Semiparametric Estimation and Inference on Structural Target Functions using Machine Learning and Influence Functions

Alicia Curth*
University of Oxford
University of Cambridge
and
Ahmed M. Alaa
UCLA
and
Mihaela van der Schaar
University of Cambridge
UCLA
The Alan Turing Institute
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Abstract

The main goal of this paper is to construct a class of learning algorithms that are of practical value to applied researchers in fields such as biostatistics, epidemiology and econometrics, where the need to learn from incompletely observed information – e.g. in settings involving counterfactual inference, missingness and censoring – is ubiquitous. To do so, we propose a new learning framework which we call ‘IF-learning’ due to its reliance on influence functions (IFs) and generic machine learning. We characterise the fundamental limits of what is achievable in terms of estimation and inference using this learning framework by providing some first provable guarantees for fully nonparametric settings, leveraging both well-known and more recent general results from semiparametric statistics. Our framework is problem- and model-agnostic and can thus be used to estimate a broad variety of target parameters of interest in applied statistics. Namely, we can consider any target function, arising as an identifiable functional from a statistical model, for which an efficient influence function of a population-averaged version exists in analytic form. Throughout, we put particular focus on so-called coarsening at random or doubly robust problems with partially unobserved information. This includes problems of high practical interest such as treatment effect estimation and inference in the presence of missing outcome data. Within this framework, we then propose two general learning algorithms that leverage ideas from the theoretical analysis: the ‘IF-learner’ which relies on large samples and outputs entire target functions without confidence bands, and the ‘Group-IF-learner’, which outputs only an approximation to a function but can give confidence guarantees if sufficient information on coarsening mechanisms is available. We close with a simulation study on inferring conditional average treatment effects and risk ratios in randomized control trials.

From a theoretical viewpoint, to achieve our goal, we need to enable essentially assumption-free and efficient estimation and inference on structural target parameters that are functions of continuous inputs (and hence infinite-dimensional) arising in semiparametric statistical models. Such parameters are not pathwise differentiable and an IF does not exist. As a direct extension of approaches existing for low-dimensional target parameters, we propose a simple solution with intuitive appeal: we propose and define the concept of a pointwise limiting IF to replace the true IF when it does not exist, and suggest learning the pointwise expected value of this limiting uncentered efficient IF from data. Even though we cannot evaluate the expected value of this limiting IF at each point directly, we can approximate it by leveraging generic data-adaptive nonparametric regression methods, and machine learning in particular, to learn it as a pseudo-outcome from data in otherwise standard nonparametric regression. We can then use this idea to characterise the plug-in bias of plug-in estimators for structural target functions whenever the IF of the population-averaged version of the target functional does exist. This allows us to approximately correct for plug-in bias over a full function by pointwise adjustment and to construct estimators that are asymptotically pointwise efficient.

Keywords: Heterogeneous Inference, Counterfactual Inference, Causal Inference, Missing Outcomes, Nonparametric Regression, Efficient Estimation, Randomized Control Trials
1 Introduction

Machine learning is increasingly transitioning from being a tool for prediction to taking over problems of interest classically within the domain of statistics, where the core focus is on estimation and inference instead of prediction. Because of the inherent flexibility of machine learning models and their data-adaptive nature, this has opened up completely new possibilities for estimating possibly very complex structural target functions, instead of focusing only on low-dimensional parameters such as population averages. Arguably the most advanced example of this is the area of causal inference. In the last 10 years, there have been substantial advances in the development of methods for data-adaptive heterogeneous treatment effect estimation from both experimental and observational data using machine learning (see e.g. Bica et al. (2020) for a comprehensive overview). However, with some notable exceptions (e.g. Alaa and van der Schaar (2018a), Athey and Imbens (2016), Athey et al. (2019), Chernozhukov et al. (2018b), Kennedy (2020) and Wager and Athey (2018)) theoretical results making statistical guarantees for estimation and enabling inference are mostly lacking - as is the case for most areas of machine learning (Chernozhukov et al., 2018b).

Data-adaptive, machine-learning-based estimators have potential applications in many fields relying on applied statistics to empirically determine the effects of interventions, policies and treatments, and could be used to shift the focus from average treatment effect estimation towards flexibly investigating heterogeneity of effects across populations. One such potential application, which motivates the authors of this paper, is the move towards more personalised medicine and healthcare. In particular, the discovery of heterogeneous treatment effects in clinical trials could improve both the ability to treat patients and increase mechanistic understanding of underlying diseases. Clinical trials generally take place in small sample regimes, so it is important that estimators be efficient in their use of data. Additionally, regulatory agencies require the quantification of statistical significance of findings and possible bias. If these factors can be accounted for, machine learning has immense potential to change the nature of clinical trials (Zame et al., 2020). There are other applications in healthcare, where given that we can make guarantees on consistency or worst-case performance, it might be enough to give personalised treatment recommendations because models have been trained on large (observational) data sets. Both types
of settings – learning from small experimental samples or large observational samples – require at least some ability to give statistical guarantees on the performance of a learning algorithm.

While the problem of heterogeneous treatment effect estimation has received considerable attention in related literature over the last few years, we take the stance that it is no different than most other problems in applied statistics. As long as a parameter is identifiable from observed data and well-defined in terms of the underlying (unknown) statistical model, statistical estimation of any parameter has the same structure and inherent problems. This indicates that we can separate the issues of identification and estimation completely (van der Laan and Rose [2011]). While it is thus necessary to carefully consider conditions under which treatment effect estimates can be interpreted as causal (such as those developed within the Neyman-Rubin Potential Outcomes framework (Neyman [1923], Rubin [1978]), or the graphical approach coined by Pearl [2009]), from a statistical viewpoint there is, strictly speaking, no need for a separate statistical literature on treatment effect estimation when identifiability is assumed.

With this in mind, we maintain a very general problem set-up in this paper and take a semiparametric, essentially assumption-free approach to estimating functions of continuous inputs that arise as identifiable functionals from statistical models. On the one hand, this class of functions includes more well-studied parameters such as the conditional mean and the conditional outcome probability in standard regression and binary classification problems, respectively. On the other hand, it also includes problems where data is coarsened at random, which have interesting doubly robust structure that we can exploit for efficient and robust estimation. Such coarsening occurs in many scenarios of practical interest to empirical researchers in biostatistics, epidemiology and econometrics (Rubin and van der Laan [2008b]) and typical examples include the estimation of causal parameters such as the conditional average treatment effect (CATE), as well as the estimation of the conditional mean of an outcome when it is missing at random or censored at random. With particular focus on such coarsening problems, we aim to generally characterise the fundamental limits of semiparametric estimation and inference when estimating entire target functions using a generic machine learning algorithm.

We do so by extending the standard notion of plug-in bias correction via influence functions (see e.g. Robins et al. [2017]) from the low-dimensional to the infinite-dimensional
case by learning an approximation to the expected value of a pointwise limiting efficient influence function from data, leading to a new learning framework we call ‘IF-learning’. We then propose two general learning algorithms that leverage these ideas – the ‘IF-learner’ and the ‘Group-IF-learner’ – which are best suited to learn in large and small sample regimes, respectively. After reviewing and developing necessary theory, we finally return to our motivating example of inferring CATE, as well as other causal parameters, from randomised control trials (RCTs) with a simulation study.

1.1 Motivation, Intuition and Implications

This paper builds on a straightforward question related to plug-in estimation. Plug-in estimation exploits that target parameters of interest in applied statistics, such as (conditional) means can almost always be written as a functional of the underlying statistical model (van der Laan and Rose, 2011). Since the statistical model is unknown, we can plug in a data-driven estimate of this model. Years of exciting research by particularly van der Laan and colleagues (see e.g. the exhaustive overviews in van der Laan and Rose (2011) and van der Laan and Rose (2018)) have established the idea that machine learning methods are naturally well-suited for this task. Unfortunately, plug-in estimation can lead to plug-in bias, and the targeted maximum likelihood estimation (TMLE) literature starting with van der Laan and Rubin (2006), as well as Robins and colleagues (e.g. in Robins et al. (2017)) have derived bias correction procedures based on efficient scores and efficient influence functions (EIFs) that can be applied when target parameters are low-dimensional.

Using TMLEs, recent work presented in van der Laan and Rose (2018) has provided new ideas for infinite-dimensional pointwise plug-in bias adjustment based on least favourable parametric sub-models and kernel smoothers. While this allows the authors to make some model-specific, problem-generic guarantees, the proposed approach is limited to the use of nonparametric kernel smoothers and requires familiarity with the specifics of the TMLE framework. In this paper, we are motivated by the intuitive appeal of constructing general ‘off-the-shelf’ machine learning-based plug-in estimators, whose estimates can then be bias-corrected using influence functions. As we discuss later, we believe that the simple intuition of plug-in bias correction via influence functions – a procedure similar to a Newton-Raphson Step – could be of great intuitive appeal for practitioners (which is also the topic of the recent paper Fisher and Kennedy (2020)). Yet, so far, general procedures for plug-in bias
correction using influence functions directly seem to only exist for low dimensional target parameters such as population means. For a schematic overview of the capabilities of approaches in related literature, see Table 1.

| Approach                        | Infinite-dim. | Problem Model | Based on | Plug-in estimation | Inference |
|---------------------------------|---------------|---------------|----------|--------------------|-----------|
| Robins et al. (2017)            |               | Generic, Generic | EIF     | ✓                  | ✓         |
| Wager and Athey (2018)          | ✓             | CATE, Forest  | EE       | ✓                  | ✓         |
| Nie and Wager (2020)            | ✓             | CATE, Generic | Loss     | ✓                  | ✓         |
| Lee et al. (2017)               | ✓*            | CATE, Local-linear | EIF     | ✓                  | ✓         |
| Fan et al. (2020)               | ✓*            | CATE, Local-linear | NO      | ✓                  | ✓         |
| Kennedy (2020)                  | ✓             | CATE, Generic | EIF     | ✓                  | ✓         |
| Athey et al. (2019)             | ✓             | Generic, Forest | EE       | ✓                  | ✓         |
| Chernozhukov et al. (2018b)     | ✓*            | Generic* Generic | EE      | ✓                  | ✓         |
| Foster and Syrgkanis (2019)     | ✓             | Generic, Generic | NO      | ✓                  | ✓         |
| Semenova and Chernozhukov (2020)| ✓*           | Generic, LS Series | NO      | ✓                  | ✓         |
| van der Laan et al. (2018)      | ✓             | Generic, Smoothing | TMLE    | ✓                  | ✓         |
| IF-learning (ours)              | ✓             | Generic, Generic | EIF     | ✓                  | ✓         |

‘Infinite-dim.’ denotes whether the target parameter is infinite dimensional. The column ‘Plug-in estimation’ denotes whether the proposed estimator is a plug-in estimator in the semiparametric sense. The column ‘inference’ indicates whether the authors attempted to characterise conditions under which standard inference, e.g. based on a central limit theorem, is possible. * denotes with additional qualifications/assumptions. CATE denotes Conditional Average Treatment effect. LS denotes Least Squares. We use the following abbreviations for concepts that methods are based on: Estimating Equations (EE), Efficient Influence Function (EIF), Loss-based (Loss), Neyman-Orthogonality (NO), Targeted Maximum Likelihood Estimation (TMLE).

Table 1: Conceptual overview of existing approaches for estimation and inference on infinite-dimensional structural target parameters and their capabilities

We were thus primarily motivated by a very simple question: how can we correct for plug-in bias that arises when we use a generic machine learning model for plug-in estimation of an infinite-dimensional structural target functional – a function – using influence functions? The very unsatisfying technical answer to this question is: we cannot, because infinite-dimensional parameters are not pathwise differentiable (van der Laan et al. 2018), and by extension the efficient influence function and the van Mises expansion, which are needed for plug-in bias adjustment, do not exist. But the intuitive answer a machine
learner would give, which lead to this paper, is a different one: we might not be able to correct for the plug-in bias exactly, but we can approximately do it. That is because there exists a sequence of parameters that approach our target parameter in a pointwise limit, but are pathwise differentiable, so an EIF exists for them. Therefore, instead of using the true EIF (which does not exist) for plug-in bias adjustment, we propose and develop the concept of a pointwise limiting uncentered EIF, whose expected value we can learn from data using pseudo-outcome regression and then subsequently use to approximately adjust entire functions for pointwise first-order plug-in bias. We believe that this relatively simple idea has important implications for both theorists and practitioners:

In theory, this gives us a tool to approximately analyse plug-in bias of entire functions in a pointwise limit, using essentially the same methods that have already been developed for low-dimensional settings. The beauty of the approach lies in the fact that, because the expected value of the limiting sequence that we consider is the target function itself, we can show that estimating this pointwise expectation from data requires no additional assumptions except the standard regularity conditions associated with the nonparametric regression method of choice. By extension, due to the role of the EIF in the characterisation of efficient estimators, we can also use these ideas to characterise efficiency, since estimators built on this limiting EIF are approaching the pointwise efficient estimator and should hence be asymptotically pointwise efficient. Further, because low-dimensional estimators based on EIFs are Gaussian under some regularity conditions, standard inference is possible under some stricter assumptions on the data generating process if we estimate the EIF using neighbourhood smoothers that choose appropriate data-adaptive neighbourhoods. For example, we can feed the pseudo-outcomes that we construct to the random forests proposed in [Wager and Athey (2018)] and [Athey et al. (2019)], which guarantee pointwise asymptotic Gaussianity under some stricter assumptions.

