Valid Instrumental Variables Selection Methods using Auxiliary Variable and Constructing Efficient Estimator

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Abstract

In observational studies, we are usually interested in estimating causal effects between treatments and outcomes. When some covariates are not observed, an unbiased estimator usually cannot be obtained. In this paper, we focus on instrumental variable (IV) methods. By using IVs, an unbiased estimator for causal effects can be estimated even if there exists some unmeasured covariates. IV methods are useful, however, they sometimes suffer from weak IV and invalid IV problems. In this paper, we propose the moment type estimator which overcomes the major IV problems at once. To achieve this, we consider the situation where some auxiliary variables such as the Negative Control Outcomes can be used. One of the important points of our proposed method is that there are no necessity to specify not only the set of valid IVs but also the proportion of them in advance: this point is different from previous methods. We prove the proposed estimator has the same asymptotic variance as Generalized Method of Moments; the semiparametric efficiency. Also, we confirm properties of our method and previous methods through simulations.

Keywords: Causal inference, Exclusion restriction, Instrumental variable, Mendelian randomization, Negative control outcome, Semiparametric efficiency, Variable selection, Unmeasured covariates
1 Introduction

In observational studies, we are usually interested in estimating causal effects between treatments and outcomes, however, there are serious risks of estimating biased causal effects unless covariates (or confounding; hereafter, we call “covariates”) are appropriately adjusted. When all covariates are observed, the covariates can be adjusted and an unbiased estimator for causal effects can be obtained; the situation of “no unmeasured confounding” (or “strong ignorability”, c.f. Hernán and Robins, 2020 and Rosenbaum and Rubin, 1983). No unmeasured confounding is one of the sufficient assumptions to estimate an unbiased estimator for causal effects. Whereas, when some covariates are not observed, an unbiased estimator usually cannot be obtained; the situations where there are some unmeasured covariates. Therefore, another sufficient assumption need to be used. In this paper, we focus on instrumental variable (IV) methods.

Regarding IV methods, many theoretical results have been derived and there exists many applications in econometrics (Sargan, 1958, White, 1982, Andrews, 1990, Newey, 1990, Imbens, 2002, Hong et al., 2003, Liao, 2013, Kolesár et al., 2013, and DiTraglia, 2016). In biometrics and related fields, some theoretical results and applications have been appeared in recent years (Brookhart and Schneeweiss, 2007, Baiocchi et al., 2014, Kang et al., 2016, Bowden et al., 2016 Burgess et al., 2017, Hartwig et al., 2017, and Orihara, 2021). IVs need to satisfy three conditions:

IV conditions

1) Related to treatments

2) No direct effects to outcomes (exclusion restriction)

3) No correlations between IVs and unmeasured covariates

Variables satisfying the above three conditions are called as “valid IVs”, and not valid IVs are called as “invalid IVs” in this paper especially when emphasizing the validity. By using
IVs, an unbiased estimator for causal effects can be estimated even if there exists some unmeasured covariates (c.f. Hayashi, 2000 and Baiocchi et al., 2014). IV methods are useful, however, sometimes suffer from “weak IV problem”, especially in Mendelian Randomization (MR); using genetic variants as IVs. Weak IV problem occurs when there are weak correlations between treatments and IVs. In MR, constructing an allele score by using many DNA alleles as IVs is one of the solutions. (Pierce et al., 2011 and Burgess et al., 2017). Note that an allele score is assumed as a weighted linear combination of IVs, and the weights are estimated by ad-hoc procedures (Burgess et al., 2017); there are no theoretical justification for the estimated weights except for some situations. Constructing a linear combination of IVs (i.e. an allele score) solves weak IV problems; however, there are risks estimating biased causal effects by including some invalid IVs.

Not only in MR but also other fields, there are many interests to estimate unbiased causal effects when there are some invalid IVs. IV condition 1) can be assessed simply by confirming from datasets, whereas, some schemes (e.g. sensitivity analysis) are applied to confirm condition IV condition 2) and 3) (Baiocchi et al., 2014). From here, we introduce important results to date with IV condition 2) and 3) deviations, respectively. Regarding IV condition 2), there are some important results. Kang et al., 2016 have derived an estimator that has consistency and asymptotic normality only when there were more than half of valid IVs in candidates of IVs (i.e. the set of candidates of IVs includes valid IVs and invalid IVs), and linear relationships between outcomes and treatments and between treatments and valid IVs respectively. Also, valid IVs can be selected by using shrinkage methods. Their result leads continuous discussions and further sophisticated results (Guo et al., 2018 and Windmeijer et al., 2019). Kolesár et al., 2013 also have derived the similar estimator under different but strong assumptions. Bowden et al., 2016 and Hartwig et al., 2017 propose simple but important estimating procedures from the viewpoint of genetics. However, their methods have not proved theoretical features such as consistency and asymptotic normality. In MR, the violation of IV condition 2) is derived from horizontal pleiotropy (Davies et al.,
Since horizontal pleiotropy derives two or more phenotypes, it is possible that genetic variants relate to outcomes directly. To overcome this problem, we confirm that it is possible some genetic variants are correlated with some phenotype (except for interested one) or not. Regarding IV condition 3), there are also important results. As a very important and famous conclusion, Sagan, 1958 has proposed a statistical test judging there are some invalid IVs or not in candidates of IVs when assuming overidentifying restriction; there are more candidates of IVs than treatments. However, the test cannot answer which candidates are invalid. DiTraglia, 2016 has proposed an information criterion selecting IVs based on Focused Information Criterion (Claeskens and Hjort, 2003). Since the information criterion selects variables from candidates of IVs so that the mean squared error of an estimator of causal effects becomes small, it doesn’t select the valid IVs exactly. Liao, 2013 has proposed a shrinkage method not only to estimate parameters but also to select parameters. However, their methods need a very strong assumption: we have to know exactly which candidates are valid IVs or not. Andrews, 1999 has also proposed an information criterion selecting valid IVs without the strong assumption. The information criterion has the similar features as ordinary model selection criterions by selecting a penalty term only when there are linearity of interested parameters.

As described in the previous paragraph, there are important results to solve IV condition 2) and 3) violation. However, there may be some applicational problems since we need to know a) the feature of genetic variants in advance or b) some model assumptions. In this paper, we apply another assumption: using auxiliary variables which include Negative Control Outcomes (NCOs; Tchetgen Tchetgen, 2014, Miao and Tchetgen Tchetgen, 2018, Sanderson et al., 2020, Shi et al., 2020, and Katsoulis et al., 2021) to relax assumptions such as a) and b) even a little. NCO is a variable it relates to unobserved variables but does not relate to IVs and treatments directly; only through unobserved variables. By using NCOs, the correlation between some genetic variants and some phenotypes or unmeasured covariates can be detected without considering the feature of genetic variants in advance. In
this paper, we propose the new two-step estimating procedure: an allele score is estimated in the first step, and an outcome model is estimated in the second step. We also prove that our proposed estimator has good theoretical properties. In particular, the estimator has the same asymptotic variance as Generalized Method of Moments (GMM, see Imbens, 2000); the semiparametric efficiency. This efficiency is achieved by the construction of the allele score in the first step. Also, our proposed method can be used for both dichotomous treatment and nonlinear outcome model situations. One of the important point of our proposed method is that the method may overcome the problems of IV condition 2) and 3) violation all at once. This is because our discussion assumes only minimum model constructions, and the key variable is only NCO. In other words, phenotypes affected by horizontal pleiotropy and unmeasured covariates are the same in some theoretical settings.

The remainder of the paper proceeds as follows. In section 2, we discuss the situation where all candidates of IVs are valid. We show that parameters of a linear combination of IVs can be estimated through a linear estimating equation and our proposed method has the same asymptotic variance as GMM. In section 3, we explain a selection method of the valid IVs without prior informations and the method has useful properties. In section 4, we confirm properties of our method and previous methods through simulation dataset. Important regularity conditions, all proofs, and all figures are given in appendix.

2 Situations where all instrumental variables are valid

At first, we discuss the situation where all candidates of IVs are valid; we need not select valid IVs. Let \( n \) be the sample size. \( T_i \in T \subset \mathbb{R}, X_i \in \mathbb{R}^p, U_i \in \mathbb{R}, Z_i \in \mathbb{R}^K, \) and \( Y_i \in \mathbb{R} \) denote the treatment, a vector of covariates, an unobserved variable, a vector of IVs, and an observed outcome respectively, where the r.v.s have appropriate moment conditions. Note that when \( T = \{0, 1\} \), it means binary treatment situations. We assume that \( i = 1, 2, \ldots, n \)
are i.i.d. samples. Throughout this paper, the following linear model is assumed:

\[ y_i = t_i \beta_t + x_i^\top \beta_x + u_i, \]  

(2.1)

where \( E[U_i] = 0 \), \( Var(U_i) = \sigma^2 < \infty \) and \( \beta = (\beta_t, \beta_x^\top)^\top \). Note that our results can be expanded to nonlinear situation, however, we consider only linear model to clarify the relationship between GMM. Also, we assume that \( U_i \perp \perp (Z_i, X_i) \) and \( U_i \not\perp T_i \). Note that the covariates are regarded as constant: \( X_i \equiv 1 \), and this is common situation of MR. When estimating \( \beta \) by using OLS, there may be some biases; therefore, the following estimating equation is used (c.f. Hayashi, 2000, Burgess et al., 2017):

\[
\sum_{i=1}^{n} \begin{pmatrix} h(z_i) \\ x_i \end{pmatrix} \left( y_i - (t_i \beta_t + x_i^\top \beta_x) \right) = 0_{p+1},
\]  

(2.2)

where \( h(\cdot) \) is \( K \)-dimensional or less measurable function. If the model (2.1) is correct, then the estimating equation (2.2) becomes

\[
E \left[ \begin{pmatrix} h(Z) \\ X \end{pmatrix} (Y - (T \beta_t^0 + X^\top \beta^0)) \right] = E \left[ \begin{pmatrix} h(Z) \\ X \end{pmatrix} \right] E [Y - (T \beta_t^0 + X^\top \beta^0)] = 0_{p+1},
\]

where the superscript “0” of parameters means the true value of parameters. Therefore, the solution of the estimating equation (2.2) becomes the consistent estimator. Under some regularity conditions, the following asymptotic normality holds:

\[
\sqrt{n} \left( \hat{\beta}^{IV} - \beta^0 \right) \xrightarrow{L} N \left( 0_{p+1}, (\Gamma_1)^{-1} \Sigma_1 (\Gamma_1^\top)^{-1} \right), \]

(2.3)
where
\[
\Sigma_1 = E \left[ \begin{pmatrix} HU \\ XU \end{pmatrix} \otimes^2 \right] = \sigma^2 \begin{pmatrix} E[H^2] & E[H X^T] \\ E[X H^T] & E[X X^T] \end{pmatrix}, \quad \Gamma_1 = \begin{pmatrix} E[H T] & E[H X^T] \\ E[T X] & E[X X^T] \end{pmatrix},
\]
and \( \Gamma_1 \) is non-singular matrix. Note that estimators of (2.1) are expressed as
\[
\hat{\beta}^{(i)} = \left( \hat{\beta}_t^{(i)}, \hat{\beta}_x^{(i)} \right)^T,
\]
e.g. \( \hat{\beta}^{IV} \) means ordinary IV estimator.

