ESTIMATION AND INference OF TREATMENT EFFECTS WITH
L²-BOOSTING IN HIGH-DIMENSIONAL SETTINGS

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Abstract. Boosting algorithms are very popular in Machine Learning and have proven very useful for prediction and variable selection. Nevertheless in many applications the researcher is interested in inference on treatment effects or policy variables in a high-dimensional setting. Empirical researchers are more and more faced with rich datasets containing very many controls or instrumental variables, where variable selection is challenging. In this paper we give results for the valid inference of a treatment effect after selecting from among very many control variables and the estimation of instrumental variables with potentially very many instruments when post- or orthogonal L²-Boosting is used for the variable selection. This setting allows for valid inference on low-dimensional components in a regression estimated with L²-Boosting. We give simulation results for the proposed methods and an empirical application, in which we analyze the effectiveness of a pulmonary artery catheter.

Key words: L²-Boosting, instrumental variables, treatment effects, post-selection inference, high-dimensional data.

1. Introduction

Boosting algorithms are very popular in Machine Learning and have proven very useful for prediction and variable selection. Nevertheless in many applications the researcher is interested in inference on selected variables. In many cases there are so-called treatment or policy variables which the researcher would like to learn about and make inferences, in particular in a high-dimensional setting. Increasing digitization in many fields of life make large datasets available for research. Typical applications are the estimation of a treatment effect after selecting from among very many control variables and the estimation of instrumental variables when there are potentially very many instruments. We provide results for valid inference in these settings when post- or orthogonal L²-Boosting is applied for the variable selection. Usually, inference after model selection leads to invalid results. This has been highlighted by Pötscher and Leeb in a series of papers. Here we use orthogonalized moment conditions (Chernozhukov et al. (2016)) and recent results on the rate of convergence of L²-Boosting which yields valid post-selection inference (Spindler and Luo (2016)).

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Boosting algorithms represent one of the major advances in machine learning and statistics in recent years. Freund and Schapire’s AdaBoost algorithm for classification (Freund and Schapire (1997)) has attracted much attention from the machine learning community as well as in statistics. Many variants of the AdaBoost algorithm have been introduced and proven to be very competitive in terms of prediction accuracy in a variety of applications, with a strong resistance to overfitting. Boosting methods were originally proposed as ensemble methods, which rely on the principle of generating multiple predictions and majority voting (averaging) of the individual classifiers (cf. Bühlmann and Hothorn (2007)). An important step in the analysis of boosting algorithms was Breiman’s interpretation of boosting as a gradient descent algorithm in a function space, inspired by numerical optimization and statistical estimation (Breiman (1996), Breiman (1998)). Building on this insight, Friedman, Hastie and Tibshirani (2000) and Friedman (2001) embedded boosting algorithms into the framework of statistical estimation and additive basis expansion. This also enabled the application of boosting to regression analysis. Boosting for regression was proposed by Friedman (2001), and then Bühlmann and Yu (2003) defined and introduced $L_2$-Boosting. An extensive overview of the development of boosting and its manifold applications is given in the survey Bühlmann and Hothorn (2007).

In the present paper we give results for valid inference on treatment effects in a high-dimensional setting. Boosting has proven very valuable for prediction, but we show in this paper that it can also be applied for causal search. In particular we consider the case of the estimation of a treatment effect with very many control variables, and the estimation of instrumental variables (IVs) with very many potential instruments. The first case, the estimation of a treatment effect with very many control variables, can also be interpreted as inference on a preselected variable in a high-dimensional linear regression model estimated with $L_2$-Boosting. Our estimation method relies on the so-called orthogonalized moment conditions. This theory was developed by Belloni, Chernozhukov, Hansen, and coauthors, in a series of papers. The case of instrumental variables is analyzed in Belloni et al. (2012), the treatment effect case in Belloni, Chernozhukov and Hansen (2014). Surveys with extensions of the general idea are Chernozhukov et al. (2016) and Chernozhukov, Hansen and Spindler (2015).

To ground the discussion, as an empirical application we examine a randomized trial of the pulmonary artery catheter (PAC) that was carried out in 65 intensive care units in the UK between 2001 and 2004 (Harvey et al. (2005)). This study got a lot of attention from the scientific community under the name the “PAC-man” study. The PAC is a monitoring device commonly inserted into critically ill patients while staying in intensive care units. It provides continuous measurements of cardiac activity. However, the insertion of a PAC is an invasive procedure, bringing the risk of complications and imposing significant costs (\$). An early study based on observational data found that a PAC had a negative effect on the survival chances of patients and led to increased costs for the health care sector (Connors et al. (1996)). This finding was the motivation for a randomized trial to evaluate PAC interventions. In that study, around 1,000 patients (approx. 50% treatment and control groups) participated, and a large number of covariates were collected. If,
First, we explain, in Section 2, the problems in estimating treatment effects in high-dimensional settings. In Section 3, $L_2$-Boosting and two variants, to which our results apply, are introduced. In Section 3, we present the formal results for valid inference on (low-)dimensional treatment effects in a possibly high-dimensional setting. A simulation study and an empirical application are given in Sections 4 and 5. Finally, we conclude (Section 6).