In practice, our approach only requires knowing the analytical form of the EIF for the population average of the target of the problem at hand, which can then be used to construct pseudo-outcomes using the observed data and a plug-in model. For many problems of practical interest, these are given in [van der Laan and Robins (2003)] and/or [Tsiatis (2007)], and can be combined using simple rules of calculus. For example, for most coarsening at random problems, the EIF takes the familiar form of an augmented inverse propensity weighted estimator. Further, we would like to point out that because we rely
on plug-in models and a pseudo-outcome regression stage, we can leverage any existing
model-architecture with minimax performance guarantees for each part of our problem.
As we can show that our approach leads to the asymptotically most efficient estimates
from a semiparametric statistics viewpoint, this implies for practice that the current trend
in statistical machine learning to build model architectures that are tailored to a specific
problem only (e.g. treatment effect estimation) is not always necessary and might actually
do more harm than good if it results in knowledge not being properly shared between
communities. Instead, we conclude that constructing machine learning algorithms that are
provably rate-optimal for any general regression problem might be the best way to truly
advance the field of high-dimensional inference.

1.2 Related literature

We draw our inspiration from ideas proposed in the econometrics, biostatistics, semipara-
metric statistics, causal inference and (statistical) machine learning communities. Due to
the sheer breadth of related topics, this review cannot be exhaustive. Instead, we focus on
key ideas from these fields that shaped the approach presented in this paper. Throughout
sections 4 and 5, we highlight similarities and differences with related literature in more
detail.

We start with the field of econometrics, where the last five years have seen exciting
developments in terms of using machine learning for estimation of and inference on (het-
erogeneous) treatment effects – which motivated much of this paper. The ideas most
relevant to us were shaped by the focus on heterogeneous inference using tree-based meth-
ods in Athey and Imbens (2016), Wager and Athey (2018) and Athey et al. (2019), on the
one hand, and the focus on exploiting generic machine learning methods for the estimation
of structural target parameters in the recent work of Chernozhukov and colleagues (e.g.
Chernozhukov et al. (2018a), Semenova and Chernozhukov (2020) and Chernozhukov et al.
(2020)) on the other. While the former builds on classical ideas from the Neyman-Rubin
Potential outcomes framework (Neyman (1923), Rubin (1978)), developed to maturity for
average treatment effect estimation over the last 30 years in econometrics (Athey et al.,
2017), much of the latter builds on a new property the authors refer to as Neyman or-
thogonality, a notion relying on estimating equations and orthogonal scores (Chernozhukov
et al., 2018a).
The latter also motivated the ‘orthogonal statistical learning’ framework presented in [Foster and Syrgkanis (2019)], which, like our proposed framework, relies on double robustness albeit with a different focus: Instead of enabling high-dimensional parameter estimation and inference (the goal of the present paper), [Foster and Syrgkanis (2019)] focus on using orthogonality to optimally bound excess risk. Thus, our approaches are complementary in nature and connections could be explored in future work. Further, many of the questions we initially tried to tackle in this paper were motivated by the inspiring discussion of the fundamental limits of using generic machine learning for heterogeneous treatment effect inference from experimental studies in [Chernozhukov et al. (2018b)]. We also adapt a proposal of [Chernozhukov et al. (2018b)] (which is itself built on findings of [Genovese et al. (2008)]) – to learn only ‘key features’ of a function instead of the function itself to facilitate inference – for one of our learning algorithms.

In biostatistics, there exist slightly older ideas contained in the more mature literature on targeted learning, which has been focused on developing smart strategies for plug-in estimation using parametric submodels and estimating equations based on influence functions. We took much of the excellent formalisation of problems of interest in statistics from this literature (as well as from the framework of ‘empirical efficiency maximisation’ proposed in [Rubin and van der Laan (2008b)], but did not yet explore further connections between our approach and the broad literature on targeted maximum likelihood estimators (TMLEs) as originally proposed in [van der Laan and Rubin (2006)]. In particular, the ideas presented in [van der Laan et al. (2018)] are inherently related to the infinite-dimensional plug-in bias problem we are trying to solve, and are the closest idea to ours (as we will discuss later). How to combine these ideas would be very interesting to explore in future work. Additionally, while we also do not yet incorporate the idea of super learning ([van der Laan et al. 2007]), this idea seems complementary to our approach.

Instead of the approaches discussed above, we ultimately found the notion of (low-dimensional) plug-in estimation and bias correction as it characteristic for [Robins et al. (2017)]’s work on (higher-order) influence functions the most natural breeding ground for our idea. The simple mathematical intuition and elegance behind using efficient influence functions and Taylor expansion/Newton-Raphson Step-like bias correction procedures naturally gave rise to the idea that we propose in this paper. We also build on the ground-breaking work of Robins and colleagues that lead to the characterisation of many coarsening
at random problems in semiparametric statistics in terms of their efficient influence func-
tions 30 years ago, as summarised in van der Laan and Robins (2003) and Tsiatis (2007).
The recent work of Newey and Robins (2018) on achieving fast rates also seems to be
complementary to the approach presented here, even though we have not yet explored this
idea in detail.

Because of their inherent mathematical elegance, influence functions have recently be-
gun to rise to popularity also in the machine learning community. In Alaa and van der
Schaar (2020a) and Alaa and van der Schaar (2020b), they were used to characterise un-
certainty in deep learning, albeit using a different property of the influence function more
natural to the field of robust statistics originally coined by Hampel (1986). Using the notion
of influence function that we are interested in here, Alaa and van der Schaar (2019)
use influence functions to adjust for plug-in bias when choosing between different methods
for treatment effect estimation via cross-validation. The original questions posed in this
paper were inspired partially by this work.

Finally, our approach relates to some ideas from the causal inference community within
machine learning, due to its focus on building model-agnostic algorithms for CATE estima-
tion, often referred to as meta-learners (e.g. Nie and Wager (2020) and Künzel et al. (2019)).
The recently independently proposed doubly robust CATE meta-learner of Kennedy (2020),
as well as similar two-step estimators presented previously in Lee et al. (2017) and Fan et al.
(2020), are special cases of one of the algorithms that we propose in this paper, as our ‘IF-
learner’ reduces to the same estimator in the context of CATE estimation. A similar idea
to ours in the special case of estimating treatment effects of continuous treatments was also
proposed in Kennedy et al. (2017). Additionally, an important and more general result on
error bounds for pseudo-outcome regression proposed in Kennedy (2020) paved the way for
most of the rate-optimality discussions later in this paper. Kennedy (2020) also discusses
the fundamental limits of CATE estimation in fully nonparametric settings, and a similar
discussion for Bayesian nonparametric settings was presented in Alaa and van der Schaar
(2018a) and Alaa and van der Schaar (2018b).

Overall, to the best of our knowledge, not much existing work has attempted to charac-
terise the fundamental limits of using generic machine learning for estimation and inference
on general structural target functions to the same extent as the quite simple and intuitive
approach we propose allows us to do. We view our approach as a direct extension of the
work of Robins et al. (2017) (and 30 years of preceding work) to the infinite-dimensional case. We see our closest relatives in Athey et al. (2019), Chernozhukov et al. (2018b), Foster and Syrgkanis (2019), Semenova and Chernozhukov (2020) and van der Laan et al. (2018), who all explore slightly different angles to the same problem, as we highlighted in Table 1. Throughout the paper, we therefore highlight parallels with existing ideas and how it might be possible to incorporate them into our framework.

1.3 Contributions

First and foremost, we aim to contribute to the growing and extremely important literature that tries to apply traditional ideas from statistics to the arsenal of data adaptive algorithms popularised in the machine learning community mainly due to their impressive predictive performance, with the ultimate goal to allow these methods to help us answer questions in areas that are currently still restricted to the focus on simple population averages due to the need to quantify uncertainty and bias. We hope to do so in this paper by highlighting the inherent usefulness of the concept of the efficient influence function (even if it does not exist exactly) to characterise the ability of machine learning models (or data-adaptive nonparameteric models more generally) to learn structural target functions of high interest in fields such as biostatistics and econometrics. We make a number of contributions to the literature, which we categorize by the branches of statistics we consider them most relevant for:

1. **Semiparametric statistics:** We extend (i) the notion of plug-in bias removal and (ii) the notion of semiparametrically efficient estimation to entire target functions, by developing the concept of a pointwise limiting efficient influence function to replace the standard definition of the efficient influence function when a parameter is infinite-dimensional. To the best of our knowledge, we are the first to make this proposition. Further, we suggest learning an approximation of the pointwise expected value of this limiting uncentered efficient influence function using pseudo-outcome regression and are the first to show that doing so requires no additional assumptions except for those associated with the regression method of choice. This learnt approximation of the EIF can be used for plug-in debiasing and enables us to find estimates of functions that fulfil well-known notions of efficiency in a pointwise manner (at least asymptotically).
We also characterise the fundamental limits of this approach in fully nonparametric settings using both old and more recent results from related literature (in particular a recent result on pseudo-outcome regression provided by Kennedy (2020)).

2. **Applied statistics:** We provide new insights into what is achievable when learning structural target functions arising in a wide range of problems of interest in applied statistics – namely problems for which the efficient influence function of a population-averaged version of the target parameter does exist in analytic form. The results on nonparametric plug-in estimation and plug-in bias removal that we provide confirm that there is no magical approach that removes all bias from nonparametric learning; rather our analysis confirms that Stone (1980)’s nonparametric minimax rate remains the best that we can do to estimate any function without further assumptions. However, our approach allows us to re-characterise problems that are normally considered harder than simple regression due to the presence of incomplete information, investigate how their difficulty relates to regression and identify scenarios in which we can actually attain oracle rates that match those of standard nonparametric regression. A particularly interesting result of this investigation is that our debiased plug-in estimators in coarsening at random problems can achieve oracle rates whenever sufficient information about the coarsening mechanism is available, which means that incorporating domain knowledge into machine learning can substantially lower the bar on data requirements. We also illustrate this finding in a simple simulation study.

3. **Statistical machine learning:** We use these ideas to propose two new and very general learning algorithms for estimation of infinite-dimensional target parameters from observed data. The first – the ‘IF-learner’ – estimates the full target function using our approximation of the EIF, without the ability to perform inference unless further assumptions are made. The second – the ‘Group-IF-learner’ – only approximates the target function coarsely but allows to perform inference on this approximation by grouping observations by data-adaptively determined heterogeneity groups (inspired by the algorithm presented in Chernozhukov et al. (2018b)). We hope that these very general algorithms can serve as templates for many problems of practical interest, in particular for problems with coarsening at random structure. Therefore, we also plan
to release a ‘sklearn-style’ python implementation of our methods\footnote{Work in progress.} which we also aim to update as we develop our ideas further.

**Structure of the paper** We proceed as follows: In the following section we describe the problem setting that we consider and give an outlook on our approach. Sections 3 and 4 are very theoretical in nature, and are intended to anchor our proposals in classical ideas from semiparametric statistics. Nonetheless, we give specific examples throughout to highlight practical implications. In Section 3 we briefly review key concepts from semiparametric statistics that are necessary for general understanding of the origins of our proposals. Section 4 presents our key theoretical arguments, and highlights some first implications of combining our proposals with existing theoretical results. Sections 5 and 6 contain the content that could be of main interest to practitioners: Section 5 constructs the proposed learning algorithms, and Section 6 contains a simulation study on estimation of different causal parameters from RCT data. Section 7 concludes and highlights avenues of future research within our framework.

## 2 Problem setting and outlook

We discuss a very general problem setting covering many problems of interest in fields such as biostatistics and econometrics. By preserving this generality we are able to maintain a framework that can handle both well-studied standard problems, such as inference on a conditional mean on the one hand, and more intricate problems, such as treatment effect estimation, estimation under missing data and censoring, on the other. Throughout, we give examples to illustrate otherwise abstract concepts, with a focus on treatment effect estimation in randomised control trials (RCTs), the main motivating example of this paper. In this section, we will first characterise the class of problems we are most interested in, then formalise our theoretical framework and finally give an outlook on our proposed approach.

### 2.1 Problem setting

Generally, we assume that we observe a sample of size $n$ of observations $O \sim P_0 \in \mathcal{P}$, where $O$ usually contains some $d$-dimensional covariate information $X \in \mathcal{X}$, some outcome
information and possibly other variables (see below). Our target parameter is an infinite-dimensional functional of the underlying statistical model \( \psi \equiv \psi(\mathbb{P}_0) \), which is most often a function of the form \( \psi(\cdot) \equiv \psi(\mathbb{P}_0)(\cdot) : \mathcal{X} \to \mathbb{R} \).

In the class of coarsening at random problems we are most interested in, we assume some additional structure \([\text{Rubin and van der Laan } 2008b]\). We assume that there exists a true underlying statistical model \( F_0 \in \mathcal{F} \) generating data \( Z = (Y^*, X) \). \( Y^* \) denotes a (possibly multivariate) outcome variable, and the \( d \)-dimensional vector \( X \in \mathcal{X} \) contains observed characteristics associated with an observation. Within this model, our interest lies in making inferences on a structural target function, \( \psi : \mathcal{X} \to \mathbb{R} \), of the form

\[
\psi(x) = \mathbb{E}_{F_0}[h(Y^*)|X = x]
\]

i.e. the conditional expectation of a function \( h(\cdot) \) of the outcome variable \( Y^* \).