From here, we consider how to select the function \( h(\cdot) \) such that the asymptotic variance of (2.3) is minimized. As describing in Introduction, an allele score that means a linear combination of IVs is well considered in MR (Burgess et al., 2017):
\[
h(z_i) = \gamma^T z_i = \sum_{k=1}^K \gamma_k z_{ik}, \quad (2.4)
\]
where \( \gamma \in \mathbb{R}^K \). Note that \( h(z_i) \) is also IVs. For instance in Burgess et al., 2017, the parameters \( \gamma \) are estimated as the inverse of standard deviations of each IVs; some ad-hoc procedures are used to estimate \( \gamma \). In fact, \( \gamma \) can be considered as the solution of a linear estimating equation under a model (2.1). Furthermore, the estimator \( \hat{\gamma} \) can be estimated such that the asymptotic variance of (2.3) becomes minimum; that is, a IV estimator can be estimated as “best”.

**Proposition 1.**
Assume that \( \Gamma_1 > O \). When C.1 and C.2 hold, the solution of the following estimating equation \( \hat{\gamma} \) gives the minimal asymptotic variance of \( \hat{\beta}^{IV} \):
\[
\left( E[Z^2] - E[Z X^T] E[X X^T]^{-1} E[X Z^T] \right) \gamma - \left( E[Z T] - E[Z X^T] E[X X^T]^{-1} E[T X] \right) = 0_K
\]
(2.5)
Then, the asymptotic variance becomes

\[
\begin{aligned}
\left( (\Gamma'_{1})^{-1} \Sigma_{1} (\Gamma'_{1})^{-1} \right)_{(1,1)} &= \sigma^2 \Omega^{-1}_{opt}, \\
\left( (\Gamma'_{1})^{-1} \Sigma_{1} (\Gamma'_{1})^{-1} \right)_{(1,2)} &= \left( (\Gamma'_{1})^{-1} \Sigma_{1} (\Gamma'_{1})^{-1} \right)_{(2,1)}^{\top} = -\sigma^2 \Omega^{-1}_{opt} E[TX^{\top}] E[XX^{\top}]^{-1}, \\
\left( (\Gamma'_{1})^{-1} \Sigma_{1} (\Gamma'_{1})^{-1} \right)_{(1,1)}' &= E[XX^{\top}]^{-1} + \sigma^2 \Omega^{-1}_{opt} E[XX^{\top}]^{-1} E[TX] E[TX^{\top}] E[XX^{\top}]^{-1},
\end{aligned}
\]

where

\[
\Omega_{opt} = \left( E[ZZ^{\top}] - E[XX^{\top}] E[XX^{\top}]^{-1} E[TX] \right)^{\top} \left( E[ZZ^{\top}] - E[XX^{\top}] E[XX^{\top}]^{-1} E[XX^{\top}] \right)^{-1} \times \left( E[ZZ^{\top}] - E[XX^{\top}] E[XX^{\top}]^{-1} E[TX] \right)
\]

Note 1.
The solution of (2.5) \( \hat{\gamma} \) means the OLS estimator for \( Z \) when \( T \) and \((Z, X)\) are regarded as a response variable and objective variables, respectively. If there are linear relationships between \( T \) and \((Z, X)\), \( \hat{\gamma} \) becomes the consistent estimator for coefficient of \( T \).

Note 2.
The result of Proposition 1 has different optimality of Newey, 1990. Newey, 1990 has to detect the true model of \( T \), whereas our methods does not; our methods does not have any concern about misspecification of the model. Rather, our methods are regarded as expansion of Two-stage IV method (White, 1982).

From the result of Proposition 1 we can estimate the weights of an allele score so that the asymptotic variance of \( \hat{\beta}^{IV} \) becomes minimal. By the way, as a well-known fact, the GMM has the semiparametric efficiency; the asymptotic variance of (2.3) is minimized when the function \( h(\cdot) \) is selected as

\[
h(Z_i) = (Z_{i1}, \ldots, Z_{iK})^{\top}.
\]
Under this situation, the following asymptotic normality holds:

\[
\sqrt{n} \left( \hat{\beta}^{GMM} - \beta^0 \right) \xrightarrow{L} N \left( 0, \left( \Gamma_1 \Sigma_1^{-1} \Gamma_1^\top \right)^{-1} \right),
\]

(2.7)

where \( \Sigma_1 \) and \( \Gamma_1 \Sigma_1^{-1} \Gamma_1^\top \) are non-singular matrix. From the next theorem, we can derive the important conclusion that \( \hat{\beta}^{IV} \) also has the semiparametric efficiency.

**Theorem 1.**

*When C.1 and C.2 hold, the asymptotic variance related to \( \hat{\beta}^{GMM} \) is the same as (2.6).*

As mentioned previously, the solution of (2.5) \( \hat{\gamma} \) gives the minimal asymptotic variance of \( \hat{\beta}^{IV} \); it is one of a different point from GMM. By using the feature, we can propose the valid IVs selection method in the next section.

### 3 Situations where some instrumental variables are invalid

In the previous section, we discussed the situation where all \( Z \) are valid IVs, but in the case of a large number of IVs such as genetic variants, there are risks that estimating biased causal effects by including some invalid IVs. In this section, we discuss the situation where some of candidates of IVs \( (Z_{\ell+1}, \ldots, Z_K) \) do not satisfy at least IV condition 2) or 3) explained at Introduction; in other words, \( (Z_{\ell+1}, \ldots, Z_K) \) are invalid IVs.

Invalid IVs do not satisfied IV condition 2) or 3); mathematically denoted as \( Z_j \not\perp \perp U, j \in \{\ell + 1, \ldots, K\} \) in this paper. From IV condition 2), \( U \) is considered as an “unmeasured phenotype” affected by horizontal pleiotropy. From IV condition 3), \( U \) is considered as an “unmeasured covariate”. Since \( U \) is an unobserved variable, the nature of the variable itself cannot be directly examined from the data. This is because we need to clarify relationship between IVs and an unmeasured variable from another viewpoint; Kang et al., 2014 assume the proportion of valid IVs and linear models, and Liao, 2013 and DiTraglia, 2016 assume the
set of valid IVs are correctly specified. The common denominator is the prior information of IVs is necessary. In this paper we apply another assumption: using auxiliary variables which are included in Negative Control Outcomes (NCOs; Tchetgen Tchetgen, 2014, Miao and Tchetgen Tchetgen, 2018, Sanderson et al., 2020, Shi et al., 2020, and Katsoulis et al., 2021). NCO is the variable that relates to unobserved covariates but does not relate to IVs and treatments directly; only through unobserved covariates. By using NCO, we need not specify not only the set of valid IVs but also the proportion of them in advance. Therefore, our methods are more useful than the previous methods when using auxiliary variables. Note that the auxiliary variable can be considered as one-dimensional in this paper, this limitation is not essential and can theoretically be extended to two or more dimensions. The NCO has been used in epidemiological studies as a way to check for the effects of unobserved covariates. Here, we present a case study of the relationship between water quality and diarrhea in children as presented in Miao and Tchetgen Tchetgen, 2018, and review a real-life example of NCO.

Khush et al. (2013) studied the association between water quality and child diarrhea in rural Southern India. Escherichia coli in contaminated water can increase the risk of diarrhea, but is unlikely to cause respiratory symptoms such as constant cough, congestion, etc. Khush et al. observed a slightly higher diarrhea prevalence at higher concentrations of Escherichia coli; however, repeated analysis shows a similar increase in risk of respiratory symptoms, which suggests that at least part of the association between Escherichia coli and diarrhea is a result of confounding. (Miao and Tchetgen Tchetgen, 2018, p.7)

At first, we introduce mathematically assumptions for unobserved variables, NCOs, and candidates of IVs to continue the discussion of the following this paper.

Assumption 1.

Unobserved covariates $U \in \mathbb{R}$, Negative Control Outcome (NCO) $M \in \mathbb{R}$, and candidates of
IVs

\[ Z = (Z_1, \ldots, Z_\ell, Z_{\ell+1}, \ldots, Z_K)^\top \in \mathbb{R}^K \]

assume the following assumptions:

1. \( \mathbb{E}[M] = 0 \)

2. \( M = M(U) + \varepsilon, \ \varepsilon \perp \perp (T, X, Z), \ \mathbb{E}[\varepsilon] = 0, \ \text{Var}(\varepsilon) < \infty \)

3. \( |\mathbb{E}[Z_kM]| > w > 0, \text{ if } k \in \{\ell + 1, \ldots, K\} \)

1. is not an essential assumption, but to simplify the discussion below. 2. is an assumption for detect valid IVs from the candidates. Under 1 and 2., when \( k \in \{1, \ldots, \ell\}, \)

\[ \mathbb{E}[Z_kM] = \mathbb{E}[M(U)\mathbb{E}[Z_k|U]] = \mathbb{E}[M(U)]\mathbb{E}[Z_k] = 0. \]

3. expresses the relationship between invalid IVs and NCO. By utilizing from 1 to 3., it is possible to identify valid and invalid IVs by NCO.

**Note 3.**

Assuming \( M(U) = U\delta + \varepsilon. \) The model satisfy 1 and 2. About 3.,

\[ |\mathbb{E}[Z_kM]| = |\mathbb{E}[Z_kU]|||\delta| > w. \]

Therefore, Assumption 3 can be reduced to an assumption about the magnitude of an unmeasured variable between unobserved covariates and invalid IVs.

**Note 4.**

In this paper, we make three assumptions about NCO, in particular 2 and 3. seem to be strong. For 2., the similar assumptions are made in Miao and Tchetgen Tchetgen, 2018 (auxiliary variables and IVs are conditionally independent given unobserved covariates (\( M \perp \perp Z|U) \)), and NCO is, for this purposes, only related to unobserved covariates; 2.
is considered to be natural. 3. is a necessary assumption since assuming the general formulation of \( M(U) \) in 2. assumes a general system of functions. As confirming in Note 3, if a linear model can be assumed between \( M \) and \( U \), then the assumption of covariance between \( M \) and \( U \) turns out to be sufficient.

Note 5.
When there are no NCO but at least one of the candidates of valid IVs can be detected, the valid IVs can be used as auxiliary variables; the same situation as Liao, 2013 and DiTraglia, 2016. In this situation, the following discussions and proofs also hold (see Appendix C).

