A robust fusion-extraction procedure with summary statistics in the presence of biased sources

Ruoyu Wang, Qihua Wang*

Academy of Mathematics and Systems Science, Chinese Academy of Sciences, Beijing 100190, China, and University of Chinese Academy of Sciences, Beijing 100049, China.

Wang Miao

School of Mathematical Sciences, Peking University, Beijing 100871, China

Abstract

Information from multiple data sources is increasingly available. However, some data sources may produce biased estimates due to biased sampling, data corruption, or model misspecification. This calls for robust data combination methods with biased sources. In this paper, a robust data fusion-extraction method is proposed. In contrast to existing methods, the proposed method can be applied to the important case where researchers have no knowledge of which data sources are unbiased. The proposed estimator is easy to compute and only employs summary statistics, and hence can be applied to many different fields, e.g., meta-analysis, Mendelian randomization, and

*qhwang@amss.ac.cn
distributed systems. The proposed estimator is consistent even if many data sources are biased and is asymptotically equivalent to the oracle estimator that only uses unbiased data. Asymptotic normality of the proposed estimator is also established. In contrast to the existing meta-analysis methods, the theoretical properties are guaranteed even if the number of data sources and the dimension of the parameter diverges as the sample size increases. Furthermore, the proposed method provides a consistent selection for unbiased data sources with probability approaching one. Simulation studies demonstrate the efficiency and robustness of the proposed method empirically. The proposed method is applied to a meta-analysis data set to evaluate the surgical treatment for moderate periodontal disease and to a Mendelian randomization data set to study the risk factors of head and neck cancer.

**Keywords:** Data fusion; Inverse variance weighting; Mendelian randomization; Meta-analysis; Robust statistics.
1 Introduction

In the big data era, it is common to have different data sources addressing a specific scientific problem of interest. An important question is how to combine these data to draw a final conclusion. In practice, due to privacy concerns or data transmission restrictions, individual-level data from different sources are usually not all available to the researcher. For some data sources, researchers only have access to certain summary statistics. To combine data information efficiently in this scenario, plenty of methods have been developed in the literature of meta-analysis, including the confidence distribution methods (Singh et al., 2005; Xie et al., 2011; Liu et al., 2015), the generalized method of moments (GMM), empirical likelihood-based methods (Sheng et al., 2020; Qin et al., 2015; Chatterjee et al., 2016; Kundu et al., 2019; Zhang et al., 2019, 2020), and calibration methods (Lin and Chen, 2014; Yang and Ding, 2020). In many cases, estimators provided by meta-analysis methods are as efficient as the pooled estimators that use all the individual-level data (Olkin and Sampson, 1998; Mathew and Nordstrom, 1999; Lin and Zeng, 2010; Xie et al., 2011; Liu et al., 2015). Moreover, meta-analysis methods have been applied to large-scale data sets to reduce the computation and communication complexity (Jordan, 2013; Fan et al., 2014; Wang et al., 2016), even though all individual-level data are available in this scenario.

Ideally, all data sources can provide valid summary statistics (or consistent local estimates) based on data from them, respectively. Unfortunately, the summary statistics (or local estimates) from some data sources may be invalid (or inconsistent) due to biased sampling, data corruption, model misspecification or other problems. Typical examples include the Simpson’s paradox in meta-analysis (Hanley and Thériault, 2000), the invalid instrument problem in Mendelian randomization (Qi and Chatterjee, 2019; Burgess et al., 2020) and Byzantine failure problem in distributed estimation (Lamport et al., 1982; Yin et al., 2018; Tu et al., 2021).

Example 1 (Simpson’s paradox in meta-analysis). The dataset reported by Hanley and Thériault (2000) consists of five case-control studies that examine the role of high voltage power lines in the etiology of leukemia in children. Hanley and Thériault (2000) point out that different data fusion methods provide opposite conclusions. The reason is that three
studies are conducted among the entire population, while two other studies undertake their investigation among the subpopulations living close to the power lines and thus suffer from biased sampling. Thus, two biased studies lead the final meta-analysis estimator to be biased. In this illustrative example, one knows which studies are biased and thus can just remove these studies. However, in practice, we seldom have such knowledge.

**Example 2 (Mendelian randomization with invalid instruments).** In Mendelian randomization, single nucleotide polymorphisms (SNPs) are used as instrumental variables to evaluate the causal effect of a risk factor on the outcome. A SNP is a valid instrumental variable if (i) it is associated with the risk factor of interest; (ii) there is no confounder of the SNP-outcome association and (iii) it does not affect the outcome directly. See the Mendelian randomization dictionary (Lawlor et al., 2019) for more details. Suppose we have access to summary data representing the estimated effect of the $k$th SNP on the risk factor ($\tilde{\beta}_k$), and on the outcome ($\tilde{\gamma}_k$) for $k = 1, \ldots, K$. If the $k$th SNP is a valid instrument, then $\tilde{\gamma}_k / \tilde{\beta}_k$ is a consistent estimator of the true causal effect. As data on several SNPs are available, we can use meta-analysis methods to produce a final estimator. However, in practice, a SNP may be an invalid instrument due to pleiotropy, linkage disequilibrium, and population stratification. In this case, $\tilde{\gamma}_k / \tilde{\beta}_k$ is no longer consistent and traditional meta-analysis methods can lead to biased estimates. In practice, however, it is hard to know which instrument is valid.

**Example 3 (Byzantine failures in distributed systems).** To reduce the computational burden with large-scale data, the calculation of estimators is often conducted on distributed systems. Summary statistics are calculated on each local machine and transmitted to the central machine. The central machine produces the final estimator by combining these summary statistics. In practice, some local machines may produce wrong results and hence are biased sources due to hardware or software breakdowns, data crashes, or communication failures, which is called the “Byzantine failures”. Usually, one does not know which machines have Byzantine failures. Byzantine failures may deteriorate the performance of many divide-and-conquer methods.

As shown in the above three examples, many issues can result in biased estimation from
a particular data source. In this paper, we call a data source biased if it produces an estimate that does not converge to the parameter of interest. Most of the aforementioned meta-analysis methods are not robust against the presence of biased sources, with the exception of Singh et al. (2005); Shen et al. (2020) and Zhai and Han (2022). Nevertheless, the method proposed in Singh et al. (2005) is limited to the one-dimensional parameter case. Moreover, to apply the method of Singh et al. (2005) and Shen et al. (2020), there must be at least one known unbiased data source for reference. While the paper was submitted for review, Zhai and Han (2022) proposed a data fusion method based on the empirical likelihood, which can deal with summary statistics from biased data sources. Their method relies on the parametric conditional density model and requires individual-level data from a data source that is known to be unbiased. However, such an unbiased data source is often unavailable in practice. The main challenge for such a problem is that we do not know which data sources are biased, and hence one cannot remove the biased data sources from these data sources directly. Clearly, the use of biased data sources is adverse to defining a consistent estimator for the parameter of interest. This paper proposes a fusion-extraction procedure to define a consistent estimator and an asymptotically normal estimator, respectively, by combining all the summary statistics from all the data sources in the presence of biased sources. In contrast to existing methods, the proposed method is applicable without any knowledge on which sources are unbiased.

The proposed fusion-extraction procedure uses only summary statistics from different data sources and consists of two stages. In the first stage, we fuse the summary statistics from different data sources and obtain an initial estimator by minimizing the weighted Euclid distance from the estimators of all data sources. In the second stage, with the assistance of the initial estimator and the penalization method, we extract information from the unbiased sources and obtain the final estimator via a convex optimization problem. Both optimization problems in the two stages can be solved efficiently. Biased data sources do not affect the consistency of our method, as long as the proportion of unbiased sources among all sources is not too small. Moreover, our method can be implemented without knowledge on which data sources are unbiased. This makes our method more practical.
The theoretical properties of our estimator are investigated under some mild conditions. We first show the consistency of the initial estimator produced by the first stage. Then we show that with this initial estimator, the final estimator produced by the second stage optimization is close in terms of Euclid norm to the oracle estimator that uses only unbiased data sources. Furthermore, it is shown that the extraction procedure in the second stage can consistently select unbiased sources. Based on these “oracle properties”, the asymptotic normality of the proposed estimator is also established. The established theorems are general in the sense that the number of data sources, $K$, and the dimension of parameter, $d$, can diverge as sample size increases. To our knowledge, no existing literature considers the meta-analysis problem in the presence of unknown biased sources when both $K$ and $d$ diverge.

Our method is robust to biased data sources and computationally simple, and hence can be applied to many different fields, e.g. meta-analysis, Mendelian randomization, and distributed system. Besides its generality, it has some attractive properties across different fields. In contrast to existing works in meta-analysis with heterogeneous data sources (Singh et al., 2005; Shen et al., 2020; Zhai and Han, 2022), the proposed method does not require knowledge on which data sources are unbiased. In the field of Mendelian randomization with invalid instruments (Han, 2008), our method does not require that at least half of the instruments are valid while allowing for multiple or diverging number of treatments. Furthermore, our method can also be applied to the distribution system with Byzantine failures (Lamport et al., 1982; Yin et al., 2018). In contrast to the existing work (Tu et al., 2021), the asymptotic normality of our method is guaranteed without requiring the proportion of biased sources among all sources to converge to zero. Moreover, our estimator has a faster convergence rate compared to that of Tu et al. (2021) if the proportion of biased sources does not converge to zero.

Simulations under different scenarios demonstrate the efficiency and robustness of the proposed method. The proposed method is applied to a meta-analysis data set (Berkey et al., 1998) to evaluate the surgical treatment for moderate periodontal disease, and a Mendelian randomization data set (Gormley et al., 2020) to study the risk factors of head
and neck cancer. The real data analysis results show the robustness of the proposed method empirically.

The rest of this paper is organized as follows. In Section 2, we suggest a two-stage method to provide an estimator for the parameter of interest in the presence of biased sources. In Section 3.1, we investigate the theoretical properties of the proposed estimator under certain general conditions on convergence rate. Under further assumptions, we establish the asymptotic normality of the proposed estimator in Section 3.2. Simulation studies were conducted to evaluate the finite sample performance of our method in Section 4, followed by two real data examples in Section 5. Further simulation studies and all proofs are deferred to the supplementary material due to limited space.

2 Estimation in the presence of biased sources

2.1 Identification

Suppose $\theta_0$ is a $d$ dimensional parameter of interest and $K$ data sources can be used to estimate this parameter. Each data source provides an estimator for the parameter of interest. Estimators from some data sources may be inconsistent for $\theta_0$. The data sources that provide inconsistent estimators are called biased data sources but we do not know which data sources are biased. For $k = 1, \ldots, K$, let $\tilde{\theta}_k$ be the estimate from the $k$th source, $n_k$ the sample size of the $k$th source, $n = \sum_{k=1}^{K} n_k$ and $\tilde{\pi}_k = n_k/n$. Estimates from different sources may be constructed using different methods and let $\theta^*_k$ be their probability limits respectively, i.e., $\|\tilde{\theta}_k - \theta^*_k\| \to 0$ in probability for $k = 1, \ldots, K$, where $\| \cdot \|$ is the Euclid norm. Then a data source is biased if $\theta^*_k \neq \theta_0$. We assume that some of the sources are unbiased in the sense that $\theta^*_k = \theta_0$ but we do not know which are unbiased. Let $\mathcal{K}_0 = \{k : \theta^*_k = \theta_0\}$ be the set of indices of unbiased sources and $b^*_k = \theta^*_k - \theta_0$ be the bias of source $k$. Throughout this paper, we assume $\|b^*_k\|$ is bounded away from zero for $k \in \mathcal{K}_0^c = \{1, \ldots, K\} \setminus \mathcal{K}_0$. Since we do not have any knowledge about $\mathcal{K}_0$, we do not know whether $\theta^*_k$ equals to the parameter of interest or not. Fortunately, the following proposition shows that $\theta_0$ can be identified as a weighted geometric median of $\theta^*_k$ for
$k = 1, \ldots, K$ if the proportion of data from unbiased sources among all data is larger than a certain threshold.