Unfortunately, in most scenarios of general interest in this paper, we do not observe \( Y^* \), but instead obtain information only on a coarsened variable \( Y = C(Y^*, C) \). Here, \( C \) is a coarsening variable determining what we observe (and the mapping \( C \) is deterministic). Such coarsening mechanisms are prevalent in settings involving, for example, counterfactual inference, missing data or censoring. In high information settings (e.g. learning from experimental data), we assume that the stochastic coarsening mechanism \( C|X \sim G_0(\cdot) \) is known or easily estimable, while in low information settings (e.g. learning from observational data) we leave it completely unspecified.

Thus, instead of \( \{Z_i\}_{i=1}^n = \{(Y_i^*, X_i)\}_{i=1}^n \) we observe a random sample \( \{O_i\}_{i=1}^n = \{(Y_i, X_i, C_i)\}_{i=1}^n \), where \( Y_i \) is the observed coarsened variable (and hence could also contain no information), drawn i.i.d. from a probability distribution \( O \sim \mathbb{P}_0(\cdot) = \mathbb{P}_{F_0,C_0}(\cdot) \), determined by the statistical model \( F_0 \) and the coarsening mechanism \( G_0 \). While we do not observe \( Y^* \), we make the assumption that we can nonetheless identify \( \psi(x) \) from the observed data. We thus consider problems in which we can construct signals \( \tilde{Y} = f(O) \), such that \( \mathbb{E}_{\mathbb{P}_0}[\tilde{Y}|X = x] = \psi(x) \) (at least asymptotically). Fortunately, as discussed above, once identification of the target parameter is guaranteed, all remaining problems are statistical in nature and concern only estimation of the target.

Before we move on, we will give some examples to illustrate the wide range of problems our framework allows us to consider. We begin with standard regression and classification
problems, because they are trivial examples of coarsening at random problems (as there is no coarsening). Further, the main motivating example in this paper, which is also discussed in more depth in section 6, is discovering evidence for heterogeneous treatment effects in a RCT. We maintain this example throughout as it is not only well-known and of high interest in many communities but also allows us to highlight the value of having knowledge of the coarsening mechanism (here: treatment assignment mechanism). Finally, we give two more examples that we will not treat in detail but present here to illustrate the sheer breadth of problems that our proposed framework can incorporate.

**Example 2.1. Standard regression and binary classification** The most simple example for a such a target function that we could be interested in is that of nonparametric regression, where we try to estimate the conditional mean \( \psi(x) = E_{P_0}[Y|X=x] \) from data without making any assumptions on the data-generating process. Here, \( O_i = Z_i = (Y_i, X_i) \), since there is no coarsening, i.e. \( \tilde{Y} = Y \). The same holds for the conditional success probability \( \psi(x) = P_0(Y=1|X=x) = E_{P_0}[1\{Y = 1\}|X = x] \) in binary classification.

**Example 2.2. Motivating example: Conditional Average Treatment Effects in RCTs** Assume that we have a binary treatment \( W \in \{0, 1\} \), which is assigned according to a known propensity score \( \pi_0(x) = P_0(W = 1|X = x) \), and we are interested in an individualised treatment effect: the difference between the potential outcomes \( Y_i(0) \) if individual \( i \) does not receive treatment \( (W_i = 0) \) and \( Y_i(1) \) if treatment is administered \( (W_i = 1) \). If we had access to both potential outcomes, then the individual treatment effect \( Y_i(1) - Y_i(0) \) would be a natural outcome of interest. However, by the fundamental problem of causal inference, we only ever observe one of the two potential outcomes. Therefore, the majority of existing literature focuses on the conditional average treatment effect (CATE), \( \tau(x) = E[Y(1) - Y(0)|X=x] \), the expected treatment effect for an individual with covariate values \( X = x \).

In this case, \( Y^* = (Y(0), Y(1)), h(Y^*) = Y(1) - Y(0) \) and \( \psi(x) = \tau(x) \). We observe only \( Y = WY(1) + (1-W)Y(0) \), the potential outcome associated with the received treatment, so the treatment indicator \( W \) acts as the coarsening variable. Under some additional assumptions (discussed in section 6), we can construct an unbiased Horvitz-Thompson-type signal \( \tilde{Y} = (\frac{W}{\pi_0(X)} - \frac{(1-W)}{\pi_0(X)})Y \) \( \text{(Horvitz and Thompson, 1952)} \) for the estimand of interest from the observed data – which, as we will illustrate throughout, is not the best way of estimating the CATE.
Example 2.3. Other causal parameters in RCTs While much of the causal inference literature in machine learning concentrates on (C)ATE, it is not actually the only parameter of practical interest (Rubin and van der Laan, 2008b). For example, if we let $\mu_0(x)$ and $\mu_1(x)$ denote the expected values of the potential outcomes, and the potential outcomes are binary, i.e. $Y(w) \in \{0,1\}$, then the relative risk $f_{RR}(\mu_0(x), \mu_1(x)) = \frac{\mu_1(x)}{\mu_0(x)}$ or the odds ratio $f_{OR}(\mu_0(x), \mu_1(x)) = \frac{\mu_1(x) / (1-\mu_1(x)}/\mu_0(x) / (1-\mu_0(x))$ are often the parameters of natural interest in RCTs.

Example 2.4. Missing outcome data Another well-known example of coarsening at random is that of missing outcome data (e.g. in a clinical trial). Here, we observe $O_i = (A_i, Y_i, A_i, X_i)$, where $A_i \in \{0,1\}$ is a missingness indicator and $Z_i = (Y_i, X_i)$. If we know that data is missing at random, i.e. the probability of missingness $\pi_0(x) = P_0(A = 1|X = x)$ is determined only by covariate information, then $\psi(x) = E_{P_0}[Y|A = 1, X = x]$, the expected outcome of those subjects with missing data, would be the functional of interest. Clearly, this problem has a structure very similar to that of treatment effect estimation, and also admits a Horvitz-Thompson-type signal $\tilde{Y}$. A similar argument holds also for the expected outcome value of censored outcomes.

2.2 Theoretical framework

We approach the problem from a semiparametric statistics viewpoint, because we wish to make little to no parametric assumptions on the data generating distribution $P_0$, which in reality could be arbitrarily complex. Thus, we wish to impose (parametric) restrictions only when we are sure that they are a feature of the underlying problem. Our interest in $P_0$ is purely motivated by the target functional $\psi = \psi(P_0)$ – all other components of $P_0$ are nuisance parameters to us. Some of these nuisance parameters are more important for estimation of $\psi$ than others, sometimes we refer to those parameters that are needed for (efficient) inference on $\psi$ as $Q \equiv Q(P_0)$. For example, $Q$ often includes parameters such as conditional mean functions, while the distribution of zero-mean error terms can often be completely ignored.

In classical semiparametric statistics, the target parameter is typically very low-dimensional – e.g. a one-dimensional population average such as the average treatment effect. In stark contrast to this, recall that our target parameter is itself a function $\psi : X \rightarrow \mathbb{R}$ and hence infinite-dimensional. We assume continuous covariates throughout, yet our approach is
also of practical use if covariates are discrete but high dimensional. In the settings that we consider, \( \Psi = \mathbb{E}_{X \sim \mathbb{P}_0[\psi(x)]] \), the population average of our target parameters, has been well-studied. Estimation of and inference on \( \psi \) itself is still very much a topic of active research.

Unfortunately, there are some fundamental limits to what we can achieve in terms of estimating \( \psi \) using frequentist non- or semiparametric statistics. Even in arguably the simplest setting, assumption-free nonparametric regression (i.e. no coarsening), Chernozhukov et al. (2018b) point out that the minimax rate of convergence of nonparametric regression is \( n^{-\frac{p}{p+d}} \) (Stone, 1980), where \( p \) is the number of continuous and bounded derivatives of the function \( f(x) \) we are trying to learn and \( d \) is the dimension of \( x \). Thus, for fixed \( p \) and \( d \) small but increasing with \( n \), e.g. \( d \geq \log(n) \), there exists no minimax consistent estimator of \( f(x) \) in general (Chernozhukov et al., 2018b). Further, the minimax rate makes clear that the finite sample performance of nonparametric estimators deteriorates rapidly with increasing dimension \( d \) for \( n \) fixed. Inference on generic nonparametric function estimates is even more difficult – in fact, adaptive confidence sets do not exist even for low dimensional nonparametric problems (Genovese et al., 2008), as bias tends to dominate sampling error (Chernozhukov et al., 2018b).

Motivated by these ideas, we aim to characterise the limits of estimating general structural target functions using generic nonparametric machine learning methods (for which we only need to be able to give minimax performance guarantees), and use our findings to construct algorithms that are of practical value to applied researchers.

2.3 Outlook: IF-learning

The fundamental limits of nonparametric regression discussed above highlight that we cannot have it all: assumption-free estimation and inference on the full function \( \psi \) is impossible, and particularly so with increasing dimension \( d \). Therefore, we have to give something up: we cannot have the ability to estimate an entire function, the ability to perform inference on the entire function, the ability to consider high-dimensional data, and the ability to make no assumptions all simultaneously. As we illustrated in the introduction, which of these abilities we are willing to give up may highly depend on the context. For example, when estimating treatment effects of new drugs in clinical trials with small sample sizes, it might be much more important to retain the ability to perform valid statistical
inference than to be able to make individualised treatment recommendations, while the opposite may be true when building an in-hospital decision support system for daily practice trained on a large observational data-set.

In this paper, we develop a new learning framework we call ‘IF-learning’, relying on efficient influence functions in their capacity to enable plug-in bias removal and efficient estimation, which we exploit to facilitate estimation and inference on high-dimensional parameters using generic machine learning methods. Within this framework, we propose two first learning algorithms that consider the two natural settings outlined above. The two settings – access to experimental and observational data – differ not only in the amount of available data (sample size), but also in the amount of information available to the statistician: In experimental settings, some features of underlying the statistical model $P_0$ are more likely to be known, transforming our fully nonparametric problem to a proper semiparametric problem. For example, in a RCT, the subset of variables affecting treatment assignment, the parametric form of the random selection mechanism, or even the exact propensity score may be known, which is less likely to be the case in observational studies. In this paper, we therefore propose one learning algorithm for each setting:

1. The ‘IF-learner’ for low-information, high sample size settings, in which we have access to large amounts of possibly low-quality data (e.g. unknown extent of selection on observables in treatment effect estimation), and rely on the assumption that the data-set is large enough such that finite sample bias is negligible. The proposed learning algorithm, the ‘IF-learner’ outputs an estimate of a full function that allows for individualised predictions – for which statistical guarantees cannot be given beyond a minimax convergence rate, unless stricter assumptions are made. In this setting, we are bound to using data-sets that are not ‘too high-dimensional’, i.e. $d < \log(n)$.

2. The ‘Group-IF-learner’ for high-information, low sample size settings, in which we have access to small amounts of high-quality data, e.g. from a RCT in which propensity scores are known. There, we cannot rely on asymptotic rate results only, however, due to information on e.g. selection mechanisms, we can obtain unbiased estimates for which standard inference is possible if we focus on a lower-dimensional approximation of our target. This algorithm outputs group-averaged target estimates with standard confidence intervals for adaptively determined heterogeneity groups.
To enable consistent estimation of high-dimensional functionals in settings where not all data is observed, we first need to develop simple strategies for plug-in bias removal based on pseudo-outcome regression. This is the main focus in the theoretical part of this paper (Sections 3 and 4). We also rely on semiparametric efficiency theory to construct estimators that are approximately efficient. For both, we make heavy use of a limiting approximation to the expected value of the uncentered efficient influence function of our target parameter $\psi$, concepts that we will introduce and define in the following two sections.

3 Theoretical Background

We begin by briefly reviewing key concepts and strategies used in semiparametric statistics to construct estimates of low-dimensional target parameters. In the remainder of this paper, we will build on and generalise these ideas to high-dimensional target parameters. We refer the reader to van der Vaart (2014), Kennedy (2016) and particularly Fisher and Kennedy (2020) for excellent introductions to influence functions and related concepts, and how these arise in the class of problems that we are most interested in. For more exhaustive treatment of existing approaches in semiparametric statistics, tailored mainly to applications in biostatistics, we refer to Tsiatis (2007), van der Laan and Robins (2003) and van der Laan and Rose (2011).

The concepts of main interest in this paper are the influence functions (IF) and, in particular, the efficient influence function (EIF) of a target parameter. Influence functions arise naturally in multiple areas of statistics, most prominently in the area of robust statistics, where the influence function of an estimator originally measures the robustness of an estimator to outliers (Hampel, 1986). This is not the use case of interest for influence functions in this paper. Instead, we build on influence functions as they are used in semiparametric statistics, namely in the context of (i) plug-in estimation and plug-in bias correction and (ii) characterisation of asymptotically efficient estimators. We will first introduce influence functions generally, and will then discuss these two aspects in turn. As is standard in most of the literature, unless stated otherwise, we will assume in this section the simple problem in which our target is a population average $\Psi(\mathbb{P}_0) \equiv \Psi = \mathbb{E}_{x \sim \mathbb{P}_0}[\psi(x)]$. 

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3.1 Influence functions

It is beyond the scope of this paper to explain how influence functions are derived using the geometrical intuition of tangent spaces, for a comprehensive introduction we refer to [Tsiatis (2007)]. Instead, we give an intuitive introduction relating influence functions of statistical parameters to derivatives of analytical functions, inspired by the discussion in [Fisher and Kennedy (2020)].

