \gamma_6 \sim \text{Unif}(-0.01, 0.01) \), \( \alpha_{jk} \sim \text{Unif}(-10, 10) \), \( b_j, b_{ijk} \sim \text{Bernoulli}(0.5) \), \( \overline{m}(X) \) is the mean of the main effect terms preceding it, and the treatment effect curve \( f(A) = A/4 + (\frac{2}{(A/100+1/2)^3} - (A-40)^2)/100 \). For the constant treatment effect setting, \( \delta(X) = 0 \), and for the heterogeneous treatment effect setting,

\[
\delta(X) = \gamma_{11} \bar{X}_1 + \gamma_{12} \bar{X}_2 + \sum_{j=3}^{8} \sum_{k=1}^{s} \left\{ \eta_{11jk} b_{11jk} \bar{X}_1 + \eta_{12jk} b_{12jk} \bar{X}_2 \right\} \tilde{X}_{j,k}
\]

where \( \tilde{X}_{j,k} = I(X_j = k) - I(X_j = \overline{k}) \), \( \eta_{11jk}, \eta_{12jk} \sim \text{Unif}(-0.5, 0.5) \), and \( b_{11jk}, b_{13jk} \sim \text{Bernoulli}(0.5) \).

We generate 100 different draws of the coefficients (\( \eta, \gamma, \) and \( b \) terms) in the outcome model above, allowing for the simulation study to explore a wide variety of outcome models. For each of these 100 outcome model draws, we replicate the simulation experiment 1000 times. For each replication, a random subsample of size \( n < 9368 \) is drawn without replacement from the 9368 units, and outcomes for these units are generated from the outcome model. The simulation process is repeated for each of the sample sizes \( n = 100, 200, 400, 800, 1600, 3200 \).

We also consider a simulation setting with the heterogeneous treatment effect where 50 additional variables are added to the covariate vector so that the overall dimension is 68. The 50 additional variables are generated so that they are correlated with both the response and treatment while preserving the original values of the response and treatment. To generate the additional variables, we first draw random variables from a normal distribution with mean \( = (\overline{X}_1 + \overline{X}_2)/2 \) and variance \( = (\text{var}(X_1) + \text{var}(X_2))/2 \), where \( X_1 \) is the age started to smoke and \( X_2 \) is the age last smoked. We then use a Cholesky decomposition to induce an \( AR(1) \) correlation structure with correlation parameter \( \rho = -1/3 \), where the correlation structure is with respect to the expanded vector \( (Y, A, X_{nv1}, \ldots, X_{nv50}) \), where \( X_{nvj} \) are the added variables and the \( AR(1) \) correlation structure is modified in such a way that \( A \) and \( Y \) remain unchanged.
but the added variables have strong correlations jointly with $A$ and $Y$ and thus impact the finite sample error in estimating the ADRF if the added variables are not properly adjusted for. This variance structure is used so that the variation of the noise variables is comparable to that of the continuous covariates in the NMES data.

All methods are evaluated with a measure of the mean absolute bias (MAB) and integrated root mean squared error (IRMSE), both of which are used for evaluation of estimates of the ADRF in Kennedy et al. (2017). MAB and IRMSE are defined as

$$MAB = \int_A \left| \frac{1}{S} \sum_{s=1}^{S} \hat{\mu}_s(a) - \mu(a) \right| \hat{f}_A(a) da$$

and

$$IRMSE = \int_A \left[ \frac{1}{S} \sum_{s=1}^{S} \left\{ \hat{\mu}_s(a) - \mu(a) \right\}^2 \right]^{1/2} \hat{f}_A(a) da,$$

where $\hat{f}_A(a)$ is a kernel density estimate of the marginal density of the treatment variable, $s$ indexes the simulation replications, and $A$ is a trimmed version of the support of the treatment variable that excludes pack years greater than 80. We calculate the MAB and IRMSE statistics for each of the 100 different outcome model settings and then compute their averages over the 100 settings.

