Incremental causal effects

Dominik Rothenhäusler and Bin Yu

1Department of Statistics
2Department of Electrical Engineering and Computer Sciences
University of California, Berkeley

August 1, 2019

Abstract

This is a draft. The ignorability assumption is a key assumption in causal inference. It is commonly made, but often violated in observational studies. In this paper, we investigate a local version of this assumption for continuous treatments, where potential outcomes are independent of the treatment assignment only in a neighborhood of the current treatment assignment. Similarly, we introduce a local version of the overlap condition, where the positivity assumption only holds in a neighborhood of observations. Under these local assumptions, we show that the effect of shifting a continuous treatment variable by a small amount across the whole population (termed incremental treatment effect) is still identifiable, and that the incremental treatment effect is equal to the average derivative or average partial effect. Moreover, we prove that in certain regression settings, estimating the incremental effect is easier than estimating the average treatment effect in terms of asymptotic variance and more robust to additive confounding. For high-dimensional settings, we develop a simple feature transformation that allows for doubly-robust estimation and doubly-robust inference of incremental causal effects. Finally, we compare the behaviour of estimators of the incremental treatment effect and average treatment effect on simulated data.

1 Introduction

The estimation of treatment effects has a long history in many disciplines and is of central interest in many scientific endeavours. Often, data from a randomized experiment is not available and one has to resort to observational data. In this case, practitioners usually mitigate the problem using regression adjustment, matching, inverse probability weighting or instrumental variables regression.

The overall goal in causal inference is to estimate the effect of intervening on a treatment $T$ on an outcome $Y$. Average treatment effect and conditional average treatment effect are often the quantities of interest in causal inference, where a treatment variable $T$ is set to the same level across a certain population. In the Neyman-Rubin model, if $Y(t)$ denotes the potential outcome of a unit with continuous treatment assignment $t$ (Rubin, 1974; Splawa-Neyman et al., 1990), this can be expressed as
where the expectation is taken over a subpopulation or superpopulation of units. However, there also exist other notions of interventions. For continuous treatment one may want to estimate the effect of shifting a pre-interventional (potentially random) assignment $T$ by an infinitesimal amount across a certain population. Mathematically, this can be expressed as

$$\frac{\mathbb{E}[Y(T + \delta)] - \mathbb{E}[Y(T)\delta]}\delta$$

for deterministic $\delta > 0$ close to zero, (1)

where the expectation is taken over a subpopulation or superpopulation of units.

This notion of intervention is much less used in parts of the causal inference community. In the econometrics literature, under weak ignorability, incremental treatment effects are often identified via $\mathbb{E}[\partial_t \mathbb{E}[Y|X, T]]$ for some covariates $X$, which is sometimes called average marginal effect or average partial effect (Powell et al., 1989; Cameron and Trivedi, 2005; Wooldridge, 2005). To differentiate the causal estimand from the particular identification strategy, in analogy to Kennedy (2018) we will call the estimand in equation (1) an incremental treatment effect.

Practitioners have to decide how to specifically formulate a domain question and which notion of intervention to employ to answer the domain question. Of course, these notions correspond to different domain questions, and the domain question is one of the most important factors for the choice of intervention notion. We would argue that issues of identification, robustness to confounding and difficulty of the estimation task (asymptotic error) should also play important roles in the choice of intervention notion.

As mentioned previously, treatment effects are often estimated under the assumptions of weak ignorability and the overlap condition. However, these assumptions can be unrealistic or hard to justify if the data is observational. We introduce a local ignorability assumption and a local overlap condition, which are weaker than their more general counterparts. Roughly speaking, the local ignorability assumption states that potential outcomes are independent of the current treatment assignment in a neighborhood of observations. It will turn out that incremental treatment effects are identifiable under these assumptions, while average treatment effects are not. To the best of our knowledge, tailor-made assumptions to identify incremental treatment effects have not been defined previously.

In situations where the practitioner suspects some latent confounding, it would be sensible to employ a notion which is the least sensitive to confounding, if possible. We will see that incremental effects are often more robust under worst-case confounding than average treatment effects if the weak ignorability assumption is slightly violated.

If the signal-to-noise ratio is very low, then estimation of average treatment effects might be highly variable and thus uninformative. We will discuss situations in which incremental treatment effects can be estimated with lower asymptotic error than average treatment effects. This includes situations where the signal to noise ratio is low. Thus, estimating incremental treatment effects is potentially more informative than estimating average treatment effects.
Causal inference from observational data is known to be challenging and prone to mistakes (Rosenbaum, 2002), with sometimes devastating effects for human lives. Revisiting the conceptual foundations of the field may help us develop notions of interventions that can be estimated more reliably and are thus more informative in practice. In this work, we investigate advantages and disadvantages of incremental treatment effects compared to average treatment effects under the ignorability assumption and overlap condition. We hope that our work aids practical decisions on choice of intervention notions to answer a specific domain question.

1.1 Related work

For discrete treatments, Kennedy (2018) defines incremental propensity score interventions by multiplying the odds of receiving treatment. The author shows that the overlap assumption is not necessary to identify incremental propensity score interventions and develops an efficiency theory with corresponding nonparametric estimators.

Asymptotic equivalence of several estimators of the average partial effect in parametric settings has been shown in Stoker (1991). To the best of our knowledge, semiparametric estimation of average derivatives has first been discussed in Powell et al. (1989). More recently, Chernozhukov et al. (2013) and Hirshberg and Wager (2017) derived semiparametrically efficient estimators of linear functionals of the conditional expectation function. In Hirshberg and Wager (2017), this is achieved under Donsker assumptions, while Chernozhukov et al. (2018) employ a sparsity assumption on either the approximation of the Riesz representer or the approximation to the regression function.

When there exists a binary instrumental variable with non-compliance, average treatment effects are usually not identifiable. In Angrist et al. (1996), the authors show that under a monotonicity assumption, interventions on the subgroup of compliers, the so-called local average treatment effect is still identifiable. In fact, estimating the effect of this "weaker" notion of intervention in cases where the average treatment effect is not identifiable is increasingly popular in certain parts of the causal inference community (Imbens, 2010).

In models based on structure equations, incremental interventions can be seen as a special case of “parametric” or “imperfect” interventions (Eberhardt and Scheines, 2007; Korb et al., 2004; Tian and Pearl, 2001). Korb et al. (2004) argue that naively estimating (deterministic) causal effects using Bayesian networks can be misleading and discuss different types of indeterministic interventions. In the context of structure learning, Eberhardt and Scheines (2007) have shown that causal systems of \( N \) variables can be identifiable using one parametric intervention. Tian and Pearl (2001) do structure learning based on local mechanism changes, which are a more general notion of intervention than incremental effects.

1.2 Our contribution

We show that the effect of incremental interventions is identifiable under a local ignorability assumption and a local overlap condition, which can be seen as relaxed versions of their more general counterparts.
In parametric and semi-parametric settings, if the distribution of the treatment variable given the covariates is Gaussian, we show that incremental subpopulation causal effects can be estimated efficiently with usually lower asymptotic error than average treatment effects. Furthermore, we show that the estimation of incremental causal effect in a regression setting in the population case is usually less sensitive to additive unobserved confounding compared to the estimation of average treatment effects.

We propose a feature transformation “incremental effect orthogonalization” that facilitates estimation and inference of high-dimensional incremental causal effects. Our method is based on a feature transformation in the first step and running a de-sparsified lasso on the transformed data. The de-sparsifying technique is similar to the ones developed for high-dimensional linear regression (Zhang and Zhang, 2014; Javanmard and Montanari, 2014; Van de Geer et al., 2014; Belloni et al., 2014) but due to the randomness in treatment assignment the asymptotic variance formula differs from existing approaches for inference in high-dimensional regression models. We modify a robust version of the de-sparsifying approach which was introduced in Bühlmann and van de Geer (2015). Our novel technique has a double-robustness property, in the sense that if one of two models is well-specified, we obtain asymptotically valid estimation and inference. The main advantage compared to existing approaches for the estimation of incremental treatment effects is that after a simple feature transformation, off-the-shelf software for estimation in high-dimensional linear models can be used.

To substantiate the claims of our theoretical results, we compare the behaviour of estimators of the incremental treatment effect and average treatment effect on simulated data. We also cover simulations settings where the assumptions of some of our theoretical results are violated and discover that the conclusions are fairly robust.

The rest of the paper is organized as follows. In Section 2 we introduce the model class. In Section 3 we discuss identification of the incremental treatment effect under a local ignorability and local overlap condition. In Section 4 we discuss models in which estimating incremental treatment effects is more robust under confounding and can be done with lower asymptotic error than estimating average treatment effects. Furthermore, we introduce a feature transformation that facilitates computing doubly robust estimation and inference in high-dimensional settings. Finally, in Section 5 we validate our theoretical results on simulated data.

2 Motivation and setup

We are interested in the causal effect of a continuous treatment variable $T$ on an outcome $Y$ in the presence of some covariates $X \in \mathbb{R}^d$. We use the Neyman-Rubin potential outcome framework (Rubin, 1974; Splawa-Neyman et al., 1990) and assume a super population or distribution $P$ of $(Y(t), T, X)$ from which $N$ independent draws $(Y_i(t), T_i, X_i)$ are given, where $Y_i(t)$ is the potential outcome of $Y$ under treatment $T = t$. Without any assumptions or adjustment, an observed association between $T$ and $Y$ might simply be due to some confounding variable that affects both the treatment and the outcome. A commonly made assumption in such a setting is weak ignorability (Rosenbaum and Rubin, 2005).
which states that the treatment assignment is independent of the outcome, conditional on some covariates $X$. Formally, this assumption is often written as

$$\{Y(t), t \in \mathbb{R}\} \perp T | X,$$  \hspace{1cm} (2)

where $Y(t)$ is defined as the potential outcome of $Y$ under treatment $T = t$. In addition, it is common to assume that the overlap condition holds, which can be written as

$$p(t|x) > 0 \text{ for all } t, x,$$ \hspace{1cm} (3)

where $p(t|x)$ is the conditional density of $T$ given $X$ and $p(x)$ is the density of $X$. If both weak ignorability and the overlap condition holds, the average treatment effect $E[Y(t)] - E[Y(t')]$ for some choice of $t, t' \in \mathbb{R}$ can be estimated via regression, matching, inverse probability weighting or combinations of these methods, see for example [Rosenbaum, 2002]. In particular,

$$E[Y(t)] - E[Y(t')] = E[E[Y|X, T = t]] - E[E[Y|X, T = t']],$$

where the outer expectation is taken over the distribution of $X$. In practice there are cases where the assumption in equation (2) might be unrealistic. For example, if $T$ describes the dose of a medication, the patients receiving high doses of the medication may be a completely different population than the patients receiving low doses of the medication, even conditional on the covariates $X$. If $X = \text{"severity of symptoms"}$ and there is a patient that has severe symptoms and receives a very low dose, this might be due to the doctor making an exceptional decision due to an exceptional circumstance that is not encoded in the data set. This exceptional circumstance might also affect the outcome. It could also be that the patient willingly decides to take only a lower dose than usual. Consequently, this patient may make other decisions that affect $Y(t)$ that are not encoded in $X$. These and similar effects are usually modelled as confounding. Many methods have been developed to deal with the problem of confounding in observational studies, most notably the instrumental variables approach and the regression discontinuity design [Wright, 1928; Thistlethwaite and Campbell, 1960; Lee and Lemieux, 2010; Imbens and Rubin, 2015]. However, these methods have assumptions that are often unrealistic or hard to justify in practice.

In the following we will show that incremental causal effects are identifiable in scenarios where the ignorability assumptions holds locally in subgroups of patients with similar treatments but not necessarily across all patients. Average treatment effects are not identifiable in this setting.

Throughout the paper we assume that Stable Unit Treatment Value Assumption [Rubin, 1980; Hernan and Robins, 2010] holds, which says that the potential outcomes are well-defined and that there is no interference between units, i.e. that the potential outcome of one individual is only a function of the treatment assignment to this individual and not of the others. Formally, this assumption can be expressed as $Y_i(T) = Y_i(T_i)$ for $T = (T_1, \ldots, T_n)$. Strictly speaking, this assumption is not necessary for the formulation of our identification results as they are stated as the expected effect of one intervention on one individual sampled from a population. However, in practice we are interested in the effect of interventions on groups of individuals. Hence, to be able to interpret our results in this fashion, a no-interference assumption is necessary.
2.1 Local ignorability

From the ignorability assumption, by conditioning on $T$, the following condition follows immediately. Ignoring measure-theoretic special cases where the condition below is not well-defined, it is practically equivalent to the ignorability assumption.