For a distribution $\mathbb{P}$ with density $p$ we can define a distribution $\mathbb{P}_\epsilon$ with density $p_\epsilon$ given by

$$p_\epsilon(o) = (1 - \epsilon)p(o) + \epsilon \tilde{p}(o)$$  \hspace{1cm} (2)

with $\tilde{p}(o)$ the density of another distribution $\tilde{\mathbb{P}}$ and $\epsilon$ small. Since our target parameter $\Psi(\mathbb{P})$ is a functional of a distribution, we can use $\mathbb{P}_\epsilon$ to evaluate the sensitivity of our target $\Psi$ to small changes along a path $\{\mathbb{P}_\epsilon\}_{\epsilon \in [0,1]}$ where $\epsilon$ at the end points 0 and 1 reduces $\mathbb{P}_\epsilon$ to the original distributions $\mathbb{P}$ and $\tilde{\mathbb{P}}$, respectively.

Now assume we have a given plug-in model $\tilde{\mathbb{P}}$ for $\mathbb{P}$ and we would like to use the intuition of the path along small changes $\epsilon$ defined above to correct the bias induced by evaluating $\Psi$ at the wrong distribution $\tilde{\mathbb{P}}$ instead of $\mathbb{P}$. If $\Psi$ was an analytical function, we would do so by using a Newton-Raphson step or a first-order Taylor-expansion (which would leave us with the same result). It turns out that plug-in bias correction for functionals can be handled using the exact same idea, and we only need a functional generalization of a derivative to essentially use the same procedures. This is the influence function.

**Definition 1. Influence Function** (adapted from [Fisher and Kennedy (2020)])

For a given functional $\Psi$, an influence function for $\Psi$ is any function $\dot{\Psi}$ satisfying

$$\frac{\partial \Psi(\mathbb{P} + \epsilon(\tilde{\mathbb{P}} - \mathbb{P}))}{\partial \epsilon} \bigg|_{\epsilon=0} = \int \dot{\Psi}(O, \mathbb{P})(d\tilde{\mathbb{P}} - d\mathbb{P})$$  \hspace{1cm} (3)

and

$$\int \dot{\Psi}(O, \mathbb{P})d\mathbb{P} = \int (D_{\Psi,\mathbb{P}}(O) - \Psi)d\mathbb{P} = 0$$  \hspace{1cm} (4)

Property (4) implies that the uncentered influence function $D_{\Psi,\mathbb{P}}(O)$ is unbiased for $\Psi$, i.e. that $\int D_{\Psi,\mathbb{P}}(O)d\mathbb{P} = \Psi$. This property is the basis for the construction of regular and asymptotically linear (RAL) estimators based on influence functions in semiparametric
statistics (see e.g. Tsiatis (2007)). In practice, \( \dot{\Psi} \) need not be unique – if restrictions are placed on the underlying model the number of influence functions is infinite. In fully nonparametric models, the influence function is unique and (if it exists) is referred to as the \textit{efficient influence function} because it can be used to construct the most efficient semiparametric RAL estimator of \( \Psi \). Because of this property, we will only consider efficient influence functions in this paper, and sometimes drop the term efficient for brevity. Finally, by extension of the intuition of derivatives of analytical functions, many of the standard rules of calculus such as the chain- and product rules hold for influence calculus, implying that influence functions for some seemingly complex parameters can be built up from simple building blocks. The simulation study contained in section 6 will highlight one such example.

Unfortunately, infinite-dimensional parameters in nonparametric models, e.g. parameters that arise as functions of continuous variables, are not pathwise differentiable, which is tied to the intuition that singletons are not \( \mathbb{P}_0 \)-measurable (van der Laan et al., 2018). Therefore, influence functions are not defined for our problems of interest. This is the main topic of this paper, which we will revisit in section 4. Before we move on, we give two important examples of influence functions that we will use throughout this paper.

\textbf{Example 3.1. Conditional mean} In generic (unrestricted) nonparametric regression, the efficient influence function of \( \Psi \), for \( \psi(x) = \mathbb{E}_\mathbb{P}[Y|X = x] \), is \( \dot{\Psi}(O; \mathbb{P}) = Y - \Psi \). That is \( D_{\Psi, \mathbb{P}}(O) = Y \) is independent of nuisance parameters.

\textbf{Example 3.2. Average treatment effect} For the average treatment effect, \( \Psi = \mathbb{E}_{\mathbb{P}_0}[\tau(x)] \), the uncentered efficient influence function is given by

\[
D_{\Psi, \mathbb{P}}(O) = \left( \frac{W}{\pi_0(X)} - \frac{(1 - W)}{1 - \pi_0(X)} \right) Y + \left[ \left( 1 - \frac{W}{\pi_0(X)} \right) \mu_1(x) - \left( 1 - \frac{1 - W}{1 - \pi_0(X)} \right) \mu_0(X) \right]
\]

with \( \mu_w(x) = \mathbb{E}_{\mathbb{P}_0}[Y(w)|X = x] = \mathbb{E}_{\mathbb{P}_0}[Y|W = w, X = x] \). This has the same form as the well-known augmented inverse propensity weighted (AIPW) estimator (Robins and Rotnitzky, 1995).
3.2 Plug-in estimation and correcting for plug-in bias

These influence functions naturally arise in plug-in estimation. Plug-in estimation exploits that Ψ is a functional mapping a statistical model \( P \in \mathcal{P} \) to Ψ(\( P \)) ∈ \( \mathbb{R} \). If we can construct an estimator \( \hat{P} \) of \( P_0 \) from a sample \( D = \{O_i\}_{i=1}^n \sim P_0 \), we could estimate \( \Psi(P_0) \) by \( \Psi(\hat{P}) \). Unfortunately, such plug-in estimators often inherit considerable first-order bias from the nonparametric estimators \( \hat{Q} \) contained in \( \hat{P} \), i.e. the estimators for high-dimensional nuisance parameters \( Q(P_0) \) needed for estimation of \( \Psi \). Intuitively, this is the case because \( \hat{P} \) is often not well-targeted towards estimating \( \Psi \) optimally, and instead estimates the components \( Q(P_0) \) too well. Since \( \Psi(P_0) \) and \( \Psi(\hat{P}) \) are evaluations of the same functional at different inputs, we can conceptualise this bias using a generalisation of the Taylor expansion to functionals, the van Mises expansion of Ψ(\( P \)):

\[
\Psi(\hat{P}) - \Psi(P_0) = \int \dot{\Psi}(O; \hat{P})d(\hat{P} - P_0) + R_2(\hat{P}, P_0) = -\int \dot{\Psi}(O; \hat{P})dP_0 + R_2(\hat{P}, P_0) \tag{5}
\]

where \( R_2 \) is a second order remainder. If it exists, the EIF discussed in the previous section satisfies \[\text{[5]}\] with lowest variance, so we will generally consider \( \dot{\Psi}(O; \hat{P}) = D_{\Psi,\hat{P}}(O) - \Psi \). Equation \( \text{[5]} \) suggests that we can approximately remove the first-order bias by using the following adjusted estimator:

\[
\tilde{\Psi}(\hat{P}) = \Psi(\hat{P}) + \frac{1}{n} \sum_{i=1}^n \dot{\Psi}(O_i; \hat{P}) = \frac{1}{n} \sum_{i=1}^n D_{\Psi,\hat{P}}(O_i) \tag{6}
\]

where the second equation follows from the expression for the EIF.

**Remark 3.1.** Here, we consider only only first order bias adjustment. If the second-order remainder decays too slowly, we can do better in theory by also using higher-order influence functions [Robins et al., 2008]. In practice, higher-order influence functions, while correcting for higher-order bias, can also add substantial variance in finite samples [van der Vaart, 2014].

3.3 Inference on plug-in estimators

From equation \[\text{[5]}\] and \[\text{[6]}\] it becomes obvious that we can write the plug-in bias-adjusted estimator \( \tilde{\Psi} \) as a regular asymptotically linear (RAL) estimator obtained from a sample of
size $n$, i.e.

$$\sqrt{n}(\hat{\Psi} - \Psi) = \frac{1}{\sqrt{n}} \sum_{i=1}^{n} D_{\Psi,\hat{P}}(O_i) + o_{P_0}(1)$$

(7)

if (i) $\sqrt{n}R_2(\hat{P}, P_0)$ is negligible ($o_{P_0}(1)$) and (ii) the finite sample bias induced in $\Psi$ by approximating $P$ with $\hat{P}$ is negligible. (i) can be achieved if $O_{P_0}(R_2(\hat{P}, P_0)) = n^{-1/2}$, whereas (ii) needs that $\hat{\Psi}(\hat{P})$ is fit on an independent sample to that used for estimating $\hat{P}$ (unless we are restricting our attention to model classes $P$ that are Donsker) and that $\Psi(\hat{P})$ is consistent for $\Psi(P_0)$ in $l_2$-norm. If these conditions hold, then $\hat{\Psi}(\hat{P})$ is asymptotically unbiased and $\sqrt{n}(\hat{\Psi} - \Psi)$ is asymptotically normal with mean zero and minimum attainable variance (the semiparametric equivalent of the parametric Cramer-Rao Lower bound).

4 Efficient estimation and inference on structural target functions

In this section, we first introduce our main theoretical contributions: developing the concept of a pointwise limiting uncentered efficient influence function and characterising assumptions necessary to learn it from data. Then, we compare our proposal to approaches in related literature, and finally provide some first provable guarantees leveraging existing results from semiparametric statistics. Throughout, we illustrate the practical implications of our suggestions.

4.1 The expected value of the pointwise limiting uncentered efficient influence function

This paper is based on the following, very intuitive idea: Although the efficient influence function (EIF) does not exist for infinite-dimensional target parameters (van der Laan et al., 2018), we propose to construct a limiting EIF by considering pointwise limits over influence functions of parameters which are pathwise differentiable. Throughout, we will use only the uncentered EIF $D_{\Psi,\hat{P}}$ of the population parameter $\Psi$ (since the centering term is not needed for estimation because it cancels in equation (6)) but will often refer to it as
EIF for brevity.

To illustrate our idea (and for the grouping-based learning algorithm discussed in section 5.2), we begin by characterising the EIF and efficient estimators of partition-based group-averaged targets. We loosely define a (fixed) partition of the input space $\mathcal{X}$ as $\pi = \{A_k^\pi \subset \mathcal{X} : A_k^\pi \cap A_j^\pi = \emptyset \forall k \neq j, \cup_{k=1}^{K^\pi} A_k^\pi = \mathcal{X}\}$ for some $K^\pi \geq 1$ and, for ease of exposition, let $\pi$ be any type of connected partition, e.g. those consisting of voronoi cells.

We first characterise the semiparametrically efficient estimator of the target within the $k^{th}$ cell of our partition, $\Psi_k^\pi = \mathbb{E}_{P_0}[\psi(x)|x \in A_k^\pi]$.

**Proposition 1.** If $\hat{\Psi} = \frac{1}{n} \sum_{i=1}^{n} D_{\Psi,P_0}(O_i)$ is the asymptotically efficient estimator for the population mean $\Psi(P_0) = \mathbb{E}_{P_0}[\psi(x)]$ based on the efficient influence function of the form $D_{\Psi,P_0}(O_i) - \Psi(P_0)$, then $\hat{\Psi}_k^\pi = \frac{1}{|A_k^\pi|} \sum_{i:X_i \in A_k^\pi} D_{\Psi,P_0}(O_i)$ is the asymptotically efficient estimator for $\Psi_k^\pi$.

**Proof.** The proof is very straightforward and can be obtained using either influence function calculus or by contradiction using the efficient estimator of the population average of $\psi$. We state both proofs in the Appendix, since they motivated the main idea of this paper. $\Box$

Based on this result, we can construct a target parameter that is arbitrarily close to $\psi(x)$ but for which both the EIF and a RAL efficient estimator do exist. For any $x \in \mathcal{X}$, if we define a sequence of cells $A_x^\epsilon = [x-\epsilon, x+\epsilon]$, indexed by $\epsilon > 0$, the EIF of the target parameter $\Psi_{x,\epsilon} = \mathbb{E}_{P_0}[\psi(x)|x \in A_x^\epsilon]$ does exist for all $\epsilon > 0$ and the uncentered EIF is given by

$$D_{A_x^\epsilon,P_0}(O) = \frac{\mathbb{1}\{X \in A_x^\epsilon\}}{P_0(X \in A_x^\epsilon)} D_{\Psi,P_0}(O)$$

resulting in efficient estimator $\hat{\Psi}_{x,\epsilon} = \frac{1}{|A_x^\epsilon|} \sum_{i:X_i \in A_x^\epsilon} D_{\Psi,P_0}(O_i)$.