3.1 Asymptotic properties of the proposed method

From here, we update the proposed method introduced in the previous section, and we propose the new method different from existing methods to estimate causal effects while selecting valid IVs. Note that to simplify the following discussions, we assume \( E[XX^\top] = I_p \), but the assumption is not essential. In the proposed method, the weights \( \gamma \) can be estimated as the solution to the estimation equation (2.5):

\[
(E[Z \otimes^2] - E[ZX^\top]E[XZ^\top]) \gamma - (E[Z^T] - E[ZX^\top]E[TX]) = 0_K
\]

When there exists both valid and invalid IVs in the candidates, the weights related to valid IVs \( \gamma_{val} = (\gamma_0, \ldots, \gamma_{\ell})^\top \) would like to be estimated from the estimation equation (2.5); the other weights \( \gamma_{inv} = (\gamma_{\ell+1}, \ldots, \gamma_K)^\top \) would like to be estimated as 0, or convergence sequences to 0. As the estimator of (2.5), the following estimating equation can be considered:

\[
\frac{1}{n} \sum_{i=1}^{n} \begin{pmatrix}
(Z_{i1}^2 - \sum_{j=1}^{p} Z_{1j} X_j^2) I_{\tau 1} + \kappa_1 I_{\tau 1} & & & \\
& \cdots & \cdots & \\
& & Z_{iK}^2 - \sum_{j=1}^{p} Z_{Kj} X_j^2 & I_{\tau K} + \kappa_1 I_{\tau K}
\end{pmatrix} \gamma = A_i
\]
\[
= \frac{1}{n} \sum_{i=1}^{n} \left( \frac{Z_{1i}T_i - \sum_{j=1}^{p} Z_{1j}X_{ij}^T X_j}{I_{\tau 1} + \kappa_{2n} I_{\tau 1}} \right) \] (3.1)

where \( \gamma = (\gamma_{val}^T, \gamma_{inv}^T)^T \), \( \kappa_1 \in \mathbb{R}, \kappa_{2n} = o \left( \frac{1}{\sqrt{n}} \right) \),

\[
\bar{Z}_kX_j = \frac{1}{n} \sum_{i=1}^{n} Z_{ik}X_{ij}, \quad \bar{T}X_j = \frac{1}{n} \sum_{i=1}^{n} T_iX_{ij}
\]

\[
I_{\tau k} = \Phi_\tau (\hat{w}_k + w) \Phi_\tau (w - \hat{w}_k), \quad \bar{I}_{\tau k} = 1 - I_{\tau k}, \quad (3.2)
\]

\[
I_{\tau k}^0 = \Phi_\tau (w^0_k + w) \Phi_\tau (w - w^0_k), \quad \bar{I}_{\tau k}^0 = 1 - I_{\tau k}^0, \quad (3.3)
\]

\[
\hat{w}_k = \frac{1}{n} \sum_{i=1}^{n} Z_{ki}M_i, \quad w^0_k = \mathbb{E}[Z_kM], \quad (3.4)
\]

and \( \Phi_\tau(\cdot) \) is CDF of \( \mathcal{N}(0, \tau^2) \). (3.2), (3.3) are estimators and the true values of the smooth weight function (c.f. Yang and Ding, 2017, Fig.1), respectively. From here, we confirm formulas (3.1)-(3.4). At first, we assume \( Z_k \) is valid. Then, \( \mathbb{E}[Z_kM] = 0 \), and

\[
I_{\tau k}^0 = \Phi_\tau (0 + w) \Phi_\tau (w - 0) \rightarrow 1 \quad (\tau \downarrow 0).
\]

Therefore, it is expected that

\[
I_{\tau k} = \Phi_\tau (\hat{w}_k + w) \Phi_\tau (w - \hat{w}_k) \overset{P}{\rightarrow} 1 \quad (n \to \infty, \tau \downarrow 0).
\]
Whereas, we assume $Z_{k'}$ is invalid. Then, $|E[Z_{k'}M]| > w$, and

$$I_{rk'}^0 = \Phi_\tau (w_{k'}^0 + w) \Phi_\tau (w - w_{k'}^0) \rightarrow 0 \quad (\tau \searrow 0).$$

Therefore, it is expected that

$$I_{rk'} = \Phi_\tau (\hat{w}_{k'} + w) \Phi_\tau (w - \hat{w}_{k'}) \overset{P}{\rightarrow} 0 \quad (n \rightarrow \infty, \tau \searrow 0).$$

In summary, about (3.1), it is expected that weights $\gamma_{val}$ of valid IVs and $\gamma_{inv}$ of invalid IVs are consistent asymptotically with solutions of following estimating equations respectively:

$$\gamma_{val} = \frac{1}{n} \sum_{i=1}^{n} \begin{pmatrix} Z_{11}^2 - \sum_{j=1}^{p} Z_1 X_j^2 & \cdots & Z_{11} Z_{ii} - \sum_{j=1}^{p} Z_1 X_j X_{\ell j} & \cdots & Z_{1i}^2 - \sum_{j=1}^{p} Z_{\ell j} X_j^2 \end{pmatrix} \rightarrow_A A_i =: A_i$$

$$= \frac{1}{n} \sum_{i=1}^{n} \begin{pmatrix} (Z_{1i} T_i - \sum_{j=1}^{p} Z_1 X_j T_j) & \cdots & (Z_{K_i} T_i - \sum_{j=1}^{p} Z_K X_j T_j) \end{pmatrix} =: b_i,$$

$$\kappa_1 \times \text{diag}(1, \ldots, 1) \gamma_{inv} = 0$$

To prove the above expectations, we confirm properties of $\gamma$ through the following two steps:

**Step 1**) Derive an asymptotic equivalent random variable to (3.1)

**Step 2**) By using random variable derived at Step 1), confirming mathematical properties of the following formula:

$$\dot{\gamma} = \left( \sum_{i=1}^{n} A_i \right)^{-1} \sum_{i=1}^{n} b_i.$$
Note 6.

The reason why the ordinary indicator function (which take 1 in some range and 0 in others) is not used in (3.2), (3.3) is that the use of the indicator function renders the ordinary asymptotic theory useless.

When assuming $\tau \equiv \tau_n \searrow 0$, the following lemma can be obtained.

Lemma 1.

Considering the following equation:

$$
\frac{1}{n} \sum_{i=1}^{n} (b_i - A_i \gamma) - \frac{1}{n} \sum_{i=1}^{n} \left\{ \begin{pmatrix} \tilde{b}_i \\ \kappa_{2n} 1_{K-\ell} \end{pmatrix} - \begin{pmatrix} \tilde{A}_i \\ O_{\ell \times K-\ell} \\ O_{\ell \times K-\ell} \end{pmatrix} \begin{pmatrix} \kappa_1 I_{K-\ell} \end{pmatrix} \right\} = \frac{1}{n} \sum_{i=1}^{n} \left( b_i - \begin{pmatrix} \tilde{b}_i \\ \kappa_{2n} 1_{K-\ell} \end{pmatrix} \right) - \frac{1}{n} \sum_{i=1}^{n} \left( A_i - \begin{pmatrix} \tilde{A}_i \\ O_{\ell \times K-\ell} \end{pmatrix} \begin{pmatrix} \kappa_1 I_{K-\ell} \end{pmatrix} \right) \gamma. \quad (3.6)
$$

A sufficient condition that the following equations:

$$
\frac{1}{n} \sum_{i=1}^{n} c_{i1k} = o_p \left( \frac{1}{\sqrt{n}} \right), \quad \frac{1}{n} \sum_{i=1}^{n} c_{i2k}(\gamma) = o_p \left( \frac{1}{\sqrt{n}} \right) \quad (3.7)
$$

are satisfied for $\forall \gamma$ and each $k$ is

$$
\left( \frac{|w - \hat{w}_k|}{\tau_n} \right)^{-1} \exp \left\{ -\frac{1}{2} \frac{(w - \hat{w}_k)^2}{\tau_n^2} \right\} = o_p \left( \frac{1}{\sqrt{n}} \right). \quad (3.8)
$$

Lemma 1 gives the sufficient order to satisfy (3.7), but (3.8) is hard to interpret. We assume that

$$
b_n = \sqrt{n} \left( \frac{|w - \hat{w}_k|}{\tau_n} \right)^{-1} \exp \left\{ -\frac{1}{2} \frac{(w - \hat{w}_k)^2}{\tau_n^2} \right\}. \quad (3.8)
$$

- When $(|w - \hat{w}_k|/\tau_n) = O_p(n)$,

$$
b_n = O_p \left( \frac{1}{\sqrt{n}} \right) \times O_p \left( \exp \left( -n^2 \right) \right) = o_p(1)
$$
• When \( \frac{|w - \hat{w}_k|}{\tau_n} = O_p(\sqrt{\log n}) \),

\[
b_n = O_p \left( \frac{\sqrt{n}}{\sqrt{\log n}} \right) \times O_p \left( n^{-\frac{1}{2}} \right) = o_p(1)
\]

• When \( \frac{|w - \hat{w}_k|}{\tau_n} = O_p(\sqrt{\log \log n}) \),

\[
b_n = O_p \left( \frac{\sqrt{n}}{\sqrt{\log \log n}} \right) \times O_p \left( (\log n)^{-\frac{1}{2}} \right) = o_p \left( \frac{\sqrt{n}}{\sqrt{\log n \log n}} \right)
\]

From the above, one of a limit of an order satisfied \([3.8]\) is \( \frac{|w - \hat{w}_k|}{\tau_n} = O_p(\sqrt{\log n}) \).

Then, since \( \hat{w}_k \) is a sample mean, a lower limit of an order for \( \tau_n \) is

\[
\tau_n^2 = O_p \left( \frac{1}{\log n} \right).
\]

From Lemma 1, the root-n consistency of \( \hat{\gamma} \) is satisfied.

**Proposition 2.**

*When C.1 holds, under the conditions of Lemma 1,*

\[
\hat{\gamma} = \left( \sum_{i=1}^{n} A_i \right)^{-1} \sum_{i=1}^{n} b_i \xrightarrow{\text{P}} \begin{pmatrix} E[\bar{A}]^{-1} E[\bar{b}] & \gamma_0^{val} \\ 0_{K-\ell} & \gamma_0^{inv} \end{pmatrix}.
\]

(3.9)

Also, if \( \left| E \left[ (\bar{b} - \bar{A}\gamma_0^{val}) \otimes 2 \right] \right| < \infty \), then each \( k \),

\[
\hat{\gamma}_{val,k} - \gamma_0^{val,k} = O_p \left( \frac{1}{\sqrt{n}} \right), \quad \hat{\gamma}_{inv,k} = o_p \left( \frac{1}{\sqrt{n}} \right).
\]

Note that \( \gamma_0^{val} \) is the solution of \([2.5]\), and \( \gamma_0^{inv} = 0_{K-\ell} \). In other words, the weights related to invalid IVs are not used when estimating \( \hat{\beta}^{IV} \). By using \( \hat{\gamma} \), an estimating equation for \( \beta \)
can be constructed:

\[ \sum_{i=1}^{n} \begin{pmatrix} \hat{\gamma}^\top z_i \\ x_i \end{pmatrix} (y_i - (t_i\beta_t + x_i^\top \beta_x)) = 0_{p+1}. \]  

(3.10)

Regarding \( \beta \), the following property holds:

**Theorem 2.**

When C.1 and C.2 hold, \( \hat{\beta} \) has the following asymptotical property:

\[ \sqrt{n} \left( \hat{\beta}^{IV} - \beta^0 \right) \xrightarrow{L} N \left( 0_{p+1}, (\Gamma_2)^{-1} \Sigma_2 (\Gamma_2)^{-1} \right), \]  

(3.11)

where \( \gamma^0 = \left( (\gamma^0_{val})^\top, (\gamma^0_{inv})^\top \right)^\top \equiv \left( \gamma^0_{val}^\top, 0_{K-\ell}^\top \right)^\top \) and

\[ \Sigma_2 = E \left[ \begin{pmatrix} (\gamma^0)^\top ZU \\ XU \end{pmatrix} \otimes 2 \right], \quad \Gamma_2 = \begin{pmatrix} E[(\gamma^0)^\top ZT] & E[(\gamma^0)^\top ZX^\top] \\ E[TX] & I_p \end{pmatrix}. \]

**Theorem 2** shows that \( \hat{\beta}^{IV} \) can be satisfied semiparametric efficiency when there are some invalid IVs; therefore the conclusions derived in the previous section hold. One of the important points in **Theorem 2** is that the IV estimator does not affect the asymptotic variance when applying the proposed method. This is because the variability of valid IVs is independent of unobserved covariates, and the variability of invalid IVs becomes 0 by selecting \( \kappa_{2n} = o(1/\sqrt{n}) \).