The MAB and IRMSE results for the constant treatment effect setting are displayed in Table 1 and the results for the heterogeneous treatment effect setting are displayed in Table 2. Results for any method are not shown if no numerical solution is found in more than 75% of the replications. The standard DCOWs performed the best in terms of both MAB and IRMSE across all sample sizes among all non-doubly-robust estimators, only being outperformed by the doubly-robust estimator that uses DCOWs as weights. DCOWs with exact first order moment decorrelation performed similarly to, but slightly worse than standard DCOWs, for both the non-doubly-robust estimator and the doubly-robust estimator, though the performance was much worse for $n = 100$, as the exact constraints may have been too stringent for the sample size. The estimators using standard GPS weights, both doubly-robust and non-doubly-robust, performed poorly in terms of both MAB and IRMSE for small to moderate sample sizes, though the doubly-robust estimator with gamma regression-based weights performed well in terms of MAB and IRMSE for larger sample sizes. The machine learning approaches to GPS estimation (GBM and BART) performed relatively poorly in terms of MAB and IRMSE for small
sample sizes, with BART performing better than GBM for small sample sizes, but with similar but slightly better performance for GBM for large sample sizes. Among the GPS-based methods, GBM and BART generally yielded the lowest MAB and IRMSE across the sample size settings, except for the doubly-robust gamma GPS estimator. Among the moment balancing approaches, entropy balancing with decorrelation induced only for first and second order moments and not interactions performed the best in terms of MAB and IRMSE, though for small sample sizes, entropy balancing frequently failed to arrive at a solution. For the heterogeneous setting, entropy balancing with decorrelation induced only for first order moments performed the best, likely due to numerical instability of adding more moment constraints. The CBPS estimator yielded worse performance than did entropy balancing overall, though it did not face the convergence problems of entropy balancing for small sample sizes. Entropy balancing with higher order moment constraints failed to arrive at a solution far more frequently and performed poorly even for large sample sizes, likely due to the strictness of the exact moment constraints.

The results for the heterogeneous effect setting with 50 additional noise variables are displayed in Table 3. Again, DCOWs performed the best among all methods in terms of both MAB and IRMSE for all sample sizes except $n = 100$, where the doubly-robust gamma GPS estimate was slightly better in terms of IRMSE.

Additional simulation results under the same setting of Vegetabile et al. (2021) can be found in the supplementary file wherein our weights also yielded the best performance across all sample size settings. The main difference was that DCOWs without doubly-robust estimators performed slightly better than DCOWs with doubly-robust estimators, likely due to substantial misspecification of the outcome model.

5 Analysis of mechanical power data

We use the Medical Information Mart for Intensive Care III (MIMIC-III) database Johnson et al. (2016) to study the impact of a large degree of mechanical power of ventilation on mortality among critically ill patients in an ICU using electronic health record (EHR) data. Our study and the construction of the cohort from the MIMIC-III database is based the original study of Neto et al. (2018) and the code provided by the authors located at https://github.com/
Table 1: Mean absolute bias (MAB) and integrated root mean squared error (IRMSE) for the constant treatment effect setting.