As we let $\epsilon$ go to zero, the pointwise limit of the EIF is undefined since the term $\frac{\mathbb{1}\{X \in A_x^\epsilon\}}{P_0(X \in A_x^\epsilon)}$ in (8) is not well-behaved – because singletons are not $P_0$-measurable. However, the efficient estimator $\hat{\Psi}_{x,\epsilon}$ does have a pointwise limit if $\exists \epsilon \in \{1, \ldots, n\} : X_i = x$ which is $\hat{\Psi}_{x,0} = \frac{1}{|\{i:X_i = x\}|} \sum_{i:X_i = x} D_{\Psi,P_0}(O_i)$ (and is undefined otherwise). Further, since estimators based on the uncentered influence function are unbiased for their target, this indicates that, if there is a value $X_i \in \{1, \ldots, n\} : X_i = x$ in our data-set, and $P_0$ is known, then $\mathbb{E}_{P_0}[\hat{\Psi}_{x,0}] = \mathbb{E}_{P_0}[D_{\Psi,P_0}(O)|X = x] = \psi(x)$. This naturally leads to the idea to construct an approximate limiting notion of an efficient influence function. We define the concept
of the pointwise limiting uncentered efficient influence function of an infinite-dimensional target parameter that arises as a function of continuous inputs $X$ as follows:

**Definition 2. Pointwise limiting uncentered efficient influence function**

We define a function $D_{\psi(x),\mathbb{P}}(O) : x \mapsto \mathbb{R}$ to be the pointwise limiting uncentered efficient influence function for $\psi(x)$ (where $\psi \equiv \psi(\mathbb{P})$ and $\psi(x) : \mathcal{X} \to \mathbb{R}$ is a function of continuous inputs) if it can be written as the product of the uncentered efficient influence function $D_{\Psi,\mathbb{P}}(O)$ of the population average $\Psi(\mathbb{P}) = \mathbb{E}_{X \sim \mathbb{P}}[\psi(X)]$, and an indicator function $1\{X = x\}$. Thus, we define $D_{\psi(x),\mathbb{P}}(O) := 1\{X = x\}D_{\Psi,\mathbb{P}}(O)$, which has the immediate consequence that $D_{\psi(x),\mathbb{P}}(O)$ is also unbiased for $\psi(x)$ since:

$$
\mathbb{E}_{\mathbb{P}}[D_{\psi(x),\mathbb{P}}(O)] = \mathbb{E}_{\mathbb{P}}[D_{\Psi,\mathbb{P}}(O)|X = x] = \psi(x)
$$

Relative to the true limit over existing uncentered influence functions $\lim_{\epsilon \to 0} \frac{1\{X \in A_\epsilon^x\}}{\mathbb{P}(X \in A_\epsilon^x)} D_{\Psi,\mathbb{P}}(O)$, we have thus replaced the ill-behaved term $\frac{1\{X \in A_\epsilon^x\}}{\mathbb{P}(X \in A_\epsilon^x)}$ with its expectation 1 and an indicator $1\{X = x\}$.

This new definition thus replaces Definition 1 given in Section 3.1 (which holds only for finite-dimensional parameters) in the case of infinite-dimensional target parameters. If we had oracle knowledge of $\mathbb{P}_0$, we could use this idea to construct $\psi(x)$ by pointwise estimation. However, the pointwise efficient estimator which estimates $\mathbb{E}[D_{\psi(x),\mathbb{P}_0}(O)]$ by the empirical average over all observations with $X = x$ clearly is not feasible if $X$ is continuous. This can even be the case if Definition 1 holds – namely when $X$ is discrete but high dimensional. However, we can leverage ideas from nonparametric statistics and machine learning to **learn** the pointwise expected value from data – if we could evaluate the analytical form $D_{\psi(x),\mathbb{P}_0}(O)$ for each point in our data-set and regress it on $X$, we could approximate its expected value, $\psi(x)$ itself, by using standard nonparametric regression methods.

Below, we show that approximating the expected value of the pointwise limiting EIF using nonparametric regression is not only intuitively appealing, but also mathematically reasonable – because we can estimate the expected value of this function in finite samples under the same conditions necessary to estimate $\psi(x)$ itself from the data. This means that, in an oracle setting, our approach requires no assumptions that the statistician was not originally willing to make to estimate $\psi(x)$ itself. For example, if one assumes that the
parameter of interest can be estimated at nonparametric minimax rates, then so can the expected value of our pointwise limiting uncentered efficient influence function, and the same argument holds for faster rates.

**Theorem 1. Learning the expected value of the pointwise limiting uncentered efficient influence function**

Given access to an oracle with knowledge of the true \( P \) and a learning algorithm \( A \), we can learn the expected value of the approximate limiting influence function \( D_{\psi(x),P}(O) \) from data at the minimax rate associated with \( A \) under no additional assumptions than the standard assumptions associated with standard regression using \( A \).

If \( A \) is a generic nonparametric regression estimator, and \( \psi(x) \) is \( p \)-smooth, then the convergence rate of this oracle regression is Stone (1980)'s minimax rate \( n^{-p/(2p+d)} \), under the standard regularity conditions (sketched in appendix 8.2).

**Proof.** Since \( E_P[D_{\psi(x),P}(O)] = E_P[D_{\psi,P}(O)|X = x] = \psi(x) \), and we are in an oracle setting, i.e. have knowledge of the model \( P \), we can evaluate \( D_{\psi(x),P}(O_i) \) from data whenever we have an observation \( O_i \) for which \( X_i = x \). Therefore, we can think of \( D_{\psi} \equiv D_{\psi(x),P}(O) \) as a pseudo-outcome in nonparametric regression with conditional mean \( \psi(x) \) and some random error. Thus, if we assume that \( \psi(x) \) is estimable from the data using regression methods \( A \), then it must be possible to do so using the ‘canonical’ pseudo-outcome \( D_{\psi} \).

For generic nonparametric regression, the assumptions that need to be placed on the underlying statistical model \( P_0 \) include some regularity conditions on the fixed function \( \psi(x) \), and the main requirement for the random pseudo-outcomes \( D_{\psi} \) are bounded first and second moments. For a sketch of the full conditions as originally characterised by Stone (1980), refer to appendix 8.2.

As this estimator is also infeasible due to a lack of oracle knowledge of \( P_0 \) in practice, we propose a two-stage estimator which first estimates a plug-in model \( \hat{P} \) from the data, and then (analogously to the low-dimensional setting discussed in section 3.2) removes the plug-in bias in \( \psi(\hat{P}) \) by learning the expected value of the EIF, through regression of \( D_{\psi,\hat{P}}(O) \) on \( X \). As we will show in section 4.3, to be able to make guarantees on this estimator, we will have to perform the two steps on two separate samples, which is intuitively obvious due to the inherent risk of overfitting and follows by direct extension from the low-dimensional case discussed in section 3.3.
Before we illustrate the power of this very intuitive and simple idea by highlighting how it can be combined with existing results from semiparametric statistics to allow for point-wise consistent estimation and inference in section 4.3, we briefly compare our estimation procedure to existing approaches for estimation of infinite-dimensional target parameters in semiparametric statistics.

4.2 Relationship to existing work

Analysing the limits of estimation of infinite-dimensional structural target parameters – functions of continuous inputs – has received little attention in related literature so far. The only other work we are aware of that actively tries to use ideas from semiparametric statistics to enable estimation and inference on general infinite-dimensional targets using plug-in debiasing methods is van der Laan et al. (2018). They suggest a targeted maximum likelihood learning approach that approximates the target parameter by a family of pathwise differentiable target parameters, namely kernel smoothed versions of $\psi(x)$ in a neighbourhood of each target value of $x$. Using TMLEs, they are able to make strict theoretical guarantees about this estimator. With inherently related goals, Semenova and Chernozhukov (2020) develop semiparametric theory for estimation of generic functions that are dependent on only a subset of a possibly high-dimensional vector of covariates using least squares series estimators and the assumption that nuisance parameters can be estimated at near-$n^{-1/4}$ rate.

The approach we propose is related to that of van der Laan et al. (2018), but is radically simpler and relies on finding an approximation to the limit of the expected value of the uncentered efficient influence function, and not a limit on the parameter itself. Further, even though we could use kernel smoothers to finally estimate the pointwise expected value, we prefer to keep the discussion generic and allow our end-user to specify the learning algorithm. Therefore, we rely only on the argument that any nonparametric machine learning model with appropriate minimax guarantees should be able to learn any function $\psi$ provided it is sufficiently regular. Thus, the kernel estimators suggested in van der Laan et al. (2018) (as well as similar estimators discussed in Kennedy et al. (2017)) could be used in our setting, and specific assumptions could lead to better guarantees than the very general model-free approach we discuss.

In two well-studied problem settings, a problem-specific version of our problem-agnostic
estimator has been previously proposed. First, in the trivial case when there is no coarsening and we are concerned with the estimation of the conditional outcome mean, our approach is equivalent to nonparametric regression. This is because the efficient influence function of the mean in standard nonparametric regression is \( Y \) itself, and therefore oracle knowledge on \( P \) adds no new information on nuisance parameters. Second, the problemspecific doubly robust estimators for CATE discussed e.g. in Kennedy (2020), Lee et al. (2017) and Fan et al. (2020) are equivalent to our estimator when the target parameter is CATE. Finally, similar ideas are also the basis continuous treatment effect estimator of Kennedy et al. (2017).

Therefore, the main contribution of our work relative to existing theoretical work is that we have constructed a very simple theoretical tool that allows for essentially assumption-free and model-free approximate pointwise plug-in bias adjustment of plug-in estimators for general targets that are functions of continuous inputs. From there, as discussed in the next section, we can leverage both well-known and more recent results from different communities to show that using this conceptually simple idea to construct estimators leads to essentially trivially provable guarantees, particularly in high information settings. In particular, we rely on a recent general result due to Kennedy (2020) which allows to bound the error of pseudo-outcome regression with estimated or imputed components. In section 5, we will show that our theoretical tool can also be immediately used to construct learning algorithms that can be used in practice.

### 4.3 Practical implications of approximate plug-in bias correction using pseudo-outcome regression

The first natural question that arises in the pseudo-outcome regression set-up we constructed in section 4.1 are how the rate of convergence of this estimator compares to the oracle rate, and how it compares to the original plug-in estimator.

The key to answering these questions is given in the recent work of Kennedy (2020), providing a general result to bound the error of pseudo-outcome regression with imputed or estimated components, which gives us the ability to bound the error of our plug-in estimates when estimated using two independent samples of size \( n \). For completeness we state Kennedy (2020)’s theorem in appendix 8.3. To be able to bound the error in
plug-in pseudo-outcome regression, we need a mild assumption on the second-stage regression model (see appendix 8.3) necessary to ensure stability of the second stage regression (Kennedy, 2020). Further, we make the following very weak assumptions on the set-up for plug-in pseudo-outcome regression for an infinite-dimensional target parameter \( \psi(x) \).

**Assumption 4.1. Set-up of plug-in-based, bias-corrected pseudo-outcome regression**

We assume the following set-up for our plug-in-based, bias-corrected pseudo-outcome regression:

- We use sample splitting or cross fitting for the plug-in regression. In a sample-splitting set-up, let \( O_0^n = (O_{01}, \ldots, O_{0n}) \) and \( O_1^n = (O_{11}, \ldots, O_{1n}) \) denote the two independent samples used for first- and second-stage regression, respectively.

- We have plug-in estimator \( \bar{\psi}(x) \) based on some first stage model \( \hat{P} \).

- We have a plug-in bias-corrected estimator \( \hat{\psi}(x) \) based on the plug-in pseudo-outcome \( D_{\Psi, \hat{P}}(O) \) which we use as a target in the second stage pseudo-outcome regression.

- There is an oracle equivalent \( \tilde{\psi}(x) \) of \( \hat{\psi}(x) \) from an infeasible regression of the true \( D_{\Psi, \hat{P}}(O) \) on \( X \).

- \( \psi(x) \) is sufficiently regular so that Theorem 1 holds and we can learn the expected value of the limiting uncentered efficient influence function from data.

These two assumptions, and Kennedy (2020)'s theorem immediately give us the following result:

**Corollary 1. Error bound for plug-in-based, bias-corrected pseudo-outcome regression estimators of structural target functions**

Under assumptions 8.1 and 4.1 we have the following result for pseudo-outcome regression of \( D_{\Psi, \hat{P}}(O) \) on \( X \)

\[
\mathbb{E} [\{\hat{\psi}(x) - \bar{\psi}(x)\}^2] \lesssim \mathbb{E} [\{\hat{\psi}(x) - \bar{\psi}(x)\}^2] + \mathbb{E} [\{\mathbb{E}[\tilde{\psi}(x)|X = x, O_0^n] - \psi(x)\}^2] \quad (10)
\]

**Proof.** This follows directly from the assumptions and Kennedy (2020)'s theorem. \( \square \)
Because the shape of the second-order remainder term on the right hand side depends on the specific target parameter of interest, it is not immediately clear what this result implies in general. Therefore, it can be instructive to consider specific examples. First, since plug-in bias correction should have no effect when estimating the mean $\mu(x) = \mathbb{E}_P[Y|X=x]$ in simple nonparametric regression, as we have shown in section 3 that the uncentered EIF $(D_{\mu,P} = Y)$ is independent of $P$ by construction, it is reassuring that the second term here will be zero since there is no second-order remainder in nonparametric regression. Thus, as expected, nonparametric regression attains the oracle rate. Further, in the class of coarsening at random problems this remainder has the familiar doubly robust form, meaning that the plug-in bias removal step halves the requirements on convergence also in the higher-dimensional case, which is a familiar notion extending directly from the standard, low-dimensional case. Hence, plug-in bias removal plays a similar role of ‘lowering the bar’ also in high-dimensional settings (refer to appendix 8.4 for an example of how this works mathematically in CATE estimation).