2. Econometric Considerations / Estimation of Treatment Effects

The goal is to estimate the treatment effect $\alpha$ of a treatment variable $D$ on an outcome variable $Y$, namely

$$Y = \gamma + \alpha D + \varepsilon,$$

where $\gamma$ denotes the intercept and $\varepsilon$ a statistical error term. There are two reasons for including covariates $X = (X_1, \ldots, X_p)$ in equation 1 for the estimation of the treatment effect. First, covariates improve the precision of the estimation of the average treatment effect in randomized control trials (RCTs). This argument has already been made in Cox (1958). Second, in observational studies, additional covariates might establish unconfoundedness, meaning that given the variables in $X$, the treatment is as randomized and there are no unobserved cofounders. For a book length treatment of this argument, we refer to Imbens and Rubin (2015). Formally, this means

$$Y = \gamma + \alpha D + g(X) + \varepsilon, \mathbb{E}(\varepsilon|D, X) = 0,$$

with $g(\cdot)$ a function of the covariates.

The next question is which variables to include in equation 1 from a set of potential covariates. In high-dimensional settings, when the number of covariates $p$ is larger than the sample size $n$, variable selection is inevitable, as, e.g., the least squares estimate is not well defined. Even when $p$ is smaller than $n$ but the ratio $p/n$ is high, ordinary least squares estimates are unreliable and again variable selection is needed. Including too many (noise) covariates might disguise the true treatment effect. For example, a study to evaluate the pulmonary artery catheter (PAC), which is analyzed in Bloniarz et al. (2016) and which we will also cover, contains 1013 observations and 55 potential covariates. In medical applications, often interaction effects might be prevalent, leading in all to $500 - 1000$ two-way interactions in this example and to a high-dimensional setting with $p$ very large compared to $n$, or even $p \gg n$.

In a naive approach, one might first select the relevant covariates by classical $t$-tests or modern machine learning methods, like Lasso and boosting, and then estimate the treatment effect by including only the selected variables and continue with standard inference methods. But this procedure, although often used in applied work, might...
fail to provide a valid post-selection inference. This has been worked out by Leeb and Pötscher (Leeb and Pötscher (2005)). We demonstrate this by a simple simulation study with one treatment variable and one covariate. The data generating process is given by

\[ y_i = d_i \alpha + x_i \beta + \epsilon_i, \quad d_i = x_i \gamma + v_i, \]

with \( \alpha = 0.5, \beta = 0.2, \gamma = 0.8 \). The noise is normally distributed \( \epsilon_i \sim N(0,1) \) and \( (d_i, x_i) \sim N \left( 0, \begin{bmatrix} 1 & 0.8 \\ 0.8 & 1 \end{bmatrix} \right) \). We apply \( L_2 \)-Boosting, which is explained later in more detail for variable selection in the naive approach. The results for 500 repetitions of the scaled estimate \( \hat{\alpha} \) are displayed in Figure 1b. The resulting distribution is highly biased, shows heavy tails and is not in line with a standard normal distribution. To provide valid post selection inference with boosting, we apply the double selection approach which is described in Section 4 in detail. Figure 1a shows the empirical distribution of the estimates when employing the double selection methods. They are nearly unbiased and can be approximated by a normal distribution. The intuition of the double selection method is that it cures the omitted variables bias which is introduced by imperfect model selection of machine learning methods by running an auxiliary regression / step. As mentioned, details will be provided later.

3. \( L_2 \)-Boosting

In this section we describe the \( L_2 \)-Boosting algorithm, namely the original boosting algorithm for regression defined in Bühlmann and Yu (2003) and two variants (orthogonal and post-boosting)\(^1\).

To define the boosting algorithm for linear models, we consider the following regression setting:

\[ y_i = x_i' \beta + \epsilon_i, \quad i = 1, \ldots, n, \]  

(2)

\(^1\)A more detailed exposition of the algorithms can be found in Spindler and Luo (2016).
with a vector $x_i = (x_{i,1}, \ldots, x_{i,p_n})$ consisting of $p_n$ predictor variables, $\beta$ a $p_n$-dimensional coefficient vector, and a random, zero-mean error term $\varepsilon_i$, $E[\varepsilon_i|x_i] = 0$. Without loss of generality, we will assume that the regressors are standardized and have unit variance. Further assumptions will be imposed in the next sections.

We allow the dimension of the predictors $p_n$ to grow with the sample size $n$. Also the case $\text{dim}(\beta) = p_n \gg n$ is allowed. In this setting a so-called sparsity condition is unavoidable. This means that there is a large set of potential variables, but the number of variables which have non-zero coefficients, denoted by $s$, is small compared to the sample size, i.e., $s \ll n$. This can be weakened to approximate sparsity, to be defined and explained later. More precise assumptions will also be made later. In the following, we will drop the dependence of $p_n$ on the sample size and denote it by $p$ if no confusion will arise.

$X$ denotes the $n \times p$ design matrix where the single observations $x_i$ form the rows. $X_j$ denotes the $j$th column of the design matrix, and $x_{i,j}$ the $j$th component of the vector $x_i$. We assume a fixed design for the regressors. We assume that the regressors are standardized with mean zero and variance one, i.e., $E_n[x_{i,j}] = 0$ and $E_n[x_{i,j}^2] = 1$ for $j = 1, \ldots, p$.