| Method         | n = 100 | n = 200 | n = 400 | n = 800 | n = 1600 | n = 3200 |
|----------------|---------|---------|---------|---------|----------|----------|
| Unweighted     | 11.461  | 17.488  | 11.283  | 13.182  | 11.246   | 12.297   | 11.254  | 11.799  | 11.237  | 11.491  |
| GPS (normal)   | 10.145  | 27.180  | 15.033  | 29.187  | 10.112   | 13.978   | 10.084  | 12.693  | 10.006  | 11.162  |
| GPS (gamma)    | 9.340   | 23.994  | 9.892   | 19.269  | 9.993    | 15.831   | 10.122  | 13.781  | 10.104  | 11.182  |
| GPS (normal,DR)| 8.315   | 30.551  | 11.081  | 33.342  | 13.216   | 30.293   | 15.370  | 27.736  | 15.324  | 21.199  | 15.769  | 18.312  |
| GPS (gamma,DR) | 7.045   | 26.437  | 6.866   | 16.463  | 6.905    | 12.044   | 6.920   | 10.168  | 6.768   | 8.985   | 6.745   | 7.612   |
| CBPS           | 9.871   | 25.398  | 12.463  | 23.375  | 14.055   | 22.016   | 14.064  | 18.802  | 14.970  | 17.546  | 15.712  | 16.847  |
| GBM            | 8.190   | 24.328  | 7.551   | 17.298  | 7.105    | 12.498   | 7.379   | 10.432  | 7.524   | 9.225   | 7.746   | 8.589   |
| BART           | 6.550   | 17.206  | 7.275   | 14.423  | 8.023    | 12.326   | 8.638   | 11.292  | 9.033   | 10.659  | 9.446   | 10.366  |
| Entropy (1)    | ——      | ——      | 9.409   | 17.880  | 9.166    | 12.946   | 9.161   | 11.321  | 9.023   | 10.258  | 8.952   | 9.537   |
| Entropy (2)    | ——      | ——      | 8.909   | 25.080  | 9.343    | 15.520   | 8.927   | 12.360  | 8.503   | 10.456  | 8.231   | 9.245   |
| Entropy (2,int)| ——      | ——      | ——      | ——      | ——      | ——      | ——      | ——      | ——      | 8.998   | 253.786 | 10.974  | 16.780  |
| DCOW           | 4.684   | 12.294  | 3.866   | 8.383   | 3.495    | 6.245    | 3.522   | 4.947   | 2.992   | 4.075   | 2.750   | 3.416   |
| DCOW (dm)      | 4.522   | 16.465  | 3.907   | 8.988   | 3.544    | 6.364    | 3.376   | 5.018   | 3.001   | 4.147   | 2.775   | 3.497   |
| DCOW (DR)      | 3.904   | 9.284   | 3.335   | 6.455   | 2.663    | 4.586    | 2.196   | 3.388   | 1.919   | 2.661   | 1.753   | 2.189   |
| DCOW (dm,DR)   | 3.905   | 11.567  | 3.459   | 6.919   | 2.828    | 4.806    | 2.356   | 3.568   | 2.057   | 2.817   | 1.873   | 2.320   |

alistairewj/mechanical-power. As there are widely-used formal guidelines that influence the management of ventilation among patients with respiratory distress (Siegel et al., 2019; Papazian et al., 2019), there are many observable factors in EHR data that are highly related to the mechanical power of ventilation. Many of these are also closely related to patient mortality. The guidelines involve consideration both of factors individually and also of many interactions of these factors. In addition, as the exposure, the mechanical power of ventilation, is itself a complex summary of multiple manipulable elements of a ventilator, the guidelines are not directly related to the exposure, but have a strong indirect effect on the power of ventilation. Thus, the dependence between observable factors and the exposure level is highly complex; methods to control for confounding in this setting must be able to handle such complexity.

Patients included in the study were at least 16 years of age and received invasive mechanical ventilation for at least 48 hours. The study contains 5014 patients, and the treatment variable of interest is the amount of energy generated by the mechanical ventilator measured by the mean of the largest and smallest mechanical power of ventilation in Joules per minute in the
Table 2: Mean absolute bias (MAB) and integrated root mean squared error (IRMSE) for the heterogeneous treatment effect setting.