Corollary 1 immediately leads to the following result on convergence rates:

**Corollary 2.** *Minimax convergence rates for generic nonparametric estimation of infinite-dimensional target parameters using plug-in-based, bias-adjusted pseudo-outcome regression*

Suppose the assumptions of Corollary 1 hold. Further, assume that the target function $\psi$ is $p$-smooth and can be estimated with minimax rate $n^{-\frac{p}{2p+d}}$ where $d$ is the dimension of $x$. Then

$$\mathbb{E} \left[ \{\hat{\psi}(x) - \psi(x)\}^2 \right] \lesssim \max(n^{-\frac{2p}{2p+d}}, O_p(R_2))$$

(11)

where $R_2 = \mathbb{E} \left[ \left\{ \mathbb{E}[\hat{\psi}(x)|X=x, O_n] - \psi(x) \right\}^2 \right]$. In particular, if the order of the oracle term dominates the remainder term, we can achieve oracle rates with the proposed plug-in estimator, i.e. if

$$O_p(R_2) \lesssim n^{-\frac{2p}{2p+d}}$$

(12)

**Proof.** This follows directly from the assumptions and Corollary 1.

**Remark 4.1. Higher-order influence functions**

By extension from the low-dimensional case, it would be interesting to investigate whether
there is the possibility to further improve upon this generic lower bound by correcting plug-in bias by using an approximation of higher-order influence functions as proposed in Robins et al. (2008). Since higher-order influence functions add variance even in the low-dimensional setting (van der Vaart, 2014), we conjecture that the increase in variance due to this additional approximation may well outweigh the benefits in terms of bias, but a more in-depth investigation might be worthwhile for future research.

For the special case of coarsening at random problems, i.e. problems possessing doubly robust properties, the second-order remainder has a special form, which we briefly discussed above. The property that only either the coarsening mechanism or the outcome regressions have to be consistently estimated has been extensively studied and exploited in the context of low-dimensional inference (see e.g. Rubin and van der Laan (2008b)). In particular, it is well-known that this structure can be exploited to achieve root-n convergence of the average treatment effect when we can give a correctly specified parametric model for either component of the problem. For cases where the propensity score or censoring mechanism is known, Rubin and van der Laan (2008b) exploit such ideas in an interesting manner to achieve a notion they call ‘empirical efficiency’ by regression adjustment targeting a measure of variance instead of goodness of fit. Corollary 2 suggests that we can leverage similar properties also for high-dimensional inference. Corollary 2 also shows that the requirements on how much structure needs to be known can be substantially relaxed when the aim is only to attain oracle rates. This is formalised below.

**Corollary 3. Exploiting information in coarsening at random problems**

For coarsening at random problems which are not fully nonparametric because we are able to exploit some known underlying structure, our proposed pseudo-outcome regression approach can easily attain oracle rates. If, for example, we know anything about the underlying (i) sparsity (or the subset of covariates that determine the propensity score, (ii) its parametric form or even (iii) the exact propensity scores, substantially lowers the bar to achieve oracle rates.

**Proof.** This is immediate from the form of the double-robust remainder $R_2$. Sparsity decreases $d$ in the nonparametric minimax rate, parametric forms allow convergence at root-n rate and the exact propensity score results in zero reminder.
This shows that incorporating domain knowledge can substantially help us in achieve oracle rates. Importantly, this domain knowledge does not have to be reflected in exact parametric forms. Even imposing some exclusion restrictions, such as excluding certain functional forms, can help reducing the difficulty of the problem by moving from a fully nonparametric to a semiparametric problem. Particularly in applications in biostatistics and medicine, such knowledge could be inferred from mechanistic understanding of diseases and domain knowledge on daily practice, e.g. by identifying variables that are more or less likely to influence missingness or selection bias. In applications from econometrics, such domain knowledge could stem from, for example, well-established theoretical models of micro- and macroeconomic theory.

**Remark 4.2. Known propensity scores and oracle efficiency**

The most trivial case in which this is true is when the coarsening mechanism is known, e.g. if the propensity score is known because we are in a RCT setting. It follows from the results above that in such settings we automatically achieve the oracle bound as $R_2$ is zero by construction. This gives a new argument why simple plug-in estimation (without bias correction) is not optimal especially when coarsening mechanisms are known. Interestingly, this is true even when the coarsening mechanism is independent of covariates and we have complete randomization. This adds to the empirical efficiency argument made in low-dimensional inference by Rubin and van der Laan (2008).

With the discussion in this section, we have highlighted the immense potential of using our limiting notion of the efficient influence function to construct and analyse estimators, in a way that is analogous to the well-studied low-dimensional case. By analogy of our approach with Kennedy (2020)'s approach in the CATE setting, it would be a straightforward and interesting next step to extend the arguments made therein on how to improve upon the simple bound given in Corollary 1 for the special case of CATE estimation to the general case presented here, particularly by leveraging the ideas on fast remainder rates recently presented in Newey and Robins (2018).

**Remark 4.3. Central limit theorems for EIF-based pseudo-outcome regression**

If we wanted to achieve convergence to a CLT, we would need that both the remainder term $R_2$ and the squared error of the oracle regression converge at root-n rates. Clearly, by Corollary 2 this is impossible without making further assumptions on the structure of
the problem and the nature of the regression estimator. However, for some data-adaptive nonparametric machine learning methods based on neighbourhood smoothing, there already exist conditions that are milder than parametric assumptions, under which they lead to a CLT asymptotically. We exploit this idea here to show the implications of our work for (efficient) inference if one is willing to make stronger assumptions. As an example, we propose using the random forests described in Wager and Athey (2018), which have some special properties (e.g. more randomness) that enable inference, for both regression stages. Because RAL estimators based on the EIF are asymptotically Gaussian with the smallest attainable variance, we conjecture that the estimator for treatment effect estimation in Wager and Athey (2018) and the generic estimators proposed in Athey et al. (2019) based on estimating equations are not optimal for inference in terms of efficiency, at least asymptotically. Combining our ideas with the theory developed in these papers thus seems to be a fruitful alley for future research. Further, for doubly robust problems, we conjecture that the conditions on the first stage regressions could be weakened in analogy with the low-dimensional case.

5 Learning algorithms within the IF-learning framework

Based on the theoretical discussion presented in the previous section, we propose two general learning algorithms that can be used for estimation and inference for the broad class of problems of interest discussed in this paper. We begin with our main algorithm, the general ‘IF-learner’ which follows naturally from the pseudo-outcome regression set-up in the previous section. After that, we characterise a grouped version, the Group-IF-learner, which we believe could be of independent practical interest low sample size settings where we cannot rely on asymptotics but may have information on the coarsening mechanism.

5.1 IF-learner

Our main proposal, the ‘IF-learner’, is the algorithm that arises naturally from our assumptions on the pseudo-outcome regression set-up, and is presented in Algorithm. Here, we rely on cross-fitting (as discussed in e.g. Chernozhukov et al. (2018a) and Kennedy.
to be more efficient in our use of data. Instead of cross-fitting, one could also use a single sample split and perform the two-stage procedure on separate samples.

Algorithm 1 IF-learner

1: Inputs: A sample $\mathcal{D} = \{O_i\}_{i=1}^n$, a target parameter $\psi$ with associated population averaged influence function $D_{\psi,\mathcal{P}}(O)$ which depends only on a subset of all nuisance parameters $Q \equiv Q(\mathcal{P})$, a learning algorithm $\mathcal{A}$, and a number $K$ of cross-fitting folds to create

2: First stage: plug-in model estimation
3: split the sample $\mathcal{D}$ in $k$ non-overlapping folds
4: for $k \leftarrow 1 : K$ do
5: Fit nuisance models $\hat{Q}_{-k} = \mathcal{A}(\mathcal{D}_{-k})$ on all but the $k^{th}$ fold
6: Predict $\hat{D}_i = D_{\psi,\mathcal{P}}(O_i)$ for $O_i \in \mathcal{D}_k$ using the nuisance model $\hat{Q}_{-k}$
7: end for

8: Second stage: plug-in bias correction step
9: estimate $\hat{\psi}(x)$ as a function of $x$ by regressing $\{\hat{D}_i\}_{i=1}^n$ on $\{X_i\}_{i=1}^n$ as $\hat{\psi}(x) = \mathcal{A}(\{\hat{D}_i, X_i\}_{i=1}^n)$
10: Output: $\hat{\psi}(x)$, a model that can output pointwise estimates of $\psi$

For the example of generic CATE estimation from observational data, the input learning algorithms would be two generic regression estimators for the potential outcome regressions, and an estimator for the propensity score. In the CATE case, our IF-learner therefore reduces to the ‘DR-learner’ recently independently proposed in Kennedy (2020), as well as similar two-stage estimators discussed in Lee et al. (2017) and Fan et al. (2020). If there is some additional knowledge on the structure of the problem, e.g. sparsity, covariates used for selection or functional forms, this could be incorporated by choosing only estimators that reflect this knowledge. As we have shown in Corollary 3, this can immediately lead to the algorithm achieving oracle rates. In particular, in large experimental studies where the propensity score is known, this should lead to immediate achievement of oracle rates.

The algorithm can, however, be used for many more problem settings, particularly for other problems with coarsening at random structure. As we will show in section 6, this algorithm could, for example, be used to infer causal parameters that have not received as much attention in the machine learning literature, such as risk ratios. Further, we note that while the algorithmic description uses the same learning algorithm $\mathcal{A}$ for all models, that is certainly not necessary in practice, and separate learners could be used for each part of the problem. As discussed in section 4.2, pointwise inference using the IF-learner
is possible only under more restrictive assumptions on the data generating process and for a restrictive choice of learning algorithms $A$.

**Remark 5.1. Super Learning**

The first stage of this algorithm also lends itself to the easy extension of incorporating super-learning [van der Laan et al., 2007] for model selection to improve finite sample performance, which would be an interesting idea to develop further.

### 5.2 Group-IF-learner

The second algorithm we propose here is motivated by the observation of Chernozhukov et al. (2018b) that if we focus on estimating key features of a function instead of the function itself, this can facilitate inference. Of the ‘key features’ proposed in Chernozhukov et al. (2018b) for treatment effect estimation, we are particularly interested in ‘Sorted Group Average Treatment Effects’ (GATES), which provide a coarse summary of treatment effect heterogeneity by heterogeneity groups. In particular, the authors propose the following algorithm for constructing GATES based on $G$ groups and known propensity scores:

1. Split the data in two samples, an auxiliary sample $D_A$ and an estimation sample $D_E$.
2. Fit a treatment effect model $\tilde{\psi}(x)$ and a baseline model $\tilde{\mu}(x) = \mathbb{E}[Y | X = x, W = 0]$ on $D_A$.
3. Predict $\tilde{\psi}(X_i)$ for the estimation sample $D_E$, and build groups of individuals that are most similar in terms of their treatment effects by grouping observations in $G$ groups according to the empirical quantiles of their estimated treatment effects $\{\tilde{\psi}(X_i)\}_{i \in D_E}$.

   Within these groups, estimate treatment effects by orthogonalised weighted regression, possibly including $\tilde{\mu}(x)$ as a covariate to improve precision.

Because of sample splitting, often also referred to as honesty [Athey and Imbens, 2016], and known propensity scores, the within-group estimates are unbiased and standard inference is possible. However, we see two points of possible improvements to this algorithm. First, the regression adjustment procedure proposed in Chernozhukov et al. (2018b) is not optimal from the standpoint of efficiency, as we have shown the true form of the efficient estimator for group-averaged target parameters in Proposition 1, which is an AIPW estimator in the CATE case. Second, if the first stage model badly overfits to the auxiliary
sample, then the groups are created based on noise only – which is irreversible because partitioning is a hard-thresholding operation. While this does not invalidate inference, it could substantially decrease the usefulness of the proposed algorithm particularly in small samples.

The ‘Group-IF-learner’ we propose is an improved version of the GATES approach proposed in Chernozhukov et al. (2018b), in which we use our IF-learner to remove the first-order plug-in bias in the first stage of the algorithm to obtain a better baseline for partitioning. We then improve the second stage by using the efficient estimators based on the efficient influence function. Note that, because we are now considering actual groups as in Proposition 1, the efficient influence function exists in the standard sense. This leads to the algorithm described in Algorithm 2.

**Algorithm 2 Group-IF-learner**

1: Inputs: All inputs of Algorithm 1. $G$, the number of groups to be created
2: Split the sample $D$ into two non-overlapping groups $D_A$ and $D_E$
3: **First stage: Learning step**
4: Fit nuisance models $\hat{Q}_A = A(D_A)$
5: Create auxiliary, plug-in debiased model $\tilde{\psi}(x)$ by using the IF-learner (Algorithm 1)
6: **Second stage: Estimation step**
7: Split $D_E$ into $G$ groups by using the empirical quantiles of $\tilde{\psi}(x)$
8: Estimate $\Psi_g$ for each group $g$ by using the empirical average $\hat{\Psi}_g = \frac{1}{n_g} \sum_{i \in g} D_{\Psi,\hat{P}}(O_i)$
   and an unbiased empirical variance estimate $\frac{1}{n_g(n_g-1)} \sum_{i \in g} (D_{\Psi,\hat{P}}(O_i) - \hat{\Psi}_g)$
9: Output: $\{\hat{\Psi}_g\}_{g=1}^G$ and associated variance estimates.

Due to sample-splitting, the within-group estimates are asymptotically unbiased and Gaussian if the nuisance parameters in the first stage are estimated at the rates discussed in section 3.3. Thus, this discretisation is not useful in high-dimensional cases where there is no information available. However, in randomised experiments (as was the setting in Chernozhukov et al. (2018b)) and other coarsening-at-random problems where the coarsening mechanism is known, this estimator is unbiased even in finite samples due to the double robustness property of the efficient influence function and asymptotically Gaussian (Rubin and van der Laan, 2008b), and thus allows for standard inference. Thus, our second algorithm is suited more to high-information, low-sample size settings – which is the case for RCTs.
Remark 5.2. **Accounting for uncertainty induced by sample splitting**

To obtain final GATES estimates, Chernozhukov et al. (2018b) repeat the grouping procedure for multiple data splits into estimation and auxiliary samples, resulting in a number of point estimates and confidence intervals that are aggregated into one estimate by group and associated confidence intervals by a tailored and new assumption-free procedure developed by the authors (Chernozhukov et al., 2018b). We did not yet attempt to incorporate this idea further, however because our learner should be more stable due to first-stage bias correction and second stage efficient estimation, we conjecture that this would only improve our algorithm relative to that of Chernozhukov et al. (2018b).