**Proposition 1.** If

$$\sum_{k \in \mathcal{K}_0} \tilde{\pi}_k > \left\| \sum_{k \in \mathcal{K}_0} \tilde{\pi}_k b_k^* \right\|,$$

then

$$\theta_0 = \arg \min_{\theta} \sum_{k=1}^K \tilde{\pi}_k \left\| \theta_k^* - \theta \right\|.$$

See the supplementary material for the proof of this proposition. The proposition shows that $\theta_0$ can be uniquely determined by $\theta_k^*$ for $k = 1, \ldots, K$ if (1) holds. Note that

$$\left\| \sum_{k \in \mathcal{K}_0} \tilde{\pi}_k b_k^* \right\| \leq \sum_{k \in \mathcal{K}_0} \tilde{\pi}_k .$$

Thus a sufficient condition for (1) is

$$\sum_{k \in \mathcal{K}_0} \tilde{\pi}_k > \sum_{k \in \mathcal{K}_0} \tilde{\pi}_k$$

or equivalently

$$\sum_{k \in \mathcal{K}_0} \tilde{\pi}_k > \frac{1}{2} .$$

Inequality (4) requires more than half of the data come from unbiased data sources, which is related to the majority rule widely adopted in the invalid instrument literature (Kang et al., 2016; Bowden et al., 2016; Windmeijer et al., 2019). The previous analysis implies that (1) is true under (4). Next, we illustrate that (1) can still hold even though less than a half of the data come from unbiased sources with a toy example. Suppose $d = 3$, $K = 6$, $\theta_0 = (0, 0, 0)^T$, $\tilde{\pi}_k = 1/6$, $b_1^* = b_2^* = (0, 0, 0)^T$, $b_3^* = (1, 0, 0)^T$, $b_4^* = (-2, 0, 0)^T$, $b_5^* = (0, 1, 0)^T$ and $b_6^* = (0, 0, 1)^T$. In this case, $\sum_{k \in \mathcal{K}_0} \tilde{\pi}_k = 1/3 < 1/2$, however, $\left\| \sum_{k \in \mathcal{K}_0} \tilde{\pi}_k b_k^* \right\| = \sqrt{2}/6 < 1/3$ and hence (1) is satisfied. In Section 4, we provide a further example where only 20% of the data come from unbiased sources and (1) still holds. Theoretically, if the equality in (3) holds, (1) is equivalent to (4); otherwise (1) is weaker than (4). The equality in (3) holds only if all $b_k^*$’s lie occasionally on the same direction, which is rarely true because the biases are often irregular in practice.
In Proposition 1, the quantity $\tilde{\pi}_k$ can be viewed as the weight attached to the $k$-th data source for $k = 1, \ldots, K$. It is observed in meta-analysis that small studies tend to be of relatively low methodological quality and are more likely to be affected by publication and selection bias (Sterne et al., 2000). Thus we use the weights $\{\tilde{\pi}_k\}_{k=1}^K$ that attach small weights to data sources with small sample sizes in this paper.

By replacing $\theta^*_k$ by $\hat{\theta}_k$ in equation (2), we can construct an estimator for $\theta_0$. Further, we use the defined estimator as an initial estimator to obtain a more efficient estimator.

### 2.2 Estimation

According to Proposition 1, we propose the following estimator $\tilde{\theta}$ that minimizes the weighted distance from $\tilde{\theta}_k$,

$$
\tilde{\theta} = \text{arg min}_{\tilde{\theta}} \sum_{k=1}^K \tilde{\pi}_k \| \tilde{\theta}_k - \tilde{\theta} \|.
$$

(5)

This optimization problem is convex and can be solved efficiently by routine algorithms.

We show the consistency of $\tilde{\theta}$ in Section 3. However, according to the well-known trade-off between robustness and efficiency (Hample et al., 2005; Lindsay, 1994), the robust estimator $\tilde{\theta}$ may not be fully efficient. Also, it may have a large finite sample bias because $\tilde{\theta}$ uses summary statistics from biased sources. Our simulations confirm this. The large finite sample bias implies that $\tilde{\theta}$ may not be $n^{1/2}$-consistent or asymptotically normal. Here we give a concrete example. Suppose $d = 1$, $K \to \infty$, $n_k = n/K$, $\tilde{\theta}_k \sim N(\theta^*_k, 1/n_k)$ for $k = 1, \ldots, K$ and $\tilde{\theta}_k$’s are independent of each other. Assume $\theta_0 = 0$, $\theta^*_k = \theta_0 + b^*_k$, $b^*_k = 0$ for $k = 1, \ldots, \lfloor (1/2 + \tau)K \rfloor$ and $b^*_k = 1$ for $k = \lfloor (1/2 + \tau)K \rfloor + 1, \ldots, K$, where $0 < \tau < 1/2$. In the supplementary material, we show

$$
P \left( \tilde{\theta} - \theta_0 \geq \frac{K^{1/2}h_*}{n^{1/2}} \right) \to 1,
$$

(6)

where $h_* = \Phi^{-1}((3/8 + \tau/4)/(1/2 + \tau))$ and $\Phi$ is the cumulative distribution function of standard normal distribution. Because $h_* > 0$ and $K \to \infty$, (6) implies $\tilde{\theta}$ is not $n^{1/2}$-consistent.

Besides the aforementioned issue, the covariance structure of $\tilde{\theta}_k$ for $k = 1, 2, \ldots, K$ is not considered in the construction of the estimator $\tilde{\theta}$ and this may lead to a loss of efficiency.
These facts motivate us to propose an estimator which is not only $n^{1/2}$-asymptotically normal but also more efficient by using penalization technique and incorporating covariance structures of $\hat{\theta}_k$ for $k = 1, 2, \ldots, K$.

It is well known that the oracle inverse-variance weighted (IVW) estimator

$$\hat{\theta}_{IVW} = \arg \min_{\theta} \sum_{k \in K_0} \frac{\tilde{\pi}_k}{2} (\hat{\theta}_k - \theta)^T \hat{V}_k (\hat{\theta}_k - \theta)$$

is the most efficient meta-analysis estimator and asymptotically normal if $K_0$ is known and $n_k^{1/2}(\hat{\theta}_k - \theta_k^*) \rightarrow N(0, \Sigma_k)$ for each $k$ in $K_0$ (Lin and Zeng, 2010; Xie et al., 2011; Burgess et al., 2020), where $\hat{V}_k$ is a consistent estimator of $\Sigma_k^{-1}$ for $k \in K_0$. See Shen et al. (2020) for further discussion on the optimality of $\hat{\theta}_{IVW}$. In general, $\hat{V}_k$’s can be any positive definite matrices if an estimator for $\Sigma_k^{-1}$ is unavailable (Liu et al., 2015) and $\hat{\theta}_{IVW}$ is still $\sqrt{n}$ consistent and asymptotically normal under certain regularity conditions. However, $\hat{\theta}_{IVW}$ is infeasible if $K_0$ is unknown. Next, we develop a penalized inverse-variance weighted estimation method, which obviates the need to know $K_0$ and is asymptotically equivalent to $\hat{\theta}_{IVW}$ under mild conditions.

To obtain a feasible estimator, we first replace $K_0$ with $\{1, \ldots, K\}$ and obtain the objective function

$$\sum_{k=1}^{K} \frac{\tilde{\pi}_k}{2} (\hat{\theta}_k - \theta)^T \hat{V}_k (\hat{\theta}_k - \theta).$$

(8)

Simply minimizing (8) with respect to $\theta$ may produce an inconsistent estimator because some of $\hat{\theta}_k$’s may not converge to $\theta_0$. Noticing that $|\|\hat{\theta}_k - \theta_0 - b_k^*\| | \rightarrow 0$ in probability for $k = 1, \ldots, K$, we add bias parameters $b_k$’s to (8) and get

$$\sum_{k=1}^{K} \frac{\tilde{\pi}_k}{2} (\hat{\theta}_k - \theta - b_k)^T \hat{V}_k (\hat{\theta}_k - \theta - b_k).$$

(9)

One may expect to recover $\theta_0$ and $b_1^*, \ldots, b_K^*$ by minimizing (9) with respect to $\theta, b_1, \ldots, b_K$. Unfortunately, it is not the case because, for any given $\theta$, (9) is minimized as long as $b_k$ takes $\hat{\theta}_k - \theta$ for $k = 1, \ldots, K$. Hence $\theta, b_1, \ldots, b_K$ that minimize (9) are not necessarily close to $\theta_0, b_1^*, \ldots, b_K^*$. To resolve this problem, we leverage the fact that $b_k^* = 0$ for $k \in K_0$ and impose penalties on $b_k$ to force $b_k$ to be zero and leave $b_k$ for $k \in K_0^c$ unconstrained. Hence we want to impose a large penalty on $b_k$ for $k \in K_0$ and impose no or a small penalty.
on $b_k$ for $k \in K_0$. To this end, we make use of the consistent estimator $\tilde{\theta}$ and define the following estimator

$$(\tilde{\theta}^T, \tilde{b}_1^T, \ldots, \tilde{b}_K^T)^T \in \arg \min_{\theta, b_1, \ldots, b_K} \sum_{k=1}^K \left\{ \frac{\tilde{\pi}_k}{2} (\tilde{\theta}_k - \theta - b_k)^T \tilde{V}_k (\tilde{\theta}_k - \theta - b_k) + \lambda \tilde{w}_k \| b_k \| \right\}, \quad (10)$$

where $\tilde{w}_k = \| \tilde{b}_k \|^{-\alpha}$, $\tilde{V}_k$ is some weighting matrix and $\lambda$ is a tuning parameter with $\alpha > 0$ and $\tilde{b}_k = \tilde{\theta}_k - \tilde{\theta}$ being an initial estimator of $b_k^*$. For $k \in K_0$, $\tilde{w}_k$ tends to be large because $\tilde{b}_k \to 0$ in probability. Thus $b_k$ may be estimated as zero in (10) for $k \in K_0$. On the other hand, because $\| \tilde{b}_k \| \to \| b_k^* \| > 0$ for $k \in K_0^c$, a smaller penalty is imposed on $b_k$ for $k \in K_0^c$ compared to $k \in K_0$. The optimization problem in (10) produces a continuous solution and is computationally attractive due to its convexity (Zou, 2006). We propose $\hat{\theta}$ as an estimator for $\theta_0$. The form of (10) is akin to the adaptive Lasso (Zou, 2006) and the group Lasso (Yuan and Lin, 2006). The optimization problem in (10) can be rewritten as an adaptive group lasso problem and solved efficiently by the R package ggLasso (https://cran.r-project.org/web/packages/gglasso/index.html). It is noted that $\tilde{\theta}$ makes contribution to $\hat{\theta}$ through $\tilde{w}_k$. This may help to select the estimates from un bias sources and control the bias of $\hat{\theta}$. We show in Section 3 that this $\hat{\theta}$ performs as well as the oracle estimator $\hat{\theta}_{IVW}$.

### 2.3 Implementation in examples

Equations (5) and (10) provide two general estimating procedures in the presence of biased data sources and can be applied to many specific problems. Only estimates $\tilde{\theta}_k$ from different data sources are required to conduct the proposed procedure. Specifically, in Example 1, we can take $\tilde{\theta}_k$ to be the estimate from the $k$th study for $k = 1, \ldots, 5$. In Example 2, we let $\tilde{\theta}_k = \gamma_k / \tilde{\beta}_k$ and use the proposed procedure to deal with the invalid instrument problem. In Example 3, we use the output of each local machine as $\tilde{\theta}_k$’s and apply our method to mitigate the effects of Byzantine failures. We investigate the theoretical properties of the proposed fusion-extraction procedure in the next section since they are of wide application.
3 Theoretical properties

3.1 Consistency and oracle properties

In this subsection, we provide asymptotic results for the estimators proposed in Section 2.2. In our theoretical development, both the dimension of parameter $d$ and the number of sources $K$ are allowed to diverge as $n \to \infty$. Let

$$\delta = \sum_{k \in K_0} \tilde{\pi}_k - \left\| \sum_{k \in K_0} \tilde{\pi}_k \frac{b_k^*}{\|b_k^*\|} \right\|.$$ 

Then (1) is equivalent to $\delta > 0$ and we have the following theorem.

**Theorem 1.** If $\delta > 0$ and $\delta^{-1} \max_k \|\tilde{\theta}_k - \theta_k^*\| \to 0$ in probability, then $\|\hat{\theta} - \theta_0\| \to 0$ in probability.

Proof of this theorem is relegated to the supplementary material. Theorem 1 establishes the consistency of $\tilde{\theta}$ under the condition that $\delta$ is not too small and that $\tilde{\theta}_k$ converges uniformly for $k = 1, \ldots, K$. If $K$ is fixed, the condition $\delta^{-1} \max_k \|\tilde{\theta}_k - \theta_k^*\| \to 0$ in probability can be satisfied as long as $\delta$ is positive and bounded away from zero. Having established the theoretical property of the initial estimator $\tilde{\theta}$, next we investigate the theoretical properties of $\hat{\theta}$ defined in (10). As pointed out previously, $\hat{\theta}_{IVW}$ is an oracle estimate that uses summary data from unbiased sources only by combining them in an efficient way (Lin and Zeng, 2010; Xie et al., 2011). It is of interest to investigate how far away the proposed estimator $\hat{\theta}$ departs from the oracle estimator $\hat{\theta}_{IVW}$ is. To establish the convergence rate of $\|\hat{\theta} - \hat{\theta}_{IVW}\|$, the following conditions are required. For any symmetric matrix $A$, let $\lambda_{\min}(A)$ and $\lambda_{\max}(A)$ be the minimum and maximum eigenvalue of $A$, respectively. We use $\| \cdot \|$ to denote the Euclid and spectral norm when applying to a vector and a matrix, respectively.