| Method                | $n = 100$   | MAB | IRMSE | $n = 200$   | MAB | IRMSE | $n = 400$   | MAB | IRMSE | $n = 800$   | MAB | IRMSE | $n = 1600$  | MAB | IRMSE | $n = 3200$  | MAB | IRMSE |
|-----------------------|-------------|-----|-------|-------------|-----|-------|-------------|-----|-------|-------------|-----|-------|-------------|-----|-------|-------------|-----|-------|
| Unweighted            | 20.075      | 28.198 | 19.865 | 24.382      | 23.999 | 34.649 | 26.269      | 33.482 | 27.298 | 31.335      | 27.982 | 29.873 |
| GPS (normal)          | 16.490      | 36.634 | 20.904 | 36.562      | 23.999 | 34.649 | 26.269      | 33.482 | 27.298 | 31.335      | 27.982 | 29.873 |
| GPS (gamma)           | 15.597      | 33.153 | 15.491 | 26.710      | 15.263 | 22.321 | 14.942      | 19.740 | 14.698 | 18.013      | 14.414 | 16.031 |
| GPS (normal,DR)       | 12.062      | 41.168 | 15.197 | 40.612      | 17.611 | 36.146 | 19.466      | 32.248 | 19.562 | 25.719      | 19.958 | 22.685 |
| GPS (gamma,DR)        | 12.021      | 38.538 | 11.194 | 25.270      | 10.856 | 18.518 | 10.553      | 15.730 | 10.341 | 14.197      | 10.235 | 11.970 |
| CBPS                  | 17.990      | 36.480 | 20.534 | 33.170      | 22.074 | 31.068 | 20.669      | 26.016 | 20.196 | 23.072      | 20.213 | 21.503 |
| GBM                   | 15.174      | 34.035 | 13.646 | 25.480      | 12.849 | 19.368 | 12.832      | 16.467 | 12.908 | 14.925      | 13.089 | 14.087 |
| BART                  | 13.372      | 26.339 | 13.141 | 21.772      | 13.753 | 18.902 | 14.286      | 17.460 | 14.712 | 16.654      | 15.118 | 16.245 |
| Entropy (1)           | ——          | ——    | 12.066 | 24.966      | 21.030 | 24.964 | 19.368      | 23.016 | 19.085 | 20.917      | 19.958 | 22.685 |
| Entropy (2)           | ——          | ——    | 15.737 | 36.405      | 15.872 | 24.570 | 14.401      | 19.456 | 13.181 | 16.191      | 12.242 | 13.928 |
| Entropy (2, int)      | ——          | ——    | ——     | ——          | ——     | 14.777 | 13.628      | 13.628 | 14.777 | 13.628      | 13.628 | 13.628 |
| DCOW                  | 6.718       | 18.517 | 6.083  | 13.254      | 5.818  | 10.552 | 5.569       | 8.852  | 5.400  | 7.703       | 5.329  | 6.830  |
| DCOW (dm)             | 7.999       | 27.130 | 6.366  | 14.836      | 5.943  | 11.074 | 5.699       | 9.226  | 5.536  | 8.038       | 5.500  | 7.129  |
| DCOW (DR)             | 5.778       | 16.726 | 5.220  | 12.206      | 4.891  | 9.780  | 4.735       | 8.311  | 4.829  | 7.422       | 5.055  | 6.753  |
| DCOW (dm,DR)          | 6.447       | 21.900 | 5.569  | 13.414      | 5.158  | 10.321 | 5.007       | 8.760  | 5.088  | 7.823       | 5.276  | 7.074  |

For all methods, balance statistics, including our developed criterion (8) and weighted correlations between first order moments and pairwise interactions of covariates and mechanical power, are summarized in Table 4. In terms of weighted marginal correlations, the version of...
Table 3: Mean absolute bias (MAB) and integrated root mean squared error (IRMSE) for the heterogeneous treatment effect setting with 50 noise variables added.