6 Simulation study: Treatment effect estimates in RCTs

To illustrate the immense potential the theoretical analysis presented in this paper could have for practitioners eager to use machine learning for heterogeneous estimation and inference, we provide a simulation case-study below, with which we aim to convince practitioners of the intuitive appeal and simplicity of our framework.

6.1 Assumptions and set-up

In this section, we return to our main motivating example: Estimating (possibly) heterogeneous treatment effects in RCTs. Recall that in this case we have observations \( O_i = (Y_i, X_i, W_i) \) with binary treatment \( W_i \in \{0, 1\} \) which is assigned according to known propensity score \( \pi_0(x) = P_0(W = 1|X = x) \). We are interested in estimating quantities such as the CATE, \( r(x) = E_{F_0}[Y(1) - Y(0)|X = x] \), which are functions of the two potential outcome regressions. The CATE and its population average, the average treatment effect (ATE), \( \Upsilon = E_{P_0}[r(x)] \), as well as other such parameters are identifiable from our data under two assumptions:

**Assumption 6.1. Unconfoundedness:** Treatment is randomised, with treatment assignment probability \( \pi_0(x) \) depending only on the covariates. That is,

\[
Y(0), Y(1) \perp W | X
\] (13)
Assumption 6.2. **Overlap:** The treatment assignment probability is uniformly bounded away from zero and one, that is,

\[ 0 < \pi_0(x) < 1 \text{ for all } x \in \mathcal{X} \tag{14} \]

i.e. we observe each potential outcome with positive probability.

Since both aspects are under control of the experimenter, they are likely to hold in practice. Further, we also need to assume that both \( Y(0) \) and \( Y(1) \) have finite variance under \( \mathbb{P}_0 \). Last, we note that within our framework we also make the assumption that our observations \( \{O_i\}_{i=1}^n \) are i.i.d. – that is, they are mutually independent. In clinical trials, this might not always be the case, as treatment assignment is often randomised under the restriction that a fixed number of participants is assigned to each trial arm in order to avoid severe imbalances (Friedman et al., 2015), making the assignments dependent (Rubin and van der Laan, 2008a). Such dependent sampling scheme in the context of empirical efficiency maximisation is discussed in Rubin and van der Laan (2008a), and it would be interesting to investigate whether their results could be used for heterogeneous inference within our framework. For now, we restrict our attention to the more common i.i.d. assumption.

Recall from example 3.2. that the uncentered efficient influence function of the ATE is given by

\[
D_{\Psi_{\mathbb{P}}}(O) = \left( \frac{W}{\pi_0(X)} - \frac{(1-W)}{1-\pi_0(X)} \right) Y + \left[ \left( 1 - \frac{W}{\pi_0(X)} \right) \mu_1(x) - \left( 1 - \frac{1-W}{1-\pi_0(X)} \right) \mu_0(X) \right]
\]

with \( \mu_w(x) = \mathbb{E}_{\mathbb{P}_0}[Y(w)|X=x] = \mathbb{E}_{\mathbb{P}_0}[Y|W=w,X=x] \) which we can use as a pseudo-outcome in our regression framework. Note that when the propensity score is known, this estimator is unbiased regardless of the quality of the two regression function estimators. This is because the first term is the standard inverse-propensity weighted Horvitz-Thompson estimator (Horvitz and Thompson, 1952) which is unbiased if \( \pi_0 \) is known, and the second term has zero expectation (Rubin and van der Laan, 2008b).
6.1.1 Targets that are other functions of the potential outcome regressions

In clinical trials and other experimental studies, in particular when the outcome variable is binary, the target parameter of interest is often not the (C)ATE $\mu_1(x) - \mu_0(x)$, but a transformation $f(\mu_0(x), \mu_1(x))$ of the expected potential outcomes such as a risk ratio (Rubin and van der Laan 2008b). Due to the generality of our approach, our framework can naturally handle these cases as well. Rubin and van der Laan (2008b) show that the EIF for generic population-averages $f(\mu_0(x), \mu_1(x))$ is given by

$$IF_{f(\mu_0(x), \mu_1(x)), P}(O) = IF_{\mu_0, P}(O) \frac{\partial}{\partial \mu_0} f(\mu_0, \mu) + IF_{\mu_1, P}(O) \frac{\partial}{\partial \mu_1} f(\mu_0, \mu_1)$$

where $IF_{\mu_0, P}$ is the centered efficient influence function of the potential outcome mean $\mu_0$. This can be naturally incorporated as an alternative pseudo-outcome. This gives our framework a considerable advantage over most other heterogeneous treatment effects estimation methods, which typically output only conditional average treatment effects. For risk ratios $f_{RR}(\mu_0(x), \mu_1(x)) = \frac{\mu_1(x)}{\mu_0(x)}$ and odds ratios $f_{OR}(\mu_0(x), \mu_1(x)) = \frac{\mu_1(x)}{1-\mu_1(x)} / \frac{\mu_0(x)}{1-\mu_0(x)}$, and the relevant partial derivatives $[\frac{\partial}{\partial \mu_1} f(\mu_0, \mu_0), \frac{\partial}{\partial \mu_0} f(\mu_0, \mu_0)]$ are given by $[\mu_0^{-1}, -\mu_1 \mu_0^{-2}]$ and $[\frac{1-\mu_0}{(1-\mu_1)^2 \mu_0}, \frac{-\mu_1}{(1-\mu_1) \mu_0^2}]$, respectively (Rubin and van der Laan 2008b).

Below, we provide an example using risk-ratios (RR), for which the population-average uncentered EIF is given by:

$$D_{RR, P}(O) = \frac{1}{\mu_0(X)} \left[ \frac{W}{\pi_0(X)} Y + \left( 1 - \frac{W}{\pi_0(X)} \right) \mu_1(X) - \mu_1 \right]$$

$$- \frac{\mu_1(X)}{\mu_0^2(X)} \left[ \frac{1 - W}{1 - \pi_0(X)} Y + \left( 1 - \frac{1 - W}{1 - \pi_0(X)} \right) \mu_0(X) - \mu_0 \right] + \frac{\mu_1}{\mu_0}$$

6.2 Experiments

In this section we illustrate what our results can imply in practice using a very simple example which is meant to highlight performance differences between plug-in estimators and bias-corrected estimators in experimental studies with relatively large size (section 6.2.1) and smaller size (section 6.2.2). To do so, we revisit the example setting used in Kennedy (2020), which is based on a difficult piecewise polynomial baseline effect function $\mu_0(x)$ from Györfi et al. (2006), while the treatment effect $\tau(x) = \tau = 0$ is not only constant.
but also zero. This set-up illustrates very well how plug-in bias affects data-adaptive target estimates even when the covariates are only one-dimensional. Thus, we stick to this simple example for the purpose of illustrating the impact of plug-in debiasing.

Kennedy (2020) used this example to highlight the difficulty of plug-in learners without bias correction step to handle observational problems in which there is (i) a very difficult baseline model and (ii) strong (unknown) selection bias, for which a propensity score has to be estimated. Since in RCTs and other experimental studies the randomisation probabilities are known, one might be tempted to think that our learner does not add much in the setting where there is randomisation and the propensity scores are known. As we have tried to highlight throughout section 4, this could not be further from the truth: particularly when one of the nuisance functions is known, we asymptotically achieve oracle rates and hence optimal convergence without further assumptions. We illustrate this idea using some evidence from simulations. Refer to section 9 in the Appendix for an overview of our experimental settings.

6.2.1 Large samples and the IF-learner

For the example of CATE estimation, we present results in Figure 1. The three settings allow us to show that (i) our learner converges faster that an uncorrected plug-in estimator even under pure randomisation ($\pi_0(x) = \pi_0 = 0.5$), (ii) performs a lot better than plug-in estimation when propensity scores are known even for relatively modest sample sizes and (iii) for fixed training sample size ($n=500$) even performs better when randomisation is assumed, but there is some form of unknown selection bias. The latter might sound counter-intuitive but hinges on the observation that the second-stage regression acts like a regularizer on the first stage regression output.

To illustrate that our framework can handle other causal parameters, we use the same set-up (difficult baseline, no treatment effect) but this time to estimate risk-ratios as discussed in the previous section. To do so, we used the same baseline function, but now as the success probability of a Bernoulli-GLM. Refer to section 9 in the Appendix also for the exact simulation specification and estimation strategies used in this scenario. Results are presented in Figure 2.

In the RR setting, a trade-off between small and large sample performance becomes much more obvious than in the CATE setting above: because $Y$ is binary while the
pseudo-outcome $D_{RRP}(O)$ in the second stage is continuous, the estimation problem is more difficult and substantially more data is needed to remove error induced in the second stage regression due to small sample variance. Therefore, the IF-learner only appears to outperform the plug-in estimator in finite samples in settings where an experiment is not fully randomised.

6.2.2 Small samples and the Group-IF-learner

We now turn to illustrating the performance of our Group-IF-learner in small samples, which is often the case for RCTs. We use the original CATE example with strong selection
on observables according to a known propensity score for illustrative purposes. Simulation
results are presented in Table 2.

We make three interesting observations. First, by comparing the first and the last row of
Table 2, we observe that our learner indeed outperforms the base learner of Chernozhukov
et al. (2018b) (here we only consider the version without repeated sample splitting) for
training sample sizes \( n < 1000 \). Second, by comparing rows three and five, we observe
that this seems to mainly be driven by replacing the second stage orthogonalised weighted
regression in Chernozhukov et al. (2018b) with the group-wise efficient estimator derived in
Proposition 1. Third, we note that this is due to the fact that, for very small samples (most
significantly for \( n < 200 \)), the plug-in bias removal step actually decreases the performance
of our learner – this is analogous to what we observed above in the RR case. There is
thus a clear trade-off between removing plug-in bias of the plug-in estimator, and inducing
larger variance by doing so in small samples.

| Method/ Training observations | 50     | 100    | 200    | 500    | 1000   | 2000   |
|------------------------------|--------|--------|--------|--------|--------|--------|
| Chernozhukov et al. (2018b)  | 3.098  | 1.137  | 0.344  | 0.036  | 0.011  | 0.005  |
|                              | (0.291)| (0.071)| (0.035)| (0.004)| (0.0005)| (0.0001)|
| Plug-in 1st stage, HT 2nd    | 1.662  | 0.910  | 0.433  | 0.175  | 0.085  | 0.044  |
|                              | (0.066)| (0.031)| (0.014)| (0.005)| (0.002)| (0.001)|
| Plug-in 1st stage, EIF 2nd   | 0.313  | 0.106  | 0.053  | 0.020  | 0.010  | 0.005  |
|                              | (0.055)| (0.005)| (0.002)| (0.0006)| (0.0003)| (0.0002)|
| IF-learner 1st stage, HT 2nd | 1.705  | 0.919  | 0.429  | 0.173  | 0.086  | 0.043  |
|                              | (0.072)| (0.034)| (0.013)| (0.005)| (0.003)| (0.001)|
| IF-learner 1st stage, EIF 2nd| 0.570  | 0.195  | 0.061  | 0.021  | 0.011  | 0.005  |
|                              | (0.072)| (0.012)| (0.002)| (0.0007)| (0.0003)| (0.0001)|

HT denotes Horvitz-Thompson estimator, EIF denotes efficient influence function estimator (here:
AIPW estimator). Standard error of the mean-MSE over 500 simulations in parentheses

Table 2: MSE of different methods for different number of training observations

Remark 6.1. **Bias-variance trade-off in finite samples**

In all of our approaches, there is a clear trade-off in terms of finite/small sample variance
and plug-in bias correction. Our rate results hold asymptotically, however, in finite samples
the variance induced by first-stage (overfitted) estimates can outweigh the asymptotic bene-
fits of our plug-in debiasing procedure. Therefore, it would be of great interest to investigate
whether approaches such as super-learning (van der Laan et al., 2007) could help in finding the right type and degree of regularisation for first stage models.

7 Conclusion

In this paper, we attempted to unify ideas from semiparametric statistics, econometrics, biostatistics, machine learning and causal inference to characterise the fundamental limits of using generic machine learning algorithms for essentially assumption-free inference on structural target functions which arise in many problems of practical interest in applied statistics. We proposed a very simple and intuitive idea, based on an approximation of the limiting uncentered efficient influence function, which allowed us to approximately characterise pointwise efficiency, consistency, plug-in bias and even the possibility to achieve pointwise Gaussianity of target functions and have given some first conditions under which each is possible using results that were already available in the literature. We believe that our proposals could have great potential in helping the field of applied statistics realise more of the inherent potential of the recent advances in machine learning.