In this paper, we propose the following procedures to estimate unbiased causal effects when some auxiliary variables can be obtained:

1. \( \hat{\gamma} \) can be estimated with selecting valid IVs as the solution of (3.1); therefore, the weight estimators for a linear combination of IVs can be derived to estimate unbiased causal effects.

2. By applying \( \hat{\gamma} \) to (3.10), an unbiased causal effects can be obtained. Note that the
estimator has the same asymptotic variance as GMM; it has semiparametric efficiency.

### 3.2 Tuning parameters

To implement our proposed method, we have to decide tuning parameters \((\kappa_1, \kappa_{2n}, \tau, w)\). \(\kappa_1\) and \(\kappa_{2n}\) control the variability of \(\hat{\gamma}_{inv}\) (see (B.19) in appendix). As is clear from (B.19), \(\kappa_1\) should be set as large as possible and \(\kappa_{2n}\) should be set as small as possible. From these settings, we can estimate \(\hat{\gamma}_{inv}\) near 0. In the following simulation and data analysis, these parameters are set as mentioned above. \(\tau\) is also easy to be set since it is only use for the proof of Theorem 2. Therefore, to implement the proposed method, \(\tau\) should be set as small as possible.

However, \(w\) is hard to decide and need to be decided very carefully. This is because \(w\) decide the cut-off point whether the candidates of IVs are valid or not. When \(w\) is set as small value, invalid IVs tend not to be selected; whereas, some valid IVs may not be selected. Therefore, the efficiency of the estimator becomes decrease. On the other hand, when \(w\) is set as large value, the inefficiency is improved; whereas, some invalid IVs may not be selected. Therefore, the estimator may have some bias. This relationship is similar as type 1 error and type 2 error in the context of statistical tests. To decide the cut-off point, we consider a decision method following statistical test contexts. We consider the statistics (3.4). Since the statistics is an ordinary sample mean, it becomes

\[
\frac{\frac{1}{\sqrt{n}} \sum_{i=1}^{n} Z_{ki} M_i}{\sqrt{E[Z_{ki}^2] E[M_i^2]}} \xrightarrow{L} N(0, 1),
\]

when \(Z_k\) is a valid IV. Then, we consider the probability \(\alpha\) that is “at least one covariance between a valid IV and the NCO exceeds a cut-off point \(w\)”. Under these settings, \(w\) can be decided to satisfy the following probability:

\[
\Pr \left( \frac{\frac{1}{\sqrt{n}} \sum_{i=1}^{n} |Z_{ki} M_i|}{\sqrt{E[Z_{ki}^2] E[M_i^2]}} > w \right) \leq \frac{\alpha}{K}
\]
Actually,
\[
\Pr\left( \bigcup_{k=1}^{K} \left\{ \frac{1}{\sqrt{n}} \sum_{i=1}^{n} |Z_{ki}M_i| \sqrt{\frac{E[Z_k^2]}{E[M^2]}} > w \right\} \right) \leq \sum_{k=1}^{K} \Pr \left( \frac{1}{\sqrt{n}} \sum_{i=1}^{n} |Z_{ki}M_i| \sqrt{\frac{E[Z_k^2]}{E[M^2]}} > w \right) \leq \alpha.
\]

Specifically, \( w \) becomes \( |z_{\alpha}| \), where \( z_{\alpha} \) is the \( \alpha \) percent point of the standard normal distribution. We use the cut-off point for the following simulations and data analyses.

On the other hand, we can also consider the probability \( 1 - \beta \) that is “all covariances between invalid IVs and the NCO exceed the cut-off point \( w \)”. When \( Z_k \) is an invalid IV,
\[
\frac{1}{\sqrt{n}} \sum_{i=1}^{n} Z_{ki}M_i \sqrt{\frac{E[Z_k^2]}{E[M^2]}} \xrightarrow{L} N \left( \frac{1}{\sqrt{n}} \frac{E[Z_kM]}{\sqrt{E[Z_k^2]E[M^2]}}, \frac{Var(Z_kM)}{E[Z_k^2]E[M^2]} \right)
\]
from the similar calculation as previous one. Then,
\[
1 - \beta = \Pr \left( \bigcap_{k=\ell+1}^{K} \left\{ \left\{ \frac{1}{\sqrt{n}} \sum_{i=1}^{n} Z_{ki}M_i \sqrt{\frac{E[Z_k^2]}{E[M^2]}} < -w \right\} \cup \left\{ \frac{1}{\sqrt{n}} \sum_{i=1}^{n} Z_{ki}M_i \sqrt{\frac{E[Z_k^2]}{E[M^2]}} > w \right\} \right\} \right) \\
\geq \sum_{k=\ell+1}^{K} \Pr \left( \left\{ \frac{1}{\sqrt{n}} \sum_{i=1}^{n} Z_{ki}M_i \sqrt{\frac{E[Z_k^2]}{E[M^2]}} < -w \right\} \cup \left\{ \frac{1}{\sqrt{n}} \sum_{i=1}^{n} Z_{ki}M_i \sqrt{\frac{E[Z_k^2]}{E[M^2]}} > w \right\} \right) - (K - \ell - 1) \\
= 1 - \sum_{k=\ell+1}^{K} \Pr \left( \frac{1}{\sqrt{n}} \sum_{i=1}^{n} |Z_{ki}M_i| \sqrt{\frac{E[Z_k^2]}{E[M^2]}} < w \right) \\
\geq 1 - \sum_{k=\ell+1}^{K} \Phi \left( \frac{w - \sqrt{n} \frac{E[Z_kM]}{\sqrt{E[Z_k^2]E[M^2]}}}{\sqrt{Var(Z_kM)E[Z_k^2]E[M^2]}} \right).
\]

Therefore, when \( n \to \infty \), the above probability becomes sufficient large; whereas, when \( K - \ell \) is relatively large, the above probability may not become sufficient large. Also, the probability depends on the correlation between invalid IVs and the NCO: \( E[Z_kM] \). In other words, to identify both valid and invalid IVs from the many candidates of IVs, we need
3.3 For nonlinear outcomes

In this paper, we assume continuous outcomes (or, linear relationship between an outcome and a treatment); however, it is common to apply nonlinear outcomes such as binary outcomes in biometrics. In this subsection, we would like to consider the expansion of the above considered model.

As mentioned above, our methods can be expand to a nonlinear model. However, expanding to another type of outcomes such as binary outcome is not simply. We think one of the solution is log normal model:

\[
\Pr(y = 1|t_i, x_i, u_i) = \exp \left\{ t_i \beta_t + x_i^\top \beta_x \right\},
\]

where unmeasured variable \( u \) averages 0. Since the model is easy to interpret, we use it in the following data analysis. Another solution is using “approximation of binary outcome models” (Clarke and Windmeijer, 2012). Considering the following logistic regression model:

\[
\Pr(y = 1|t_i, x_i, u_i) = \expit \left\{ t_i \beta_t + x_i^\top \beta_x + u_i \right\}, \quad (3.12)
\]

Of course, the estimator solving the below estimating equation may have some biases:

\[
\sum_{i=1}^{n} \left( h(z_i) \right) \frac{y_i - \expit \left\{ t_i \beta_t + x_i^\top \beta_x \right\}}{x_i} = 0_{p+1}.
\]

This is because the true moment condition between \((h(z_i), x_i)^\top\) and \(y_i - \expit \left\{ t_i \beta_t^0 + x_i^\top \beta_x^0 \right\}\) is not 0. To solve the problem, we consider that (3.12) can be approximated by the following model:

\[
\Pr(y = 1|t_i, x_i, u_i) \approx \expit \left\{ t_i \beta_t + x_i^\top \beta_x \right\} + u_i, \quad (3.13)
\]
Obviously, the estimating equation based on (3.13) derive unbiased estimator. As mentioned in Clarke and Windmeijer (2012), the approximation (3.13) is somewhat reasonable in the sense of a first-order approximation, or when a variance of unmeasured covariates is only small.

4 Simulations

In this section, we confirm properties of our proposed method and compare with the method put forward by Liao, 2013, DiTraglia, 2016, and Gkatzionis et al., 2021. Our simulation is constructed by two situations:

1. Confirming the performance of our proposed method and the previous methods through under the setting of Liao, 2013.

2. Confirming the performance of our proposed method and the method proposed by Gkatzionis et al. (2021) through under the more realistic setting for a mendelian randomization.

Through the situation 1., we show that 1) our proposed method has the same asymptotic variance as GMM, 2) pre-specified valid IVs is not necessary to our proposed method when there are some NCOs. Through the situation 2., we show that our proposed method has the similar performance as Gkatzionis et al., 2021 when there are some NCOs. To confirm these properties, we summarize descriptive statistics of estimates for each procedure. The number of iterations for simulations is 1,000.

4.1 Setting of Liao, 2013

The simulation setting is as follows:
Candidates of IVs, treatment, and unmeasured covariate

$$(T_i, Z_{i1}, Z_{i21}, U_i, Z_{i22})^\top \overset{i.i.d.}{\sim} N_5(0_5, \Sigma), \ Z_{i22} = Z_{i22}^* + 0.5 \ast U_i$$

where

$$\Sigma = \begin{pmatrix} 1 & \sigma_{tz_1} & \sigma_{tz_{21}} & 0.4 & 0 \\ 1 & 0 & 0 & 0 & 0 \\ 1 & 0 & 0 & 0 & 1 \\ 1 & 0 & 0 & 0 & 1 \end{pmatrix}$$

1. Strong IVs: $(\sigma_{tz_1}, \sigma_{tz_{21}}) = (0.4, 0.4)$
2. Weak IVs: $(\sigma_{tz_1}, \sigma_{tz_{21}}) = (0.1, 0.3)$

Outcome

$$Y_i = 0.8 + 0.8T_i + U_i$$

Negative Control Outcome

$$M_i = 1 + \alpha_{mu}U_i + \varepsilon_{mi}, \ \varepsilon_{mi} \sim N(0, 1)$$

1. Strong NCO: $\alpha_{mu} = 1$
   $$\Rightarrow$$ Correlation between a NCO and an unmeasured covariate becomes approximately 0.71.
2. Weak NCO: $\alpha_{mu} = 0.35$
   $$\Rightarrow$$ Correlation between a NCO and an unmeasured covariate becomes approximately 0.34.