The basic principle of $L_2$-Boosting works as follows: the criterion function we would like to minimize is the sum of squared residuals, as in the ordinary least squares (OLS) case. We initialize the estimator $\hat{\beta}$ to zero (strictly speaking, a $p$-dimensional vector consisting of zeros). Then we calculate the residuals, which in this case are equivalent to the observations. Then we conduct $p$ univariate regressions, namely, we regress the residuals (in the first round, the observations) on each of the $p$ regressors, resulting in $p$ univariate regressions. Then we select the variable or regression which explains most of the residuals and update this coordinate of our estimated vector in this direction. Now we repeat this procedure (the calculation of the updated residuals, $p$ univariate regressions, and updating the estimated coefficient vector) until some stopping criterion is reached.

The version above and the orthogonal version, introduced next, are, in deterministic settings, also known as the pure greedy algorithm (PGA) and the orthogonal greedy algorithm (OGA). Boosting is a gradient descent method. In the $L_2$-case the gradient equals the residuals and the residuals are iteratively fitted by a so-called base learner, here componentwise univariate regressions. Early stopping is crucial. In the low-dimensional case the estimator converges to the OLS solution. In the high-dimensional case, overfitting can occur in the absence of early stopping. Hence, early stopping prevents overfitting and is an unusual penalization / regularization scheme.

3.1. $L_2$-Boosting. The algorithm for $L_2$-Boosting with componentwise least squares is given below.
Algorithm 1 (L₂-Boosting). (1) Start / Initialization: \( \beta^0 = 0 \) (p-dimensional vector), \( f^0 = 0 \), set maximum number of iterations \( m_{\text{stop}} \) and set iteration index \( m \) to 0.

(2) At the \((m+1)\)th step, calculate the residuals \( U^m = y_i - x_i' \beta^m \).

(3) For each predictor variable \( j = 1, \ldots, p \) calculate the correlation with the residuals:

\[
\gamma_j^m := \frac{\sum_{i=1}^n U^m_i x_{i,j}}{\sum_{i=1}^n x_{i,j}^2} = \frac{\langle U^m, x_j \rangle}{E_n[x_{i,j}^2]}.
\]

Select the variable \( j^m \) that is the most correlated with the residuals[2], i.e., \( \max_{1 \leq j \leq p} |\text{corr}(U^m, x_j)| \).

(4) Update the estimator:

\[
\beta^{m+1} = \beta^m + \gamma_j^m e_j^m
\]

and \( f^{m+1} := f^m + \gamma_j^m x_j^m \).

(5) Increase \( m \) by one. If \( m < m_{\text{stop}} \), continue with (2); otherwise stop.

For simplicity, write \( \gamma^m \) for the value of \( \gamma_j^m \) at the \( m \)th step.

The act of stopping is crucial for boosting algorithms, as stopping too late or never stopping leads to overfitting and therefore some kind of penalization is required. A suitable solution is to stop early, i.e., before overfitting takes place. “Early stopping” can be interpreted as a form of penalization. Similar to Lasso, early stopping might induce a bias through shrinkage. A potential way to decrease the bias is by “post-Boosting”, which is defined in the next section.

3.2. Post- and orthogonal L₂-Boosting. Post-L₂-Boosting is a post-model selection estimator that applies ordinary least squares (OLS) to the model selected by the first step, which is \( \ell_2 \)-Boosting. To define this estimator formally, we make the following definitions: \( T := \text{supp}(\beta) \) and \( \hat{T} := \text{supp}(\beta^m) \), the support of the true model and the support of the model estimated by \( \ell_2 \)-Boosting as described above with stopping at \( m \). The superscript \( C \) denotes the complement of the set with regard to \( \{1, \ldots, p\} \). In the context of Lasso, OLS after model selection was analyzed in Belloni and Chernozhukov (2013). Given the above definitions, the post-model selection estimator or OLS post-\( \ell_2 \)-Boosting estimator will take the form

\[
\tilde{\beta} = \arg\min_{\beta \in \mathbb{R}^p} Q_n(\beta) : \beta_j = 0 \quad \text{for each} \quad j \in \hat{T}^C.
\]

(3)

\( Q_n(\beta) \) denotes the squared sum of residuals defined as \( \sum_{i=1}^n (y_i - x_i' \beta)^2 \).

Another variant of the boosting algorithm is orthogonal boosting (oBA), or the orthogonal greedy algorithm in its deterministic version. Only the updating step is changed: an orthogonal projection of the response variable is carried out on all the variables which have been selected up to that point. The advantage of this method is that any variable is selected at most once in this procedure, while in the previous version the same variable might be selected at different steps, which makes the analysis far more complicated. More formally, the method can be described as follows, by modifying Step (4):

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2Equivalently, which fits the gradient best in an \( \ell_2 \)-sense.
Algorithm 2 (Orthogonal L2-Boosting).

\[
\hat{y}^{m+1} = f^{m+1} = P_m y \quad \text{and} \quad U_i^{m+1} = Y_i - \hat{Y}_i^{m+1},
\]

where \( P_m \) denotes the projection of the variable \( y \) on the space spanned by the first \( m \) selected variables (the corresponding regression coefficient is denoted \( \beta_m \)).