**Assumption 1** (Ignorability assumption, reformulated). Assume that

\[ Y(t)|X = x, T = t_1 \overset{d}{=} Y(t)|X = x, T = t_2 \text{ for all } t, t_1, t_2. \]

Thus, one way to think about the ignorability assumption is that, conditionally on $X = x$, the distribution of the potential outcomes is the same across patients with different treatment assignments. In the following, to deal with certain violations of equation (2) as discussed in the previous chapter, we will define a local version of this assumption.

**Assumption 2** (Local ignorability). Assume that

\[ Y(t + \delta)|X = x, T = t \overset{d}{=} Y(t + \delta)|X = x, T = t + \delta' \]  \hspace{1cm} (4)

for all $|\delta| \leq \delta_0$, $|\delta'| \leq \delta_0$, where $\delta_0 > 0$ can depend on $x$ and $t$.

Roughly speaking, we assume that patients are “comparable” (i.e. have the same potential outcome in distribution), if they have a treatment assignment that is sufficiently similar. In other words, we assume that treatment assignments are randomized locally but not necessarily globally. This can happen, for example, if a doctor has discrete groups of patients that he treats differently. Then the treatment assignment might be random between patients with similar treatments, but not between patients with very different treatments. Even if the group assignment is not observed (unobserved confounder), the incremental causal effect can be identifiable, as we will see below. Thus, the local ignorability assumption allows for some unobserved heterogeneity.

2.2 Local overlap

Now let us turn to weakening the overlap condition. In practice the overlap condition is often not satisfied. In the example discussed above, ethical considerations, among others, might prevent doctors to give a very low dose to patients with severe symptoms and a very high dose to patients with minor symptoms. If $X =$ “severity of symptoms”, then by conditioning on a large value $X = x$ we will have only very few patients with low doses, or no patients at all. This makes it exceedingly difficult to estimate the effect of giving a low dose to this group of patients. In finite samples, estimation of the average treatment effects is difficult if there exists regions where assignment variables $t$ has low density and the other treatment assignment $t'$ has high density. This issue can be exacerbated if the covariate vector $X$ is high-dimensional \cite{d'amour2017}. Roughly speaking, due to the curse of dimensionality, in high-dimensions there will often be regions where one of the treatments has low density. A similar problem appears in practice when trying to match subjects on many covariates. The more covariates we have, the harder it is to find pairs of subjects that are similar in all covariates.
High-dimensional covariates are potentially also challenging for the estimation of incremental interventions. However, compared to the problem of estimating average treatment effects, we can relax the overlap condition. In the following we assume that the density $p(t,x)$ is well-defined.

**Assumption 3 (Local overlap). Assume that $p(t,x)$ is continuous.**

Roughly speaking, we assume that if there is a patient with severity $X = x$ that gets treatment $T = t$ then the probability of another patient with the slightly different severity and treatment is nonzero.

### 2.2.1 Regularity assumption

We have to make some assumptions that guarantee that the conditional expectations mentioned in this paper are well-defined. In practice, these assumptions can be thought of as putting a smoothness condition on the potential outcomes.

**Assumption 4 (Regularity). Assume that the potential outcomes $Y(t)$ are bounded and that the derivative $Y'(t) := \partial_t Y(t)$ is continuous and bounded.**

This assumption can be slightly relaxed. Instead of asking for smoothness of the potential outcomes, we could assume a smoothness condition for the regression surface $E[Y|X = x, T = t]$. We will work with the regularity condition as defined above for reasons of simplicity.

### 3 Identification of incremental causal effects

Note that if we only have the local ignorability assumption or the local overlap condition, it is generally not possible to consistently estimate (identify) the average treatment effect

$$E[Y(t)] - E[Y(t')]$$

for some $t, t' \in \mathbb{R}$.

However, we will now show that the effect of shifting $t$ by a small amount around the current treatment can still be identifiable. In the following, we make the assumption that $Y(t)$ is bounded and continuously differentiable in $t$ with bounded derivative, c.f. Assumption 4. Together with the local ignorability assumption and the local overlap condition, it implies that $E[Y|X = x, T = t]$ is well-defined and differentiable in $t$ for all $(x,t)$ with $p(x,t) > 0$. The proof of the following result can be found in the Appendix, Section 8.2.

**Proposition 1.** If the local ignorability assumption, the local overlap condition and the regularity assumption are satisfied, then for all $(x,t)$ with $p(x,t) > 0$,

$$E[Y'(t)|X = x, T = t] = \partial_t E[Y|X = x, T = t].$$

The assumption that $Y(t)$ is bounded and differentiable with bounded derivative is made for expositional clarity and can be weakened slightly.

In the following we have to differentiate between the incremental effect for the superpopulation and the incremental effect for the subpopulation or sample. In the latter case, all statements are conditional on the units that we observe. More information for the difference between population causal effects and finite
sample causal effects can be found in \cite{imbens2015causal}, Section 1. More specifically, we will investigate estimation and inference for the expected effect of an infinitesimal shift intervention for a subpopulation or finite sample \((y_i, t_i, x_i), i = 1, \ldots, n\),

\[
\theta_{fs} := \frac{1}{n} \sum_{i=1}^{n} \mathbb{E}[Y'(t_i)|X = x_i, T = t_i],
\]

(5)

where the expectation is taken with respect to the potential outcomes \(Y\) given \(X = x\) and \(T = t\). In words, \(\theta_{fs}\) corresponds to the expected effect of an incremental intervention conditionally on \((t_i, x_i)_{i=1,\ldots,n}\). We condition on the \((t_i)_{i=1,\ldots,n}\) as we aim to estimate the effect of shifting the current treatment assignments \((t_i)_{i=1,\ldots,n}\). Note that we do not condition on \((y_i)_{i=1,\ldots,n}\) as is sometimes done in the causal inference literature for binary treatments \cite{imbens2015causal}. Conditioning on the \(y_i\), in addition to conditioning on the \(t_i\) and \(x_i\) would result in a deterministic sample and is thus not practical.

For \(n \to \infty\), under some regularity conditions, \(\theta_{fs}\) will converge to the superpopulation effect,

\[
\theta_{sp} := \mathbb{E}[Y'(T)].
\]

(6)

Here, the expectation is taken over \(T, X, Y\). In words, \(\theta_{sp}\) corresponds to the expected effect of an incremental intervention on the superpopulation. We want to emphasize that the interpretation of these causal effects is different from the most common notion of interventions, so-called average treatment effects, surgical interventions or do-interventions. The population effect answers the question: "How will the average outcome change if we change the treatment of all patients by a small amount, i.e. use treatment assignment \(T' = T + \delta\) across all patients" for some \(\delta\) close to zero. Note that the quantities of interest are in general also different from

\[
\mathbb{E}[Y'(t)],
\]

which corresponds to first setting the value of \(T\) to \(t\) across the whole population and than varying that intervention by a small amount. In the next section we will discuss general properties of estimation and inference of the effect in equation (5) and equation (6).

4 Estimating incremental effects in regression settings

In this section we discuss various aspects of estimation and inference for incremental causal effects. In Section 4.1 we discuss settings for which the error of efficiently estimating the effect of shift interventions is lower than the error of efficiently estimating average treatment effects. In Section 4.2 we show that estimation of incremental interventions is often less sensitive to confounding than estimation of average treatment effects. In Section 4.3 we discuss a feature transformation that facilitates obtaining confidence statements in high-dimensional scenarios. The main advantage compared to existing approaches \cite{powell1989regression, hirshberg2017estimation, chernozhukov2018high} is that after a simple feature transformation, off-the-shelf software for estimation and inference in high-dimensional linear models can be used.
4.1 Variance comparison

We have made the empirical observation (c.f. Section 5) that in both low- and high-dimensional settings the squared error of estimating the sample average treatment effect is often larger than the squared error of estimating the sample effect of incremental interventions for comparable estimators. In this section, using a toy model, we will provide some theoretical justification for this effect.

We assume that we observe i.i.d. observations $(x_i, t_i, y_i)$ of distribution $P$ that follow the additive noise model

$$Y = f^0(T, X) + \epsilon,$$

where $\epsilon$ is independent of $T$ and $X$, $E[\epsilon] = 0$ and $\text{Var}(\epsilon) = \sigma^2$. We assume that $f^0$ is differentiable in $t$, i.e. we make a smoothness assumption on how the treatment affects the outcome. As an example, $y$ could be the math score of a student in a test, $t$ the study time after class and $x$ pre-treatment covariates such as age and gender. $\epsilon$ could be the influence of some other unmeasured factors that are independent of $X$ and $T$ but have an influence on the math score. In the easiest case, the function $f^0$ is linear in its arguments, but often there will be interactions between the pre-treatment covariates and study time after class. If $x = "\text{doing at least two hours of sports per week}"$, then the effect of studying on the outcome $y$ might be stronger if the student does enough sports.

Under the assumptions of Proposition we have $\theta^\epsilon = \frac{1}{n} \sum_{i=1}^n \bar{f}(t_i, x_i)$.

We can estimate $\theta^\epsilon$ via a two-stage procedure in parametric settings. First, choose twice differentiable basis functions $b_1, \ldots, b_p$. These functions can for example include linear terms, polynomials, radial basis functions or wavelets. Then, solve the least-squares problem

$$\hat{\beta} = \arg \min_{\beta} \sum_{i=1}^n \left( y_i - \sum_{k=1}^p b_k(t_i, x_i) \beta_k \right)^2.$$

Finally, estimate the derivative via $\hat{\tau}(t, t') = \frac{1}{n} \sum_{i=1}^n \frac{\hat{f}(t, x_i) - \hat{f}(t', x_i)}{t - t'}$.

where $\hat{f} = \sum_{k} \hat{\beta}_k f_k(t_i, x_i)$. Under weak ignorability, this is an estimator of the (normalized) sample average treatment effect

$$\tau_{\theta^\epsilon}(t, t') := \frac{1}{n} \sum_{i=1}^n \frac{E[Y(t)|X = x_i, T = t] - E[Y(t')|X = x_i, T = t']}{t - t'}.$$

Define $B$ as the linear span of $b_1, \ldots, b_p$. Write $X_{j, i} = b_j(t_i, x_i)$. The proof of the following theorem can be found in the Appendix. Here and in the following, to be able to use partial integration we tacitly assume that $b_k(t, x)p(t|x) \to 0$ and $\partial b_k(t, x)p(t|x) \to 0$ for fixed $x$ and $t \to \infty$.

**Theorem 1** (Asymptotic variance comparison). Assume that the data $(y_i, t_i, x_i)$, $i = 1, \ldots, n$ is i.i.d. and follows the model in equation . Furthermore, assume that $\partial b_i p(t, x) \in B$ and $f^0 \in B$. Let $b_1(t, x), \ldots, b_p(t, x)$ be differentiable and let $(b_k(T, X))_{k=1,\ldots,p}$ and $(\partial b_k(T, X))_{k=1,\ldots,p}$ have finite second moments.
If the conditional distribution $p(t|x)$ is Gaussian for all $x$ with constant variance, then for all $t, t' \in \mathbb{R}$,
\[
\limsup_{n \to \infty} \frac{\mathbb{E}[(\hat{\theta} - \theta_{fs})^2|X]}{\mathbb{E}[(\hat{\tau} - \tau_{fs})^2|X]} \leq 1.
\]

If $-\partial_t^2 \log p(t|x)$ is non-increasing in $|t|$, then for all $t \in \mathbb{R}$ and $t' = 0$ we have
\[
\limsup_{n \to \infty} \frac{\mathbb{E}[(\hat{\theta} - \theta_{fs})^2|X]}{\mathbb{E}[(\hat{\tau} - \tau_{fs})^2|X]} \leq 1.
\]

Roughly speaking, the theorem shows that the simple plug-in estimator $\hat{\theta}$ has asymptotically lower error or the same error as $\hat{\tau}$ if $B$ is large enough and $p(t|x)$ is Gaussian. The difference in asymptotic variance can be drastic, as we will see in the simulation section. Hence, the concept of incremental interventions might be helpful in situations where the signal-to-noise ratio is too low for drawing any conclusions from $\hat{\tau}$.

If the errors are Gaussian, then the estimators above are both asymptotically efficient for estimating their respective target quantities (Van der Vaart, 2000). In this setting, the result above shows that in low-dimensional scenarios, estimating incremental causal effects is easier in terms of optimal asymptotic variance.