Note that $Z_{22}$ is the invalid IV in the candidates of IVs; we would like to use $Z_1, Z_{21}$.

At first, our proposed method is compared with the previous methods: GMM and pro-
posed by Liao, 2013 and DiTraglia, 2016. We confirm the two scenarios:

1. We know some valid IVs (i.e. $Z_1$) and NCO (i.e. $M$)

   Under this situation, not only our proposed method but also the methods of Liao, 2013 and DiTraglia, 2016 work well.

2. We do not know some valid IVs, but know NCO

   Under this situation, the methods of Liao, 2013 and DiTraglia, 2016 do not work well. Whereas, our proposed method also work well.

Regarding the method of Liao, 2013, we use an Adaptive LASSO-type penalty and tuning parameters are selected as $\lambda_n = 0.1$ and $\omega = 1$. Regarding our proposed method, the tuning parameters for proposed methods are selected as $(\kappa_1, \kappa_2, \tau) = (10000, 0.01, 0.01)$. Also, the important tuning parameter $\omega$ is selected by 10-fold cross validation.

Regarding the methods of Liao, 2013 and DiTraglia, 2016, $(Z_1, Z_{21})$ is known as the valid IVs, and we would like to decide that $Z_{22}$ is valid or not. Also, the NCO can be used; therefore all methods can estimate valid estimators for causal effects. Summaries each estimator for causal effects are in Table 1. Under Strong IV situation, our proposed method and Liao, 2013 can estimate valid estimates. Although DiTraglia, 2016 has a large variance, a median of estimates is valid to some extent. Under Weak IV situation, all methods have larger variance than Strong IV situation. In particular, the variance of our proposed method is relatively larger than Liao, 2013 in small sample whereas being reversed in large sample. Regarding our proposed method, the strength of NCO has little effect on the parameter estimation.
Table 1: Summary of estimators for causal effects by situations

| Information of IV | Setting of IV | Setting of NCO | Method | Small sample n = 500 | Large sample n = 200 |
|-------------------|---------------|----------------|--------|----------------------|----------------------|
|                   |               |                |        | Mean (SD) Median (Range) | Mean (SD) Median (Range) |
|                   |               |                |        | | Bias | RMSE | Bias | RMSE |
| -                 | Strong IV     | Strong NCO     | Proposed | 0.874 (0.161) | 0.837 (0.58, 1.53) | 0.074 | 0.177 | 0.810 (0.037) | 0.811 (0.67, 0.92) | 0.010 | 0.039 |
|                   |               |                |        | | | | | | | | | |
|                   | Weak NCO      | Proposed       | 0.840 (0.162) | 0.828 (0.40, 2.75) | 0.040 | 0.167 | 0.813 (0.056) | 0.810 (0.65, 1.08) | 0.013 | 0.058 |
| -                 | Weak IV       | Strong NCO     | Proposed | 0.880 (0.208) | 0.856 (-0.57, 1.87) | 0.080 | 0.223 | 0.822 (0.080) | 0.814 (0.61, 1.26) | 0.022 | 0.083 |
|                   |               |                |        | | | | | | | | | | |
| Specify valid IVs| Strong IV     | -              | Liao, 2013 | 0.801 (0.087) | 0.802 (0.49, 1.34) | 0.001 | 0.087 | 0.829 (0.107) | 0.803 (0.66, 1.28) | 0.029 | 0.111 |
|                   |               |                | DiTraglia, 2016 | 0.799 (0.081) | 0.801 (0.50, 1.04) | 0.001 | 0.081 | 0.799 (0.040) | 0.799 (0.66, 0.92) | 0.001 | 0.040 |
|                   |               |                | GMM | 0.799 (0.081) | 0.801 (0.50, 1.04) | 0.001 | 0.081 | 0.799 (0.040) | 0.799 (0.66, 0.92) | 0.001 | 0.040 |
|                   | Weak IV       | -              | Liao, 2013 | 0.823 (0.186) | 0.815 (0.35, 2.10) | 0.023 | 0.188 | 0.879 (0.252) | 0.811 (0.61, 1.99) | 0.079 | 0.265 |
|                   |               |                | DiTraglia, 2016 | 0.806 (0.139) | 0.811 (0.35, 1.15) | 0.006 | 0.139 | 0.803 (0.070) | 0.804 (0.61, 1.00) | 0.003 | 0.070 |
|                   |               |                | GMM | 0.806 (0.139) | 0.811 (0.35, 1.15) | 0.006 | 0.139 | 0.803 (0.070) | 0.804 (0.61, 1.00) | 0.003 | 0.070 |
| Unspecify valid IVs| Strong IV     | -              | Liao, 2013 | 1.359 (0.214) | 1.368 (0.76, 1.94) | 0.559 | 0.599 | 1.270 (0.156) | 1.259 (0.93, 1.67) | 0.470 | 0.496 |
|                   |               |                | DiTraglia, 2016 | 1.200 (0.143) | 1.208 (0.72, 1.64) | 0.400 | 0.425 | 1.215 (0.064) | 1.213 (1.01, 1.42) | 0.415 | 0.420 |
|                   |               |                | GMM | 1.215 (0.125) | 1.213 (0.87, 1.64) | 0.415 | 0.434 | 1.215 (0.064) | 1.213 (1.01, 1.42) | 0.415 | 0.420 |
|                   | Weak IV       | -              | Liao, 2013 | 2.844 (0.588) | 2.780 (0.98, 7.93) | 2.044 | 2.127 | 2.647 (0.533) | 2.796 (1.32, 4.03) | 1.847 | 1.923 |
|                   |               |                | DiTraglia, 2016 | 2.715 (0.538) | 2.632 (1.17, 8.08) | 1.915 | 1.989 | 2.703 (0.223) | 2.687 (2.10, 3.77) | 1.903 | 1.916 |
|                   |               |                | GMM | 2.715 (0.538) | 2.632 (1.37, 8.08) | 1.915 | 1.989 | 2.703 (0.223) | 2.687 (2.10, 3.77) | 1.903 | 1.916 |
4.2 Setting under a mendelian randomization

The simulation setting is as follows (refer to Gkatzionis et al., 2021):

Candidates of IVs

\[ Z_{ik} \sim \text{Binom}(2, p_{zk}), \quad p_{zk} \sim \text{Unif}(0.1, 0.9), \quad k = 1, 2, \ldots, 30 \]

Unmeasured covariates

\[ U_i = (Z_{i1} - 2p_{z1}, \ldots, Z_{i40} - 2p_{z40}) \alpha + \varepsilon_{ui}, \quad \varepsilon_{ui} \sim N(0, 0.1^2), \]

\[ \alpha^\top = (0, \ldots, 0, \underbrace{\tilde{\alpha}_{25}^\top}_{25 \ \text{SNPs}}, \underbrace{0}_{5 \ \text{SNPs}}), \quad \tilde{\alpha}_k \sim N(0.4, 0.2^2) \]

From these settings, the former 25 SNPs \((k = 1, 2, \ldots, 25)\) are “valid IVs”, and the latter 5 SNPs \((k = 26, \ldots, 30)\) are “invalid IVs”. Also, \(\frac{1}{n} \sum_{i=1}^{n} U_i \xrightarrow{p} 0\).

Treatment

\[ T_i = (Z_{i1}, \ldots, Z_{i30}) \beta + U_i, \quad \beta_k = 0.5 + |\tilde{\beta}_k|, \quad \tilde{\beta}_k \sim N(0, 0.5^2) \]

Outcome

\[ Y_{ti} = 1 + 0.3T_i + U_i \]

Negative Control Outcome

\[ M_i = 1 + U_i + \varepsilon_{mi}, \quad \varepsilon_{mi} \sim N(0, 1) \]

In this simulation, the proposed estimator is compared with the ordinary GMM and the method of Gkatzionis et al. (2021)
Table 2: Summary of estimators for causal effects

| Method                  | Sample size: $n = 5000$ |
|-------------------------|--------------------------|
|                         | Mean (SD)                | Median (Range) | |Bias|RMSE|
| Proposed                | 0.304 (0.003)            | 0.304 (0.296, 0.315) | 0.004 |0.005|
| Gkatzionis et al., 2021 | 0.322 (0.010)            | 0.318 (0.308, 0.357) | 0.022 |0.024|
| GMM                     | 0.368 (0.006)            | 0.368 (0.349, 0.388) | 0.068 |0.068|

5 Conclusions and Future Works

In this paper, we proposed the new IV estimator which use a linear combination of IVs. When there are some invalid IVs exists, our proposed method can select the valid IVs by using a negative control outcome or some auxiliary variable. Whether selecting valid IVs or not, we showed that our proposed estimator has the same efficiency of the generalized methods of moments estimator. We confirm performances of our proposed method and some previous methods through simulations. Whether the strength of a negative control outcome, our proposed method work well; the strength of IVs are more important. Not only large sample but also small sample situation, the performance of our proposed method is superior to the previous methods in many situations. Also, our proposed method work by using valid IVs when a negative control outcome cannot be used.

We believe that our proposed estimator has important impact on the biometrics and related fields, specifically in mendelian randomization. As I mentioned in Introduction, there are many works related to IV methods, however, the universal solution selecting valid IVs is not exist. Our results show that by using an auxiliary variable such as a negative control outcome, we can construct an efficient estimator for causal effects. Since researches related to using negative control outcomes increase in recent years (Tchetgen Tchetgen, 2014, Miao and Tchetgen Tchetgen, 2018, Sanderson et al., 2020 and Shi et al., 2020), our results may become one of the key conclusion to solve the important problem. On the other hand, some auxiliary variables is necessary to our proposed method, but we think this is correct intuitively. Since we cannot observe unmeasured covariates, we have to observe a fluctuation.
of some proxy variables; this is the role of an auxiliary variable. I will mention later, an idea of proxy variable is recently considered.