**Condition 1.** $\sum_{k \in K_0} \tilde{\pi}_k$ is bounded away from zero.

**Condition 2.** There are some deterministic matrices $V_k^*$ ($k \in K_0$), such that $\max_{k \in K_0} \|\tilde{V}_k - V_k^*\| = o_P(1)$ where $\tilde{V}_k$ is the weighting matrix appearing in (10). Moreover, the eigenvalues of $V_k^*$ are bounded away from zero and infinity for $k \in K_0$. 




**Condition 3.** \( K = O(n^{\nu_1}), \delta > 0 \) and \( \delta^{-1} \max_k \| \tilde{\theta}_k - \theta_k^* \| = O_P(n^{-\nu_2}) \) for some \( \nu_1 \in [0, 1) \) and \( \nu_2 \in (0, 1) \).

Condition 1 assumes that the proportion of data from unbiased data sources is bounded away from zero, which is a reasonable requirement. The weighting matrix \( \tilde{V}_k \) may affect the performance of the resulting estimator. In many cases, the optimal choice of \( \tilde{V}_k \) is shown to be the inverse of \( \tilde{\theta}_k \)'s asymptotic variance matrix (Lin and Zeng, 2010; Liu et al., 2015).

Condition 2 can be easily satisfied if the inverses of the estimated asymptotic variance matrices are used and \( d, K \) are not too large (Vershynin, 2018; Wainwright, 2019). There are some difficulties in estimating the asymptotic variance matrix and its inverse when the dimension is high (Wainwright, 2019). In addition, sometimes the estimated asymptotic variance matrix is not available from the summary statistics (Liu et al., 2015). However, Condition 2 just requires \( \tilde{V}_k \) to converge to some nonsingular matrix. In these cases, we can simply take \( \tilde{V}_k \) to be the identity matrix for \( k = 1, \ldots, K \) and Condition 2 can always be satisfied. Condition 3 assumes the number of data sources \( K \) is not too large. The convergence rate in Condition 3 can be satisfied by many commonly-used estimators, e.g., the maximum likelihood estimator and lasso-type estimators, under certain regularity conditions (Spokoiny, 2012; Battey et al., 2018). Then we are ready to state the theorem.

**Theorem 2.** Under Conditions 1, 2 and 3, if \( \lambda \asymp 1/n \) and \( \alpha > \max\{\nu_1\nu_2^{-1}, \nu_2^{-1} - 1\} \), we have

\[
\| \hat{\theta} - \hat{\theta}_{IVW} \| = O_P \left( \frac{K}{n} \right).
\]

Proof of this theorem is in the supplementary material. Theorem 2 establishes the convergence rate of \( \| \hat{\theta} - \hat{\theta}_{IVW} \| \), which indicates that the proposed estimator is close to the oracle estimator. If \( K = o(n^{1/2}) \), then \( \| \hat{\theta} - \hat{\theta}_{IVW} \| = o_P(n^{-1/2}) \) and our proposal is asymptotically equivalent to the oracle estimator up to an error term of order \( o_P(n^{-1/2}) \). The estimator proposed in Shen et al. (2020) possesses the similar asymptotic equivalence property. However, theoretical results in Shen et al. (2020) require \( d \) and \( K \) to be fixed, which is not required by Theorem 2. Moreover, implementation of the estimator proposed in Shen et al. (2020) requires at least one known unbiased data source. In contrast, we do not need any information about \( K_0 \) to calculate \( \hat{\theta} \).
Theorem 2 is generic in the sense that it only relies on some convergence rate conditions and does not impose restrictions on the form of \( \tilde{\theta}_k \). In practice, \( \tilde{\theta}_k \) may be calculated based on complex data, such as survey sampling or time-series data, via some complex procedure, such as deep learning or Lasso-type penalization procedure. In these cases, Theorem 2 holds consistently as long as Conditions 2 and 3 are satisfied. Moreover, Theorem 2 does not require \( \tilde{\theta}_k \)’s to be independent of each other, which ensures validity of the theorem in meta-analysis with overlapping subjects (Lin and Sullivan, 2009) or one sample Mendelian randomization (Minelli et al., 2021).

When solving (10), we also get an estimator \( \hat{b}_k \) of the bias. A question is whether \( \{\hat{b}_k\}_{k=1}^K \) selects the unbiased sources consistently, that is, whether \( \hat{K}_0 = K_0 \) with probability approaching one, where \( \hat{K}_0 = \{k : \hat{b}_k = 0\} \). To assure this selection consistency, a stronger version of Condition 2 is required.

**Condition 4.** For some deterministic matrices \( V_k^* (k = 1, \ldots, K) \), such that \( \max_k \|\tilde{V}_k - V_k^*\| = o_P(1) \) where \( \tilde{V}_k \) is the weighting matrix appears in (10). Moreover, the eigenvalues of \( V_k^* \) are bounded away from zero and infinity for \( k = 1, \ldots, K \).

This condition requires that Condition 2 holds not only for \( k \in K_0 \) but also for \( k \in K_0^c \), which is still a mild requirement. Then we are ready to establish the selection consistency.

**Theorem 3.** Under Conditions 1, 3 and 4, if \( \lambda \asymp 1/n \) and \( \alpha > \max\{\nu_1\nu_2^{-1}, \nu_2^{-1} - 1\} \), we have

\[
P(\hat{K}_0 = K_0) \to 1
\]

provided \( \min_{k \in K_0^c} \tilde{\pi}_k > C_\pi / K \) and \( K \log n/n \to 0 \) where \( C_\pi \) is some positive constant.

Proof of this theorem is relegated to the supplementary material.

### 3.2 Asymptotic normality

In this subsection, we establish the asymptotic normality of the proposed estimator \( \hat{\theta} \). Under Conditions 1, 2 and 3, if \( K = o(n^{1/2}) \), then \( \|\hat{\theta} - \hat{\theta}_{IVW}\| = o_P(n^{-1/2}) \). If \( \hat{\theta}_{IVW} \) is \( n^{1/2} \)-asymptotically normal, then \( \hat{\theta} \) is \( n^{1/2} \)-asymptotically normal and has the same asymptotic variance as \( \hat{\theta}_{IVW} \). There exist some results on asymptotic normality of \( \hat{\theta}_{IVW} \) in the
literature. However, these results either focus on the fixed dimension case (Lin and Zeng, 2010; Zhu et al., 2021) or are only suited to some specific estimators under sparse linear or generalized linear model (Battey et al., 2018). Here, we establish the asymptotic normality of \( \hat{\theta}_{IVW} \), and hence of \( \hat{\theta} \) in a general setting where \( d \) and \( K \) can diverge and \( \tilde{\theta}_k (k \in K_0) \) can be any estimator that admits uniformly an asymptotically linear representation defined in the following. Suppose the original data from the \( k \)th source \( Z_1^{(k)}, \ldots, Z_{n_k}^{(k)} \) are i.i.d. copies of \( Z^{(k)} \) and the data from different data sources are independent from each other. Then we are ready to state the condition.

**Condition 5** (Uniformly asymptotically linear representation). For \( k \in K_0 \), there is some function \( \Psi_k(\cdot) \) such that \( E[\Psi_k(Z^{(k)})] = 0 \) and

\[
\tilde{\theta}_k - \theta_0 = \frac{1}{n_k} \sum_{i=1}^{n_k} \Psi_k(Z_i^{(k)}) + R_k, \tag{11}
\]

where \( R_k \) satisfies \( \max_k \|R_k\| = o_P(n^{-1/2}) \).

Some examples satisfying Condition 5 will be discussed later. With the assistance of the uniformly asymptotically linear representation condition (Condition 5), we can establish the asymptotic normality of \( \hat{\theta}_{IVW} \) and hence of \( \hat{\theta} \).

**Theorem 4.** Suppose Conditions 1, 3 and 5 hold. If (i) \( \nu_1 < 1/2 \); (ii) there are some deterministic matrices \( V_k^* \), \( k \in K_0 \), such that \( \max_{k \in K_0} \|\tilde{V}_k - V_k^*\| = o_P(n^{-1/2+\nu_2}) \); (iii) for \( k \in K_0 \), the eigenvalues of \( V_k^* \) and \( \text{var}[\Psi_k(Z^{(k)})] \) is bounded away from zero and infinity; (iv) for \( k \in K_0 \), \( u \in \mathbb{R}^d \), \( \|u\| = 1 \) and some \( \tau > 0 \), \( E[|u^T \Psi_k(Z^{(k)})|^{1+\tau}] \) are bounded; (v) \( \lambda \asymp 1/n \) and \( \alpha > \max\{\nu_1\nu_2^{-1}, \nu_2^{-1} - 1\} \), then for any fixed \( q \) and \( q \times d \) matrix \( W_n \) such that the eigenvalues of \( W_n V_n^* \) are bounded away from zero and infinity, we have

\[
n^{1/2}I_n^{-1/2}W_n(\hat{\theta} - \theta_0) \to N(0, I_q)
\]

in distribution, where \( I_q \) is the identity matrix of order \( q \).

\[
I_n = \sum_{k \in K_0} \tilde{\pi}_k H_{n,k} \text{var}[\Psi_k(Z^{(k)})] H_{n,k}^T
\]

with \( H_{n,k} = W_n V_0^{-1} V_k^* \) and \( V_0^* = \sum_{k \in K_0} \tilde{\pi}_k V_k^* \).
Proof of this theorem is in the supplementary material. Many estimators have the asymptotically linear representation (11) with \( R_k = o_P(n_k^{-1/2}) \), see for instance Bickel et al. (1993); Spokoiny (2013); Zhou et al. (2018) and Chen and Zhou (2020). For these estimators, Condition 5 is satisfied if remainder terms \( R_k \)'s are uniformly small for \( k \in \mathcal{K}_0 \) in the sense that \( \max_{k \in \mathcal{K}_0} \| R_k \| = o_P(n^{-1/2}) \). If \( K \) is fixed, then \( \max_{k \in \mathcal{K}_0} \| R_k \| = o_P(n^{-1/2}) \) as long as \( \tilde{\pi}_k \)'s are bounded away from zero. For the case where \( K \to \infty \), in the supplementary material, we show that Condition 5 holds under some regularity conditions if \( \tilde{\theta}_k \)'s are M-estimators, i.e.

\[
\tilde{\theta}_k = \arg \min_{\theta} \frac{1}{n_k} \sum_{i=1}^{n_k} L_k(Z_i^{(k)}, \theta),
\]

for \( k = 1, \ldots, K \), where \( L_k(\cdot, \cdot) \) is some loss function that may differ from source to source. The result on M-estimator covers many commonly used estimators, e.g., the least squares estimator and maximum likelihood estimator.

Theorem 4 establishes the asymptotic normality of \( \hat{\theta} \). Unlike the existing work that can deal with biased sources in the meta-analysis literature (Singh et al., 2005; Shen et al., 2020; Zhai and Han, 2022), both the proposed estimator \( \hat{\theta} \) and \( \tilde{\theta} \) can be obtained without any knowledge on \( \mathcal{K}_0 \). Compared to existing estimators in the literature of Mendelian randomization that focus on a one-dimensional parameter (Kang et al., 2016; Bowden et al., 2016; Windmeijer et al., 2019; Hartwig et al., 2017; Guo et al., 2018; Ye et al., 2021), the proposed \( \hat{\theta} \) is applicable to the case where a multidimensional parameter is of interest. Moreover, the corresponding theoretical results are more general in the sense that they allow for the divergence of both \( d \) and \( K \) as the sample size increases. Thus besides univariable Mendelian randomization, our method can also be applied to multivariable Mendelian randomization (Burgess and Thompson, 2015; Rees et al., 2017; Sanderson et al., 2019) in the presence of invalid instruments. Recently, Tu et al. (2021) developed a method that can deal with biased sources and also allows \( d \) and \( K \) to diverge. In contrast to their work, the estimator obtained by our method achieves the \( n^{1/2} \)-asymptotic normality without requiring the proportion of biased sources among all sources to converge to zero. According to the discussion after Proposition 1, the asymptotic normality of \( \hat{\theta} \) is guaranteed even if more than half of the data come from biased sources. Therefore, our method is quite robust.
against biased sources and this is confirmed by our simulation results in the next section.