The second part of Theorem 1 indicates that estimating incremental causal effects is not easier than estimating treatment effects in terms of asymptotic error if the distribution of $T$ given $X$ is long-tailed. We will investigate this further in Section 5. While the theoretical result above makes relatively strong assumptions on the distribution of $T$, in practice the effect seems fairly robust.

### 4.2 Robustness to additive confounding

In this section we discuss how estimation of average treatment effects and incremental causal effects behaves in the population case if the ignorability assumption is slightly violated. We will show that average treatment effects are usually more sensitive to worst-case confounding than incremental causal effects in this setting. Before we proceed, we need some additional notation.

Let $\mathbb{P}_{\text{unconf}}$ denote the distribution of $(Y, T, X)$ and assume that we weak ignorability and overlap condition holds under $\mathbb{P}_{\text{unconf}}$. Then, the average treatment effect is identifiable via $\tau_{sp} = \tau(\mathbb{P}_{\text{unconf}})$, where
\[
\tau(\mathbb{P}) = \frac{\mathbb{E}[E[Y|X = x, T = t] - E[E[Y|X = x, T = t']]}{t - t'},
\]
for some $t \neq t'$. Analogously, the incremental effect can be identifiable via $\theta_{sp} = \theta(\mathbb{P}_{\text{unconf}})$, where
\[
\theta(\mathbb{P}) = \mathbb{E}[-\partial_t \log p \cdot Y] = \mathbb{E}[\partial_t E[Y|X, T]].
\]

In the following we investigate how the functionals $\tau(\cdot)$ and $\theta(\cdot)$ behave under additive confounding.

We assume that there is some additive confounding $\delta$ in $Y$, i.e. we assume that $(Y, T, X)$ has the same distribution under $\mathbb{P}_{\text{conf}}$ as $(Y + \delta, T, X)$ under
Let $P$ be the set of distributions $P$ for which the second moment of $\delta$ is bounded by $\epsilon$. For all $\epsilon > 0$, define
\[
\text{sens}_{\text{ATE}}(\epsilon) = \max_{P_{\text{conf}} \in P} |\tau(P_{\text{unconf}}) - \tau(P_{\text{conf}})|, \quad \text{and}
\text{sens}_{\text{incr}}(\epsilon) = \max_{P_{\text{conf}} \in P} |\theta(P_{\text{unconf}}) - \theta(P_{\text{conf}})|.
\]

In words, $\text{sens}_{\text{ATE}}(\epsilon)$ and $\text{sens}_{\text{incr}}(\epsilon)$ quantify how robust the identification methods $\theta(P)$ and $\tau(P)$ are under slight violations of the ignorability assumption. The proof of the following result can be found in the Appendix.

**Theorem 2.** For all $\epsilon > 0$ we have
\[
\text{sens}_{\text{incr}}(\epsilon) = \sqrt{\epsilon E[-\partial^2_t \log p]},
\]
\[
\text{sens}_{\text{ATE}}(\epsilon) = \infty.
\]

As an example, if $p(t|x)$ is Gaussian with variance $\sigma^2$, then $\text{sens}_{\text{incr}}(\epsilon) = \frac{\sqrt{\epsilon}}{\sigma}$.

This result shows, that estimating the average treatment effect from observational data via the ignorability assumption is oftentimes less robust to confounding than estimating the effect of incremental interventions if the ignorability assumption is slightly violated. Of course, this result is conservative as we are dealing with worst-case confounding in an $\epsilon$-ball around the unconfounded distribution $P_{\text{unconf}}$.

### 4.3 Doubly-robust estimation and confidence intervals under sparsity

In this section we describe a simple procedure to derive asymptotically valid confidence intervals using the lasso. “Doubly robust” is meant in the sense that the method yields asymptotically valid confidence intervals if the function class $B$ either contains $\partial_t \log p(t, x)$ or $f^0$. The method we describe is based on the method on page 6 in B"uhlmann and van de Geer (2015). However, we will transform the features in a pre-processing step. This transformation will depend on the observations $(t_i, x_i)$ and change for every $n$, which adds some complexity. The benefit of this pre-processing step is to reduce the problem of estimating incremental treatment effects to a problem of estimating a single component in a high-dimensional, potentially misspecified linear model. As a result, existing software such as the R-package hdi (Meier, 2013) can be used to efficiently estimate incremental treatment effects. Of course, the results below also extend to the low-dimensional case, i.e. to the case where the number of features $p$ is fixed and the number of observations $n$ goes to infinity.

As above, consider basis functions $b_1(t, x), \ldots, b_p(t, x)$ of $B$ which are potentially non-linear. To make notation simpler without loss of generality we assume that $b_1(t, x) = t$. Assume we have an i.i.d. sample $(y_i, t_i, x_i)$, $i = 1, \ldots, n$, and define the feature matrix $X$ via $X_{k,i} = b_k(t_i, x_i)$, the target vector $Y = (y_1, \ldots, y_n)^T$ and the transformed feature matrix $\tilde{X}$ via
\[
\tilde{X}_{k,i} = \begin{cases} t_i & \text{for } k = 1, \\ b_k(t_i, x_i) - t_i \frac{1}{n} \sum_{i=1}^n \partial_t b_k(t_i, x_i) & \text{for } k > 1. \end{cases}
\]
Proposition 2. The following proposition is a direct result of the observation above. This can be thought of as an orthogonalization step. Thus, we refer to this technique “incremental effect orthogonalization”.

By construction, for $k > 1$ the features $(\tilde{X}_{k,i})_{i=1,...,n}$ are asymptotically uncorrelated of the Riesz representer of the average partial effect, $(-\partial \log p(t_i, x_i))_{i=1,...,n}$. Using implicit or explicit orthogonality properties is common in semiparametric approaches. For general functionals the orthogonalization step can be more involved, see for example Chernozhukov et al. (2018). The intuition behind the orthogonalization step is as follows: If we define the transformed functions $b_k = b_k(t, x) - t\alpha_k$ with $\alpha_k = \frac{1}{n} \sum_{i=1}^{n} \partial_t b_k(t_i, x_i)$ for $k > 1$ and $b_k = t$ for $k = 1$, then also $b_1, \ldots, b_p$ is a basis of $\mathcal{B}$. Hence, if $f^0 \in \mathcal{B}$, we can write it as $f^0 = \sum \beta_k^0 b_k$. And in particular, we have the average derivative

$$\theta_{fs} = \frac{1}{n} \sum_{i=1}^{n} \partial_t f^0(t_i, x_i) = \sum_{k=1}^{p} \beta_k^0 \frac{1}{n} \sum_{i=1}^{n} \partial_t \tilde{b}_k = \beta_1^0. \quad (10)$$

The following proposition is a direct result of the observation above.

**Proposition 2.** Assume that $b_1, \ldots, b_p$ is a basis of the function class $\mathcal{B}$. Assume that $Y = f^0(T, X) + \epsilon$ for $\epsilon$ independent of $X, T$ and that $f^0 \in \mathcal{B}$. Let $(y_i, t_i, x_i)_{i=1,...,n}$ be i.i.d. with the same distribution as $(Y, T, X)$ and denote $E_\epsilon$ the expectation with respect to the $\epsilon_i = y_i - f^0(t_i, x_i)$. Then,

$$\theta_p = \beta_1^0,$$

where

$$\beta_0^0 = \arg\min_\beta E_\epsilon \left[ \frac{1}{n} \sum_{i=1}^{n} (y_i - \sum_k \tilde{b}_k(t_i, x_i)\beta_k)^2 \right].$$

Thus, we have transformed the problem of estimation and inference for subpopulation or sample incremental causal effects $\theta_{fs}$ to the problem of doing estimation and inference of one component in a (potentially high-dimensional) linear model. Several approaches have been developed to do inference in high-dimensional linear models (Meinshausen et al. 2009; Liu and Yu 2013; Zhang and Zhang 2014; Javanmard and Montanari 2014; Van de Geer et al. 2014; Belloni et al. 2014). However, using one of these methods with the transformed data $(\tilde{X}, Y)$ does not guarantee that we still have asymptotically valid inference if the Riesz representer $\partial_t \log p(t, x) \in \mathcal{B}$, but $f^0 \not\in \mathcal{B}$. In other words, this approach does not automatically guarantee a double robustness property. In the following we discuss how to obtain double robustness properties for estimating $\theta_{sp}$.

Define the two lasso estimators

$$\hat{\gamma} := \arg\min_\gamma \| \hat{X}_1 - \hat{X}_{-1}\gamma \|_2^2 / n + 2\lambda_1 \| \gamma \|_1,$$

$$\hat{\beta} := \arg\min_\beta \| Y - \hat{X}\beta \|_2^2 / n + 2\lambda_1 \| \beta \|_1.$$

Furthermore, define the desparsified estimator for the first component

$$\hat{\beta}_1^{\text{despar}} = \frac{\hat{Z}^T Y}{\hat{Z}^T \hat{X}_1} - \sum_{k>1} \frac{\hat{Z}^T \hat{X}_k}{\hat{Z}^T \hat{X}_1} \hat{\beta}_k,$$

where

$$\hat{Z} = X_1 - \hat{X}_{-1}\hat{\gamma}.$$
To formulate the assumptions and the result, we need some additional notation.

**Notation.** For $j \geq 1$ we define

$$\tilde{X}_k^0 = b_k(t_i, x_i) - t_i \mathbb{E}[\partial b_k(t_1, x_1)],$$

$$\gamma^0 = \arg\min_{\gamma} \mathbb{E}[\|X_1 - \tilde{X}_0^0 \gamma\|^2_2],$$

$$\beta^0 = \arg\min_{\beta} \mathbb{E}[\|Y - \tilde{X}_0^0 \beta\|^2_2],$$

$$\tilde{Z}_0 = X_1 - \tilde{X}_0^0 \gamma^0,$$

$$\hat{\epsilon} = \epsilon = Y - \tilde{X}_0^0 \beta^0.$$

**Assumptions.** As mentioned before, our work builds on Bühlmann and van de Geer (2015). In comparison to their work, the main difference in terms of assumptions is that we added assumption (A8), see below. As in our setting $\log(p) / n \to 0$, assumption (A8) means that the $\ell_1$-norm of the population regression coefficient $\beta^0$ is bounded and that the $\ell_1$ norm of $\gamma^0$ grows slower than $\sqrt{n / \log(p)}$. Thus, we consider the added assumption (A8) as rather weak. Viewed in total, the assumptions are strong and in particular require that the nonlinear functions $b_k$ and $\partial b_k$ and the error terms are bounded.

(A1) $\mathbb{E}[(\tilde{X}_0^0)^\top \tilde{X}_0^0] / n$ has smallest eigenvalue lower bounded by $C_1 > 0$.

(A2) We assume that there exists a constant $C_2$ such that $\mathbb{P}[|b_k(t_i, x_i)| > C_2] = 0$ and the $\mathbb{P}[|\partial b_k(t_i, |x_i)| > C_2] = 0$ for all $k$.

(A3) $\|\tilde{Z}_0\|_\infty \leq C_3 < \infty$.

(A4) $s_1 = |\{k : \gamma_k^0 \neq 0\}| = o(\sqrt{n / \log(p)})$

(A5) $s_0 = |\{k : \beta_k^0 \neq 0\}| = o(\sqrt{n / \log(p)})$

(A6) The normalized asymptotic error is bounded from below: for

$$u^2 = \text{Var} \left( \frac{\epsilon_1 \tilde{Z}_0^0}{\mathbb{E}[\tilde{Z}_0^0]^\top \tilde{X}_0^0] + \sum_k \partial b_k(t_1, x_1) \beta_k^0} \right),$$

we have $v^2 \geq C_4 > 0$.

(A7) The error is bounded $\|\epsilon\|_\infty \leq V$.

(A8) $\|\beta^0\|_1$ is bounded by a constant and $\|\gamma^0\|_1 = o(\sqrt{n / \log(p)})$.

The assumptions (A5) and (A7) can be relaxed. For details, see Bühlmann and van de Geer (2015). Now let us turn to the result.