Our proposed method has many interesting points, but there are also many future works. First of all, our discussions assume the valid outcome model. If we misspecify the model, of course our proposed estimator does not have even the consistency. Okui et al., 2012 and Ogburn et al, 2015 have proposed a doubly robust estimator in the sense that we only need to specify the correct model either an outcome or instrumental variables. Our proposed method may be extended as having double robustness by applying their ideas. Also, Miao and Tchetgen Tchetgen, 2018 and Cui et al., 2020 have proposed a doubly robust estimator regarding instrumental variables and a negative control outcome. Their idea is that instrumental variables and a negative control outcome are regarded as proxy variables of observed covariates. As discussed in our paper, our estimator also use some auxiliary (proxy) variables; therefore the idea may compatible with our method. Secondly, our proposed method assume continuous outcomes. In biometrics and related fields, not only discrete outcomes but also time-to-event type outcomes are considered. Recently, some methods overcoming a problem of unobserved covariate have been proposed in recent years (Tchetgen Tchetgen et al., 2015, Kianian et al., 2019, Martínez-Camblor et al., 2019, and Ying et al., 2019). Out proposed method should be extended to apply various type of data. Thirdly, we also consider a selection method not only outcome models for observed covariates but also tuning parameters. Regarding outcome models for observed covariates, we usually do not have interest in the model. Therefore, we need to consider a semiparametric model selection methods (Su and Zhang, 2012 and Liu et al., 2013). Regarding tuning parameters, we concluded that the parameters have little effect on a parameter estimation, but it may relate to data. As Liao, 2013, we need to consider a method of tuning parameters selection. Fourthly, our method uses a linear combination of IVs, but we need not restrict the situation. Since we would like to show semiparametric efficiency, we consider a linear combination. Darolles et al., 2011 and Deaner, 2019 have considered properties of nonparametric instrumental variable meth-
ods. By applying their results, we can extend to non-linear situations. Finally, in our paper, we assume the fixed number of instrumental variables. In the econometrics, the situation where the number of instrumental variables also increase when sample size increase is well considered. We wonder the situation need to be considered in the biometrics, but we should derive the result in the situation.
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A Important regularity conditions

Throughout our papers, the following two regularity conditions are important:

C.1
\[ E[Z \otimes^2] - E[ZX^\top]E[XX^\top]^{-1}E[XX^\top] > 0 \]

C.2
\[ E[ZT] - E[ZX^\top]E[XX^\top]^{-1}E[XX^\top] ≠ 0 \]

C.1 means valid relationship between \( Z \) and \( X \); it shows only relationship of variables. Whereas, C.2 is regarded as a kind of IV condition 1). If
\[ E[XT] - E[ZX^\top]E[XX^\top]^{-1}E[XX^\top] = 0, \]
i.e., \( γ^0 = 0 \), a linear combination of IVs does not work. Therefore, an IV estimator cannot be constructed.

B Proofs

B.1 Proof of Proposition 1

We use the following lemma that is well-known conclusion (c.f. Harville, 2006) when showing the Proposition 1.

Lemma 2.

A means \( m \times m \) non-singular matrix, \( d \) means \( m \)-dimension vector. \( \forall x \setminus \{0\} \in \mathbb{R}^m \),
\[ \frac{x^\top Ax}{(d^\top x)^2} ≥ (d^\top A^{-1}d)^{-1}, \]
the equation holds when \( x \propto A^{-1}d \).
From here, we prove **Proposition 1**. At first, we calculate $\Gamma^{-1}_1$:

$$
\Gamma^{-1}_1 = \left( \begin{array}{c}
\left( E[HT] - E[H\mathbf{X}^T] E[\mathbf{X}^T]^{-1} E[TX] \right)^{-1} \\
- \left( E[\mathbf{X}^T] - \frac{E[TX] E[H\mathbf{X}^T]}{E[HT]} \right)^{-1} \frac{E[TX]}{E[HT]} \end{array} \right) - \left( \begin{array}{c}
\left( E[HT] - \frac{E[H\mathbf{X}^T]}{E[HT]} \right)^{-1} \left( E[\mathbf{X}^T] - \frac{E[TX] E[H\mathbf{X}^T]}{E[HT]} \right)^{-1} \\
- \left( E[\mathbf{X}^T] - \frac{E[TX] E[H\mathbf{X}^T]}{E[HT]} \right)^{-1} \end{array} \right) .
$$

By using Sherman-Morrison formula (c.f. Harville, 2006),

$$
\left( E[\mathbf{X}^T] - \frac{E[TX] E[H\mathbf{X}^T]}{E[HT]} \right)^{-1} = E[\mathbf{X}^T]^{-1} + \frac{E[\mathbf{X}^T]^{-1} E[TX] E[H\mathbf{X}^T] E[\mathbf{X}^T]^{-1}}{1 - E[H\mathbf{X}^T] E[\mathbf{X}^T]^{-1} E[TX] / E[HT]}
$$

Therefore,

$$
\frac{E[H\mathbf{X}^T]}{E[HT]} \left( E[\mathbf{X}^T] - \frac{E[TX] E[H\mathbf{X}^T]}{E[HT]} \right)^{-1} = \frac{E[H\mathbf{X}^T] E[\mathbf{X}^T]^{-1}}{E[HT] - E[H\mathbf{X}^T] E[\mathbf{X}^T]^{-1} E[TX]},
$$

$$
\left( E[\mathbf{X}^T] - \frac{E[TX] E[H\mathbf{X}^T]}{E[HT]} \right)^{-1} \frac{E[TX]}{E[HT]} = \frac{E[\mathbf{X}^T]^{-1} E[TX]}{E[HT] - E[H\mathbf{X}^T] E[\mathbf{X}^T]^{-1} E[TX]}. 
$$

We continue to calculate the variance components:

$$
(\Gamma_1)^{-1} \Sigma_1 = \sigma^2 \left( \begin{array}{c}
\left( \frac{E[H^2] - E[H\mathbf{X}^T] E[\mathbf{X}^T]^{-1} E[H\mathbf{X}]}{E[HT] - E[H\mathbf{X}^T] E[\mathbf{X}^T]^{-1} E[TX]} \right) \end{array} \right),
$$

$$
(\Gamma_1)^{-1} \Sigma_1 (\Gamma_1^T)^{-1} = \sigma^2 \left( \begin{array}{c}
\left( \frac{E[H^2] - E[H\mathbf{X}^T] E[\mathbf{X}^T]^{-1} E[H\mathbf{X}]}{E[HT] - E[H\mathbf{X}^T] E[\mathbf{X}^T]^{-1} E[TX]} \right) \end{array} \right) \left( \begin{array}{c}
\left( \frac{E[H^2] - E[H\mathbf{X}^T] E[\mathbf{X}^T]^{-1} E[H\mathbf{X}]}{E[HT] - E[H\mathbf{X}^T] E[\mathbf{X}^T]^{-1} E[TX]} \right) \end{array} \right)^T \left( \begin{array}{c}
O^\top \\
I_p
\end{array} \right)
$$

(B.1)
where

\[
D = E[XX^\top]^{-1} + \frac{E[H^2] - E[HX^\top]E[XX^\top]^{-1}E[HX]}{(E[HT] - E[HX^\top]E[XX^\top]^{-1}E[TX])^2}E[XX^\top]^{-1}E[TX]E[XX^\top]^{-1}E[XX^\top]^{-1}
\]

The (1,1) component of (B.1) is

\[
\frac{E[H^2] - E[HX^\top]E[XX^\top]^{-1}E[HX]}{(E[HT] - E[HX^\top]E[XX^\top]^{-1}E[TX])^2} = \frac{\gamma^\top \left( E[Z^\otimes 2] - E[ZX^\top]E[XX^\top]^{-1}E[XZ^\top] \right) \gamma}{\gamma^\top \left( E[ZT] - E[ZX^\top]E[XX^\top]^{-1}E[TX] \right)^2}.
\]

(B.2)

By using Lemma 2, the minimum value of (B.2) can be derived. Therefore, when

\[
\gamma \propto \left( E[Z^\otimes 2] - E[ZX^\top]E[XX^\top]^{-1}E[XZ^\top] \right)^{-1} \left( E[ZT] - E[ZX^\top]E[XX^\top]^{-1}E[TX] \right)
\]

(B.3)

the asymptotic variance related to \( \hat{\beta}^{IV} \) becomes minimum.

### B.2 Proof of Theorem 1

To describe simply, we use the following descriptions:

\[
\Sigma_1 = \sigma^2 \begin{pmatrix} E[H^\otimes 2] & E[HX^\top] \\ E[XH^\top] & E[XX^\top] \end{pmatrix} = \begin{pmatrix} A & B^\top \\ B & C \end{pmatrix}, \quad \Gamma_1 = \begin{pmatrix} E[HT] & E[HX^\top] \\ E[TX] & E[XX^\top] \end{pmatrix} = \begin{pmatrix} F & B^\top \\ G & C \end{pmatrix}
\]

At first, we calculate the inverse matrix of \( \Sigma_1 \):

\[
\Sigma_1^{-1} = \begin{pmatrix} (A - B^\top C^{-1}B)^{-1} & -A^{-1}B^\top (C - BA^{-1}B^\top)^{-1} \\ -(C - BA^{-1}B^\top)^{-1} BA^{-1} & (C - BA^{-1}B^\top)^{-1} \end{pmatrix} = \begin{pmatrix} D & -A^{-1}B^\top E \\ EBA^{-1} & E \end{pmatrix},
\]

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\[
\Gamma_1^\top \Sigma_1^{-1} = \begin{pmatrix}
F^\top D - G^\top EBA^{-1} & -F^\top A^{-1}B^\top E + G^\top E \\
BD - CEB^{-1} & -BA^{-1}B^\top E + CE
\end{pmatrix}.
\] (B.4)

About the (2,2) component of (B.4), by using

\[-BA^{-1}B^\top E + CE = (C - BA^{-1}B^\top) (C - BA^{-1}B^\top)^{-1} = I_p,
\]

\[
\Gamma_1^\top \Sigma_1^{-1} \Gamma_1
= \begin{pmatrix}
F^\top DF - G^\top EBA^{-1}F + G^\top EG - F^\top A^{-1}B^\top E G
F^\top DB^\top - G^\top E B^{-1}B^\top + G^\top E C - F^\top A^{-1}B^\top EC \\
G + BDF - CEB^{-1}F 
BDB^\top - CEB^{-1}B^\top + C
\end{pmatrix}.
\] (B.5)

From here, we calculate each component of (B.5). At first, about (2,1):

\[
BDF - CEB^{-1}F = (B - CEB - CEBA^{-1} (C - BA^{-1}B)) DF
= (B - CEB + CEBA^{-1}(A - B^\top C^{-1})B) DF
= (B - CE(C - BA^{-1}B^\top) C^{-1}B) DF
= (B - C(C - BA^{-1}B^\top)^{-1}(C - BA^{-1}B^\top) C^{-1}B) DF
= \mathbf{0}_K.
\]

Next, about (1,2):

\[
-G^\top EBA^{-1}B^\top + G^\top EC = G^\top E (C - BA^{-1}B^\top)
= G^\top (C - BA^{-1}B^\top)^{-1}(C - BA^{-1}B^\top)
= G^\top.
\]
At last, about (2,2):

\[ BDB^T - CEBA^{-1}B^T = O_K \]

From the above, (B.5) is

\[ \Gamma_1^T \Sigma_1^{-1} \Gamma_1 = \begin{pmatrix} F^T DF - 2G^T EBA^{-1}F + G^T EG & G^T \\ G & C \end{pmatrix}, \tag{B.6} \]

Therefore,

\[
\begin{pmatrix} \Gamma_1^T \Sigma_1^{-1} \Gamma_1 \end{pmatrix}^{-1} \\
\begin{pmatrix} (F^T DF - 2G^T EBA^{-1}F + G^T EG - G^T C^{-1}G)^{-1} \\ C^{-1} + G^T C^{-1}G \end{pmatrix}^{-1} \\
= \begin{pmatrix} (F^T DF - 2G^T EBA^{-1}F + G^T EG - G^T C^{-1}G)^{-1} G^T C^{-1} \\ C^{-1} + G^T C^{-1}G \end{pmatrix}.
\]