4 Simulation

In this section, we conducted three simulation studies to evaluate the empirical performance of the proposed methods. We consider different combinations of $d$ and $K$, with $d = 3, 18$ and $K = 10, 30$.

4.1 Least squares regression

First, we consider the case where $\tilde{\theta}_k$’s are obtained via least squares. Let $1_s$ be the $s$ dimensional vector consisting of 1’s and $\otimes$ be the Kronecker product. In this simulation, the data from the $k$th source are generated from the following data generation process:

$$X_k \sim N_d(0, 3I_d), \ Y_k \mid X_k \sim N_d(X_k^T(\theta_0 + b_k^*), 1),$$

where $I_d$ is the identity matrix of order $d$, $\theta_0 = 1_{d/3} \otimes (2, 1, -1)^T$, $(b_1^*, \ldots, b_K^*) = 1_{K/10} \otimes 1_{d/3} \otimes B$ and

$$B = \begin{pmatrix}
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & -1 & 1 & 1 & -2 & -2 & 5 & -1 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & -1 & 1 & 2 & -2 & 5 & 1 \\
0 & 0 & 0 & -1 & 1 & 2 & -2 & 5 & 1
\end{pmatrix}.$$

(12)

From each data source, an i.i.d sample of size $n_s$ is generated. We consider three different values of $n_s$, namely, $n_s = 100, 200$ or 500. In this simulation setting, only 20% of the data come from unbiased sources. However, the biases do not lie in the same direction and it can be verified that $\delta > 0$ by straightforward calculations. Let $\tilde{\theta}_k$ be the least squares estimator from the $k$th data source. In the simulation, we simply take $\tilde{V}_k$ to be identity matrix to ensure that all the conditions on $\tilde{V}_k$ in this paper are satisfied. We compute the naive estimator $\sum_{k=1}^K \tilde{\theta}_k/K$, the oracle estimator $\hat{\theta}_{IVW}$, the $iFusion$ estimator proposed by Shen et al. (2020), the initial estimator $\tilde{\theta}$ and the proposed estimator $\hat{\theta}$. Note that the $iFusion$ estimator is infeasible unless at least one data source is known to be unbiased. In this section, we always assume that the first data source is known to be unbiased when computing the $iFusion$ estimator. This information is not required by $\tilde{\theta}$ and $\hat{\theta}$. The following table presents the norm of the bias vector (NB) and summation of the component-wise standard
error (SSE) of these estimators calculated from 200 simulated data sets for all the four combinations of $d$ and $K$ with $d = 3, 18$ and $K = 10, 30$.

[Insert Table 1 about here.]

The naive estimator has a large bias which renders its small standard error meaningless. The bias of all the other estimators decreases as $n^*$ increases. The iFusion estimator performs similarly to the oracle estimator when $d$ and $K$ are small. However, if $d = 18$ and $K = 30$, it has a much larger standard error compared to the oracle estimator and $\hat{\theta}$. The initial estimator $\tilde{\theta}$ performs well in terms of standard error. Nevertheless, it has a far larger bias compared to the oracle estimator and $\hat{\theta}$, especially when $d$ and $K$ are large. The reason may be that it is not $\sqrt{n}$-consistent. The performance of $\tilde{\theta}$ is similar to the oracle estimator. This confirms the asymptotic equivalence between $\hat{\theta}$ and $\hat{\theta}_{IVW}$ established in Section 3.1.

Next, we evaluate the performance of our methods when all the data sources are unbiased. We set $b^*_k$ to be a zero vector for $k = 1, \ldots, K$ while keeping other parameters unchanged. In this scenario, the naive estimator reduces to the oracle estimator. NB and SSE of the estimators calculated from 200 simulated data sets for all the combinations of $d$ and $K$ are summarized in the following table.

[Insert Table 2 about here.]

Table 2 shows that the iFusion estimator has a slightly larger bias and a much larger standard error compared to other estimators when $d = 18$. All other estimators have similar performance when there are no biased sources. This implies that there is little loss of efficiency to apply our methods when all the sources are unbiased.

### 4.2 Logistic regression

In this subsection, we conducted a simulation study under the scenario where the responses are binary and $\tilde{\theta}_k$’s are obtained via logistic regression. All simulation settings are the same as in Section 4.1 except for that $Y_k \mid X_k \sim \text{Bernoulli}(t(X_k^T(\theta_0 + b^*_k)))$ and $\hat{\theta}_k$ is the maximum likelihood estimator of logistic regression model from the $k$th data source, where $t(x) = \exp(x)/(1 + \exp(x))$ is the logistic function, $\theta_0 = 0.1 \times 1_{d/3} \otimes (2, 1, −1)^T$, $(b^*_1, \ldots, b^*_K) = 0.5 \times 1_{K/10}^T \otimes 1_{d/3} \otimes B$ and $B$ is defined in (12). We add a small ridge penalty
when solving $\tilde{\theta}_k$ to avoid the problem that the maximum likelihood estimator may not be uniquely determined in finite sample (Silvapulle, 1981). NB and SSE of these estimators calculated from 200 simulated data sets are summarized in the following table.

[Insert Table 3 about here.]

The naive estimator has a large bias and the bias does not decrease as $n_*$ increases. The bias of all the other estimators decreases as $n_*$ increases. The $iFusion$ estimator has a bias similar to that of the oracle estimator. Its standard error is much larger than the oracle estimator and $\hat{\theta}$ especially when $d, K$ are large and $n_*$ is small. The initial estimator $\tilde{\theta}$ has a much larger bias compared to the oracle estimator and the proposed estimator $\hat{\theta}$, which are consistent with the simulation results under least squares regression. The performance of $\hat{\theta}$ is similar to the oracle estimator.

Next, we evaluate the performance of our methods when all the data sources are unbiased. We set $b^*_k$ to be the zero vector for $k = 1, \ldots, K$ while keeping other parameters unchanged. The naive estimator reduces to the oracle estimator in this scenario. NB and SSE of the estimators calculated from 200 simulated data sets are summarized in the following table.

[Insert Table 4 about here.]

All the estimators have similar performance in Table 4 except for that $iFusion$ estimator has a much larger standard error compared to other estimators, and there is little loss of efficiency to apply our methods when all the sources are unbiased.

### 4.3 Mendelian randomization with invalid instruments

We consider Mendelian randomization with invalid instruments in this subsection. To closely mimic what we will encounter in practice, we generate data based on a real-world data set, the BMI-SBP data set in the R package `mr.raps` (version 0.4) of Zhao et al. (2020). The data set contains estimates of the effects of 160 different SNPs on Body Mass Index (BMI) $\{\bar{\beta}_k\}_{k=1}^{160}$ and the corresponding standard error $\{\bar{\sigma}_1,k\}_{k=1}^{160}$ from a study by the Genetic Investigation of ANthropometric Traits consortium (Locke et al., 2015) (sample size: 152893), and estimates of the effects on Systolic Blood Pressure (SPB) $\{\bar{\gamma}_k\}_{k=1}^{160}$ and the
corresponding standard error \( \{\bar{\sigma}_{2,k}\}_{k=1}^{160} \) from the UK BioBank (sample size: 317754). The goal is to estimate the causal effect of BMI on SPB.

In this simulation, we generate data via the following process:

\[
\hat{\beta}_k \sim N(\bar{\hat{\beta}}_k, \bar{\sigma}_{1,k}^2), \quad k = 1, \ldots, 160,
\]
\[
\bar{\gamma}_k \sim N(\bar{\beta}_k \theta_0 + 0.15 + 3\bar{\beta}_k, \bar{\sigma}_{2,k}^2), \quad k = 1, \ldots, 100
\]
and
\[
\bar{\gamma}_k \sim N(\bar{\beta}_k \theta_0, \bar{\sigma}_{2,k}^2), \quad k = 101, \ldots, 160
\]
where \( \theta_0 = 1 \). Then \( \hat{\theta}_k \) is given by \( \bar{\gamma}_k / \bar{\hat{\beta}}_k \). Under this data generation process, 100 out of 160 instruments are invalid instruments. We apply the proposed methods to estimate \( \theta_0 \) based on \( \hat{\theta}_k \)’s. For comparison, we apply five standard methods in Mendelian randomization, namely the MR-Egger regression (Bowden et al., 2015), the weighted median method (Bowden et al., 2016), the IVW method, the weighted mode method (Hartwig et al., 2017) and the robust adjusted profile score method (RAPS, Zhao et al., 2020). Results of these five methods are calculated by the R package TwoSampleMR (https://github.com/MRCIEU/TwoSampleMR). Bias and standard error (SE) of the estimators based on 200 simulations are summarized in the following table.

[Insert Table 5 about here.]

Table 5 shows that \( \hat{\theta} \) has the smallest bias among all the estimators. The standard error of the proposed \( \hat{\theta} \) is smaller than other estimators except for the weighted median. However, the weighted median estimator has a much larger bias compared to \( \hat{\theta} \).

5 Real Data Analysis

5.1 Effects of surgical procedure for the treatment of moderate periodontal disease

In this subsection, we apply our methods to the data set provided in Berkey et al. (1998).

Data used in this subsection are available from the R package mvmeta (https://cran.r-project.org/package=mvmeta).
The data set contains results of five randomized controlled trials comparing the effect of surgical and non-surgical treatments for moderate periodontal disease. In all these studies, different segments of each patients’ mouth were randomly allocated to different treatment procedures. The two outcomes, probing depth (PD) and attachment level (AL), were assessed from each patient. The goal of treatment is to decrease PD and to increase AL around the teeth. The data set provides the estimated benefit of surgical treatment over non-surgical treatment in PD and AL (positive values mean that surgery results in a better outcome). The sample size of each study and estimated covariance matrix of the estimators are also available. The inverse-variance weighted method using all data sources produces an estimator $(0.307, -0.394)$ for the effect on (PD, AL). By applying our methods, we obtain $\tilde{\theta} = (0.260, -0.310)$ and $\hat{\theta} = (0.282, -0.303)$. Next, we assess the robustness of our methods against the bias of the published results. To do this, we add a perturbation $t \times (1, -3)$ to the first published result in the data set. After perturbing, the first published result becomes a biased estimator for the parameter of interest. We plot the resulting estimates with different values of $t$ in the following figure.

Figure 1 shows that $\tilde{\theta}$ and $\hat{\theta}$ provide quite stable estimates under different values of $t$ compared to the IVW estimator. Based on the reported estimated covariance matrices and the asymptotic normality of $\hat{\theta}$, we conduct two hypothesis testings to test whether these effects are significant. The $p$-values of the two-sided tests for effect on PD and AL are $1.660 \times 10^{-7}$ and $5.278 \times 10^{-15}$, respectively. This suggests that both effects are significant at 0.05 significance level. The 95% confidence intervals for effects of the surgical treatment on PD and AL based on $\hat{\theta}$ are $[0.176, 0.387]$ and $[-0.379, -0.227]$, respectively. In summary, our result suggests that the surgical treatment has a positive effect on PD and a negative effect on AL and our result is robust against potential bias in the results of the five published trials.
5.2 Effects of smoking and alcohol in head and neck cancer

Head and neck cancer is the sixth most common cancer in the world. Established risk factor of this cancer includes smoking and alcohol. However, researchers only have a limited understanding of the causal effect of these risk factors due to the unmeasured confounding (Gormley et al., 2020). Thanks to the recent developments in the genome-wide association study (GWAS), Mendelian randomization (Katan, 2004) has become a powerful tool to tackle the unmeasured confounding problem (Kang et al., 2016; Bowden et al., 2016; Windmeijer et al., 2019; Hartwig et al., 2017; Guo et al., 2018; Zhao et al., 2020; Ye et al., 2021). In Mendelian randomization analysis, as discussed in Example 2, each SNP is used as instrumental variables to estimate the causal effect and the estimator is consistent if the SNP is a valid instrument. The final estimator is obtained via combining the estimators produced by each SNP to improve the efficiency. However, if some SNPs are invalid instruments due to pleiotropy, linkage disequilibrium, and population stratification, the final estimator may be biased.