**Theorem 3** (Similar to Proposition 9 in Bühlmann and van de Geer (2015)). Assume (A1)–(A8) and let $(y, x, t_i)$ be i.i.d. Then, for $\lambda x = D_2 \sqrt{\log(p) / n}$ with $D_2$ sufficiently large and $\lambda = D_1 \sqrt{\log(p) / n}$ with $D_1$ sufficiently large and $\sqrt{\log(p) / n} \to 0$,

$$\sqrt{n} \left( \beta_1^{\text{despar}} - \beta_1^0 \right) \xrightarrow{d} N(0, 1),$$

(11)
where \( \hat{\sigma}^2 \) is the empirical variance of

\[
\hat{\sigma}^2 = \frac{\hat{\epsilon}_i Z_i}{(Z_i)^\top X_1/n} + \sum_k \partial_t b_k(t, x_i) \hat{\beta}_k, \text{ for } i = 1, \ldots, n.
\]

Note that we neither assumed \( f^0 \in \mathcal{B} \) nor \( \partial_t \log p(t, x) \in \mathcal{B} \). The following result shows under which conditions we have \( \hat{\beta}_0 \rightarrow \mathbb{E}[\partial_t \mathbb{E}[Y|X, T]] \). The result is a variation of well-known results for doubly robust estimation of causal parameters, see for example [Bang and Robins (2005)]. For reasons of completeness, we include a proof in the Appendix.

Lemma 1. If \( f^0 \in \mathcal{B} \) or \( \partial_t \log p(t, x) \in \mathcal{B} \), then

\[ \hat{\beta}_0 = \mathbb{E}[\partial_t \mathbb{E}[Y|X, T]]. \]

This shows that estimation and inference is doubly robust: if one of the two functions \( f^0 \) or \( \partial_t \log p \) lie in \( \mathcal{B} \), we obtain consistency for the average partial effect, i.e., \( \hat{\beta}_0^{\text{dpar}} \rightarrow \mathbb{E}[\partial_t \mathbb{E}[Y|X, T]] \) with asymptotically valid confidence intervals. If both \( f^0 \in \mathcal{B} \) and \( \partial_t \log p(t|x) \in \mathcal{B} \) then the proposed estimator reaches the semiparametric efficiency bound. A sketch of this result can be found in the Appendix, Lemma 5.

While we do not show rate double robustness (i.e., trading off performance of \( \hat{\gamma} \) and \( \hat{\beta} \)) for reasons of simplicity, such results can be obtained by a variation of the current proofs. Note that we assume that the sparsity is of order \( o(\sqrt{n}/\log(p)) \). This condition might be weakened by using sample splitting, analogously as in [Chernozhukov et al. (2017)]. Last but not least, we believe that this trick is applicable for more general functionals beyond the average derivative.

## 5 Simulations

In Section 5.1 we discuss a very simple low-dimensional model, where the features are drawn from a Gaussian or t-distribution. In Section 5.2 the covariates are taken from the enhancer data set.

### 5.1 Synthetic data set

In this section we compare estimation and inference for the sample incremental causal effects \( \theta_{\text{fs}} \) and the (relative) sample average treatment effect \( \tau_{\text{fs}} \) as defined in Section 4.1 in very simple scenarios. In the first scenario we generate \( n \) samples according to the following R-code:

```r
f <- function(t) { 3*t + t^2}
t <- rnorm(n=n)
y <- f(t) + runif(n)
```

We fit a cubic model \( y \sim t + t^2 + t^3 \) using ordinary least squares and then we use the simple plug-in estimators \( \hat{\theta} \) to estimate \( \theta_{\text{fs}} \) and \( \hat{\tau} \) to estimate \( \tau_{\text{fs}} \) with \( t_1 = \frac{1}{2}, t' = -\frac{1}{2} \) as defined in Section 4.1.

As we are fitting a linear model, asymptotically valid confidence intervals for both the incremental treatment effect and the average treatment effect can be readily computed using standard formulae. Coverage, average length of the
resulting confidence intervals and root mean-squared error for varying sample size $n$ are given in the table below. Note that the model is well-specified, thus we expect asymptotically correct coverage for both estimators for their specific target quantities. In both cases, coverage is approximately correct.

|       | n=10 | n=20 | n=50 | n=100 | n=200 |
|-------|------|------|------|-------|-------|
| CI coverage incr | 0.97 | 0.96 | 0.95 | 0.95  | 0.94  |
| CI coverage subpopulation ATE | 0.97 | 0.95 | 0.94 | 0.92  | 0.94  |
| CI length incr | 1.01 | 0.40 | 0.19 | 0.12  | 0.08  |
| CI length subpop. ATE | 1.78 | 0.91 | 0.49 | 0.32  | 0.22  |
| RMSE incr | 0.24 | 0.10 | 0.05 | 0.03  | 0.02  |
| RMSE subpop. ATE | 0.42 | 0.22 | 0.12 | 0.09  | 0.06  |

However, note that the average length of confidence intervals for the effect of the incremental effect is much lower than the respective length for the average treatment effect. This is expected and in line with our theory as the assumptions for Theorem 1 hold. Now let us turn to a case where the model is misspecified. We generate $n$ samples according to

\[
f(t) = 3t + t^2 + t^3 + \text{abs}(t) \\
t \sim \text{rt}(n, \text{df}=4) \\
y = f(t) + \text{runif}(n)
\]

Then, we fit a cubic model $y \sim t + t^2 + t^3$ using ordinary least squares and then use simple plug-in estimators for the sample incremental effect and the average treatment effect as above. However, in this case, neither of the confidence intervals are asymptotically valid due to model misspecification. Coverage, average length of the (asymptotically invalid) confidence intervals and root mean-square error are given in the table below.

|       | n=10 | n=20 | n=50 | n=100 | n=200 |
|-------|------|------|------|-------|-------|
| CI coverage incr | 0.82 | 0.72 | 0.62 | 0.53  | 0.37  |
| CI coverage subpopulation ATE | 0.96 | 0.92 | 0.74 | 0.52  | 0.28  |
| CI length incr | 0.81 | 0.32 | 0.17 | 0.12  | 0.09  |
| CI length subpop. ATE | 3.83 | 1.76 | 0.90 | 0.58  | 0.39  |
| RMSE incr | 0.24 | 0.14 | 0.09 | 0.08  | 0.08  |
| RMSE subpop. ATE | 0.90 | 0.45 | 0.36 | 0.37  | 0.38  |

Notably, while both confidence intervals have asymptotically incorrect coverage, incremental causal effects have lower root mean-squared error and lower asymptotic variance. Thus, while the assumptions for Theorem 1 do not hold in this case, estimating incremental interventions is still easier in terms of asymptotic mean squared-error for our choices of estimators.

Of course, there exist scenarios where estimating the effect of incremental effects is considerably harder than estimating average treatment effects. For example, in our experience performance suffers if the distribution of $T$ is extremely heavy-tailed or if the conditional expectation $\mathbb{E}[Y | X = x, T = t]$ is very variable close to the edge of the observation space. In this case, estimating an average treatment effect $\tau(t, t')$, where $t$ and $t'$ are in the bulk of the observations, is relatively easy compared to estimating incremental causal effects. More
simulation experiments are needed to understand the benefits and drawbacks of both estimands under a variety of scenarios.

5.2 Simulations based on an enhancer data set

We aim to investigate estimation of the average derivative in using the transformation proposed in Section 4.3. To increase the realism of our simulation study, we consider features from a real-world data set. More specifically, we consider the activity of \( p = 36 \) transcription factors in Drosophila embryos on \( n = 7809 \) segments of the genome \( \text{Li et al., 2008, MacArthur et al., 2009} \). As the features are heavy-tailed, a square-root transform was performed. The activity of the transcription factors is obtained using the following approach: A transcription-specific antibody is used to filter segments of DNA from the embryo. The filtered segments are measured using microarrays and mapped back to the genome, resulting in a genome-wide map of DNA binding for each transcription factor. Then, \( n = 7809 \) segments of the genome are selected based on background knowledge about enhancer activity. The main effects and interactions of transcription factors form a \( 7809 \times 666 \)-dimensional feature matrix \( X \). We consider two simulation settings which differ in the way the vector \( \beta^0 \) is formed. In one case, the non-zero entries of \( \beta^0 \) are constant 1, whereas in the other case the non-zero entries of \( \beta^0 \) are sampled from an exponential distribution:

**Exponential** \( \beta^0 \): As a feature vector, we randomly select a subset \( S \subset \{1, \ldots, 666\} \) of size eight of the main effects and interactions of the transcription factors. For each of the effects \( k \in S \cup \{1\} \), we draw \( \beta^0_k \sim \exp(\lambda) \) with \( \lambda = \sqrt{10} \) and \( \beta^0_k = 0 \) otherwise.

**Constant** \( \beta^0 \): For the feature vector we randomly select a subset \( S \subset \{1, \ldots, 666\} \) of size eight. For each of the selected \( k \in S \cup \{1\} \), we set \( \beta^0_k = 1 \), and set \( \beta^0_k = 0 \) for \( k \notin S \). We draw \( n \) samples \( \epsilon_i \) from a standard Gaussian distribution with unit variance.

Then, we form observations

\[
y_i = X_i \cdot \beta + \epsilon_i.
\]

We report both the mean-squared error and coverage for \( \theta_k \), corresponding to the first component for varying sample size using the method described in Section 4.3. For fairness of comparison, we use an analogous trick for estimating the average treatment effect. As treatment effect, we consider

\[
\tau(t, t'),
\]

where \( t \) and \( t' \) are both randomly drawn from the empirical distribution of \( T \). The results can be found in Table 1 and Table 2.

Evidently, in this simulation setting, estimating the average treatment effect results in higher asymptotic variance as estimating the incremental effect. This is in line with the theory presented in Section 4.1. This phenomenon seems relatively robust. Similar results for varying choices of simulation parameters can be found in the Appendix.
Table 1: Root mean-squared error of estimating the sample average treatment effect and sample incremental treatment effect. The estimator of incremental causal effects exhibits consistently a lower error. The noise is drawn from a centered Gaussian distribution with unit variance. For the feature vector, a subset of size eight is randomly selected from $S \subset \{1, \ldots, 666\}$. For each of the $k \in S \cup \{1\}$, we draw $\beta_0^k \sim \exp(\lambda)$ with $\lambda = \sqrt{10}$ and set $\beta_0^k = 0$ otherwise.

|       | n=200 | n=300 | n=400 | n=600 | n=800 | n=1000 | n=1500 |
|-------|-------|-------|-------|-------|-------|--------|--------|
| incr  | 0.123 | 0.102 | 0.084 | 0.086 | 0.058 | 0.050  | 0.043  |
| ate   | 0.189 | 0.151 | 0.155 | 0.138 | 0.115 | 0.111  | 0.091  |

Table 2: Root mean-squared error of estimating the sample average treatment effect and sample incremental treatment effect. The estimator of incremental causal effects exhibits consistently a lower error. The noise is drawn from a centered Gaussian distribution with unit variance. For the feature vector, a subset of size eight is randomly selected from $S \subset \{1, \ldots, 666\}$. For each of the $k \in S \cup \{1\}$, we set $\beta_0^k = 1$ and for $k \not\in S \cup \{1\}$ we set $\beta_0^k = 0$.

|       | n=200 | n=300 | n=400 | n=600 | n=800 | n=1000 | n=1500 |
|-------|-------|-------|-------|-------|-------|--------|--------|
| incr  | 0.134 | 0.099 | 0.095 | 0.083 | 0.075 | 0.052  | 0.045  |
| ate   | 0.442 | 0.405 | 0.324 | 0.262 | 0.295 | 0.232  | 0.165  |

6 Conclusion

The estimation of treatment effects is of central interest in many disciplines. Often, treatment effects are estimated under the assumption of weak ignorability and the overlap condition. Both of these assumptions are strong and easily violated if the data is observational. In this paper, we have showed that these assumptions can be substantially weakened for identification of incremental treatment effects. We introduced a local ignorability assumption and a local overlap condition and show that incremental treatment effects are identifiable under these two new local conditions. As an example, conditionally on $X$, treatment assignment to patients might be randomized within subgroups of patients who get similar treatments but not necessarily across patients who get very different treatments.

Furthermore, we discussed how to obtain asymptotically valid confidence intervals that are doubly robust both in terms of estimation and inference in high-dimensional settings under restrictive conditions. In some situations, a feature transformation can be used to obtain confidence intervals using standard statistical software. In simulation studies, we have seen some preliminary results indicating that the estimation of the average treatment effect using a plug-in estimator has sometimes much higher variance than a comparable estimator for the average derivative.

In a limited theoretical setting, we have shown that this difference in asymptotic error is indeed systematic. Moreover, we have showed that estimation of incremental treatment effects is usually more robust under worst-case confounding than estimation of average treatment effects in regression settings.

Causal inference from observational data is known to be unreliable and has to be done with extreme care. In high-stake scenarios such as healthcare this
can have devastating effects on human lives. Thus, we believe it is worthwhile to revisit the foundations of the field. Potentially, some notions are more reliably estimable than others and are thus more informative for practitioners. We have given some theoretical and simulation evidence for situations when it might be favourable to estimate the incremental treatment effect as opposed to estimating the average treatment effect. The next step is to investigate its performance in real-world situations.