3.3. Early Stopping. As already mentioned, early stopping is crucial in boosting to avoid overfitting. The standard approaches for determining the “optimal” stopping time are cross validation and an corrected AIC (Bühlmann (2006)). Both lack a theoretical foundation in a high-dimensional setting, although they are applied by practitioners and often given competitive results. In our analysis, in particular in the simulation study, we rely on theoretical-grounded data driven stopping rules developed in Spindler and Luo (2016). The idea is to stop the boosting algorithm when the improvement in fit is below some pre-specified threshold.

4. Inference for Treatment Effects

4.1. Inference on treatment effects after selection from among high-dimensional controls. We consider the case where a researcher is interested in estimating the treatment effect \( \alpha_0 \) of a treatment variable \( d_i \). In many situations the treatment variable is uncorrelated with the error term \( (d_i) \) only after controlling for sufficient control variables, denoted \( x_i \). Often it is not clear which set of control variables to include, in particular when many potential control variables are available. In such situations, in particular when the number of variables \( p \) is larger than the number of observations \( n \), model selection might be inevitable. Unfortunately, many modern methods, like Lasso or boosting, give consistent model selection only under very strong, in particular in applications in economics, unrealistic assumptions. Hence, relevant variables might be missed, which leads to invalid post-selection inference. To circumvent this problem, we apply the so-called double selection method (Belloni, Chernozhukov and Hansen (2014), Chernozhukov et al. (2016), Chernozhukov, Hansen and Spindler (2015)). To be able to make a valid inference on low-dimensional parameters in a high-dimensional setting, we apply the so-called double selection method. The key idea of double selection is to introduce and estimate an auxiliary regression which safeguards against model selection error of moderate size. The model we estimate is given by

\[
y_i = d_i \alpha_0 + \beta' x_i + \xi_i, \quad E[\xi_i | d_i, x_i] = 0
\]
\[
d_i = \gamma' x_i + \nu_i, \quad E[\nu_i | x_i] = 0.
\]
This method consists of the following three steps, where the first two involve selection with boosting:

1. Run a post- or orthogonal boosting regression of $d_i$ on $x_i$. The set of variables which is selected will be denoted $\hat{I}_1$.
2. Run a post- or orthogonal boosting regression of $y_i$ on $x_i$. The set of variables which is selected will be denoted $\hat{I}_2$.
3. Run an OLS regression of $y_i$ on the treatment variable $d_i$ and the set of variables selected in the first two steps. This set might be augmented by additional variables.

To analyze the double selection estimator based on $L_2$-Boosting, we impose the following assumptions. 

**A.1.**

(i) $w_i = (y_i, d_i, x_i)$, $i = 1, \ldots, n$, i.n.i.d. on $(\Omega, \mathcal{F}, P)$ obeying [6] and [7].

(ii) $||\beta||_0 \leq s$, $||\gamma||_0 \leq s$

(iii) $s^2 \log^2(p \vee n)/n \rightarrow 0$

(iv) $E[|\xi|^q + |\nu_i|^q] \leq C$ for some $q > 4$.

$max_{1 \leq i \leq p} ||X_i||_{\infty}^2 s n^{-1/2+2/q} = o_P(1)$

Assumption [1] imposes standard conditions on the data generating process. Assumption [2](ii) imposes sparsity on the two equations, (iii) restricts the growth of the number of parameters.

**A.2.** We assume that there exist constants $0 < c < 1$ and $C$ such that $0 < 1 - c \leq \phi_\epsilon(s', E_n[x_i'x_i]) \leq \phi_\epsilon(s', E_n[x_i'x_i]) \leq C < \infty$ for any $s' \leq M_0$, where $M_0$ is a sequence such that $M_0 \rightarrow \infty$ slowly along with $n$, and $M_0 \geq s$. $\phi_\epsilon(s', E_n[x_i'x_i])$ denotes the minimum over all smallest eigenvectors of $s'$-dimensional submatrices of $E_n[x_i'x_i]$. $\phi_\epsilon(s', E_n[x_i'x_i])$ is defined in an analog way for the largest eigenvectors.

These conditions are standard for the analysis of Lasso and other Machine Learning methods in a high-dimensional setting.

**A.3.** It exists constants $0 < c < C < \infty$ and $4 < q < \infty$ s.t. for $(a_i, \varepsilon_i) = (y_i, \xi_i)$ and $(a_i, \varepsilon_i) = (d_i, \nu_i)$

(i) $E[|d_i|^q]$, $c \leq E[\xi_i^q | d_i, x_i] \leq C$, $c \leq E[\nu_i^q | x_i] \leq C$ a.s. $E$ denotes the average over the expected values.

(ii) $E[|\xi_i|^q] + E[\varepsilon_i^q] + \max_{1 \leq j \leq p} \left\{ E[x_i^2 \varepsilon_i^2] + E[x_i^3 \varepsilon_i^3] + 1/\bar{E}[x_i] \right\} \leq C$

(iii) $\log^3 p / n \rightarrow 0$

(iv) $\max_{1 \leq i \leq n} \left\{ (E_n - \bar{E})[x_i^2 \varepsilon_i^2] + (E_n - \bar{E})[x_i^3 \varepsilon_i^3] \right\} + \max_{1 \leq i \leq n} \|x_i\|_\infty^2 s \log(n \vee p) / n = o_P(1)$
imposes technical conditions on the regressors and the error terms. They are fulfilled for many relevant designs.