Our DCOWs that induces first order marginal correlations between covariates and mechanical power to be zero performs the best, with the standard DCOWs and entropy balancing weights a close second. In terms of our proposed criterion (8), by definition the DCOWs yield the smallest value. However it is notable that only a small price is paid in terms of both (8) and effective sample size (ESS) in order to additionally exactly decorrelate marginal covariate moments and treatment. Among methods that do not target independence, entropy balancing has the smallest value of (8), indicating that decorrelating first order moments in this particular dataset mitigates a vast majority of the dependence between covariates and mechanical power of ventilation. We also note that exactly decorrelating second order moments using entropy balancing results in additionally instability and thus overall worse mitigation of dependence. However, exact decorrelation of marginal results in much larger standard errors of the resulting ADRF, as evidenced in Figure 2. Interestingly, both in terms of marginal weighted correlations and in terms of our proposed independence metric, the flexible machine learning approaches (GBM and BART) perform significantly worse than a simple normal model for the conditional density.
|                | Unweighted | GPS (normal) | GPS (gamma) | CBPS | GBM | BART | Entropy (1) | Entropy (2) | DCOW (dm) |
|----------------|------------|--------------|-------------|------|-----|------|-------------|-------------|-----------|
| (8)            | 21.0406    | 2.5735       | 4.2687      | 4.7127 | 12.9924 | 6.1664 | 1.0927      | 4.2621      | 0.2201    |
| $D(w)$         | 21.0406    | 2.3492       | 4.0143      | 4.3284 | 12.9604 | 5.7097 | 1.0052      | 4.0832      | 0.1436    |
| $\mathcal{E}(F_{a,w}, F_{a})$ | 0.0000     | 0.0266       | 0.0031      | 0.0099 | 0.0030 | 0.0426 | 0.0296      | 0.0006      | 0.0508    |
| $\mathcal{E}(F_{x,w}, F_{x})$ | 0.0000     | 0.1976       | 0.2513      | 0.3743 | 0.0290 | 0.4141 | 0.0579      | 0.1783      | 0.0258    |
| ESS            | 4933       | 2048         | 1832        | 1017  | 3892 | 782   | 2185        | 478         | 2232      |
| mean(|Corr|)    | 0.0697     | 0.0142       | 0.0365      | 0.0246 | 0.0577 | 0.0452 | 0.0067      | 0.0208      | 0.0067    |
| sd(|Corr|)     | 0.0821     | 0.0151       | 0.0363      | 0.0249 | 0.0609 | 0.0434 | 0.0075      | 0.0219      | 0.0064    |
| median(|Corr|) | 0.0405     | 0.0096       | 0.0260      | 0.0178 | 0.0361 | 0.0352 | 0.0046      | 0.0159      | 0.0051    |
| 95-pctl(|Corr|) | 0.2482     | 0.0439       | 0.1048      | 0.0633 | 0.2000 | 0.1177 | 0.0200      | 0.0547      | 0.0184    |
| max(|Corr|)    | 0.7877     | 0.2003       | 0.8536      | 0.4702 | 0.5682 | 0.9388 | 0.1225      | 0.5066      | 0.0839    |

Table 4: Summary statistics (mean, standard deviation, median, 95th percentile, and maximum) of the absolute weighted correlations of the first five powers of mechanical power of ventilation and all marginal moments of covariates, pairwise interactions of covariates, and up to 5th order polynomials of covariates. Summaries are over $8284 \times 5$ weighted correlations of covariate moments and mechanical power moments.

For a concrete example of how DCOWs mitigate dependence, we illustrate the unadjusted marginal dependence of the PaO$_2$/FiO$_2$ ratio and the mechanical power of ventilation. PaO$_2$/FiO$_2$ ratio is a pre-treatment covariate that characterizes acute hypoxemia, defines presence and severity of acute respiratory distress syndrome (ADRS), and plays a critical role in ventilation guidelines (Papazian et al., 2019). The PaO$_2$/FiO$_2$ ratio is also strongly associated with mortality and is thus a critical confounder in this study. We display weighted marginal dependence of the PaO$_2$/FiO$_2$ ratio and the mechanical power of ventilation with our proposed weights and with the entropy-balancing weights in Figure 1. Compared with methods that aim to exactly decorrelate specified moments, our proposed weights are able to handle nonlinear dependence between covariates and treatment even in datasets with moderately high dimension. While entropy balancing accounts for a significant proportion of dependence, there remains residual nonlinear dependence.
Figure 1: Shown are plots of the relationship between the minimum PaO$_2$/FiO$_2$ ratio on day 1 in the ICU (on a log base 10 scale) and the treatment, including an unadjusted plot (left) and plots adjusted by DCOWs and entropy balancing weights (right two plots). In the adjusted plots, the transparency of each point is proportional to its assigned weight, with lighter points indicating less weight. The blue line is a weighted nonparametric regression of the treatment on PaO$_2$/FiO$_2$ (on the log base 10 scale) and the red line is a weighted linear regression.