7 Acknowledgements

Partial supports are gratefully acknowledged from ARO grant W911NF1710005, ONR grant N00014-17-1-2176, NSF grants DMS-1613002 and IIS 1741340, and the Center for Science of Information (CSoI), a US NSF Science and Technology Center, under grant agreement CCF-0939370. BY is a Chan Zuckerberg Biohub investigator.

References

Angrist, J., Imbens, G., and Rubin, D. (1996). Identification of causal effects using instrumental variables. *Journal of the American statistical Association*, 91(434):444–455.

Bang, H. and Robins, J. (2005). Doubly robust estimation in missing data and causal inference models. *Biometrics*, 61(4):962–973.

Belloni, A., Chernozhukov, V., and Hansen, C. (2014). Inference on treatment effects after selection among high-dimensional controls. *The Review of Economic Studies*, 81(2):608–650.

Boucheron, S., Lugosi, G., and Massart, P. (2013). *Concentration inequalities: A nonasymptotic theory of independence*. Oxford university press.

Bühlmann, P. and van de Geer, S. (2011). *Statistics for High-Dimensional Data: Methods, Theory and Applications*. Springer Verlag.

Bühlmann, P. and van de Geer, S. (2015). High-dimensional inference in misspecified linear models. *Electronic Journal of Statistics*, 9(1):1449–1473.

Cameron, A. and Trivedi, P. (2005). *Microeconometrics: methods and applications*. Cambridge university press.

Chernozhukov, V., Chetverikov, D., Demirer, M., Duflo, E., Hansen, C., and Newey, W. (2017). Double/debiased/neyman machine learning of treatment effects. *American Economic Review*, 107(5):261–65.

Chernozhukov, V., Newey, W., and Robins, J. (2018). Double/de-biased machine learning using regularized riesz representers. *arXiv preprint arXiv:1802.08667*.

D’Amour, A., Ding, P., Feller, A., Lei, L., and Sekhon, J. (2017). Overlap in observational studies with high-dimensional covariates. *arXiv preprint arXiv:1711.02582*.
Eberhardt, F. and Scheines, R. (2007). Interventions and causal inference. Philosophy of Science, 74:981–995.

Hernan, M. A. and Robins, J. M. (2010). Causal inference. CRC Press.

Hirshberg, D. A. and Wager, S. (2017). Augmented minimax linear estimation. arXiv preprint arXiv:1712.00038.

Imbens, G. (2010). Better late than nothing: Some comments on deaton (2009) and heckman and urzua (2009). Journal of Economic literature, 48(2):399–423.

Imbens, G. and Rubin, D. (2015). Causal inference in statistics, social, and biomedical sciences. Cambridge University Press.

Javanmard, A. and Montanari, A. (2014). Confidence intervals and hypothesis testing for high-dimensional regression. The Journal of Machine Learning Research, 15(1):2869–2909.

Kennedy, E. (2018). Nonparametric causal effects based on incremental propensity score interventions. Journal of the American Statistical Association, pages 1–12.

Korb, K., Hope, L., Nicholson, A., and Axnick, K. (2004). Varieties of causal intervention. In Proceedings of the Pacific Rim Conference on AI, pages 322–331.

Lee, D. and Lemieux, T. (2010). Regression discontinuity designs in economics. Journal of economic literature, 48(2):281–355.

Li, X., MacArthur, S., Bourgon, R., Nix, D., Pollard, D., Iyer, V., Hechmer, A., Simirenko, L., Stapleton, M., Hendriks, C., et al. (2008). Transcription factors bind thousands of active and inactive regions in the drosophila blastoderm. PLoS biology, 6(2).

Liu, H. and Yu, B. (2013). Asymptotic properties of lasso+ mls and lasso+ ridge in sparse high-dimensional linear regression. Electronic Journal of Statistics, 7:3124–3169.

MacArthur, S., Li, X., Li, J., Brown, J., Chu, H., Zeng, L., Grondona, B., Hechmer, A., Simirenko, L., Keränen, S., et al. (2009). Developmental roles of 21 drosophila transcription factors are determined by quantitative differences in binding to an overlapping set of thousands of genomic regions. Genome biology, 10(7):R80.

Meier, L. (2013). hdi: High-Dimensional Inference. R package version 0.0-1/r2.

Meinshausen, N., Meier, L., and Bühlmann, P. (2009). P-values for high-dimensional regression. Journal of the American Statistical Association, 104:1671–1681.

Powell, J., Stock, J., and Stoker, T. (1989). Semiparametric estimation of index coefficients. Econometrica: Journal of the Econometric Society, pages 1403–1430.
Rosenbaum, P. (2002). *Observational studies*. Springer.

Rosenbaum, P. and Rubin, D. (1983). Assessing sensitivity to an unobserved binary covariate in an observational study with binary outcome. *Journal of the Royal Statistical Society: Series B (Methodological)*, 45(2):212–218.

Rubin, D. (1974). Estimating causal effects of treatments in randomized and nonrandomized studies. *Journal of educational Psychology*, 66(5):688.

Rubin, D. (1980). Discussion of "randomization analysis of experimental data in the Fisher randomization test" by D. Basu. *Journal of the American Statistical Association*, 75:591–593.

Splawa-Neyman, J., Dabrowska, D., and Speed, T. (1990). On the application of probability theory to agricultural experiments. *Statistical Science*, pages 465–472.

Stoker, T. M. (1991). Equivalence of direct, indirect, and slope estimators of average derivatives. *Nonparametric and semiparametric methods in econometrics and statistics*, pages 99–118.

Thistlethwaite, D. and Campbell, D. (1960). Regression-discontinuity analysis: An alternative to the ex post facto experiment. *Journal of Educational Psychology*, 51(6):309.

Tian, J. and Pearl, J. (2001). Causal discovery from changes. In *Proceedings of the 17th Conference on Uncertainty in Artificial Intelligence (UAI)*, pages 512–522.

Van de Geer, S., Bühlmann, P., Ritov, Y., and Dezeure, R. (2014). On asymptotically optimal confidence regions and tests for high-dimensional models. *The Annals of Statistics*, 42(3):1166–1202.

Van der Vaart, A. (2000). *Asymptotic statistics*, volume 3. Cambridge University Press.

Wooldridge, J. (2005). Unobserved heterogeneity and estimation of average partial effects. *Identification and Inference for Econometric Models: Essays in Honor of Thomas Rothenberg*, pages 27–55.

Wright, P. (1928). *Tariff on animal and vegetable oils*. Macmillan Company, New York.

Zhang, C.-H. and Zhang, S. (2014). Confidence intervals for low dimensional parameters in high dimensional linear models. *Journal of the Royal Statistical Society: Series B (Statistical Methodology)*, 76(1):217–242.
8 Appendix

8.1 Additional simulation results

| n=200 | n=300 | n=400 | n=600 | n=800 | n=1000 | n=1500 |
|-------|-------|-------|-------|-------|--------|--------|
| incr  | 0.222 | 0.174 | 0.159 | 0.136 | 0.107  | 0.097  | 0.073  |
| ate   | 0.357 | 0.240 | 0.216 | 0.190 | 0.165  | 0.166  | 0.136  |

Table 3: Root mean-squared error of estimating the sample average treatment effect and sample incremental treatment effect. The estimator of incremental causal effects exhibits consistently a lower error. The noise is drawn from a $t$-distribution with three degrees of freedom. For the feature vector, a subset of size eight is randomly selected from $S \subset \{1, \ldots, 666\}$. For each of the $k \in S \cup \{1\}$, we draw $\beta_k^0 \sim \exp(\lambda)$ with $\lambda = \sqrt{10}$ and set $\beta_k^0 = 0$ otherwise.

| n=200 | n=300 | n=400 | n=600 | n=800 | n=1000 | n=1500 |
|-------|-------|-------|-------|-------|--------|--------|
| incr  | 0.270 | 0.192 | 0.169 | 0.151 | 0.113  | 0.088  | 0.088  |
| ate   | 0.460 | 0.487 | 0.409 | 0.333 | 0.318  | 0.315  | 0.299  |

Table 4: Root mean-squared error of estimating the sample average treatment effect and sample incremental treatment effect. The estimator of incremental causal effects exhibits consistently a lower error. The noise is drawn from a centered $t$-distribution with 3 degrees of freedom. For the feature vector, a subset of size eight is randomly selected from $S \subset \{1, \ldots, 666\}$. For each of the $k \in S \cup \{1\}$, we set $\beta_k^0 = 1$ and for $k \notin S \cup \{1\}$ we set $\beta_k^0 = 0$.

8.2 Proof of Proposition 1

Proof. Without loss of generality we will drop “conditional on $X$”. In the following, choose $t$ with $p(t) > 0$. As $Y(t)$ is continuously differentiable with derivative $Y'(t)$ there exists a random variable $\xi_\delta \in [t, t + \delta]$ such that

$$\frac{Y(t + \delta) - Y(t)}{\delta} = Y'(\xi_\delta). \quad (12)$$

As the derivative $Y'(t)$ is continuous and bounded, by dominated convergence,

$$\lim_{\delta \to 0} \frac{\mathbb{E}[Y(t + \delta)|T = t] - \mathbb{E}[Y(t)|T = t]}{\delta} = \mathbb{E}[Y'(t)|T = t].$$

Now choose $\delta_0 > 0$ small enough such that both the local overlap condition and local ignorability is satisfied, i.e. such that $p(t') > 0$ for all $|t' - t| \leq \delta_0$ and that $Y(t + \delta)|T = t \leq Y(t + \delta)|T = t + \delta$ for all $|\delta| \leq \delta_0$. Hence, for $\delta$ close to zero,

$$\mathbb{E}[Y(t + \delta) - Y(t)|T = t] = \mathbb{E}[Y(t + \delta)|T = t] - \mathbb{E}[Y(t)|T = t]$$

$$= \mathbb{E}[Y(t + \delta)|T = t + \delta] - \mathbb{E}[Y(t)|T = t].$$

Dividing by $\delta$,

$$\frac{\mathbb{E}[Y(t + \delta) - Y(t)|T = t]}{\delta} = \frac{\mathbb{E}[Y(t + \delta)|T = t + \delta] - \mathbb{E}[Y(t)|T = t]}{\delta}.$$
As shown above, for \( \delta \to 0 \), the limit of the quantity on the left exists and is equal to \( E[Y'(t)|T = t] \). Thus, \( E[Y|T = t] \) is differentiable and the quantity on the left converges to \( \partial_t E[Y|T = t] \). Taking the limit on both sides concludes the proof. In particular, as \( Y(t) \) is continuously differentiable with bounded derivative, \( t \to E[Y|T = t] \) is also continuously differentiable with bounded derivative in neighborhoods where \( p(t) > 0 \).