(B.7)

About the second term of (B.7),

\[ G^T EBA^{-1}F = G^T (C^{-1} + C^{-1}BDB^T C^{-1}) BA^{-1} F \]
\[ = G^T C^{-1} BA^{-1} F + G^T C^{-1} BDB^T C^{-1} BA^{-1} F \]
\[ = G^T C^{-1} BD ((A - B^T C^{-1} B) A^{-1} + B^T C^{-1} BA^{-1}) F = G^T C^{-1} BDF \]

Next the third and fourth term of (B.7),

\[ G^T EG - G^T C^{-1}G = G^T C^{-1}G + G^T C^{-1} BDB^T C^{-1} G \]
\[ = G^T C^{-1} BDB^T C^{-1} G \]

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Therefore, (B.7) becomes

\[
\left( \Gamma_1^\top \Sigma_1^{-1} \Gamma_1 \right)_{(1,1)}^{-1} = \left( FDF^\top - 2G^\top C^{-1}BDF + G^\top C^{-1}BDB^\top C^{-1}G \right)^{-1} \\
= \left( (F - B^\top C^{-1}G)^\top D(F - B^\top C^{-1}G) \right)^{-1}.
\]

Return to the original symbols:

\[
\left( \Gamma_1^\top \Sigma_1^{-1} \Gamma_1 \right)_{(1,1)}^{-1} = \sigma^2 \left( E[HT] - E[H\mathbf{X}^\top] E[\mathbf{X}\mathbf{X}^\top]^{-1} E[TLX] \right) \left( E[H^\otimes 2] - E[H\mathbf{X}^\top] E[\mathbf{X}\mathbf{X}^\top]^{-1} E[\mathbf{X}HT] \right)^{-1} \\
\times \left( E[HT] - E[H\mathbf{X}^\top] E[\mathbf{X}\mathbf{X}^\top]^{-1} E[TLX] \right)
\]

Therefore, the asymptotic variance related to \( \hat{\beta}_t^{IV} \) consist with \( \hat{\beta}_t^{GMM} \). For the remaining components of (B.7), the same discussion is considered.

### B.3 Proof of Lemma 1

We proceed the proof by dividing (3.6) into two parts: \( c_{i1}, c_{i2}(\gamma) \). At first, regarding \( c_{i1} \),

- When \( k \in \{1, \ldots, \ell\} \),

\[
\frac{1}{n} \sum_{i=1}^{n} \left\{ \left( Z_{ik}T_i - \sum_{j=1}^{p} Z_{kX_j^T}TX_j \right) I_{rk} + \kappa_{2n} \bar{I}_{rk} - \left( Z_{ik}T_i - \sum_{j=1}^{p} Z_{kX_j^T}TX_j \right) \right\}
\]

\[
= \frac{1}{n} \sum_{i=1}^{n} \left\{ \kappa_{2n} - \left( Z_{ik}T_i - \sum_{j=1}^{p} Z_{kX_j^T}TX_j \right) \right\} I_{rk} \tag{B.8}
\]

- When \( k \in \{\ell + 1, \ldots, K\} \),

\[
\frac{1}{n} \sum_{i=1}^{n} \left\{ \left( Z_{ik}T_i - \sum_{j=1}^{p} Z_{kX_j^T}TX_j \right) I_{rk} + \kappa_{2n} \bar{I}_{rk} - \kappa_{2n} \right\}
\]

\[
= \frac{1}{n} \sum_{i=1}^{n} \left\{ \left( Z_{ik}T_i - \sum_{j=1}^{p} Z_{kX_j^T}TX_j \right) - \kappa_{2n} \right\} I_{rk} \tag{B.9}
\]
About (B.8), (B.9), since the first term \( \left( \frac{1}{n} \sum_{i=1}^{n} \{ \cdot \} \right) \) convergence to a constant in probability, we need to confirm an asymptotic property of \( I_{\tau k} \). Next, regarding \( c_{i2}(\gamma) \),

- When \( k \in \{1, \ldots, \ell\}, k' \in \{1, \ldots, \ell\} \),

  About the diagonal component of the matrix,

  \[
  \frac{1}{n} \sum_{i=1}^{n} \left\{ \left( Z_{ik}^2 - \sum_{j=1}^{p} Z_{kj} X_{j}^2 \right) I_{\tau k} + \kappa_1 \bar{I}_{\tau k} - \left( Z_{ik}^2 - \sum_{j=1}^{p} \bar{Z}_{kj} X_{j}^2 \right) \right\} = \frac{1}{n} \sum_{i=1}^{n} \left\{ \kappa_1 - \left( Z_{ik}^2 - \sum_{j=1}^{p} \bar{Z}_{kj} X_{j}^2 \right) \right\} \bar{I}_{\tau k} \]  

  (B.10)

  About the non-diagonal component of the matrix,

  \[
  \frac{1}{n} \sum_{i=1}^{n} \left\{ \left( Z_{ik} Z_{ik'} - \sum_{j=1}^{p} Z_{kj} Z_{k'j} X_{j} X_{j} \right) I_{\tau k} I_{\tau k'} - \left( Z_{ik} Z_{ik'} - \sum_{j=1}^{p} Z_{kj} Z_{k'j} \right) \right\} = \frac{1}{n} \sum_{i=1}^{n} \left\{ \left( Z_{ik} Z_{ik'} - \sum_{j=1}^{p} \bar{Z}_{kj} \bar{Z}_{k'j} \right) \right\} \left( I_{\tau k} I_{\tau k'} - 1 \right) \]  

  (B.11)

- When \( k \in \{\ell + 1, \ldots, K\}, k' \in \{\ell + 1, \ldots, K\} \),

  About the diagonal component of the matrix,

  \[
  \frac{1}{n} \sum_{i=1}^{n} \left\{ \left( Z_{ik} T_i - \sum_{j=1}^{p} Z_{kj} X_{j} X_{j} \right) I_{\tau k} + \kappa_2 \bar{I}_{\tau k} - \kappa_2 \right\} = \frac{1}{n} \sum_{i=1}^{n} \left\{ \left( Z_{ik} T_i - \sum_{j=1}^{p} Z_{kj} T_{X_{j}} X_{j} X_{j} \right) - \kappa_2 \right\} \bar{I}_{\tau k} \]  

  (B.12)

- When \( k \in \{1, \ldots, K\}, k' \in \{\ell + 1, \ldots, K\} \), or \( k \in \{\ell + 1, \ldots, K\}, k' \in \{1, \ldots, K\} \),

  About the non-diagonal component of the matrix,

  \[
  \frac{1}{n} \sum_{i=1}^{n} \left( Z_{ik} Z_{ik'} - \sum_{j=1}^{p} Z_{kj} Z_{k'j} X_{j} X_{j} \right) I_{\tau k} I_{\tau k'} \]  

  (B.13)

About (B.10)-(B.13), since the first term \( \left( \frac{1}{n} \sum_{i=1}^{n} \{ \cdot \} \right) \) convergence to a constant in proba-
bility, we need to confirm an asymptotic property of $I_{\tau k}$.

From here, we confirm when $I_{\tau k} = o_p (1/\sqrt{n})$ or $\bar{I}_{\tau k} = o_p (1/\sqrt{n})$ hold. Note that under this situation, the product $(I_{\tau k} I_{\tau k'})$ becomes $o_p (1/n)$. Regarding $I_{\tau k}$,

$$I_{\tau k} = \Phi_\tau(\hat{w}_k + w) \Phi_\tau(w - \hat{w}_k) = \frac{1}{\sqrt{2\pi \tau^2}} \int_{-\infty}^{\hat{w}_k + w} \exp \left\{ -\frac{\omega^2}{2\tau^2} \right\} d\omega \frac{1}{\sqrt{2\pi \tau^2}} \int_{-\infty}^{w - \hat{w}_k} \exp \left\{ -\frac{\omega^2}{2\tau^2} \right\} d\omega.$$

Transformation of variables as $\omega' = \omega/\tau$,

$$I_{\tau k} = \frac{1}{\sqrt{2\pi}} \int_{-\infty}^{\hat{w}_k + w} \exp \left\{ -\frac{(\omega')^2}{2} \right\} d\omega' \frac{1}{\sqrt{2\pi}} \int_{-\infty}^{w - \hat{w}_k} \exp \left\{ -\frac{(\omega')^2}{2} \right\} d\omega' = \int_{-\infty}^{\hat{w}_k + w} d\Phi \int_{-\infty}^{w - \hat{w}_k} d\Phi,$$

where $\Phi$ is CDF of $N(0,1)$. Then

$$0 < 1 - I_{\tau k} = 1 - \int_{-\infty}^{\hat{w}_k + w} d\Phi \int_{-\infty}^{w - \hat{w}_k} d\Phi$$

$$< \begin{cases} 1 - \left( \int_{-\infty}^{w - \hat{w}_k} d\Phi \right)^2 & (\hat{w}_k \geq 0) \\
1 - \left( \int_{-\infty}^{\hat{w}_k + w} d\Phi \right)^2 & (\hat{w}_k < 0) 
\end{cases}$$

$$= 1 - \left( \int_{-\infty}^{w - |\hat{w}_k|} d\Phi \right)^2,$$  \hspace{1cm} (B.14)

and

$$0 < I_{\tau k} = \int_{-\infty}^{\hat{w}_k + w} d\Phi \int_{-\infty}^{w - \hat{w}_k} d\Phi < \int_{-\infty}^{w - |\hat{w}_k|} d\Phi \hspace{1cm} (B.15)$$

satisfy.

- When $k \in \{1, \ldots, \ell\}$,

  In this situation, $\hat{w}_k \overset{P}{\to} 0$. At first, when $w \geq |\hat{w}_k|$, by using (B.14)

  $$0 < 1 - I_{\tau k} = 1 - \left( \int_{-\infty}^{w - |\hat{w}_k|} d\Phi \right)^2 = 1 - \left( 1 - \int_{-\infty}^{w - |\hat{w}_k|} d\Phi \right)^2$$

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\[
= 2 \int_{w - |\hat{w}_k| \tau_n}^{\infty} d\Phi - \left( \int_{w - |\hat{w}_k| \tau_n}^{\infty} d\Phi \right)^2 < 2 \int_{w - |\hat{w}_k| \tau_n}^{\infty} d\Phi \quad (B.16)
\]

Regarding (B.16), using an evaluation of the tail of Normal distribution (c.f. Gordon, 1941),

\[
0 < 1 - I_{\tau_k} < 2 \int_{w - |\hat{w}_k| \tau_n}^{\infty} d\Phi - \left( \int_{w - |\hat{w}_k| \tau_n}^{\infty} d\Phi \right)^2 < 2 \int_{w - |\hat{w}_k| \tau_n}^{\infty} d\Phi < \frac{2}{\sqrt{2\pi}} \left( \frac{w - |\hat{w}_k|}{\tau_n} \right)^{-1} \exp \left\{ -\frac{1}{2} \left( \frac{w - |\hat{w}_k|}{\tau_n^2} \right)^2 \right\} \]

\[
< \left( \frac{|w - \hat{w}_k|}{\tau_n} \right)^{-1} \exp \left\{ -\frac{1}{2} \left( \frac{w - \hat{w}_k}{\tau_n^2} \right)^2 \right\} .
\]

Therefore, when

\[
\left( \frac{|w - \hat{w}_k|}{\tau_n} \right)^{-1} \exp \left\{ -\frac{1}{2} \left( \frac{w - \hat{w}_k}{\tau_n^2} \right)^2 \right\} = o_p \left( \frac{1}{\sqrt{n}} \right) , \quad (B.17)
\]

\(\bar{I}_{\tau_k} = o_p (1/\sqrt{n})\) is satisfied, and \(I_{\tau_k} = 1 + o_p (1/\sqrt{n})\) is also satisfied. Next, when \(w < |\hat{w}_k|\), we can ignore the situation in the view of the convergence in probability since \(\hat{w}_k \xrightarrow{P} 0\).