For each method, we construct pointwise confidence bands of the ADRF using a nonparametric bootstrap similar to Wang and Wahba (1995). Weighted local linear regression estimates of the ADRF of mechanical power of ventilation on in hospital mortality and 95% confidence bands are displayed in Figure 2. The entropy balancing approach with higher order moments was not included due to the small effective sample size and that large number of bootstrap replications for which no numerical solution was found. While both the entropy balancing weights and the GPS estimated with a normal model exhibit reasonable control over dependence between covariates and treatment, they result in unacceptably high variance in the estimate of the ADRF.
Figure 2: Shown are weighted local linear regression estimates of the ADRF of mechanical power on the probability of in hospital mortality and pointwise 95% confidence bands estimated via a nonparametric bootstrap. 38 replications of the bootstrap resulted in no numerical solution for entropy balancing weights and are left out of the confidence interval calculation.
6 Discussion

In this paper we provide a detailed inspection of the role of weights in weighted nonparametric estimates of causal quantities involving continuous-valued exposures from observational data. This inspection shows clearly that the key source of bias depends on the degree to which the weights induce independence between the treatment and confounders. We then provide a measure that characterizes how well a set of weights mitigates the dependence between the treatment and confounders. This measure does not require any tuning parameters, making it straightforward to deploy in practice. Given some light smoothness conditions on the outcome data-generating model, this measure acts as an upper bound on the key source of systematic bias in a weighted nonparametric estimate of the ADRF. Our proposed weights, the DCOWS, which minimize our measure of dependence, provide an empirically robust means for estimating weights, as they directly target independence between the treatment and confounders. These weights are a natural complement to doubly-robust estimators, as they provide an anchor for the doubly-robust estimator: since they are guaranteed to be consistent on their own, the consistency of the doubly-robust estimator does not critically depend on the correctness of the outcome model. Thus, the outcome model can be safely used as a tool by which to reduce variability in the estimate of the ADRF.

Appendix

A Properties of stabilized generalized propensity score weights

The stabilized GPS weights $f_A(A)/f_{A|X}(A \mid X)$ have several key properties. Namely, when weighting by these weights they 1) result in independence of $A$ and $X$, 2) preserve the marginal distributions of $X$ and $A$, and 3) have mean 1. For the following, we let $g(X)$ be any function of $X$ only and let $h(A)$ be any function of $A$ only. It can be straightforwardly shown that

$$\mathbb{E}_{X,A} \left( g(X)h(A) \frac{f_A(A)}{f_{A|X}(A \mid X)} \right) = \mathbb{E}_X(g(X))\mathbb{E}_A(h(A)),$$

$$\mathbb{E}_{X,A} \left( g(X) \frac{f_A(A)}{f_{A|X}(A \mid X)} \right) = \mathbb{E}_X(g(X)),$$

and

$$\mathbb{E}_{X,A} \left( h(A) \frac{f_A(A)}{f_{A|X}(A \mid X)} \right) = \mathbb{E}_A(h(A)).$$
The first equality shows that when weighting by \( \frac{f_A(a)}{f_A(X|A)X} \), \( A \) and \( X \) are independent, as the above holds for any \( g \) and \( h \). Further, the second two equalities show that, on the weighted scale, the marginal distributions of \( X \) and \( A \) are preserved. Finally, the weights have mean 1, i.e. \( E_{X,A} \left( \frac{f_A(a)}{f_A(X|A)X} \right) = 1. \)

\[ \text{B Regularity conditions} \]

For \( (X_1, A_1), \ldots, (X_6, A_6) \overset{i.i.d.}{\sim} F_{X,A} \), define

\[ k((X_1, A_1), \ldots, (X_6, A_6)) = w(X_1, A_1)g_X(X_1, X_2, X_3)g_A(A_1, A_2, A_5, A_6)w(X_2, A_2) \]

with \( w(x, a) = \frac{f_A(a)}{f_A(X|a)X} \),

\[ g_X(X_1, X_2, X_3, X_4) = \|X_1 - X_2\|_2 - \|X_1 - X_3\|_2 - \|X_2 - X_4\|_2 + \|X_3 - X_4\|_2 \]

and

\[ g_A(A_1, A_2, A_3, A_4) = |A_1 - A_2| - |A_1 - A_3| - |A_2 - A_4| + |A_3 - A_4|. \]

Further define

\[ k_X((X_1, A_1), \ldots, (X_4, A_4)) = w(X_1, A_1)\|X_1 - X_3\|_2 + w(X_2, A_2)\|X_2 - X_4\|_2 \]

\[ - w(X_1, A_1)w(X_2, A_2)\|X_1 - X_2\|_2 - \|X_3 - X_4\|_2 \]

and

\[ k_A((X_1, A_1), \ldots, (X_4, A_4)) = w(X_1, A_1)|A_1 - A_3| + w(X_2, A_2)|A_2 - A_4| \]

\[ - w(X_1, A_1)w(X_2, A_2)|A_1 - A_2| - |A_3 - A_4|. \]

The following assumptions are required for several Lemmas and Theorems presented. These conditions amount to finite moment conditions on squares of the Euclidean norms of \( X, A \) and their products with the weights \( w(X, A) \).