A.4. With probability 1 - \( \alpha \) or larger, \( \sup_{1 \leq j \leq p} \langle X_j, \varepsilon \rangle_n \leq 2\sigma \sqrt{\frac{\log(2p/\alpha)}{n}} =: \lambda_n \) for \( \varepsilon_i = \xi_i \) and \( \varepsilon_i = \nu_i \). \( \langle X_j, \varepsilon \rangle_n \) denotes the empirical inner product.

A.5. \( \min_{j \in T} |\beta_j| \geq J, \max_{j \in T} |\beta_j| \leq J' \), \( |\alpha_0| \leq J' \) for some constants \( J > 0, J' < \infty \).

This assumption is a so-called beta-min condition for the parameters in both equations. Although it might look quite strong at first glance, it can be weakened so that the sequence of absolute values of the coefficients is decreasing with the sample size.

Moreover, we assume that in the boosting regressions early stopping takes place and the stopping criteria follow the proposals in Spindler and Luo (2016) for post- and orthogonal \( L_2 \)-Boosting, i.e. the procedure is stopped when the improvement in fit is below some pre-specified threshold.

With these assumptions, we can now formulate our main theorem.

**Theorem 1.** Let \( P_n \) be the collection of all data generating processes \( P \) for which conditions A.1–A.5 hold for a given \( n \). Then under any sequence \( P_n \in P_n \), the double-selection estimator based on post-\( L_2 \)-Boosting / orthogonal \( L_2 \)-Boosting \( \hat{\alpha} \) satisfies

\[
\sigma_n^{-1} \sqrt{n}(\hat{\alpha} - \alpha_0) \to_D N(0, 1) \tag{8}
\]

where \( \sigma_n^2 = [\hat{E}\nu_i^2]^{-1}\hat{E}[\nu_i^2 \xi_i^2 \hat{E}\nu_i^2]^{-1} \). This holds if \( \sigma_n^2 \) is replaced by \( \hat{\sigma}_n^2 = [E_n\nu_i^2]^{-1}E_n[\nu_i^2 \xi_i^2]E_n[\nu_i^2]^{-1} \) for \( \hat{\xi}_i := (y_i - d_i \hat{\alpha} - x_i'\hat{\beta})(n/(n - \hat{s} - 1))^{1/2} \) and \( \nu_i := d_i - x_i'\hat{\gamma}, i = 1, \ldots, n \), where \( \beta \) denotes the post-double selection estimator.

**Proof.** Assumptions A.1(i)–(iii), A.2, A.4, and A.5 imply, according to Spindler and Luo (2016), that condition HLMS(\( P \)) in Belloni et al. (2014) is satisfied. Conditions A.1, A.3 and A.5 imply conditions ASTE(\( P \)), SM(\( P \)) and SE(\( P \)). Hence, Theorem 2 in Belloni et al. (2014) yields the result. ■

The construction of uniform valid confidence intervals is given in the corollary.

**Corollary 4.1.** Under the assumptions of Theorem 1 and with \( c(1 - \xi) = \Phi^{-1}(1 - \xi/2) \), the confidence regions based upon \( \hat{\alpha}, \hat{\sigma}_n \) are valid uniformly in \( P \in P \):

\[
\lim_{n \to \infty} \sup_{P \in P} |P(\alpha_0 \in [\hat{\alpha} \pm c(1 - \xi)\hat{\sigma}_n\sqrt{n}]) - (1 - \xi)| = 0.
\]

4.2. **Inference on treatment effects in an instrumental variable model.** Suppose given the model

\[
\begin{align*}
y_i &= d_i\alpha_0 + \beta'x_i + \varepsilon_i, E[\varepsilon_i|z_i] = 0 \tag{9} \\
D_i &= D(z_i) = E[d_i|z_i] = \gamma'z_i. \tag{10}
\end{align*}
\]
To estimate the coefficient $\alpha_0$ of the endogenous treatment variable, we employ the following two-stage least squares (tsls) procedure: In the first step, we estimate and predict the instrument $\hat{D}_i$ by post- or orthogonal $L_2$-Boosting. Finally, we estimate $\hat{\alpha}_0$ by a regression of the outcome variable $y$ on the predicted instrument $\hat{D}_i$ and the controls.

**B.1.** The data $(y_i, d_i, x_i, z_i)$ is i.i.d. normal and obeys the linear IV model.

**B.2.** The optimal instrument function $D_i$ can be approximated by $s$ instruments which can be unknown:

$$D(z_i) = \gamma' z_i, ||\gamma|| \leq s = o(n)$$

**B.3.** (SE) We assume that there exist constants $0 < c < 1$ and $C$ such that $0 < 1 - c \leq \phi_s(s', E_n[z'_i z_i]) \leq \phi_I(s', E_n[z'_i z_i]) \leq C < \infty$ for any $s' \leq M_0$, where $M_0$ is a sequence such that $M_0 \rightarrow \infty$ slowly along with $n$, and $M_0 \geq s$.