**8.3 Proof of Theorem 1**

Proof. Take an orthogonal basis \( b_1, \ldots, b_p \) of \( \mathcal{B} \), such that \( b_1 = -\partial_t \log p(t|x) \). For \( n \) large enough, the estimator \( \hat{f} \) can be written as \( \hat{f} = \sum_k \hat{\alpha}_k b_k \) with unique \( \hat{\alpha}_1, \ldots, \hat{\alpha}_p \). Define \( X_{j,i} = b_j(t_i, x_i) \). Note that conditionally on \( X \), \( \hat{\theta}_n \) and \( \hat{\tau}_n \) are unbiased estimators of \( \theta_n \) and \( \tau_n \). Thus, in the following we will derive the conditional asymptotic variance of these estimators. The conditional variance of the vector \( \hat{\alpha} \) can be written as

\[
(X'X)^{-1}E[\epsilon^2]
\]

The conditional variance of \( \hat{\alpha} \) can thus be written as

\[
\frac{1}{n} \cdot \begin{pmatrix}
\frac{E[\epsilon^2]}{E[\epsilon^2]} & 0 & \ldots & 0 \\
\frac{E[\epsilon^2]}{E[\epsilon^2]} & 0 & & * & * \\
& & \ddots & \ddots & \ddots \\
& & & \frac{E[\epsilon^2]}{E[\epsilon^2]} & 0 & * & * \\
0 & & & * & * & * \\
\end{pmatrix} + o_P \left( \frac{1}{n} \right).
\]

Here we used that by choice of \( b_1, \ldots, b_p \) we have that \( E[b_1 b_k] = 0 \) for all \( k > 1 \). In addition, we used the formula for block-wise inversion and multiplication of matrices. Hence \( \hat{\theta}_n = \frac{1}{n} \sum_{i=1}^{n} \sum_{k} \hat{\alpha}_k \partial_t b_k(t_i, x_i) = \sum_{k} \hat{\alpha}_k \frac{1}{n} \sum_{i=1}^{n} \partial_t b_k(t_i, x_i) \) has asymptotic conditional variance

\[
\frac{1}{n} \cdot \left( E[\partial_t b_1] \ldots E[\partial_t b_p] \right) \begin{pmatrix}
\frac{E[\epsilon^2]}{E[\epsilon^2]} & 0 & \ldots & 0 \\
\frac{E[\epsilon^2]}{E[\epsilon^2]} & 0 & & * & * \\
& & \ddots & \ddots & \ddots \\
& & & \frac{E[\epsilon^2]}{E[\epsilon^2]} & 0 & * & * \\
0 & & & * & * & * \\
\end{pmatrix} \left( E[\partial_t b_1] \ldots E[\partial_t b_p] \right) + o_P \left( \frac{1}{n} \right),
\]

Using that by partial integration, \( E[\partial_t b_k] = E[b_k b_1] = 0 \) for all \( k > 1 \), \( \hat{\theta}_n \) has asymptotic conditional variance

\[
\frac{1}{n} \cdot \left( E[\partial_t b_1]^2 \frac{E[\epsilon^2]}{E[\epsilon^2]} \right) + o_P \left( \frac{1}{n} \right).
\]

We can now use that \( E[\partial_t b_1]^2 = E[b_1^2]^2 \). This gives us asymptotic conditional variance

\[
\frac{E[b_1^2]}{n} \frac{E[\epsilon^2]}{E[\epsilon^2]} + o_P \left( \frac{1}{n} \right).
\]

Through analogous argumentation we obtain that the conditional variance of \( \hat{\tau} \) is asymptotically

\[
\frac{1}{n} \cdot \begin{pmatrix}
v_1 & \ldots & v_p \end{pmatrix} \begin{pmatrix}
\frac{E[\epsilon^2]}{E[\epsilon^2]} & 0 & \ldots & 0 \\
0 & & & * & * \\
& & \ddots & \ddots & \ddots \\
& & & \frac{E[\epsilon^2]}{E[\epsilon^2]} & 0 & * & * \\
0 & & & * & * & * \\
\end{pmatrix} \begin{pmatrix}
v_1 \\
v_2 \\
\vdots \\
v_p \\
\end{pmatrix} + o_P \left( \frac{1}{n} \right).
\]
where \( v_k := \frac{E[b_k(t, X)] - E[b_k(t', X)]}{t - t'} \). Using that the submatrix denoted by “*” is positive semidefinite, the variance of \( \hat{\tau}_{fs} \) is asymptotically lower bounded by

\[
\frac{1}{n} \left( \frac{E[b_1(t, X)] - E[b_1(t', X)]}{t - t'} \right)^2 \frac{E[\epsilon^2]}{E[b_1]^2} + o_p \left( \frac{1}{n} \right).
\]

If the distribution of \( T \) given \( X \) is Gaussian with constant variance, then the second derivative of the log-density given \( X \) is constant. In this case,

\[
\left( \frac{E[b_1(t, X)] - E[b_1(t', X)]}{t - t'} \right)^2 = E[\partial_t b_1]^2.
\]

Hence, in this case, the variance of \( \hat{\tau}_{fs} \) is asymptotically lower bounded by

\[
\frac{E[b_1]^2 | E[\epsilon^2]}{n} + o_p \left( \frac{1}{n} \right).
\]

Thus, \( \liminf_{n \to \infty} \frac{\text{Var}(\hat{\tau}_{fs})}{\text{Var}(\hat{\theta}_{fs})} \geq 1 \). This completes the proof for the case where the distribution of \( T \) given \( X \) is Gaussian. Now let us turn to the case where \( t' = 0, t \in \mathbb{R}, \) and \( \partial_t b_k(t, x) \) is non-increasing in \( |t| \). Then,

\[
\left( \frac{E[b_1(t, X)] - E[b_1(0, X)]}{t} \right)^2 \frac{E[\epsilon^2]}{E[b_1]^2} \geq E[\partial_t b_1]^2 \frac{E[\epsilon^2]}{E[\partial_t b_1]} = E[b_1^2 | E[\epsilon^2]].
\]

### 8.4 Proof of Theorem 2

**Proof.** Sketch. We will first prove the result for incremental treatment effects. Set \( f_* = -\partial_t \log p(t, x) \). Then,

\[
\max_{E[|s|] \leq \epsilon} \mathbb{E}_{\text{conf}}[f_* Y] - \mathbb{E}_{\text{unconf}}[f_* Y] = \max_{E[|s|] \leq \epsilon} \mathbb{E}_{\text{unconf}}[f_* (Y + \delta)] - \mathbb{E}_{\text{unconf}}[f_* Y] = \max_{E[|s|] \leq \epsilon} \mathbb{E}_{\text{unconf}}[f_* \delta] = \sqrt{\epsilon} \sqrt{\mathbb{E}[f_*^2]}.
\]

Now, use that \( \mathbb{E}[f_*^2] = \mathbb{E}[\partial_t f_*] = \mathbb{E}[-\partial_t^2 \log p(t, x)] \). In the case of the average treatment effect use

\[
\delta = \frac{f((T - t)/\sigma)}{\sqrt{\mathbb{E}_{\text{unconf}}[f((T - t)/\sigma)^2]}}.
\]

where \( f \) is the density function of a standard Gaussian random variable. For \( \sigma \to 0, \mathbb{E}_{\text{conf}}[Y|X = x, T = t] \to \infty \), whereas \( \mathbb{E}_{\text{conf}}[Y|X = x, T = t'] \to \mathbb{E}_{\text{unconf}}[Y|X = x, T = t'] \). This concludes the proof.

### 8.5 Proof of Theorem 3 and auxiliary results

The proof follows closely Bühlmann and van de Geer (2015) with some modifications. Before we proceed, we show that the following auxiliary results hold:
(D1) \[
\max_k |\hat{\epsilon}^\top \tilde{X}_k / n| = O_P(\sqrt{\log(p) / n})
\]
\[
\max_k |\epsilon^\top (\tilde{X}_k - \tilde{X}_0) / n| = O_P(\sqrt{\log(p) / n})
\]
\[
\max_{k \neq 1} |(\tilde{X}_k^\top \tilde{Z})^\top / n| = O_P(\sqrt{\log(p) / n})
\]
\[
\max_{k \neq 1} |(\tilde{X}_k - \tilde{X}_0)^\top \tilde{Z}^\top / n| = O_P(\sqrt{\log(p) / n})
\]

(D2) \[\|\hat{\gamma}(\lambda X) - \gamma^0\|_1 = o_P(1/\sqrt{\log(p)})\]

(D3) \[\|\hat{\beta}(\lambda) - \beta^0\|_1 = o_P(1/\sqrt{\log(p)})\]

**Lemma 2** (Similar to Lemma 2 in Bühmann and van de Geer (2015)). Assume (A2), (A3) and (A7). Then, (D1) holds.

**Proof.** We will prove the first part of the statement. The other parts of the statement can be proven analogously. First, note that

\[
\text{E}\left[ \max_{1 \leq k \leq p} |n^{-1} \epsilon^\top \tilde{X}_k|^2 \right] \leq 2\text{E}\left[ \max_{1 \leq k \leq p} |n^{-1} \epsilon^\top X_k|^2 \right] + 2\text{E}\left[ \max_{1 \leq k \leq p} |\delta_k|^2 \right],
\]

where \(\delta_k = 0\) and \(\delta_k = n^{-1} \sum_i \epsilon_i \cdot n^{-1} \sum_j \beta_{ki} (t_j, x_i)\) for \(k > 1\). Using Nemirowski’s inequality (Bühmann and van de Geer [2011], Lemma 14.24) we obtain:

\[
\text{E}\left[ \max_{1 \leq k \leq p} |n^{-1} \epsilon^\top X_k|^2 \right] \leq 8 \log(2p) C_2^2 V^2 / n = O(\log(p) / n),
\]

and similarly

\[
\text{E}\left[ \max_{1 \leq k \leq p} |\delta_k|^2 \right] \leq 8 \log(2p) C_4^2 V^2 / n = O(\log(p) / n).
\]

Using equation (13) and equation (15) in equation (13) we obtain

\[
\text{E}\left[ \max_{1 \leq k \leq p} |n^{-1} \epsilon^\top \tilde{X}_k|^2 \right] = O(\log(p) / n).
\]

In the next step, we can use Markov’s inequality and \(\text{E}[\epsilon^\top \tilde{X}_k] = 0\) to conclude that

\[
\text{P}\left[ \max_{k=1, \ldots, p} |n^{-1} \epsilon^\top \tilde{X}_k| > c \right] \leq \frac{\text{E}[\max_{k=1, \ldots, p} |n^{-1} \epsilon^\top \tilde{X}_k|]}{c}
\]

\[
\leq \frac{\sqrt{\text{E}[\max_{k=1, \ldots, p} |n^{-1} \epsilon^\top \tilde{X}_k|^2]}}{c}
\]

\[= O(\sqrt{\log(p) / n}).\]

\[\square\]

**Lemma 3** (Similar to Lemma 2 in Bühmann and van de Geer [2015]). Assume (A1) and (A2) and \(\sqrt{\log(p) / n} \to 0\).

1. If (A3) and (A4) hold, then for \(\lambda X = D_2 \sqrt{\log(p) / n}\) with \(D_2\) sufficiently large we have (D2).
2. If (A7) and (A5) holds, then for \( \lambda = D_1 \sqrt{\log(p)/n} \) with \( D_1 \) sufficiently large, we have (D3).

Proof. The proof proceeds mostly as in Bühlmann and van de Geer (2015). However, there is one slight complication that the rows of \( \tilde{X} \) are not i.i.d. We will prove statement (1). The proof for statement (2) proceeds analogously.

First, we will prove the compatibility condition for the transformed data \( \tilde{X} \). To this end, note that

\[
\frac{1}{n} \tilde{X}_j \tilde{X}_k = \frac{1}{n} X_j \tilde{X}_k - \frac{1}{n} \sum_{i=1}^{n} X_{i,j} X_{i,k} \delta_k - \frac{1}{n} \sum_{i=1}^{n} X_{i,1} X_{i,k} \delta_j + \delta_k \delta_j \frac{1}{n} \sum_{i=1}^{n} X_{i,1}^2,
\tag{17}
\]

where \( \delta_j = \frac{1}{n} \sum_{i} \partial_t b_j(t_i, x_i') \) for \( j > 1 \) and \( \delta_j = 0 \) for \( j = 1 \). Using assumption (A2) and sub-Gaussian tail bounds (Boucheron et al., 2013, Chapter 2), the terms

\[
\frac{1}{n} X_j \tilde{X}_k - \frac{1}{n} \mathbb{E}[X_j \tilde{X}_k],
\delta_k - \mathbb{E}[\delta_k],
\]

are uniformly of the order \( O_P(\sqrt{\log(p)/n}) \). Hence, using equation (17), the term

\[
\max_{j,k} \frac{1}{n} \tilde{X}_j \tilde{X}_k - \frac{1}{n} \mathbb{E}[\tilde{X}_j \tilde{X}_k]
\]

is of order \( O_P(\sqrt{\log(p)/n}) \).

The sparsity assumption (A4) combined with (A1) imply that the compatibility condition holds with probability converging to one, c.f. Bühlmann and van de Geer (2011, Chapter 6.12). Using Lemma 2, we obtain \( \|\tilde{X} \|_\infty \leq O_P(\sqrt{n \log(p)}) \). Invoking an inequality for the lasso (Bühlmann and van de Geer, 2011, Chapter 6.1) with assumption (A4), we obtain statement (1).