In this subsection, we use the comprehensive smoking index (CSI) and alcoholic drinks per week (DPW) as quantitative measures of smoking and alcohol intake and conduct the analysis using the genetic data provided by Gormley et al. (2020). A copy of the data used in this subsection is available at https://github.com/rcrichmond/smoking_alcohol_headandneckcancer. The data set contains the estimated effect of 168 independent SNPs on the head and neck cancer, CSI and DPW and the corresponding standard error. Summary-level data for the effect on head and neck cancer is from a GWAS with sample size of 12,619 conducted by the Genetic Associations and Mechanisms in Oncology Network (Lesseur et al., 2016). Summary-level data for the effect on CSI is derived by Wootton et al. (2020) from the UK Biobank (sample size 462,690), and the DPW data is obtained from a GWAS with sample size 226,223 in the GWAS & Sequencing Consortium of Alcohol and Nicotine use. See Gormley et al. (2020) for further details of the data. Following Gormley et al. (2020), we conduct the univariable Mendelian randomization to analyze the causal effect of CSI and DPW separately. Estimators of the causal effect of CSI on head and neck cancer are constructed based on 108 SNPs used in Gormley et al. (2020), which produce 108 estimates.
The IVW method that uses all these 108 estimates gives the estimate of 1.791. To mitigate the invalid instrument problem, we combine these 108 estimators by the procedures proposed in this paper, which gives \( \hat{\theta} = 1.956 \) and \( \hat{\theta} = 1.856 \), respectively. The results are close to that produced by IVW method. This is in conformity with the fact that, among the 108 SNPs, no invalid instrument is identified by Gormley et al. (2020). The analysis result suggests a positive causal effect of CSI on head and neck cancer with confidence interval [0.969, 2.744] (based on \( \hat{\theta} \)).

Then the causal effect of DPW is estimated similarly based on 60 SNPs used in Gormley et al. (2020). The result of the IVW method is 2.111. The results of the proposed methods are \( \hat{\theta} = 1.622 \) and \( \hat{\theta} = 1.598 \). When analysing the causal effect of DPW, Gormley et al. (2020) identify an invalid instrument \( rs1229984 \). When \( rs1229984 \) is not included, the IVW method based on the remaining 59 SNPs gives the estimate 1.381, which is quite different from the case where \( rs1229984 \) is included. The proposed estimators based on the remaining 59 SNPs are \( \hat{\theta} = 1.619 \) and \( \hat{\theta} = 1.590 \), which are close to the case where \( rs1229984 \) is included. This demonstrates the robustness of the proposed methods against the invalid instrument \( rs1229984 \). The analysis result suggests that DPW has a positive causal effect on the head and neck cancer with confidence interval [0.414, 2.774] (based on \( \hat{\theta} \) without \( rs1229984 \)). We then compare these results with four standard methods in Mendelian randomization problem with invalid instruments, the MR-Egger regression (Bowden et al., 2015), the weighted median method (Bowden et al., 2016), the weighted mode method (Hartwig et al., 2017) and the RAPS method (Zhao et al., 2020). Results of these four methods are calculated by the R package TwoSampleMR (https://github.com/MRCIEU/TwoSampleMR). In the presence of \( rs1229984 \), the MR-Egger regression, the weighted median, the weighted mode and the RAPS method produce the estimate 2.797, 2.968, 2.837 and 2.165 for the causal effect of DPW, respectively. Without \( rs1229984 \), results of these four methods becomes 1.072, 1.397, 1.264 and 1.637, respectively. All these four standard methods appears to be much more sensitive to the invalid instrument \( rs1229984 \) compared to the proposed methods.
6 Discussion

In this paper, we present a fusion-extraction procedure to combine summary statistics from different data sources in the presence of biased sources. The idea of the proposed method is quite general and is applicable to many estimation problems. However, several questions are left open by this paper. First, the results in this paper do not apply to the conventional random-effect model in meta-analysis. It warrant further investigation to extend results in this paper to random-effect models. Second, we assume in this paper that different data sources share the same true parameter but some data sources fail to provide a consistent estimator. In practice, the true parameters in different data sources might be heterogeneous and the estimator from a data sources may converge to the true parameter of the data source (Claggett et al., 2014). In this case, (2) defines the “least false parameter” that minimizes the weighted average distance to true parameters of each data source. It is of interest to investigate the theoretical properties of $\tilde{\theta}$ and $\hat{\theta}$ in this case.
Throughout this proof, we use $B_L$ ($B_U$) to denote the lower (upper) bound of a positive sequence that is bounded away from zero (infinity).

A Details of the counter example in Section 2.2

In this subsection, we prove (6) in Section 2.2.

Proof. Let $n_*=n/K$ and $Z_k = \tilde{\theta}_k - \theta_0$. Then it is easy to verify that $\tilde{\theta} = \text{med}(\tilde{\theta}_1, \ldots, \tilde{\theta}_K)$ and hence $\tilde{\theta} - \theta_0 = \text{med}(Z_1, \ldots, Z_K)$ where med(·) is the univariate median. Let

$$F_K(z) = \frac{1}{K} \sum_{k=1}^{K} 1\{Z_k \leq z\}.$$ 

Recall that $h_* = \Phi^{-1}((3/8 + \tau/4)/(1/2 + \tau))$. By the definition of median, to prove (6), it suffices to show $F_K(h_*/\sqrt{n_*}) < 1/2$ with probability approaching one. Note that $E[1\{Z_k \leq z\}] = \Phi(\sqrt{n_*}(z - b^*_k))$ for any $z$. Letting $z = h_*/\sqrt{n_*}$, according to the Hoeffding inequality (Wainwright, 2019, Proposition 2.5), we have

$$F_K(h_*/\sqrt{n_*}) - \frac{1}{K} \sum_{k=1}^{K} \Phi(h_* - b^*_k \sqrt{n_*}) \leq K^{-\frac{1}{2}}$$ \hspace{1cm} (13)$$

with probability at least $1 - 2 \exp(-2\sqrt{K})$. Clearly, as $K \to \infty$, $1 - 2 \exp(-2\sqrt{K}) \to 1$. Notice that

$$\frac{1}{K} \sum_{k=1}^{K} \Phi(h_* - b^*_k \sqrt{n_*}) = \frac{1}{K} \sum_{k \in K_0} \Phi(h_*) + o(1)$$

$$= \frac{1}{K} \sum_{i=1}^{[(\frac{1}{2} + \tau)K]} \frac{3/8 + \tau/4}{1/2 + \tau} + o(1)$$ \hspace{1cm} (14)

$$\leq \left(\frac{1}{2} + \tau\right) \frac{3/8 + \tau/4}{1/2 + \tau} + o(1)$$

$$= \frac{3}{8} + \frac{\tau}{4} + o(1).$$

Because $3/8 + \tau/4 < 1/2$, combining (13) and (14), we have $F_K(h_*/\sqrt{n_*}) < 1/2$ with probability approaching one, which implies (6). \hfill \square

25
B Proof of Proposition 1

Proof. Let \( G(\theta) = \sum_{k=1}^{K} \tilde{\pi}_k \|\theta^*_k - \theta\| = \sum_{k \in \mathcal{K}_0} \tilde{\pi}_k \|\theta_0 - \theta\| + \sum_{k \in \mathcal{K}_0^c} \tilde{\pi}_k \|\theta_0 + b^*_k - \theta\|. \) For any \( \theta' \neq \theta_0 \), the directional derivative of \( G(\theta) \) at the point \( \theta_0 \) in the direction \( \theta' - \theta_0 \) is

\[
\|\theta' - \theta_0\| \left( \sum_{k \in \mathcal{K}_0} \tilde{\pi}_k + \sum_{k \in \mathcal{K}_0^c} \tilde{\pi}_k \frac{b^*_k (\theta' - \theta_0)}{\|b^*_k\| \|\theta' - \theta_0\|} \right) \\
= \|\theta' - \theta_0\| \left( \sum_{k \in \mathcal{K}_0} \tilde{\pi}_k + \left( \sum_{k \in \mathcal{K}_0^c} \tilde{\pi}_k \frac{b^*_k}{\|b^*_k\|} \right)^T (\theta' - \theta_0) \right) \\
\geq \|\theta' - \theta_0\| \left( \sum_{k \in \mathcal{K}_0} \tilde{\pi}_k - \left( \sum_{k \in \mathcal{K}_0^c} \tilde{\pi}_k \frac{b^*_k}{\|b^*_k\|} \right) \right) > 0.
\]

Hence Proposition 1 follows from the fact that \( G(\theta) \) is convex.

C Proof of Theorem 1

Theorem 1 is a straightforward corollary of the following Lemma.

Lemma 1. If \( \delta > 0 \), then

\[
\|\tilde{\theta} - \theta_0\| \leq 2\delta^{-1} \sum_{k=1}^{K} \tilde{\pi}_k \|\hat{\theta}_k - \theta^*_k\|.
\]

Proof. By the convexity of \( G(\theta) \) and the directional derivative given in the proof of Proposition 1, we have

\[
G(\theta) - G(\theta_0) \geq \delta \|\theta - \theta_0\|. \tag{15}
\]

Let \( \tilde{G}(\theta) = \sum_{k=1}^{K} \tilde{\pi}_k \|\hat{\theta}_k - \theta\| \). Then by the triangle inequality of the Euclid norm,

\[
|\tilde{G}(\theta) - G(\theta)| \leq \sum_{k=1}^{K} \tilde{\pi}_k \|\hat{\theta}_k - \theta^*_k\|
\]

for any \( \theta \). Thus

\[
\tilde{G}(\theta) - \tilde{G}(\theta_0) \geq G(\theta) - G(\theta_0) - 2 \sum_{k=1}^{K} \tilde{\pi}_k \|\hat{\theta}_k - \theta^*_k\|.
\]
This together with (15) proves
\[ \tilde{G}(\theta) - \tilde{G}(\theta_0) > 0 \]
for all \( \theta \) satisfying \( \| \theta - \theta_0 \| > 2\delta^{-1} \sum_{k=1}^{K} \tilde{\pi}_k \| \tilde{\theta}_k - \theta_k^* \| \). Recalling the definition of \( \hat{\theta} \) in Section 2.2, we have \( \tilde{G}(\hat{\theta}) \leq \tilde{G}(\theta_0) \) and hence \( \| \hat{\theta} - \theta_0 \| \leq 2\delta^{-1} \sum_{k=1}^{K} \tilde{\pi}_k \| \tilde{\theta}_k - \theta_k^* \| \).

\[ \Box \]

**D Proof of Theorem 2**

To prove Theorem 2, we first establish two useful lemmas. Here we just state the lemmas and the key ideas. See the next Section for the formal proof of the two lemmas are relegated.

A key step of the proof is to construct a “good event” that happens with high probability and on the good event \( \hat{\theta} \) has some desirable properties.

For any positive numbers \( \epsilon_n \) and constants \( C_L > 0 \) and \( C_U > 1 \) such that \( C_L < B_L \leq B_U < C_U \), let \( \Delta_M = \min \{ B_L - C_L, C_U - B_U \} \). We first construct three event as follows,

\[ S_1 = \{ \| \tilde{V}_k - V_k^* \| \leq \Delta_M, \ k \in K_0 \} , \]
\[ S_2 = \{ \| \hat{\theta}_{IVW} - \tilde{\theta}_k \| < (2\tilde{\pi}_k C_U)^{-1} \lambda \tilde{w}_k, \ k \in K_0 \} , \]
\[ S_3 = \left\{ \min_{k \in K_0} \frac{\lambda \tilde{w}_k}{\tilde{\pi}_k} \geq 2\epsilon_n, \ C_U \sum_{k \in K_0} \lambda \tilde{w}_k \leq B_L C_L \epsilon_n \right\} . \]

On \( S_1 \), for \( k \in K_0 \), \( \tilde{V}_k \) is close to \( V_k^* \). On \( S_2 \), for \( k \in K_0 \), the penalty coefficient of \( b_k \) in problem (10) dominates the difference between \( \hat{\theta}_{IVW} \) and \( \tilde{\theta}_k \). Hence \( b_k \)'s are likely to be penalized to zero for \( k \in K_0 \) on \( S_2 \). On \( S_3 \), the penalty coefficient of \( b_k \) is not too small for \( k \in K_0 \) and not too large for \( k \in K_0^c \). Intuitively, these three events are all good events on which \( \hat{\theta} \) would perform well. Let \( \mathcal{S} = S_1 \cap S_2 \cap S_3 \). Next, we show that \( \hat{\theta} \) is close to \( \hat{\theta}_{IVW} \) on the event \( \mathcal{S} \). The formal result is stated in the following lemma.

**Lemma 2.** On the event \( \mathcal{S} \), we have

\[ \| \hat{\theta} - \hat{\theta}_{IVW} \| \leq \epsilon_n . \]
Under Conditions 1 and 2 and some conditions on the convergence rate of $\|\tilde{\theta}_k - \theta_k^*\|$, we have $P(S) \to 1$ and hence $P(\hat{\theta} - \hat{\theta}_{IVW} \leq \epsilon_n) \to 1$ according to Lemma 2. The formal result is summarized in the following lemma. See Appendix E for the proof of Lemma 2 and 3.