**B.4.** (i) The eigenvalues of $Q = \bar{E}[D(z_i)D(z_i)']$ are bounded uniformly from above and away from zero, uniformly in $n$. $E[\varepsilon_i^2 | x_i]$ is bounded uniformly from above and from below uniformly in $i$ and $n$. Wlog, $\bar{E}[|z_j^2 \varepsilon_i^2|] = 1$, $\forall 1 \leq j \leq P$ and $\forall n$.

(ii) For some $q > 2$ and $q_\varepsilon > 2$, uniformly in $n$, $\max_{1 \leq j \leq p} E[|z_j \varepsilon_i|^3] + E[||D_i||_2 | \varepsilon_i|^{2q}] + E[|\varepsilon_i|^{3q}] + E[|d_i|_2^q] = O(1)$

(iii) $\log^3 p = o(n)$

(a) $\frac{s \log(p\vee n)}{n} n^{2/q_\varepsilon} \to 0$

(b) $\frac{s^2 \log^2(p\vee n)}{n} \to 0$

(c) $\max_{1 \leq j \leq p} E_n[|z_j^2 \varepsilon_i^2|] = O_P(1)$.

**B.5.** $\min_{j \in T} |\gamma_j| \geq J$, $\max_{j \in T} |\gamma_j| \leq J'$ for some constants $J > 0, J' \leq \infty$.

**Theorem 2.** Under conditions B.1–B.5, the IV estimator $\hat{\alpha}$ based on post-$L_2$-Boosting or orthogonal $L_2$-Boosting of the optimal instrument satisfies

$$(Q^{-1} \Omega Q^{-1})^{-1/2} \sqrt{n}(\hat{\alpha} - \alpha_0) \to_d N(0, I)$$

for $\Omega := \bar{E}[\varepsilon_i^2 D(z_i)D(z_i)']$ and $Q := \bar{E}[D(z_i)D(z_i)']$.

**Proof.** Conditions B.1, B.2, B.3 and B.5 imply that the first step regression estimated with post- or orthogonal boosting converges in prediction norm and in $L_2$ with the “Lasso”-rate, as shown in Spindler and Luo (2016). This and B.1–B.4 allows applying theorem 4 in Belloni et al. (2012), which concludes the proof. ■
5. Simulation Study

In this section we present simulation results for both settings.

5.1. Inference on treatment effects after selection from among high-dimensional controls. Here we consider the following data generating process:

\[ y_i = d_i \alpha_0 + x_i' \theta_g + \xi_i \]  
\[ d_i = x_i' \theta_m + \nu_i, \]

where \((\xi_i, \nu_i)' \sim N(0, I_2)\) with \(I_2\) the 2 \times 2 identity matrix, \(x_i \sim N(0, \Sigma)\) with \(\Sigma_{kj} = 0.5^{j-k}\). \(x_i\) consists of \(p = 100\) or \(p = 10\) components. The parameter of interest, \(\alpha_0\), is set equal to 0.5. We consider both a sparse setting and an approximate sparse setting where \(\theta_g = \theta_m\). In the sparse setting the first \(s\) coefficients are set equal to one and all other parameters \(p-s\) are equal to zero. In the approximate sparse setting the coefficient vectors are of the form \((1, 0.7^2, 0.7^3, \ldots, 0.7^{p-1})^2\). We vary both the sample size \(n\) and the sparsity index \(s\). The number of repetitions is \(R = 500\). Tables 1 and 2 show the results (bias and rejection rates) for the sparse setting with the double selection method. Tables 2 and 4 show the corresponding results for the approximate sparse setting. Under approximate sparsity the bias of the post-lasso procedure seems to be slightly smaller, while the rejection rates seem to be comparable with one exception \((n = 100, p = 100)\). But this setting might not be considered as sparse. The pattern in the exact sparsity seems to be similar. Finally, we would also like to mention that the classical \(L_2\)-boosting algorithm performs comparable to the other booting algorithms analyzed in the simulation study here, although the results are not included in the tables.

| \(n\) | \(p\) | \(s\) | post-Lasso | post-BA | oBA |
|---|---|---|---|---|---|
| 100 | 10 | 5 | 0.00 | -0.00 | 0.00 |
| 100 | 100 | 10 | -0.01 | -0.08 | 0.05 |
| 100 | 100 | 20 | -0.01 | 0.20 | 0.35 |
| 100 | 100 | 50 | 0.66 | 0.44 | 0.52 |
| 200 | 10 | 5 | -0.00 | -0.01 | 0.00 |
| 200 | 100 | 10 | -0.00 | -0.02 | 0.00 |
| 200 | 100 | 20 | -0.00 | 0.30 | 0.44 |
| 200 | 100 | 50 | -0.00 | 0.30 | 0.44 |
| 400 | 10 | 5 | -0.00 | -0.00 | 0.00 |
| 400 | 100 | 10 | -0.00 | -0.01 | 0.00 |
| 400 | 100 | 20 | 0.00 | -0.01 | 0.03 |
| 400 | 100 | 50 | 0.00 | -0.00 | 0.13 |
5.2. IV estimation with many instruments. The simulations are based on a simple instrumental variables model data generating process:

\[ y_i = \beta d_i + e_i, \]  
\[ d_i = z_i \Pi + v_i, \]  
\[ (e_i, v_i) \sim N \left( 0, \begin{pmatrix} \sigma_e^2 & \sigma_{ev} \\ \sigma_{ev} & \sigma_v^2 \end{pmatrix} \right) \text{ i.i.d.}, \]  