Proposition 3 (Similar to Proposition 7 in Bühlmann and van de Geer (2015)). Assume (A1), (A3), (A6), (A7) and (A8). Write

\[
u^2 = \text{Var} \left( \frac{\epsilon^* \tilde{Z}_1^0}{\mathbb{E}[\tilde{Z}_1^0 \tilde{X}_1]} + \sum_k \partial_t b_k(t_1, x_1) \beta_k^0 \right)
\]

Then,

\[
\sqrt{n} \left( \frac{\epsilon^* \tilde{Z}_1^0/n}{\mathbb{E}[\tilde{Z}_1^0 \tilde{X}_1]} - \sum_k (\mathbb{E}[\partial_t b_k \beta_k^0] - \mathbb{E}[\partial_t b_k \beta_k^0]) \right) \xrightarrow{d} \mathcal{N}(0, 1).
\tag{18}
\]

Proof. By assumption (A6), \( u \) is bounded from below. In addition, note that due to (A1), \( \mathbb{E}[(\tilde{Z}^0)^n X_1^0]/n \) is bounded away from zero and due to (A2) it is bounded from above. Due to (A2) and (A8), \( \sum_k \partial_t b_k \beta_k^0 \) is bounded. The proof then proceeds analogously to the proof in Bühlmann and van de Geer (2015) using the Lindeberg condition.
Proposition 4 (Similar to Proposition 8 in Bühlmann and van de Geer (2015)). Assume \( \sqrt{\log(p)/n} \to 0 \), (A1), (A2), (A3), (A6), (A7), (A8), (D1), (D2) and (D3). Then:

\[
\frac{Z^*_\epsilon}{Z^*_X} - \frac{1_{k}}{u} \left( \sum_k (E[\partial_t b_k \beta^0_k] - \hat{E}[\partial_t b_k \beta^0_k]) \right) \to \mathcal{N}(0,1) \quad (19)
\]

Proof. We have to show that the difference between equation (18) and equation (19), up to bounded factors, is away from zero and can be ignored. The difference between equation (18) and (19), up to bounded factors, is

\[
\sqrt{n} \left( \frac{Z^*_\epsilon}{Z^*_X} - \frac{e^T Z^0/n}{E[(Z^0)^T X^0_{11}]} \right).
\]

We want to show that this term goes to zero. Let us assume for a moment that

1. \( |e^T (Z^0 - \bar{Z})/\sqrt{n}| = o_P(1) \),
2. \( \hat{Z}^T X_1/n - E[(Z^0)^T X^0_{11}] = o_P(1) \),
3. \( e^T Z^0/\sqrt{n} = O_P(1) \),
4. \( E[(Z^0)^T X^0_{11}] \) is bounded away from zero.

Then,

\[
\sqrt{n} \left( \frac{Z^*_\epsilon}{Z^*_X} - \frac{e^T Z^0/n}{E[(Z^0)^T X^0_{11}]} \right) = e^T Z^0/\sqrt{n} \left( \frac{1}{Z^*_X X_1/n} - \frac{1}{E[(Z^0)^T X^0_{11}]} \right) + (e^T Z^0/\sqrt{n} - e^T \bar{Z}/\sqrt{n}) \frac{1}{Z^*_X X_1/n} = o_P(1),
\]

which is the desired result. Thus, it remains to show that the claims (1)–(4) hold. Let us first show claim (1).

\[
|e^T (Z^0 - \bar{Z})/\sqrt{n}| \leq |e^T \bar{X}_1 (\hat{\gamma} - \gamma^0)|/\sqrt{n} + |e^T (\bar{X}_1 - \bar{X}^0_{11})\gamma^0|/\sqrt{n} \leq \|e^T \bar{X}_1\|_\infty \|\hat{\gamma} - \gamma^0\|_1/\sqrt{n} + \|e^T (\bar{X}_1 - \bar{X}^0_{11})\|_\infty/\sqrt{n}\|\gamma^0\|_1
\]

Now we can use (D1), (D2) and (A8) to conclude that this term goes to zero in probability for \( n \to \infty \). This proves claim (1). Now let us turn to claim (2). Similarly as proving claim (1) we can show that

\[
|\hat{Z}^T X_1/n - (\bar{Z}^0)^T \bar{X}_1/n| = \left| \frac{1}{n} \bar{X}_1^T \bar{X}_1 (\hat{\gamma} - \gamma^0) \right| + \left| \frac{1}{n} \bar{X}_1^T (\bar{X}^0_{11} - \bar{X}_{11})\gamma^0 \right| = o_P(1).
\]

As \( \bar{X}_1 = \bar{X}^0_{11} \),

\[
|\hat{Z}^T X_1/n - (\bar{Z}^0)^T \bar{X}_1/n| = o_P(1). \quad (20)
\]
By (A2) and the law of large numbers,

\[(Z^0)^\top X^0_1/n - \mathbb{E}[(Z^0_i)^\top X^0_1] = oP(1).\]

Using equation (20) proves claim (2).

\[\left(\frac{1}{Z^0_1/n} - \frac{1}{\mathbb{E}[(Z^0_i)^\top X^0_1]}\right) = oP(1).\]

Due to (A3), (A7) and the definition of \(\epsilon, e\top Z^0 / \sqrt{n} = O_P(1)\). This proves claim (3). Claim (4) follows from assumption (A1).

**Proposition 5** (Similar to Proposition 9 in Bühlmann and van de Geer (2015)). Assume (A1), (A2), (A3), (A6), (A7), (A8), (D1), (D2) and (D3). Then, for \(\lambda_X = D_2 \sqrt{\log(p)/n}\) with \(D_2\) sufficiently large and \(\sqrt{\log(p)/n} \to 0\),

\[\sqrt{n}(\hat{\beta}_{1\text{despar}} - \beta^0_1) \sim \mathcal{N}(0,1),\]

where \(u\) is defined as in Proposition 3.

**Proof.** Let us recall the definition

\[\hat{\beta}_{1\text{despar}} = \frac{Z^\top Y}{Z^\top X_1} - \sum_{k \neq 1} \frac{Z^\top X_k \hat{\beta}_k}{Z^\top X_1} \beta^0_k.\]

Then, using that \(Y = \epsilon + X^0_1\beta^0 = \epsilon + X_1\beta^0 - \sum_{k \neq 1} X_1 (E[\partial_t b_k \beta^0_k] - E[\partial_t b_k \beta^0_k]),\)

\[\sqrt{n}Z^\top X_1(\hat{\beta}_{1\text{despar}} - \beta^0_1)\]

\[= \sqrt{n} \left(\frac{Z^\top Y}{n} - \sum_{k \neq 1} \frac{Z^\top X_k \hat{\beta}_k}{n} \beta^0_k - \frac{Z^\top X_1 \beta^0_k}{n} \right)\]

\[= \sqrt{n} \left(\hat{\beta}^\top (\epsilon - X_1 \sum_{k \neq 1} (E[\partial_t b_k] - E[\partial_t b_k])\beta^0_k + \sum_{k \neq 1} \hat{X}_k (\beta^0_k - \hat{\beta}_k))\right)\]

\[= \sqrt{n} \left(\hat{\beta}^\top (\epsilon - X_1 \sum_{k \neq 1} (E[\partial_t b_k] - E[\partial_t b_k])\beta^0_k + \hat{X}_1 \sum_{k \neq 1} (\beta^0_k - \hat{\beta}_k))\right).\]

The latter quantity in this term can be bounded,

\[\left| \frac{1}{\sqrt{n}} Z^\top X_1 \sum_{k \neq 1} (\beta^0_k - \hat{\beta}_k) \right| \leq \frac{1}{\sqrt{n}} \left\| Z^\top X_1 \right\|_{\infty} \left\| (\beta^0_k - \hat{\beta}_k) \right\|_1\]

The KKT conditions for the regression of \(\hat{X}_1\) on \(\hat{X}_1\) read as

\[\hat{X}_1^\top \hat{Z}/n + \lambda_X \hat{\kappa} = 0,\]
for $\hat{\kappa} \in [-1, 1]^{p-1}$. Thus, $\|\breve{X}_i^\top Z_i\|_\infty = O(\sqrt{n \log(p)})$. Furthermore, by assumption $\|\beta_0 - \hat{\beta}\|_1 = o_p(1/\sqrt{\log(p)})$. Thus,
\[
\left| \frac{1}{\sqrt{n}} \breve{Z}_i^\top \breve{X}_i (\hat{\beta}_0 - \hat{\beta}_1) \right| = o_p(1)
\]
Thus,
\[
\sqrt{n} \breve{Z}_i^\top \breve{X}_i (\hat{\beta}_0 - \hat{\beta}_1)
= \sqrt{n} \left( \breve{Z}_i^\top (\hat{\beta}_0 - \hat{\beta}_1) + o_p(1) \right).
\]
Rearranging yields
\[
\sqrt{n} \left( \hat{\beta}_0 - \hat{\beta}_1 \right)
= \sqrt{n} \left( \breve{Z}_i^\top (\hat{\beta}_0 - \hat{\beta}_1) + o_p(1) \right) + o_p(1).
\]

**Proposition 6** (Similar to Proposition 1 in Bühlmann and van de Geer (2015)). Assume $\sqrt{\log(p)/n} \to 0$, (A1), (A2), (A3), (A6), (A7), (A8), (D2) and (D3). Then,
\[
\hat{u}^2 = u^2 + o_p(1),
\]
where $\hat{u}^2$ is the empirical variance of
\[
\frac{\hat{Z}_i^\top \breve{X}_i}{n} - \frac{\hat{Z}_i^\top \breve{X}_i}{n} - \sum_k \hat{E} [\partial_t b_k] \hat{\beta}_k - \hat{b}_k (t_i, x_i) \hat{\beta}_k,
\]
for $i = 1, \ldots, n$ and $u^2$ is the variance of
\[
\frac{\hat{Z}_i^\top \breve{X}_i}{n} - \frac{\hat{Z}_i^\top \breve{X}_i}{n} - \sum_k \hat{E} [\partial_t b_k] \beta_0 - \hat{b}_k (t_i, x_i) \beta_0.
\]

**Proof.** Define
\[
\xi_i = \frac{\hat{Z}_i^\top \breve{X}_i}{n} - \frac{\hat{Z}_i^\top \breve{X}_i}{n} - \sum_k \hat{E} [\partial_t b_k] \beta_0 - \hat{b}_k (t_i, x_i) \beta_0
\]
and
\[
\xi_i = \frac{\hat{Z}_i^\top \breve{X}_i}{n} - \frac{\hat{Z}_i^\top \breve{X}_i}{n} - \sum_k \hat{E} [\partial_t b_k] \beta_0 - \hat{b}_k (t_i, x_i) \beta_0.
\]
By assumption (A1), $\hat{E} [\hat{Z}_i^\top \breve{X}_i]$ is bounded away from zero. Thus, by (A2), (A3), (A7) and (A8), the $\xi_i$ are bounded. Using the law of large numbers,
\[
\frac{1}{n} \sum_i \xi_i^0 = \hat{E} [\xi_i^0] + o_p(1),
\]
\[
\frac{1}{n} \sum_i (\xi_i^0)^2 = \hat{E} [(\xi_i^0)^2] + o_p(1).
\]
Thus, it suffices to show that
\[
\frac{1}{n} \sum_i \xi_i^0 - \xi_i = o_P(1),
\]
\[
\frac{1}{n} \sum_i (\xi_i^0)^2 - \xi_i^2 = o_P(1).
\]

Note that we have
\[
\left| \frac{1}{n} \sum_i \xi_i^0 - \xi_i \right| \leq \max_i |\xi_i^0 - \xi_i| \quad (21)
\]
\[
\left| \frac{1}{n} \sum_i (\xi_i^0)^2 - \xi_i^2 \right| \leq \max_i |\xi_i^0 - \xi_i| \left( \max_i |\xi_i^0 - \xi_i| + \max_i |\xi_i^0| \right)
\]

As the \( \xi_i^0 \) are bounded, using equation (21) it suffices to show that
\[
\max_i |\xi_i - \xi_i^0| = o_P(1). \quad (22)
\]

We will do this in two steps.
\[
\max_i |\xi_i - \xi_i^0| 
\]
\[
\leq \max_i \left| \frac{\epsilon_i \tilde{Z}_i^0}{\mathbb{E}[(Z_i^1)^T X_{i1}^1]} - \frac{\epsilon_i \tilde{Z}_i}{(Z)^T X_{i1}/n} \right| 
\]
\[
+ \max_i \left| \sum_k \mathbb{E}[\partial_i b_k \beta_k^0] - \partial_i b_k(t_i, x_i) \beta_k^0 - \sum_k \hat{E}[\partial_i b_k] \hat{\beta}_k - \partial_i b_k(t_i, x_i) \hat{\beta}_k \right| \quad (23)
\]

By assumption, \( \xi_i^0 \) and \( \xi_i \) are bounded. Note that
\[
\max_i \left| \sum_k \partial_i b_k(t_i, x_i) (\beta_k^0 - \hat{\beta}_k) \right| \leq \max_k |b_k(t_i, x_i)|^2 \|\beta^0 - \hat{\beta}\|_1.
\]