**Lemma 3.** Under Conditions 1 and 2, if the tuning parameter $\lambda$ satisfies

$$
\lambda^{-1} \delta^{-\alpha} \max_k \{\|\tilde{\theta}_k - \theta_k^*\|^{\alpha+1}\} \in o_P(1),
$$

then for any sequence $\epsilon_n$ such that $\lambda K / \epsilon_n \to 0$ and $\epsilon_n \lambda^{-1} \delta^{-\alpha} \max_k \{\|\tilde{\theta}_k - \theta_k^*\|^{\alpha}\} \in o_P(1),$

$$
P(\|\hat{\theta} - \hat{\theta}_{IVW}\| \leq \epsilon_n) \to 1.
$$

With the assistance of Lemma 3, we are able to prove Theorem 2.

**Proof.** Condition 3 and the fact that $\alpha > \max\{\nu_1 \nu_2^{-1}, \nu_2^{-1} - 1\}$ together imply

$$
\delta^{-(\alpha+1)} \max_k \{\|\tilde{\theta}_k - \theta_k^*\|^{\alpha+1}\} \in o_P(n^{-1}),
$$

\begin{equation}
\delta^{-\alpha} \max_k \{\|\tilde{\theta}_k - \theta_k^*\|^{\alpha}\} \in o_P(n^{-\alpha\nu_2}).
\end{equation}

Because $\lambda \asymp 1/n$, the conditions Lemma 3 is satisfied with $\epsilon_n = a_n K / n$ where $a_n$ is an arbitrary sequence of positive numbers such that $a_n \to \infty$ and $a_n n^{\nu_1 - \alpha \nu_2} \to 0$. Note that $\nu_1 - \alpha \nu_2 < 0$. Then we have

$$
P(\|\hat{\theta} - \hat{\theta}_{IVW}\| \leq a_n K / n) \to 1
$$

for arbitrary $a_n$ that diverges to infinity at a sufficiently slow rate. This indicates that $\|\hat{\theta} - \hat{\theta}_{IVW}\| = O_P(K/n)$. To see this, assuming that $n\|\hat{\theta} - \hat{\theta}_{IVW}\|/K$ is not bounded in probability, then for some $\epsilon > 0$ there is some $m_1 \geq e$ such that $P(n\|\hat{\theta} - \hat{\theta}_{IVW}\|/K > 1) \geq \epsilon$ when $n = m_1$. For $s = 2, 3, \ldots$, there is some $m_s > \max\{m_{s-1}, \epsilon^s\}$ such that $P(n\|\hat{\theta} - \hat{\theta}_{IVW}\|/K > s) \geq \epsilon$ when $n = m_s$. Let $a_n = s$ for $m_s \leq n < m_{s+1}$. Then for this sequence, we have $a_n \to \infty$ and $a_n \leq \log n$. Hence $a_n$ satisfies $a_n n^{\nu_1 - \alpha \nu_2} \to 0$. Moreover, for any positive integer $s$, $P(\|\hat{\theta} - \hat{\theta}_{IVW}\| \leq a_n K / n) \leq 1 - \epsilon$ when $n = m_s$. Thus, $\liminf_n P(\|\hat{\theta} - \hat{\theta}_{IVW}\| \leq a_n K / n) \leq 1 - \epsilon$, which contradicts to (18).
E  Proof of Lemmas 2 and 3

To prove the two lemmas, we first analyse the optimization problem (10) in the main text. We denote $\gamma = (\theta^T, b_1^T, \ldots, b_K^T)^T$ as a grand parameter vector. Let

$$\Gamma_0 = \{\gamma : \gamma = (\theta^T, b_1^T, \ldots, b_K^T)^T, b_k = 0 \text{ for } k \in \mathcal{K}_0 \text{ and } b_k \neq 0 \text{ for } k \in \mathcal{K}_0^c\},$$

and

$$L(\gamma) = \sum_{k=1}^K \frac{\pi_k}{2} (\theta_k - \theta - b_k)^T \hat{V}_k (\theta_k - \theta - b_k).$$

Consider the following oracle problem that sets the term $b_k$ to be zero in prior for $k \in \mathcal{K}_0$

$$\min_{\gamma \in \Gamma_0} \{L(\gamma) + \sum_{k \in \mathcal{K}_0^c} \lambda \hat{w}_k \|b_k\|\}.$$  \hspace{1cm} (19)

The following lemma establishes the relationship between the minimum point of this problem and the problem (10).

**Lemma 4.** Let $\mathcal{M}$ be the set of minimum points of problem (10) and $\bar{\mathcal{M}}$ be the set of minimum points of problem (19). If there exists a minimum point $\bar{\gamma} = (\bar{\theta}^T, \bar{b}_1^T, \ldots, \bar{b}_K^T)^T$ of problem (19) such that $\pi_k \|\hat{V}_k (\bar{\theta} - \bar{\theta})\| < \lambda \hat{w}_k$ for $k \in \mathcal{K}_0$, then $\mathcal{M} = \bar{\mathcal{M}}$.

**Proof.** Because $\bar{\gamma}$ is a minimum point of problem (19), it follows from the Karush-Kuhn-Tucker condition that

$$\left\{ \begin{array}{l}
\sum_{k \in \mathcal{K}_0} \pi_k \hat{V}_k (\bar{\theta}_k - \bar{\theta}) + \sum_{k \in \mathcal{K}_0^c} \pi_k \hat{V}_k (\bar{\theta}_k - \bar{\theta} - \bar{b}_k) = 0, \\
\pi_k \hat{V}_k (\bar{\theta}_k - \bar{\theta} - \bar{b}_k) = \lambda \hat{w}_k \hat{z}_k, \; k \in \mathcal{K}_0^c
\end{array} \right.$$ \hspace{1cm} (20)

where $\hat{z}_k = \bar{b}_k / \|\bar{b}_k\|$ if $\bar{b}_k \neq 0$ and $\|\hat{z}_k\| \leq 1$ if $\bar{b}_k = 0$. Because $\pi_k \|\hat{V}_k (\bar{\theta} - \bar{\theta})\| < \lambda \hat{w}_k$ for $k \in \mathcal{K}_0$, $\bar{\gamma}$ also satisfies the Karush-Kuhn-Tucker condition of problem (10) and hence $\bar{\gamma} \in \mathcal{M}$ by the convexity of problem (10).

One the one hand, for any $\bar{\gamma} \in \mathcal{M}$, because both $\bar{\gamma}$ and $\bar{\gamma}$ belongs to $\bar{\mathcal{M}}$, we have $L(\bar{\gamma}) + \sum_{k=1}^K \lambda \hat{w}_k \|\bar{b}_k\| = L(\bar{\gamma}) + \sum_{k=1}^K \lambda \hat{w}_k \|\bar{b}_k\|$. In addition, according to the above discussion, we have $\bar{\gamma} \in \mathcal{M}$. Then we have $L(\bar{\gamma}) + \sum_{k=1}^K \lambda \hat{w}_k \|\bar{b}_k\| = \min_{\gamma} \{L(\gamma) + \sum_{k=1}^K \lambda \hat{w}_k \|b_k\|\}$ and hence $L(\bar{\gamma}) + \sum_{k=1}^K \lambda \hat{w}_k \|\bar{b}_k\| = \min_{\gamma} \{L(\gamma) + \sum_{k=1}^K \lambda \hat{w}_k \|b_k\|\}$. This implies $\bar{\gamma} \in \mathcal{M}$ and proves $\bar{\mathcal{M}} \subset \mathcal{M}$.
On the other hand, for any $\gamma' \in \mathcal{M}$, because both $\gamma'$ and $\tilde{\gamma}$ belongs to $\tilde{\mathcal{M}}$, we have $L(\tilde{\gamma}) + \sum_{k=1}^{K} \lambda \tilde{w}_k \| \tilde{b}_k \| = L(\gamma') + \sum_{k=1}^{K} \lambda \tilde{w}_k \| b'_k \|$, this implies $L(\tilde{\gamma}) - L(\gamma') = \sum_{k=1}^{K} \lambda \tilde{w}_k (\| b'_k \| - \| \tilde{b}_k \| )$. Recall that, for $k \in K_0$, $\tilde{z}_k = \tilde{b}_k/\| \tilde{b}_k \|$ if $\tilde{b}_k \neq 0$ and $\| \tilde{z}_k \| \leq 1$ if $\tilde{b}_k = 0$. In addition, let $\tilde{z}_k = (\lambda \tilde{w}_k)^{-1} \tilde{\pi}_k \tilde{V}_k (\tilde{\theta}_k - \tilde{\theta})$ for $k \in K_0$. Then it is easy to verify that $\| \tilde{z}_k \| \leq 1$ for $k \in K_0$, $\| \tilde{z}_k \| < 1$ for $k \in K_0$, $\tilde{z}_k \tilde{b}_k = \| \tilde{b}_k \|$ for $k = 1, \ldots, K$, and $\nabla L(\tilde{\gamma}) = -(0^T, \lambda \tilde{w}_1 \tilde{z}^*_1, \ldots, \lambda \tilde{w}_K \tilde{z}^*_K)^T$. By the convexity of $L(\gamma)$, we have

$$0 \geq L(\tilde{\gamma}) - L(\gamma') + \nabla L(\tilde{\gamma})^T(\gamma' - \tilde{\gamma})$$

$$= \sum_{k=1}^{K} \lambda \tilde{w}_k (\| b'_k \| - \| \tilde{b}_k \| ) - \sum_{k=1}^{K} \lambda \tilde{w}_k \tilde{z}^*_k (b'_k - \tilde{b}_k)$$

$$= \sum_{k=1}^{K} \lambda \tilde{w}_k (\| b'_k \| - \tilde{z}^T b'_k)$$

$$\geq \sum_{k=1}^{K} \lambda \tilde{w}_k (\| b'_k \| - \| \tilde{z}_k \| \| b'_k \| )$$

$$\geq \sum_{k \in K_0} \lambda \tilde{w}_k \| b'_k \| (1 - \| \tilde{z}_k \| ).$$

Because $\lambda \tilde{w}_k (1 - \| \tilde{z}_k \| ) = \lambda \tilde{w}_k - \tilde{\pi}_k \| \tilde{V}_k (\tilde{\theta}_k - \tilde{\theta}) \| > 0$ for $k \in K_0$, we have $\| b'_k \| = 0$ for $k \in K_0$. Combining this with the fact that $L(\tilde{\gamma}) + \sum_{k=1}^{K} \lambda \tilde{w}_k \| \tilde{b}_k \| = L(\gamma') + \sum_{k=1}^{K} \lambda \tilde{w}_k \| b'_k \|$, we have $\gamma' \in \tilde{\mathcal{M}}$. This completes the proof of the lemma.

\[\square\]

Recall that throughout the proofs, we always use $B_L$ ($B_U$) to denote the lower (upper) bound of a sequence that is bounded away from zero (infinity). For any positive numbers $\epsilon_n$ and constants $C_L > 0$ and $C_U > 1$ such that $C_L < B_L \leq B_U < C_U$, let $\Delta_M = \min\{B_L - C_L, C_U - B_U\}$,

$$S_1 = \{ \| \tilde{V}_k - V^*_k \| \leq \Delta_M, \ k \in K_0 \},$$

$$S_2 = \{ \| \tilde{\theta}_k \| < (2\tilde{\pi}_k C_U)^{-1} \lambda \tilde{w}_k, \ k \in K_0 \},$$

$$S_3 = \{ \min_{k \in K_0} \lambda \tilde{w}_k / \tilde{\pi}_k \geq 2\epsilon_n, \ C_U \sum_{k \in K_0} \lambda \tilde{w}_k \leq B_L C L \epsilon_n \},$$

and

$$S = S_1 \cap S_2 \cap S_3.$$
Then we are ready to give the proof of Lemma 2.