where \( \beta = 1 \) is the parameter of interest. The regressors \( Z_i = (z_{i1}, \ldots, z_{i100})' \) are normally distributed \( N(0, \Sigma_Z) \) with \( \mathbb{E}[z_{ih}^2] = \sigma_z^2 \) and \( \text{Corr}(z_{ih}, z_{ij}) = 0.5^{|i-j|} \). \( \sigma_z^2 \) and \( \sigma_e^2 \) are set to unity, \( \text{Corr}(e, v) = 0.6 \). \( \sigma_v^2 = 1 - \Pi' \Sigma_z \Sigma \) so that the unconditional variance of the endogenous variable equals 1. The first stage coefficients are set according to \( \Pi = CP \). For \( P \) we use a sparse design, i.e., \( P = (1, \ldots, 1, 0, \ldots, 0) \) with \( s \) coordinates equal to one and all other \( p - s \) equal to zero. \( C \) is set in such a way that we generate

**Table 2. Simulation results double selection method: Bias, approximate sparsity**

| \( n \) | \( p \) | post-Lasso | post-BA | oBA |
|---|---|---|---|---|
| 100 | 10 | -0.00 | -0.01 | -0.01 |
| 100 | 100 | 0.00 | -0.06 | -0.05 |
| 200 | 10 | -0.00 | -0.01 | -0.01 |
| 200 | 20 | -0.00 | -0.02 | -0.02 |
| 200 | 50 | 0.00 | -0.02 | -0.02 |
| 200 | 100 | 0.00 | -0.04 | -0.04 |
| 400 | 10 | -0.00 | -0.00 | -0.00 |
| 400 | 20 | 0.00 | -0.00 | -0.00 |
| 400 | 50 | -0.00 | -0.02 | -0.02 |
| 400 | 100 | 0.01 | -0.01 | -0.01 |

**Table 3. Simulation results double selection method: Rejection Rate, exact sparsity**

| \( n \) | \( p \) | \( s \) | post-Lasso | post-BA | oBA |
|---|---|---|---|---|---|
| 100 | 10 | 5 | 0.04 | 0.04 | 0.05 |
| 100 | 100 | 10 | 0.06 | 0.08 | 0.05 |
| 100 | 100 | 20 | 0.11 | 0.10 | 0.09 |
| 100 | 100 | 50 | 0.98 | 0.96 | 0.96 |
| 200 | 10 | 5 | 0.06 | 0.06 | 0.07 |
| 200 | 100 | 10 | 0.06 | 0.06 | 0.06 |
| 200 | 100 | 20 | 0.09 | 0.09 | 0.09 |
| 200 | 100 | 50 | 0.09 | 0.09 | 0.09 |
| 400 | 10 | 5 | 0.05 | 0.06 | 0.05 |
| 400 | 100 | 10 | 0.06 | 0.05 | 0.06 |
| 400 | 100 | 20 | 0.05 | 0.07 | 0.07 |
| 400 | 100 | 50 | 0.06 | 0.06 | 0.06 |

The simulations are based on a simple instrumental variables model data generating process:

\[ y_i = \beta d_i + e_i, \]
\[ d_i = z_i \Pi + v_i, \]
\[ (e_i, v_i) \sim N \left( 0, \begin{pmatrix} \sigma_e^2 & \sigma_{ev} \\ \sigma_{ev} & \sigma_v^2 \end{pmatrix} \right) \text{ i.i.d.}, \]
### Table 4. Simulation results double selection method: Rejection Rate, approximate sparsity

| n   | p   | post-Lasso | post-BA | oBA |
|-----|-----|------------|---------|-----|
| 100 | 10  | 0.04       | 0.04    | 0.05|
| 100 | 100 | 0.08       | 0.16    | 0.15|
| 200 | 20  | 0.06       | 0.05    | 0.05|
| 200 | 50  | 0.05       | 0.05    | 0.06|
| 200 | 100 | 0.05       | 0.09    | 0.08|
| 400 | 10  | 0.08       | 0.08    | 0.08|
| 400 | 20  | 0.05       | 0.05    | 0.05|
| 400 | 50  | 0.06       | 0.06    | 0.06|
| 400 | 100 | 0.08       | 0.06    | 0.05|

The target values for the concentration parameter $\mu = \frac{n\Sigma_{10} \Pi}{\sigma_2}$ which determines the behavior of the IV estimators. We set $p = 100$ and the concentration parameter equal to 180 and vary both the sample size $n$ and the sparsity index $s$. The number of repetitions in the simulations study is again $R = 500$. We estimate the first stage and calculate the first stage predictions with $L_2$-Boosting and its variants. The simulation results in Tables 5 and 6 reveal that boosting performs comparable to post-Lasso in the examined settings concerning both bias and the rejection rates. Although we have not included the results for the “classical”boosting algorithm, as it is not covered by our theory, the empirical performance is similar to the post- and orthogonal boosting algorithms.