(A1) \( \mathbb{E}[k^2((X_1, A_1), \ldots, (X_6, A_6))] < \infty \)

(A2) \( \mathbb{E}[k_X^2((X_1, A_1), \ldots, (X_4, A_4))] < \infty \) and \( \mathbb{E}[k_A^2((X_1, A_1), \ldots, (X_4, A_4))] < \infty \)

References

Andersen, M., Dahl, J., Liu, Z., Vandenberghe, L., Sra, S., Nowozin, S. and Wright, S. (2011), ‘Interior-point methods for large-scale cone programming’, *Optimization for Machine Learning* 5583.
Chattopadhyay, A., Hase, C. H. and Zubizarreta, J. R. (2020), ‘Balancing vs modeling approaches to weighting in practice’, *Statistics in Medicine* **39**(24), 3227–3254.

Colangelo, K. and Lee, Y.-Y. (2020), ‘Double debiased machine learning nonparametric inference with continuous treatments’, *arXiv preprint arXiv:2004.03036*.

Crump, R. K., Hotz, V. J., Imbens, G. W. and Mitnik, O. A. (2009), ‘Dealing with limited overlap in estimation of average treatment effects’, *Biometrika* **96**(1), 187–199.

Dawid, A. P. (1979), ‘Some misleading arguments involving conditional independence’, *Journal of the Royal Statistical Society: Series B (Methodological)* **41**(2), 249–252.

Díaz, I. and van der Laan, M. J. (2013), ‘Targeted data adaptive estimation of the causal dose–response curve’, *Journal of Causal Inference* **1**(2), 171–192.

Fong, C., Hazlett, C. and Imai, K. (2018), ‘Covariate balancing propensity score for a continuous treatment: Application to the efficacy of political advertisements’, *The Annals of Applied Statistics* **12**(1), 156–177.

Galvao, A. F. and Wang, L. (2015), ‘Uniformly semiparametric efficient estimation of treatment effects with a continuous treatment’, *Journal of the American Statistical Association* **110**(512), 1528–1542.

Hill, J. L. (2011), ‘Bayesian nonparametric modeling for causal inference’, *Journal of Computational and Graphical Statistics* **20**(1), 217–240.

Hirano, K. and Imbens, G. W. (2004), *The Propensity Score with Continuous Treatments*, John Wiley & Sons, Ltd, chapter 7, pp. 73–84.

Huling, J. D. and Mak, S. (2020), ‘Energy balancing of covariate distributions’, *arXiv preprint arXiv:2004.13962*.

Imai, K. and Van Dyk, D. A. (2004), ‘Causal inference with general treatment regimes: Generalizing the propensity score’, *Journal of the American Statistical Association* **99**(467), 854–866.

Imbens, G. W. (2004), ‘Nonparametric estimation of average treatment effects under exogeneity: A review’, *Review of Economics and Statistics* **86**(1), 4–29.

Johnson, A. E., Pollard, T. J., Shen, L., Li-Wei, H. L., Feng, M., Ghassemi, M., Moody, B., Szolovits, P., Celi, L. A. and Mark, R. G. (2016), ‘Mimic-iii, a freely accessible critical care database’, *Scientific data* **3**(1), 1–9.

Johnson, E., Dominici, F., Griswold, M. and L. Zeger, S. (2003), ‘Disease cases and their medical costs attributable to smoking: an analysis of the national medical expenditure survey’, *Journal of Econometrics* **112**(1), 135–151.

Kallus, N. and Santacatterina, M. (2019), ‘Kernel optimal orthogonality weighting: A balancing approach to estimating effects of continuous treatments’, *arXiv preprint arXiv:1910.11972*.