**Restate of Lemma 2.** On the event $\mathcal{S}$, we have

$$\|\hat{\theta} - \hat{\theta}_{IVW}\| \leq \epsilon_n.$$  

**Proof.** Let $\tilde{\gamma} \in \tilde{\mathcal{M}}$ be any minimum point of problem (19). Then by the KKT condition (20), we have

$$\hat{\theta} = (\sum_{k \in K_0} \tilde{\pi}_k \tilde{V}_k)^{-1} (\sum_{k \in K_0} \tilde{\pi}_k \tilde{V}_k \hat{\theta}_k) + (\sum_{k \in K_0} \tilde{\pi}_k \tilde{V}_k)^{-1} (\sum_{k \in K_0} \lambda \tilde{w}_k \tilde{z}_k)$$

$$= \hat{\theta}_{IVW} + \left( \sum_{k \in K_0} \tilde{\pi}_k \tilde{V}_k \right)^{-1} \left( \sum_{k \in K_0} \lambda \tilde{w}_k \tilde{z}_k \right). \tag{21}$$

By Weyl’s Theorem, we have $\max_{k \in K_0} \{ \max \{ |\lambda_{\min}(\tilde{V}_k) - \lambda_{\min}(V_k^*)|, |\lambda_{\max}(\tilde{V}_k) - \lambda_{\max}(V_k^*)| \} \} \leq \max_{k \in K_0} \| \tilde{V}_k - V_k^* \| \leq \Delta_M$ on $\mathcal{S}_1$. Then by Condition 2, it follows

$$C_L \leq \lambda_{\min}(\tilde{V}_k) \leq \lambda_{\max}(\tilde{V}_k) \leq C_U$$

for $k \in K_0$ on $\mathcal{S}_1$. Then by Conditions 1 and 2, we have

$$\tilde{\pi}_k \| \tilde{V}_k (\hat{\theta}_k - \hat{\theta}) \| \leq \tilde{\pi}_k \| \tilde{V}_k \| \| \hat{\theta}_k - \hat{\theta}_{IVW} \| + \tilde{\pi}_k \| \tilde{V}_k \| \left( \sum_{k \in K_0} \tilde{\pi}_k \tilde{V}_k \right)^{-1} \| \sum_{k \in K_0} \lambda \tilde{w}_k \tilde{z}_k \|

\leq \tilde{\pi}_k C_U \| \hat{\theta}_k - \hat{\theta}_{IVW} \| + \tilde{\pi}_k C_U B_L^{-1} C_L^{-1} \sum_{k \in K_0} \lambda \tilde{w}_k

< \frac{\lambda \tilde{w}_k}{2} + \frac{\tilde{\pi}_k \epsilon_n}{2} < \lambda \tilde{w}_k$$

on the event $\mathcal{S}$. According to Lemma 4, we have $\mathcal{M} = \mathcal{M}$ on $\mathcal{S}$. By equation (21), for any $(\hat{\theta}^T, \hat{b}_1^T, \ldots, \hat{b}_K^T)^T \in \mathcal{M} = \tilde{\mathcal{M}}$, we have

$$\hat{\theta} - \hat{\theta}_{IVW} = \left( \sum_{k \in K_0} \tilde{\pi}_k \tilde{V}_k \right)^{-1} \left( \sum_{k \in K_0} \lambda \tilde{w}_k \tilde{z}_k \right).$$

31
This implies
\[
\|\hat{\theta} - \hat{\theta}_{IVW}\| \leq B_L^{-1} C_L^{-1} \sum_{k \in \mathcal{K}_0} \lambda \hat{w}_k \leq C_U^{-1} \epsilon_n
\]
on \mathcal{S}. Note that \(C_U > 1\) and this completes the proof of the lemma.

Next, we move on to the proof of Lemma 3.

**Restate of Lemma 3.** Under Conditions 1, and 2, if the tuning parameter \(\lambda\) satisfies
\[
\lambda^{-1} \delta^{-\alpha} \max_k \{\|\hat{\theta}_k - \theta_k^*\|^{\alpha+1}\} = o_P(1),
\]
then for any sequence \(\epsilon_n\) such that \(\lambda K / \epsilon_n \rightarrow 0\) and \(\epsilon_n \lambda^{-1} \delta^{-\alpha} \max_k \{\|\hat{\theta}_k - \theta_k^*\|\} = o_P(1),\)
\[
P(\|\hat{\theta} - \hat{\theta}_{IVW}\| \leq \epsilon_n) \rightarrow 1.
\]

**Proof.** To prove the lemma, according to Lemma 2, it suffices to prove \(P(\mathcal{S}) \rightarrow 1\) with \(C_L = 0.9 B_L, C_U = 1.1 B_U\). By Condition 2, we have \(P(\mathcal{S}_1) \rightarrow 1\). By the definition of \(\hat{\theta}_{IVW}\), we have
\[
\hat{\theta}_{IVW} - \tilde{\theta}_k = \left(\sum_{j \in \mathcal{K}_0} \tilde{\pi}_j \tilde{V}_j\right)^{-1} \left(\sum_{j \in \mathcal{K}_0} \tilde{\pi}_j \tilde{V}_j (\hat{\theta}_j - \hat{\theta}_k)\right).
\]
For \(k \in \mathcal{K}_0\), on the event \(\mathcal{S}_1\), we have
\[
\|\hat{\theta}_{IVW} - \tilde{\theta}_k\| \leq (B_L - \max_{j \in \mathcal{K}_0} \|\tilde{V}_j - V_j^*\|)^{-1} (\max_{j \in \mathcal{K}_0} \|\tilde{V}_j (\hat{\theta}_j - \hat{\theta}_k)\|)
\]
\[
\leq (B_L - \max_{j \in \mathcal{K}_0} \|\tilde{V}_j - V_j^*\|)^{-1} (B_U + \max_{j \in \mathcal{K}_0} \|\tilde{V}_j - V_j^*\|) \max_{j \in \mathcal{K}_0} \|\tilde{\theta}_j - \tilde{\theta}_k\| \quad (22)
\]
\[
\leq C_L^{-1} C_U \max_{j \in \mathcal{K}_0} \|\tilde{\theta}_j - \tilde{\theta}_k\|
\]
by Condition 2. Because for \(j \in \mathcal{K}_0, \theta_j^* = \theta_0\), we have
\[
\max_{j \in \mathcal{K}_0} \|\tilde{\theta}_j - \tilde{\theta}_k\| \leq \max_j \|\tilde{\theta}_j - \theta_0\| + \max_k \|\tilde{\theta}_k - \theta_0\| = 2 \max_j \|\tilde{\theta}_j - \theta_j^*\|. \quad (23)
\]
Note that by Lemma 1,\[
\|\tilde{\theta} - \theta_0\| \leq 2 \delta^{-1} \|\tilde{\theta}_j - \theta_j^*\|.
\]
This together with the definitions of $\hat{b}_k$ and $b_k^*$ proves
\[
\|\hat{b}_k - b_k^*\| \leq (1 + 2\delta^{-1}) \max_j \|\hat{\theta}_j - \theta_j^*\|. \tag{24}
\]
Recalling that $\bar{w}_k = 1/\|\hat{b}_k\|^\alpha$, according to (22), (23) and (24) we have
\[
S_1 \cap S_2 = S_1 \cap \{\lambda^{-1} \hat{\pi}_k \|\hat{b}_k\|\|\hat{\theta}_{1W} - \hat{\theta}_k\| < (2C_1)^{-1}, \ k \in \mathcal{K}_0 \}
\supset S_1 \cap \{2C_L^{-1}C_U\lambda^{-1}(1 + 2\delta^{-1})\alpha(\max_j \|\hat{\theta}_j - \theta_j^*\|)^{\alpha + 1} < (2C_1)^{-1}\} =: S_1 \cap S_2^*.
\]
Because $\lambda^{-1}\delta^{-\alpha}\max_j \|\hat{\theta}_j - \theta_j^*\|^{\alpha + 1} = o_P(1)$, then $P(S_2^*) \to 1$ and hence $P(S_1 \cap S_2^*) \to 1$. This implies $P(S_1 \cap S_2) \to 1$. Notice that $S_3$ can be rewritten as
\[
\{2\epsilon_n \lambda^{-1} \max_{k \in \mathcal{K}_0} \|\hat{\pi}_k\|\|\hat{b}_k\|^\alpha \} \leq 1, \sum_{k \in \mathcal{K}_0} \lambda \bar{w}_k / \epsilon_n \leq C_U^{-1}B_L C_L \}.
\]
According to (24), because $\|b_k^*\|$ is bounded away from zero for $k \in \mathcal{K}_0$,
\[
S_3 \supset \{2\epsilon_n \lambda^{-1}(1 + 2\delta^{-1})\alpha \max_k \|\hat{\theta}_k - \theta_k^*\|^{\alpha} \} \leq 1, \sum_{k \in \mathcal{K}_0} \lambda \bar{w}_k / \epsilon_n \leq C_U^{-1}B_L C_L \}
\supset \{2\epsilon_n \lambda^{-1}(1 + 2\delta^{-1})\alpha \max_k \|\hat{\theta}_k - \theta_k^*\|^{\alpha} \} \leq 1, \max_{k \in \mathcal{K}_0} \|\hat{w}_k\|\lambda K / \epsilon_n \leq C_U^{-1}B_L C_L \}
\supset \{2\epsilon_n \lambda^{-1}(1 + 2\delta^{-1})\alpha \max_k \|\hat{\theta}_k - \theta_k^*\|^{\alpha} \} \leq 1, \lambda^{-1}\epsilon_n \min_{k \in \mathcal{K}_0} \|\hat{b}_k\|^\alpha \geq C_U B_L^{-1}C_L^{-1} K \}
\supset \{2\epsilon_n \lambda^{-1}(1 + 2\delta^{-1})\alpha \max_k \|\hat{\theta}_k - \theta_k^*\|^{\alpha} \} \leq 1,
\quad (B_L - (1 + 2\delta^{-1}) \max_k \|\hat{\theta}_k - \theta_k^*\|^{\alpha}) \geq C_U B_L^{-1}C_L^{-1} \lambda K / \epsilon_n \}
\supset: S_3^*.
\]
Since $\lambda K / \epsilon_n \to 0$, we have $\lambda / \epsilon_n \to 0$. Because $\epsilon_n \lambda^{-1}\delta^{-\alpha}\max_k \|\hat{\theta}_k - \theta_k^*\|^{\alpha} = o_P(1)$, then we have
\[
(1 + 2\delta^{-1}) \max_k \|\hat{\theta}_k - \theta_k^*\| = (\epsilon_n^{-1}\lambda \times \epsilon_n \lambda^{-1}(1 + 2\delta^{-1})\alpha \max_j \|\hat{\theta}_j - \theta_j^*\|)^{\frac{1}{\alpha}} = o_P(1).
\]
Hence $P(S_3^*) \to 1$ and hence $P(S_3) \to 1$. This completes the proof. \hfill \Box

33
F Proof of Theorem 3

We first establish a lemma that is needed in the proof of Theorem 3.

Lemma 5. On the event $S$, we have $\hat{b}_k = 0$ for $k \in \mathcal{K}_0$.

Proof. According to the proof of Lemma 2, we have $\hat{M} = M$ on $S$. By the definition of $\hat{M}$, for any $(\hat{\theta}_T, \hat{b}_T^1, \ldots, \hat{b}_T^K)^T \in M = \hat{M}$, we have $\hat{b}_k = 0$ for $k \in \mathcal{K}_0$. □

Restate of Theorem 3. Under Conditions 1, 3 and 4, if $\lambda \asymp 1/n$ and $\alpha > \max\{\nu_1^{-1}, \nu_2^{-1} - 1\}$, we have

$$P(\hat{K}_0 = K_0) \to 1$$

provided $\min_{k \in \mathcal{K}_0^c} \hat{\pi}_k > C_\pi/K$ and $K \log n/n \to 0$ where $C_\pi$ is some positive constant.

Proof. As before, we let $C_L = 0.9B_L$, $C_U = 1.1B_U$, $\Delta_M = \min\{B_L - C_L, C_U - B_U\}$ and $\epsilon_n = a_n K/n$ where $a_n$ is a sequence of positive numbers such that $a_n \to \infty$ and $a_n/\log n \to 0$. Define

$$S'_1 = \{\|\hat{V}_k - V_k^*\| \leq \Delta_M, \; k = 1, \ldots, K\},$$

$$S'_2 = \{\|\hat{\theta}_{IVW} - \hat{\theta}_k\| > (\hat{\pi}_k C_L)^{-1} \lambda \hat{w}_k + \epsilon_n, \; k \in \mathcal{K}_0^c\},$$

$$S' = S'_1 \cap S'_2.$$

Recall the definition of $S$ in (16). According to Lemmas 2 and 5, we have $\|\hat{\theta} - \hat{\theta}_{IVW}\| \leq \epsilon_n$ and $\hat{b}_k = 0$ for $k \in \mathcal{K}_0$ when $S$ holds. It is straightforward to verify that the conditions of Lemma 3 is satisfied under the conditions of this theorem. Hence we have $P(S) \to 1$ according to Lemma 3. To prove this theorem, it then suffices to prove $\hat{b}_k \neq 0$ for $k \in \mathcal{K}_0^c$ on $S' \cap S$ and $P(S') \to 1$.