Due to assumption (A2), the \( b_k \) are bounded. Recall that due to (D3), \( \|\beta - \beta^0\|_1 = o_P(\sqrt{1/\log p}) \). Thus,
\[
\max_i \left| \sum_k \partial_i b_k(t_i, x_i) (\beta_k^0 - \hat{\beta}_k) \right| = o_P(1) \quad (24)
\]

Using (A2) and that \( \|\beta^0\|_1 \) is bounded, using a sub-Gaussian tail inequality (Boucheron et al. 2013, Chapter 2),
\[
\sum_k \mathbb{E}[\partial_i b_k] \beta_k^0 - \sum_k \frac{1}{n} \sum_i \partial_i b_k(t_i, x_i) \beta_k^0 = O_P(\sqrt{\log(p)/n}). \quad (25)
\]

Combining equation (24) and equation (25),
\[
\left| \sum_k \mathbb{E}[\partial_i b_k \beta_k^0] - \partial_i b_k(t_i, x_i) \beta_k^0 - \sum_k \hat{E}[\partial_i b_k] \hat{\beta}_k - \partial_i b_k(t_i, x_i) \hat{\beta}_k \right| = o_P(1).
\]
Using equation (23), it remains to show that
\[ \max_i \left| \frac{\epsilon_i \tilde{Z}_i^0}{\mathbb{E}[Z^0 | X_{i,1}]} - \frac{\epsilon_i \tilde{Z}_i}{(Z)\tau X_{i,1}/n} \right| = o_P(1) \]

Expanding the terms,
\[
\left| \frac{\epsilon_i \tilde{Z}_i^0}{\mathbb{E}[Z^0 | X_{i,1}]} - \frac{\epsilon_i \tilde{Z}_i}{(Z)\tau X_{i,1}/n} \right| \\
\leq \frac{\epsilon_i \tilde{Z}_i^0 - \epsilon_i \tilde{Z}_i}{\mathbb{E}[Z^0 | X_{i,1}]} + \left| \frac{\epsilon_i \tilde{Z}_i}{(Z)\tau X_{i,1}/n} - \frac{1}{\mathbb{E}[Z^0 | X_{i,1}]} \right| \\
\leq \frac{\epsilon_i \tilde{Z}_i^0 - \epsilon_i \tilde{Z}_i}{\mathbb{E}[Z^0 | X_{i,1}]} + \left( \epsilon_i \tilde{Z}_i - \epsilon_i \tilde{Z}_i^0 \right) \left( \frac{1}{(Z)\tau X_{i,1}/n} - \frac{1}{\mathbb{E}[Z^0 | X_{i,1}]} \right) + \epsilon_i \tilde{Z}_i \left( \frac{1}{(Z)\tau X_{i,1}/n} - \frac{1}{\mathbb{E}[Z^0 | X_{i,1}]} \right). \tag{26} \]

We have shown in Proposition 4 that
\[ \tilde{Z}\top X_{i,1}/n = \mathbb{E}[Z_0^0 X_{i,1}] + o_P(1), \]
and that the latter quantity is bounded away from zero. Furthermore, by assumption \( \max_i |\epsilon_i \tilde{Z}_i^0| \) is bounded. Using equation (26) it suffices to show that
\[ \max_i |\epsilon_i \tilde{Z}_i - \epsilon_i \tilde{Z}_i^0| = o_P(1). \]

To this end note that
\[
\max_i |\epsilon_i \tilde{Z}_i^0 - \epsilon_i \tilde{Z}_i| \\
\leq \max_i |\epsilon_i (\tilde{Z}_i^0 - \tilde{Z}_i)| + \max_i |(\epsilon_i - \epsilon_i)(\tilde{Z}_i - \tilde{Z}_i^0)| + \max_i |(\epsilon_i - \epsilon_i)\tilde{Z}_i^0| \]

Now use the following inequalities
\[
\|\tilde{Z}^0\|_\infty \leq C_3 < \infty \\
\|\tilde{Z} - \tilde{Z}^0\|_\infty = \|\tilde{X}_{-1} \gamma - \tilde{X}_{-1} \gamma^0\|_\infty \\
\leq \|\tilde{X}_{-1} (\gamma - \gamma^0)\|_\infty + \|\tilde{X}_{-1} - \tilde{X}_{-1} \gamma^0\|_\infty \\
\leq \|\tilde{X}_{-1}\|_\infty \|\gamma - \gamma^0\|_1 + \|\tilde{X}_{-1} - \tilde{X}_{-1} \gamma^0\|_\infty \|\gamma^0\|_1 \\
= o_P(1) \\
\|
\tilde{\epsilon} - \epsilon\|_\infty \leq \|\tilde{X}(\tilde{\beta} - \beta^0)\|_\infty + \|\tilde{X} - \tilde{X}^0\|_\infty \beta^0\|_\infty \\
\leq \|\tilde{X}\|_\infty \|\tilde{\beta} - \beta^0\|_1 + \|\tilde{X} - \tilde{X}^0\|_\infty \beta^0\|_1 \\
= o_P(1) \]

Here we used that by a sub-Gaussian tail bound \cite{Boucheron2013}, Chapter 2), (A2) implies \( \|\tilde{X} - \tilde{X}^0\|_\infty = O_P(\sqrt{\log(p)/n}) \). Furthermore, we used that by (A2), \( \|\tilde{X}\|_\infty = O_P(1) \), that by (D3) we have \( \|\tilde{\beta} - \beta^0\|_1 = O_P(1/\sqrt{\log(p)}) \),
by (D2) we have \( \| \hat{\gamma} - \gamma^0 \|_1 = O_P(1/\sqrt{\log(p)}) \) and by assumption \( \| \beta^0 \|_1 = O(1) \) and \( \| \gamma^0 \|_1 = o(\sqrt{n}/\log(p)) \). Hence, we have shown that
\[
\frac{1}{n} \sum_i \xi_i^0 = \xi_0 = o_P(1),
\]
and
\[
\frac{1}{n} \sum_i (\xi_i^0)^2 - \xi_i^2 = o_P(1).
\]
As argued above, this concludes the proof.

8.5.1 Proof of Theorem 3

Proof. Combine Lemma 2 and Lemma 3 with Proposition 5 and Proposition 6. Note that due to assumption (A6), \( u \) is bounded away from zero. Thus,
\[
\hat{u}^2 = 1 + o_P(1),
\]
which completes the proof.

8.6 Proof of Lemma 1

Proof. Define \( \tilde{b}_k = b_k - t E[\partial_t b_k] \) for \( k > 1 \) and \( \tilde{b}_1 = t \). By definition of \( \beta^0 \),
\[
\beta^0 = \arg \min_{\beta} E[(Y - \tilde{X}^0_0 \beta)^2] = \arg \min_{\beta} E[(Y - \sum_k \tilde{b}_k(T, X) \beta)^2].
\]
Now use Lemma 4. This implies that
\[
E[\partial_t E[Y | X = x, T = t]] = E[\sum_k \partial_t \tilde{b}_k \beta^0_k].
\]
Expanding the definition,
\[
E[\partial_t E[Y | X = x, T = t]] = \sum_k (E[\partial_t b_k] - 1_{k > 1} \partial_t t E[\partial_t b_k]) \beta^0_k
\]
\[
= \sum_k (E[\partial_t b_k] - 1_{k > 1} E[\partial_t b_k]) \beta^0_k
\]
\[
= \beta^0_1.
\]
This concludes the proof.

8.7 Proof of Lemma 4

Lemma 4. Define
\[
b^0 = \arg \min_{b \in B} E[(f^0(T, X) - b(T, X))^2],
\]
and
\[
b_* = \arg \min_{b \in B} E[(f_*(T, X) - b(T, X))^2],
\]

31
where \( f_* = -\partial_t \log p(t|x) \). If, \( \mathbb{P} \)-a.s. we have

\[
b^0(T, X) = f^0(T, X) \text{ or } b_*(T, X) = f_*(T, X),
\]
then \( \mathbb{E}[\partial_t f^0] = \mathbb{E}[\partial_t b^0] \).

**Proof.** As \( \mathbb{P} \)-a.s. we have \( b^0 = f^0 \) or \( b_* = f_* \), we also have that \( \mathbb{P} \)-a.s. \( (b^0 - f^0)(b_* - f_*) = 0 \). Hence,

\[
0 = \mathbb{E}[(b^0 - f^0)(b_* - f_*)] = \mathbb{E}[f^0 f_*] + \mathbb{E}[b^0 b_*] - \mathbb{E}[b^0 f_*] - \mathbb{E}[f^0 b_*]
\]

where \( b^0 = f^0 \) or \( b_* = f_* \). If, \( \mathbb{P} \)-a.s. we have \( b^0 = f^0 \) or \( b_* = f_* \), then the residual variance is

\[
\text{Var}((\hat{\beta}_1 - \beta_1)\text{despar}) = \text{Var}((\hat{\beta}_1 - \beta_1)\text{despar}) + \text{Var}(\partial_t f^0) + \text{Var}(\partial_t b^0).
\]

Thus, it suffices to show that

\[
0 = \mathbb{E}[f^0 f_*] - \mathbb{E}[b^0 f_*] = \mathbb{E}[\partial_t f^0] - \mathbb{E}[\partial_t b^0],
\]

completes the proof. \( \square \)

### 8.8 Proof of Lemma 5

**Lemma 5** (Semiparametric efficiency bound). Let the assumptions of Theorem 5 hold. If \( f^0 \in \mathcal{B} \) and \( \partial_t \log p(t|x) \in \mathcal{B} \), then the asymptotic variance of \( \sqrt{n}(\hat{\beta}_1\text{despar} - \beta_1^0) \) is equal to \( \text{Var}(\partial_t f^0) + \text{Var}(\epsilon)\mathbb{E}[(\partial_t \log p(T|X))^2] \).

**Proof.** Sketch. First, by Proposition 4, the asymptotic variance of \( \sqrt{n}(\hat{\beta}_1\text{despar} - \beta_1^0) \) is

\[
\frac{\text{Var}(\epsilon)\text{Var}(\tilde{Z}^0)}{\text{Var}(Z^0)^2} + \text{Var}(\partial_t f^0)
\]

Thus, it suffices to show that

\[
\text{Var}(Z_i^0) = 1/\mathbb{E}[(\partial_t \log p)^2] \text{ for } i = 1, \ldots, n.
\]

Write \( f_* = -\partial_t \log p \). Let us first consider a univariate regression of \( T \) on \( f_* - \alpha \mathbb{E}[\partial_t f_*] \). Then, the residual variance is

\[
\min_{\alpha} \mathbb{E}[(T + \alpha(f_* - \mathbb{E}[\partial_t f_*]))^2] = \min_{\alpha} \mathbb{E}[(T(1 - \alpha \mathbb{E}[\partial_t f_*]) + \alpha f_*)^2]
\]

Expanding, and using that \( \mathbb{E}[T f_*] = 1 \),

\[
\mathbb{E}[(T(1 - \alpha \mathbb{E}[\partial_t f_*]) + \alpha f_*)^2]
= \mathbb{E}[f_*^2](1 - 2\alpha \mathbb{E}[\partial_t f_*] + \alpha^2 \mathbb{E}[\partial_t f_*]^2)
+ 2\alpha(1 - \alpha \mathbb{E}[\partial_t f_*]) + \alpha^2 \mathbb{E}[f_*^2].
\]

Now we can use that \( \mathbb{E}[f_*^2] = \mathbb{E}[\partial_t f_*] \). Taking the derivative with respect to \( \alpha \), we obtain

\[
-2\mathbb{E}[T^2] \mathbb{E}[f_*^2] + 2\alpha \mathbb{E}[T^2] \mathbb{E}[f_*^2]^2 + 2 - 4\alpha \mathbb{E}[f_*^2] + 2\alpha \mathbb{E}[f_*^2]
\]
Setting this term to zero and rearranging

\[-2E[T^2]E[f_*^2] + 2 = 2\alpha E[f_*^2] - 2\alpha E[T^2]E[f_*^2]^2\]

\[= \alpha E[f_*^2](2 - 2E[f_*^2]E[T^2])\]

Thus, the solution is \(\alpha = 1/E[f_*^2]\) and the resulting residual variance is

\[\min_\alpha E[(T + \alpha(f_* - TE[\partial_tf_*]))^2] = E((f_* / E[f_*^2])^2] = 1/E[f_*^2]\]

By definition, \(f_*\) is uncorrelated with \(b_k\) for all \(k > 1\). Thus,

\[\min_{\alpha_1, \ldots, \alpha_p} E[(T - \sum_{k>1} \alpha_k \tilde{b}_k)^2] = 1/E[f_*^2].\]