- When \(k \in \{ \ell + 1, \ldots, K \}\),

In this situation, \(\hat{w}_k \xrightarrow{P} w_k\). At first, when \(w \geq |\hat{w}_k|\), we can ignore the situation in the view of the convergence in probability since \(|\hat{w}_k| \xrightarrow{P} |w_k| > w\). Next, when \(w < |\hat{w}_k|\), by using (B.15) and an evaluation of the tail of Normal distribution,

\[
0 < I_{\tau_k} < \int_{-\infty}^{w - |\hat{w}_k| \tau} d\Phi = \int_{-\infty}^{w - |\hat{w}_k| \tau_n} d\Phi = \left( \frac{|w - \hat{w}_k|}{\tau_n} \right)^{-1} \exp \left\{ -\frac{1}{2} \left( \frac{w - \hat{w}_k}{\tau_n^2} \right)^2 \right\} .
\]

Therefore, when (B.17), \(I_{\tau_k} = o_p (1/\sqrt{n})\) hold, and \(\bar{I}_{\tau_k} = 1 + o_p (1/\sqrt{n})\) also hold.

From the above, when (B.17) is satisfied, (3.6) is also satisfied.
B.4 Proof of Proposition 2

From the result of Lemma 1, \( \forall \gamma \),

\[
\frac{1}{n} \sum_{i=1}^{n} (b_i - A_i \gamma) - \frac{1}{n} \sum_{i=1}^{n} \left\{ \begin{pmatrix} \hat{b}_i \\ \kappa_2 n 1_{K-\ell} \end{pmatrix} - \begin{pmatrix} \hat{A}_i \\ O_{\ell \times K-\ell}^T \kappa_1 I_{K-\ell} \end{pmatrix} \gamma \right\} = o_p \left( \frac{1}{\sqrt{n}} \right).
\]

Therefore,

\[
0_K = \frac{1}{n} \sum_{i=1}^{n} (b_i - A_i \hat{\gamma}) - \frac{1}{n} \sum_{i=1}^{n} \left\{ \begin{pmatrix} \hat{b}_i \\ \kappa_2 n 1_{K-\ell} \end{pmatrix} - \begin{pmatrix} \hat{A}_i \\ O_{\ell \times K-\ell}^T \kappa_1 I_{K-\ell} \end{pmatrix} \hat{\gamma} \right\} + o_p \left( \frac{1}{\sqrt{n}} \right),
\]

(B.18)

\[
\hat{\gamma} = \left( \frac{1}{n} \sum_{i=1}^{n} \begin{pmatrix} \hat{A}_i \\ O_{\ell \times K-\ell}^T \kappa_1 I_{K-\ell} \end{pmatrix} \right)^{-1} \frac{1}{n} \sum_{i=1}^{n} \begin{pmatrix} \hat{b}_i \\ \kappa_2 n 1_{K-\ell} \end{pmatrix} + o_p \left( \frac{1}{\sqrt{n}} \right) P \rightarrow \begin{pmatrix} E [\hat{A}]^{-1} E [\hat{b}] \\ 0_{K-\ell} \end{pmatrix}
\]

(B.19)

From the above the first component of Proposition 2 can be proved. Next regarding (B.18), conducting the taylor expansion around \( \gamma^0 \),

\[
O_K = \frac{1}{n} \sum_{i=1}^{n} \left\{ \begin{pmatrix} \hat{b}_i \\ \kappa_2 n 1_{K-\ell} \end{pmatrix} - \begin{pmatrix} \hat{A}_i \\ O_{\ell \times K-\ell}^T \kappa_1 I_{K-\ell} \end{pmatrix} \hat{\gamma} \right\} + o_p \left( \frac{1}{\sqrt{n}} \right)
\]

\[
= \frac{1}{n} \sum_{i=1}^{n} \left\{ \begin{pmatrix} \hat{b}_i \\ \kappa_2 n 1_{K-\ell} \end{pmatrix} - \begin{pmatrix} \hat{A}_i \\ O_{\ell \times K-\ell}^T \kappa_1 I_{K-\ell} \end{pmatrix} \gamma^0 \right\}
\]

\[
- \frac{1}{n} \sum_{i=1}^{n} \begin{pmatrix} \hat{A}_i \\ O_{\ell \times K-\ell}^T \kappa_1 I_{K-\ell} \end{pmatrix} (\hat{\gamma} - \gamma^0) + o_p \left( \frac{1}{\sqrt{n}} \right).
\]
Therefore,
\[
\sqrt{n} (\hat{\gamma} - \gamma^0) = \left( \frac{1}{n} \sum_{i=1}^{n} \begin{pmatrix} \tilde{A}_i & O_{\ell \times K - \ell} \end{pmatrix} \right)^{-1} \\
\times \frac{\sqrt{n}}{n} \sum_{i=1}^{n} \left\{ \begin{pmatrix} \tilde{b}_i \\ \kappa_2 n 1_{K - \ell} \end{pmatrix} - \begin{pmatrix} \tilde{A}_i & O_{\ell \times K - \ell} \end{pmatrix} \gamma^0 \right\} + o_p(1)
\]
\[
= \left( \left( \frac{1}{n} \sum_{i=1}^{n} \tilde{A}_i \right)^{-1} \begin{pmatrix} O_{\ell \times K - \ell} \\ \frac{1}{\kappa_1} I_{K - \ell} \end{pmatrix} \right) \left( \frac{\sqrt{n}}{n} \sum_{i=1}^{n} (\tilde{b}_i - \tilde{A}_i \gamma^0_{\text{val}}) \right) + o_p(1)
\]

If \( \left| \mathbb{E} \left[ (\hat{b} - \tilde{A}\gamma^0_{\text{val}})^\otimes 2 \right] \right| < \infty \), by using the ordinary asymptotic theories for M-estimator (c.f. Van der Vaart, 2000), the second component of Proposition 2 can be proved.

### B.5 Proof of Theorem 2

Regarding (3.10), conducting the taylor expansion around \( \beta^0 \) and \( \gamma^0 \),

\[
0_{p+1} = \frac{1}{n} \sum_{i=1}^{n} \begin{pmatrix} \hat{\gamma}^\top z_i \\ x_i \end{pmatrix} \left( y_i - (t_i, x_i^\top) \right) \beta^0 \\
= \frac{1}{n} \sum_{i=1}^{n} \begin{pmatrix} (\gamma^0)^\top z_i \\ x_i \end{pmatrix} (y_i - (t_i, x_i^\top) \beta^0) - \frac{1}{n} \sum_{i=1}^{n} \begin{pmatrix} (\gamma^0)^\top z_i t_i \\ x_i x_i^\top \end{pmatrix} (\hat{\beta} - \beta^0) \\
+ \frac{1}{n} \sum_{i=1}^{n} \begin{pmatrix} (y_i - (t_i, x_i^\top) \beta^0) z_i^\top \\ O_{p \times K} \end{pmatrix} (\hat{\gamma} - \gamma^0) + o_p \left( \frac{1}{\sqrt{n}} \right).
\]
Therefore,

\[
\sqrt{n} \left( \hat{\beta} - \beta^0 \right) = \left( \frac{1}{n} \sum_{i=1}^{n} \begin{pmatrix} (\gamma^0)^\top z_i t_i & (\gamma^0)^\top z_i x_i^\top \end{pmatrix} \right)^{-1} \left\{ \frac{\sqrt{n}}{n} \sum_{i=1}^{n} \begin{pmatrix} (\gamma^0)^\top z_i u_i \\ x_i u_i \end{pmatrix} \right\} + \frac{1}{n} \sum_{i=1}^{n} \begin{pmatrix} u_i z_i^\top \\ O_{p \times K} \end{pmatrix} \sqrt{n} (\hat{\gamma} - \gamma^0) + o_p \left( \frac{1}{\sqrt{n}} \right). 
\]  

(B.20)

The second term of \{\cdot\} in (B.20) becomes

\[
\frac{1}{n} \sum_{i=1}^{n} u_i z_i \overset{P}{\to} E[UZ] = \begin{pmatrix} 0_{\ell} \\ E[UZ_{\ell+1}] \\ \vdots \\ E[UZ_K] \end{pmatrix},
\]

and the result of Proposition 2, we can show that

\[
\frac{1}{n} \sum_{i=1}^{n} \begin{pmatrix} u_i z_i^\top \\ O_{p \times K} \end{pmatrix} \sqrt{n} (\hat{\gamma} - \gamma^0) = o_p(1).
\]

Therefore, by using the ordinary asymptotic theories for M-estimator to (B.20), Theorem 2 can be proved.

C Using valid IVs as auxiliary variables

Assume that we know at least one IV $Z_0$ is valid. Therefore, a solution of the following estimating equation becomes true causal effects when (2.1) is the true outcome model:

\[
\sum_{i=1}^{n} \begin{pmatrix} z_{0i} \\ x_i \end{pmatrix} \left( y_i - (t_i, x_i^\top) \beta \right) = 0_{p+1}
\]
Also, residuals can be estimated as follows:

\[ \varepsilon_i \left( \hat{\beta}_0 \right) = y_i - (t_i, \mathbf{x}_i^\top)\hat{\beta}_0 \]

When constructing \( \hat{w}_k \), we substitute \( \varepsilon_i \left( \hat{\beta}_0 \right) \) for NCO \( M_i \):

\[ \hat{w}_k = \frac{1}{n} \sum_{i=1}^{n} Z_{ki} \varepsilon_i \left( \hat{\beta}_0 \right) , \]

and

\[ \hat{w}_k \overset{p}{\rightarrow} \mathbb{E} [Z_k U] . \]

And, we can easily confirm the discussions and proofs of Section 3. Therefore, we can identify valid and invalid IVs by using \( Z_0 \) as auxiliary variables.

\section*{D Supplementary figures}
Figure 1: Boxplot of estimators for causal effects (strong IV, n = 500)
Figure 2: Boxplot of estimators for causal effects (strong IV, n = 2000)
Figure 3: Boxplot of estimators for causal effects (weak IV, $n = 500$)
Coefficient estimates of $\beta_t$

![Boxplot of estimators for causal effects (weak IV, $n=2000$)](image)

Figure 4: Boxplot of estimators for causal effects (weak IV, $n=2000$)