As we have tried to showcase throughout the paper, we also believe that our proposals open up a plethora of interesting and new research directions, and might even bring some communities closer together. In particular, we believe that much can be learned from further exploring connections of our proposals, which are mainly based on the first-order efficient influence function of a target parameter, with other interesting concepts in low- and high-dimensional inference that have been proposed in the last 15 years. In particular, we believe that there might be interesting connections with targeted maximum likelihood estimation (van der Laan and Rose, 2011), empirical efficiency maximisation (Rubin and van der Laan, 2008b), super learning (van der Laan et al., 2007), Neyman-Orthogonality and high-dimensional locally robust semiparametric estimation (e.g. Chernozhukov et al., 2018a), Semenova and Chernozhukov (2020), Chernozhukov et al. (2020), adaptive nearest neighbourhood estimators based on random forests (Athey et al., 2019), and approaches to achieving fast rates using orthogonal statistical learning (Foster and Syrgkanis, 2019), cross-fitting (Newey and Robins, 2018) and higher-order influence functions (Robins et al., 2008). We hope to be able to explore some of these in future work.
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8 Technical appendix

8.1 Proof of Proposition 1

The proof is very straightforward and can be arrived at both from the EIF and from the efficient estimator of the population average. We state both, since they greatly helped us in developing the intuition behind our approach.

*Proof.* (1) by contradiction, using the efficient RAL estimator

We begin by noting that

\[
\Psi = \mathbb{E}_{\mathbb{P}_0}[\psi(x)] = \mathbb{E}_{\mathbb{P}_0}[\mathbb{E}_{\mathbb{P}_0}[\psi(x)|X \in A_k^\pi]] = \sum_{k=1}^{K}\mathbb{P}_0(X \in A_k^\pi)\Psi_k
\]

so the full population mean is simply a weighted average of the partition-means. Therefore, we can write

\[
\hat{\Psi} = D_{\Psi,\mathbb{P}_0}(O) - \Psi = \sum_{k=1}^{K}\left(1(X \in A_k^\pi)D_{\Psi,\mathbb{P}_0}(O) - \mathbb{P}_0(X \in A_k^\pi)\Psi_k\right)
\]
Since $\mathbb{E}_{P_0}[\hat{\Psi}] = \sum_{k=1}^K \mathbb{P}_0(X \in A_k^\pi)(\mathbb{E}_{P_0}[D_{\Psi, P_0}(O)|X \in A_k^\pi] - \Psi_k^\pi) = 0$, we must have that $\mathbb{E}_{P_0}[D_{\Psi, P_0}(O)|X \in A_k^\pi] - \Psi_k^\pi = 0$ for all $k$, so (not surprisingly)

$$
\hat{\Psi}_k^\pi = \frac{1}{|\{i : X_i \in A_k^\pi\}|} \sum_{i : X_i \in A_k^\pi} D_{\Psi, P_0}(O)
$$

is the oracle unbiased estimator for $\Psi_k^\pi$. It must also be the unique efficient estimator, since if it was not, and there existed a regular estimator with lower asymptotic variance, say $\tilde{\Psi}_k^\pi$ for each $k$, the estimator $\tilde{\Psi} = \sum_{k=1}^K \frac{1}{n} \sum_{i : X_i \in A_k^\pi} \tilde{\Psi}_k^\pi$ would be the efficient estimator for the population mean, which is a contradiction since $\hat{\Psi}$ is the unique asymptotically efficient estimator.

**Proof.** (2) using influence function calculus

This also follows when deriving the influence function using rules of simple calculus. Since $\mathbb{E}_{P_0}[\psi(X)|X \in A_k^\pi] = \frac{\mathbb{E}_{P_0} [1_{\{X \in A_k^\pi\}} \psi(X)]}{\mathbb{P}_0[1_{\{X \in A_k^\pi\}}]}$, the uncentered efficient influence function of the parameter $\Psi_{A_k^\pi}$ can be shown to be $D_{\Psi_{A_k^\pi}, P_0}(O) = \frac{1}{\mathbb{P}_0(X \in A_k^\pi)} D_{\Psi, P_0}(O)$. The most efficient estimator for the nuisance parameter capturing the empirical distribution of $X$ is the empirical distribution $P_n = \frac{1}{n} \sum_{i=1}^n \delta_{X_i}$, thus $\hat{P}(x \in A_k^\pi) = \frac{1}{n} \sum_{i=1}^n 1\{x \in A_k^\pi\}$, and substitution leads to the same expression as in Proposition 1. 

8.2 Regularity conditions for convergence in pseudo-outcome regression (Theorem 1)

We assume the following pseudo-outcome regression set-up, as implied by Theorem 1 with standard regularity conditions as characterised by Stone (1980): let $(D_{\Psi}, X)$ denote a pair of random random variables, with $D_{\Psi} \equiv D_{\Psi, P_0}(O)$ real-valued and $X \in \mathcal{X} \subseteq \mathbb{R}^d$, where $\mathcal{X}$ denotes an open neighbourhood around the origin. Let $\mathcal{G}_p$ denote the set of $p - 1$ times continuously differentiable real valued functions $g$ on $\mathbb{R}^d$ with $p$ bounded derivatives. Assume $\psi_f$ is a fixed function, and consider the set of parameters $\mathcal{P} = \{\psi_f + g : g \in \mathcal{G}\}$, of which the true pseudo-outcome regression function $\psi(x) = \mathbb{E}_{P_0}[D_{\Psi}|X = x]$ is an unknown member. Assume that the conditional variance of $D_{\Psi}$ is bounded on $\mathcal{X}$, and that the density of $X$ is absolutely continuous and bounded away from zero and one on $\mathcal{X}$. The conditional distribution is assumed to be of the form $f(d_{\Psi}|x, \psi(x))\phi(dd_{\Psi})$ with $\phi$ a measure on $\mathbb{R}$.
It is assumed that \( f(d\psi|x,t) \) is strictly positive and jointly measurable in its arguments as they vary over their support. Further, \( \int d\psi f(d|x,t)\phi(dd\psi) = E[d\psi|x,t] = t \) for \( t \) in the open interval containing \( \{\psi(x) : \psi \in \mathcal{M} \text{ and } x \in \mathcal{X}\} \), and \( f \) is twice continuously differentiable on the domain and fulfils some additional technical conditions on the log-likelihood. Then, the optimal minimax rate attainable for estimating \( \psi(x) \) by generic nonparametric regression is \( n^{-p/(2p+d)} \).

### 8.3 Result for error bounds for pseudo-outcome regression due to Kennedy (2020)

Due to the importance of Kennedy (2020)'s result for our rate-discussions, we restate the necessary assumptions as well as the theorem in slightly adapted format below:

**Assumption 8.1. Regularity of regression estimators**

We need mild two mild assumptions on the regularity of our second-stage regression estimators \( \hat{E}_n \). \( \hat{E}_n \) needs to satisfy that:

1. \( \hat{E}_n(Y|X = x) + c = \hat{E}_n(Y + c|X = x) \) for any constant \( c \)

2. If \( E[Y|X = x] = E[W|X = x] \) then

\[
\mathbb{E}\left[\{\hat{E}_n[W|X = x] - E[W|X = x]\}^2\right] \asymp \mathbb{E}\left[\{\hat{E}_n[Y|X = x] - E[Y|X = x]\}^2\right]
\]

**Theorem. Error bound for pseudo-outcome regression (Theorem 1, Kennedy (2020))**

Let \( O_0^n = (O_{01}, \ldots, O_{0n}) \) and \( O_1^n = (O_{11}, \ldots, O_{1n}) \) denote two independent training and test samples, respectively, which are all sampled from the same model \( \mathbb{P}_0 \). Let \( \hat{f}(o) = \hat{f}(o; O_0^n) \) be an estimate of a function \( f(o) \) using only the training data \( O_0^n \) and define \( m(x) \equiv E_{\mathbb{P}_0}[f(O)|X = x] \) Let \( \hat{E}_n(Y|X = x) \) denote a generic estimator of the regression function \( E[Y|X = x] \) using the test data \( O_1^n \), where \( (X_{1i}, Y_{1i}) \subseteq O_{1i}, i = 1, \ldots, n \). Assume the estimator \( \hat{E}_n \) satisfies

1. \( \hat{E}_n(Y|X = x) + c = \hat{E}_n(Y + c|X = x) \) for any constant \( c \)
2. If $E[Y|X = x] = E[W|X = x]$ then
\[ E \left[ \{\hat{E}_n[W|X = x] - E[W|X = x]\}^2 \right] \leq E \left[ \{\hat{E}_n[Y|X = x] - E[Y|X = x]\}^2 \right] \]

Let $\hat{m}(x) = \hat{E}_n[\hat{f}(O)|X = x]$ denote the regression of $\hat{f}(O)$ on the test samples, and let $\tilde{m}(x) = E_n[f(O)|X = x]$ denote the corresponding oracle regression of $f(O)$ on $X$. Then we have that:
\[ E \left[ \{\hat{m}(x) - m(x)\}^2 \right] \leq E \left[ \{\tilde{m}(x) - m(x)\}^2 \right] + E\{\hat{r}(x)^2\} \tag{16} \]
where $\hat{r}(x) = \hat{r}(x; Z^n_0) \equiv E[\hat{f}(O)|X = x, O^n_0] - m(x)$.

For i.i.d. data, two independent samples can be arrived at by randomly splitting the sample in half. Further, the same bound holds when using cross-fitting (see e.g. Chernozhukov et al. (2018a)) instead.

### 8.4 Implications of doubly robust remainders for CATE estimation

For the case of CATE estimation, Kennedy (2020) (Theorem 2) showed that
\[ \{E[\tilde{\psi}(x)|X = x, O^n_0] - \psi(x)\}^2 \leq \left( \frac{2}{\epsilon} \right) \{\pi(x) - \tilde{\pi}(x)\}^2 \{\mu_1(x) - \tilde{\mu}_1(x)\}^2 + \{\mu_0(x) - \tilde{\mu}_0(x)\}^2 \]
where $\epsilon < \tilde{\pi}(x) < 1 - \epsilon$. Then, (modulo constants) the second term on the RHS in (10) can be written as $E \left[ \{\tilde{\pi}(x) - \pi(x)\}^2 \sum_{w=0}^{\epsilon} E \left[ \{\mu_w(x) - \tilde{\mu}_w(x)\}^2 \right] \right]$, if the propensity score and the outcome regressions are fit on separate samples (double-sample splitting).

For a simple plug-in estimator, $\hat{\mu}_1 - \hat{\mu}_0$, on the other hand, the remainder is given by
\[ (\hat{\mu}_1(x) - \hat{\mu}_0(x) - \mu_1(x) - \mu_0(x))^2 \leq 2 * \{\{\mu_1(x) - \hat{\mu}_1(x)\}^2 + \{\mu_0(x) - \hat{\mu}_0(x)\}^2 \} \]
as $(a + b)^2 \leq a^2 + 2ab + b^2$.

Because the product term with the propensity score is missing, the rate of convergence of this plug-in estimator will be dominated by the slower-converging of the two regression terms, while the remainder of the doubly robust estimator converges to zero whenever
either the estimated regression functions or the estimated propensity score converge.

9 Experimental set-up

In our experiments, we revisit the example setting used in [Kennedy (2020)], which is based on a difficult piecewise polynomial baseline effect function $\mu_0(x)$ from [Györfi et al. (2006)], while the treatment effect $\tau(x) = \tau = 0$ is not only constant but also zero. This set-up illustrates very well how plug-in bias affects data-adaptive target function estimates even when the data is only one-dimensional.

Thus, we use the following piecewise polynomial baseline model specification:

$$
\mu_0(x) = 0.5 \times 1\{x \leq -0.5\}(x + 2)^2 + (x/2 - 0.875) \times 1\{-0.5 < x \leq 0\} + 1\{0 < x \leq 0.5\}(-5(x - 0.2)^2 + 1.075) + 1\{x > 0.5\}(x + 0.125)
$$

Further, we use different degrees of selection bias. For the first setting in Figures 1 and 2, we use $\pi_0(x) = \pi_0 = 0.5$, i.e. full randomization. For the second setting in Figures 1 and 2 as well as Table 2, we use

$$
\pi_0(x) = 0.1 + 0.8 \times 1\{x > 0\}
$$

the propensity score used by [Kennedy (2020)]. For the final setting in Figure 1 we use

$$
\pi_0(x) = 0.5 + 0.5 \times b \times \left| \frac{x}{2} \right|
$$

i.e. there is selection bias that selects individuals with higher absolute values in covariates into treatment, which gets stronger as $b$ increases in $[0, 1)$, but feed the model a propensity score of 0.5 as an input.

For continuous outcomes, we generate observations $Y_i$ using the same model as [Kennedy (2020)]: We simulate inputs

$$
X_i \sim Unif([-1, 1])
$$

$$
W_i \sim Ber(\pi_0(X_i))
$$

(20)
and outcomes as
\[ Y_i = W_i \ast \tau(X_i) + \mu_0(X_i) + \epsilon(X_i) \]  
(21)

with
\[ \epsilon(X_i) \sim \mathcal{N}(0, 0.2 - 0.1 \times \cos(2\pi \times x)) \]

For the binary outcome data, we keep the baseline simulations (20) but for outcome simulations instead use
\[ Y_i \sim Ber(W_i \ast \tau(X_i) + \mu_0(X_i)) \]  
(22)

For all settings, we use the same generic default estimator: whenever the outcome variable is continuous, we use a smoothing spline based on a natural cubic spline basis with 5 degrees of freedom. Whenever the outcome is binary, we use a GLM based on the same spline basis functions (which reduces to a logistic regression using spline basis functions here).

We present results that are averaged over 500 independent simulations using the same DGP, where the MSE is computed on a test-set of 1000 independent hold-out observations in each simulation.