### Table 5. Simulation results: Bias

| n   | p   | s   | post-Lasso | post-BA | oBA |
|-----|-----|-----|------------|---------|-----|
| 400 | 100 | 5   | -0.0017    | -0.0027 | -0.0021|
| 400 | 100 | 10  | 0.0060     | 0.0055  | 0.0061 |
| 400 | 100 | 20  | -0.0022    | -0.0028 | -0.0050|
| 400 | 100 | 50  | -0.0138    | -0.0031 | -0.0029|
| 800 | 100 | 5   | 0.0031     | 0.0041  | 0.0038 |
| 800 | 100 | 10  | 0.0060     | 0.0055  | 0.0061 |
| 800 | 100 | 50  | 0.0011     | 0.0025  | 0.0030 |
| 800 | 100 | 100 | -0.3618    | 0.0001  | 0.0013 |

6. Application: Analysis of the PAC-man Study

6.1. The PAC-man study. To illustrate our method, we analyze the PAC-man study mentioned in the Introduction. There were 1,013 patients who took part in this study, which was conducted as a randomized control trial. There were 506 patients treated with PAC, and 507 patients formed the control group. The research question is whether the treatment by a PAC increases the patient’s number of quality-adjusted life years (QALYs), which is the outcome variable. One QALY represents one year of life in full
Table 6. Simulation results: Rejection Rate

| n   | p  | s | post-Lasso | post-BA | oBA |
|-----|----|---|------------|---------|-----|
| 400 | 100 | 5 | 0.052      | 0.060   | 0.046 |
| 400 | 100 | 10| 0.056      | 0.050   | 0.056 |
| 400 | 100 | 20| 0.080      | 0.066   | 0.062 |
| 400 | 100 | 50| 0.044      | 0.060   | 0.058 |
| 800 | 100 | 5 | 0.062      | 0.056   | 0.058 |
| 800 | 100 | 10| 0.056      | 0.050   | 0.056 |
| 800 | 100 | 50| 0.058      | 0.044   | 0.054 |
| 800 | 100 | 100| 0.032     | 0.046   | 0.050 |

health; an in-hospital death corresponds to a QALY of zero. The dataset contains 53 covariates about each individual in the study. There are two reasons, as argued in Section 2, to use additional covariates in the analysis of this randomized control trial: First, additional covariates allow a more precise estimation of the treatment effect. Second, despite the randomized design of the study, conditioning on covariates might reinforce unconfoundedness. It might be possible that certain conditions (e.g., acute health conditions) lead to a deviation from the randomized protocol. Using a large set of covariates describing individual specific health conditions, but also hospital specific conditions, might control for such deviations. The PAC-man study was discussed widely in the literature. Bloniarz et al. (2016), which is closest to our setting, consider Lasso adjustments of treatment effect estimates in randomized experiments in a high-dimensional setting. We follow their proposal to construct the design matrix $X$ by including all main effects and two-way interactions. Interactions which are highly correlated (with a correlation larger than 0.95) are excluded. Additionally, indicators with very sparse entries (when the number of 1’s is less than 20) are also removed. This results in a total of 771 regressors. The covariates contain detailed information on the patient’s health conditions, e.g., pre-existing conditions and current health status measured by different biomarkers, and also hospital specific information. For a detailed description we refer to the documentation of the PAC-man study.

6.2. Results. We estimate the following model.

$$ y_i = \delta d_i + \beta' x_i + \varepsilon_i, i = 1, \ldots, 1013. $$

The number of QALYs are the outcome variable $y_i$. The treatment variable $d_i$ is a binary variable indicating PAC. $\varepsilon_i$ denotes the residuals. We estimate the (constant) treatment effect without any controls (baseline estimator) as is the standard approach in RCTs, but we also control for covariates. The results are presented in Table 7. The baseline estimator gives a negative treatment effect but with a $p$-value of 0.665. The

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Bloniarz et al. (2016) have in total 1172 regressors as the dataset of the PAC-man study which was provided to them contains four additional variables to which we have no access.
Table 7. Results of the PAC-man Study

|            | Baseline | BA    | post-BA | oBA   |
|------------|----------|-------|---------|-------|
| Est.       | -0.123   | 0.218 | 0.224   | -0.052|
| se         | 0.284    | 0.261 | 0.265   | 0.286 |
| p-value    | 0.665    | 0.798 | 0.801   | 0.428 |

$L_2$-Boosting algorithm (BA) and the post variant (post-BA) show a positive treatment effect, but also not significant. Surprisingly, while in the simulation study and many applications the three boosting algorithms have comparable results, the orthogonal variant (oBA) differs to a large extent from the first two versions, giving a negative estimate. But this estimate is also insignificant. An insignificant treatment effect in the PAC-man study is also in line with the results presented in Bloniarz et al. (2016).

7. Conclusion

In this paper we apply $L_2$-Boosting, namely the post- and orthogonal version for estimation of treatment effects in the setting of many controls and many instruments. We derive uniformly valid results for the asymptotic distribution of estimated treatment effects. We use the framework of orthogonalized moment conditions introduces by Belloni, Chernozhukov, Hansen and coauthors in a series of papers to derive the results. The second ingredient are results on the rate of convergence of $L_2$ given in Spindler and Luo (2016). In the simulation study our proposed method works well and is comparable with Lasso. Finally, we analyze the PAC-man study which stimulated a lot of research in Medicine and related fields. We find that the treatment effect is not significantly different from zero.
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