Kang, J. D. and Schafer, J. L. (2007), ‘Demystifying double robustness: A comparison of alternative strategies for estimating a population mean from incomplete data’, *Statistical Science* **22**(4), 523–539.

Kennedy, E. H., Ma, Z., McHugh, M. D. and Small, D. S. (2017), ‘Non-parametric methods for doubly robust estimation of continuous treatment effects’, *Journal of the Royal Statistical Society: Series B (Statistical Methodology)* **79**(4), 1229–1245.
Kish, L. (1965), *Survey sampling*, Vol. 26, John Wiley & Sons.

Mak, S. and Joseph, V. R. (2018), ‘Support points’, *The Annals of Statistics* 46(6A), 2562–2592.

Martinet, G. (2020), ‘A balancing weight framework for estimating the causal effect of general treatments’, *arXiv preprint arXiv:2002.11276*.

Naimi, A. I., Moodie, E. E., Auger, N. and Kaufman, J. S. (2014), ‘Constructing inverse probability weights for continuous exposures: a comparison of methods’, *Epidemiology* pp. 292–299.

Neto, A. S., Deliberato, R. O., Johnson, A. E., Bos, L. D., Amorim, P., Pereira, S. M., Cazati, D. C., Cordioli, R. L., Correa, T. D., Pollard, T. J. et al. (2018), ‘Mechanical power of ventilation is associated with mortality in critically ill patients: an analysis of patients in two observational cohorts’, *Intensive Care Medicine* 44(11), 1914–1922.

Papazian, L., Aubron, C., Brochard, L., Chiche, J.-D., Combes, A., Dreyfuss, D., Forel, J.-M., Guérin, C., Jaber, S., Mekontso-Dessap, A. et al. (2019), ‘Formal guidelines: management of acute respiratory distress syndrome’, *Annals of Intensive Care* 9(1), 1–18.

Robins, J. M., Hernan, M. A. and Brumback, B. (2000), ‘Marginal structural models and causal inference in epidemiology’, *Epidemiology* 11, 550–560.

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

Siegel, M. D., Hyzy, R. C. et al. (2019), ‘Ventilator management strategies for adults with acute respiratory distress syndrome’.

Stellato, B., Banjac, G., Goulart, P., Bemporad, A. and Boyd, S. (2020), ‘Osqp: An operator splitting solver for quadratic programs’, *Mathematical Programming Computation* pp. 1–36.

Székely, G. J. and Rizzo, M. L. (2013), ‘Energy statistics: A class of statistics based on distances’, *Journal of Statistical Planning and Inference* 143(8), 1249–1272.

Székely, G. J., Rizzo, M. L. and Bakirov, N. K. (2007), ‘Measuring and testing dependence by correlation of distances’, *The Annals of Statistics* 35(6), 2769–2794.

Tübbicke, S. (2020), ‘Entropy balancing for continuous treatments’, *arXiv preprint arXiv:2001.06281*.

van der Laan, M. J. and Robins, J. M. (2003), *Unified methods for censored longitudinal data and causality*, Springer Science & Business Media.

Vegetabile, B. G., Griffin, B. A., Coffman, D. L., Robbins, M. W., Cefalu, M. and McCaffrey, D. F. (2021), ‘Nonparametric estimation of population average dose-response curves using entropy balancing weights for continuous exposures’, *Health Services and Outcomes Research Methodology* 21(1), 69–110.

Wang, Y. and Wahba, G. (1995), ‘Bootstrap confidence intervals for smoothing splines and their comparison to bayesian confidence intervals’, *Journal of Statistical Computation and Simulation* 51(2-4), 263–279.

Yiu, S. and Su, L. (2018), ‘Covariate association eliminating weights: a unified weighting framework for causal effect estimation’, *Biometrika* 105(3), 709–722.
Zhu, Y., Coffman, D. L. and Ghosh, D. (2015), ‘A boosting algorithm for estimating generalized propensity scores with continuous treatments’, *Journal of Causal Inference* 3(1), 25–40.

Zubizarreta, J. R. (2015), ‘Stable weights that balance covariates for estimation with incomplete outcome data’, *Journal of the American Statistical Association* 110(511), 910–922.