First, we prove that $\hat{b}_k \neq 0$ for $k \in \mathcal{K}_0^c$ on the event $S' \cap S$. The arguments in the rest of this paragraph are derived on the event $S' \cap S$. By Weyl’s Theorem, $\max_k \{\|\lambda_{\min}(\hat{V}_k) - \lambda_{\min}(V_k^*)\|, \|\lambda_{\max}(\hat{V}_k) - \lambda_{\max}(V_k^*)\|\} \leq \max_k \|\hat{V}_k - V_k^*\| \leq \Delta_M$. Thus, for $k = 1, \ldots, K$,

$$C_L \leq \lambda_{\min}(\hat{V}_k) \leq \lambda_{\max}(\hat{V}_k) \leq C_U.$$
Because \((\hat{\theta}^T, \hat{b}_1^T, \ldots, \hat{b}_k^T)^T\) is a minimum point of problem (10) in the main text, we have
\[
\pi_k V_k(\hat{\theta}_k - \hat{\theta} - \hat{b}_k) = \lambda \hat{\theta}_k \hat{z}_k, \quad k \in \mathcal{K}_0^c
\] (25)
for some \(\|\hat{z}_k\| \leq 1\) according to the KKT condition. Thus by (25), the definition of eigenvalue and the triangular inequality, we have
\[
\pi_k C_L(\|\hat{\theta}_k - \hat{\theta}\| - \|\hat{b}_k\|) \leq \pi_k \lambda_{\min}(V_k)(\|\hat{\theta}_k - \hat{\theta}\| - \|\hat{b}_k\|) \leq \|\pi_k V_k(\hat{\theta}_k - \hat{\theta} - \hat{b}_k)\| \leq \lambda \hat{w}_k
\]
for \(k \in \mathcal{K}_0^c\). Then on \(S'_2\)
\[
\|\hat{b}_k\| \geq \|\hat{\theta}_k - \hat{\theta}\| - \|\hat{\theta}_k - \hat{\theta}\| - \|\hat{b}_k\| \\
\geq \|\hat{\theta}_k - \hat{\theta}\| - (\pi_k C_L)^{-1}\lambda \hat{w}_k \\
\geq \|\hat{\theta}_k - \hat{\theta}_{IVW}\| - \|\hat{\theta} - \hat{\theta}_{IVW}\| - (\pi_k C_L)^{-1}\lambda \hat{w}_k \\
\geq \|\hat{\theta}_k - \hat{\theta}_{IVW}\| - \epsilon_n - (\pi_k C_L)^{-1}\lambda \hat{w}_k \\
> 0.
\]
This indicates that \(\hat{b}_k \neq 0\) for \(k \in \mathcal{K}_0^c\) on the event \(S' \cap S\).

Next, we prove that \(P(S') \to 1\). By Condition 4, we have \(P(S'_1) \to 1\). Note that
\[
\hat{\theta}_{IVW} - \hat{\theta}_k = \left(\sum_{j \in \mathcal{K}_0} \pi_j V_j\right)^{-1} \left(\sum_{j \in \mathcal{K}_0} \pi_j V_j(\hat{\theta}_j - \hat{\theta}_k)\right).
\]
On the event \(S'_1\), for \(k \in \mathcal{K}_0^c\), we have
\[
\|\hat{\theta}_{IVW} - \hat{\theta}_k\| \geq (B_U + \max_{j \in \mathcal{K}_0} \|\hat{V}_j - V_j^*\|)^{-1} B_L \left(\min_{j \in \mathcal{K}_0} \|V_j^*(\hat{\theta}_j - \hat{\theta}_k)\|\right) \\
\geq (B_U + \max_{j \in \mathcal{K}_0} \|\hat{V}_j - V_j^*\|)^{-1} B_L \left(B_L - \max_{j \in \mathcal{K}_0} \|\hat{V}_j - V_j^*\|\right) \min_{j \in \mathcal{K}_0} \|\hat{\theta}_j - \hat{\theta}_k\| \\
\geq C_U^{-1} B_L C_L \min_{j \in \mathcal{K}_0} \|\hat{\theta}_j - \hat{\theta}_k\|.
\]
Because for \(k \in \mathcal{K}_0^c\) and \(j \in \mathcal{K}_0\),
\[
\|\hat{\theta}_j - \hat{\theta}_k\| \geq \|b_k^*\| - \|\hat{\theta}_j - \theta_0\| - \|\hat{\theta}_k - \theta_k^*\|,
\]
we have
\[
\min_{j \in \mathcal{K}_0, k \in \mathcal{K}_0^c} \|\hat{\theta}_j - \hat{\theta}_k\| \geq B_L - 2 \max_j \|\hat{\theta}_j - \theta_j^*\|
\]
35
Thus
\[ S'_1 \cap S'_2 = S'_1 \cap \{ ||\hat{\theta}_{IVW} - \tilde{\theta}_k|| > (\hat{\pi}_k C_L)^{-1}\lambda \tilde{w}_k + \epsilon_n, \ k \in K_0 \} \]
\[ \supset S'_1 \cap \{ C_U^{-1} B_L C_L (B_L - 2 \max_j \|\hat{\theta}_j - \theta_j^*\|) > (\min_{k \in K_0} \hat{\pi}_k C_L)^{-1}\lambda \max_k \tilde{w}_k + \epsilon_n \} \]
\[ =: S'_{2^*}. \]

According to Condition 3, \( C_U^{-1} B_L C_L (B_L - 2 \max_j \|\hat{\theta}_j - \theta_j^*\|) = C_U^{-1} C_L B_L^2 + o_P(1) \).

Recall that \( \tilde{w}_k = 1/||\tilde{b}_k||^\alpha \). Then \( \max_{k \in K_0} \tilde{w}_k = O_P(1) \) according to (24) and (17).

Since \( \min_{k \in K_0} \hat{\pi}_k > C \pi / K \) and \( \lambda < 1/n \), we have \( (\min_{k \in K_0} \hat{\pi}_k C_L)^{-1}\lambda \max_{k \in K_0} \tilde{w}_k = O_P(K/n) \). Moreover, \( \epsilon_n = o(K \log n/n) \) by definition. \( (\min_{k \in K_0} \hat{\pi}_k C_L)^{-1}\lambda \max_{k \in K_0} \tilde{w}_k + \epsilon_n = o_P(1) \) because \( K \log n/n \to 0 \). Thus \( P(S'_{2^*}) \to 1 \) and hence \( P(S') \to 1 \). This completes the proof.

\[ \square \]

G Proof of Theorem 4

Restate of Theorem 4. Suppose Conditions 1, 3 and 5 hold. If (i) \( \nu_1 < 1/2 \); (ii) there are some deterministic matrices \( V_k^*, \ k \in K_0 \), such that \( \max_{k \in K_0} ||\tilde{V}_k - V_k^*|| = o_P(n^{-1/2+\nu_2}) \); (iii) for \( k \in K_0 \), the eigenvalues of \( V_k^* \) and \( \text{var} [\Psi_k(Z^{(k)})] \) are bounded away from zero and infinity; (iv) for \( k \in K_0 \), \( u \in \mathbb{R}^d, ||u|| = 1 \) and some \( \tau > 0 \), \( E[|u^\tau \Psi_k(Z^{(k)})|^{1+\tau}] \) are bounded; (v) \( \lambda < 1/n \) and \( \alpha > \max\{\nu_1 \nu_2^{-1}, \nu_2^{-1} - 1\} \), then for any fixed \( q \) and \( q \times d \) matrix \( W_n \) such that the eigenvalues of \( W_n W_n^T \) are bounded away from zero and infinity, we have

\[ \sqrt{n}T_n^{-1/2} W_n(\hat{\theta} - \theta_0) \overset{d}{\to} N(0, I_q), \]

where \( I_q \) is the identity matrix of order \( q \), \( T_n = \sum_{k \in K_0} \hat{\pi}_k H_{n,k} \text{var} [\Psi_k(Z^{(k)})] H_{n,k}^T \), \( H_{n,k} = W_n V_0^{-1} V_k^* \) and \( V_0^* = \sum_{k \in K_0} \hat{\pi}_k V_k^* \).

Proof. According to Theorem 2, under (i), (ii), (v), Condition 1 and 3, we have

\[ ||\hat{\theta} - \hat{\theta}_{IVW}|| = o_P \left( \frac{1}{\sqrt{n}} \right). \]
Then to establish the asymptotic normality result of $\hat{\theta}$, it suffices to establish the asymptotic normality of $\hat{\theta}_{IVW}$. According to (ii), (iii) and Condition 1, we have

$$I_n^{-1/2}W_n(\hat{\theta}_{IVW} - \theta_0) = I_n^{-1/2}W_n \left( \sum_{k \in K_0} \hat{\pi}_k \hat{V}_k \right) \left( \sum_{k \in K_0} \hat{\pi}_k \hat{V}_k (\hat{\theta}_k - \theta_0) \right)$$

$$= I_n^{-1/2}W_n \left( V_0^{* - 1} + o_P(1) \right) \left( \sum_{k \in K_0} \hat{\pi}_k V_k^* (\hat{\theta}_k - \theta_0) \right)$$

$$+ I_n^{-1/2}W_n \left( V_0^{* - 1} + o_P(1) \right) \left( \sum_{k \in K_0} \hat{\pi}_k \left( \hat{V}_k - V_k^* \right) (\hat{\theta}_k - \theta_0) \right),$$

where $V_0^* = \sum_{k \in K_0} \hat{\pi}_k V_k^*$. According to (iii) and (iv), we have

$$I_n^{-1/2}W_n = O(1). \quad (26)$$

Because $\max_k \| \hat{\theta}_k - \theta_k^* \| = O_P \left( n^{-\nu_2} \right)$, $\max_{k \in K_0} \| \hat{V}_k - V_k^* \| = o_P \left( n^{-1/2+\nu_2} \right)$ and (26), we have

$$I_n^{-1/2}W_n \left( V_0^{* - 1} + o_P(1) \right) \left( \sum_{k \in K_0} \hat{\pi}_k \left( \hat{V}_k - V_k^* \right) (\hat{\theta}_k - \theta_0) \right)$$

$$= O_P \left( \max_k \| \hat{\theta}_k - \theta_k^* \| \right) O_P \left( \max_{k \in K_0} \| \hat{V}_k - V_k^* \| \right) = o_P \left( \frac{1}{\sqrt{n}} \right),$$

and hence

$$I_n^{-1/2}W_n(\hat{\theta}_{IVW} - \theta_0)$$

$$= I_n^{-1/2}W_n V_0^{* - 1} \left( \sum_{k \in K_0} \hat{\pi}_k V_k^* (\hat{\theta}_k - \theta_0) \right) + o_P \left( I_n^{-1/2}W_n V_0^{* - 1} \left( \sum_{k \in K_0} \hat{\pi}_k V_k^* (\hat{\theta}_k - \theta_0) \right) \right)$$

$$+ o_P \left( \frac{1}{\sqrt{n}} \right).$$

Thus Theorem 4 is proved if we show

$$\sqrt{n}I_n^{-1/2}W_n V_0^{* - 1} \left( \sum_{k \in K_0} \hat{\pi}_k V_k^* (\hat{\theta}_k - \theta_0) \right) \xrightarrow{d} N(0, I_q). \quad (27)$$
By Condition 5, we have
\[
\sqrt{n} I_n^{-1/2} W_n V_0^{-1} \left( \sum_{k \in K_0} \tilde{\pi}_k V_k^* (\tilde{\theta}_k - \theta_0) \right)
\]
\[
= \sqrt{n} I_n^{-1/2} W_n V_0^{-1} \left\{ \sum_{k \in K_0} \frac{\tilde{\pi}_k V_k^*}{n_k} \sum_{i=1}^{n_k} \Psi_k (Z_i^{(k)}) \right\} + o_P(1)
\]
\[
= \sum_{k \in K_0} \sum_{i=1}^{n_k} \eta_{k,i} + o_P(1),
\]
where \( \eta_{k,i} = I_n^{-1/2} W_n V_0^{-1} V_k^* \Psi_k (Z_i^{(k)}) / \sqrt{n} \). Because \( E \left[ \Psi_k (Z^{(k)}) \right] = 0 \) for \( k \in K_0 \), (iii) and (iv) implies that Lindeberg-Feller condition (Van der Vaart, 2000) is satisfied. Then (27) follows since
\[
\sum_{k \in K_0} \sum_{i=1}^{n_k} \text{var} [\eta_{k,i}] = I_n^{-1/2} I_n I_n^{-1/2} = I_q.
\]

H Uniform asymptotically linear representation of M-estimator

In this section, we establish the uniform asymptotically linear representation in the case where \( \tilde{\theta}_k \)'s are M-estimators, i.e.
\[
\tilde{\theta}_k = \arg \min_{\theta} \frac{1}{n_k} \sum_{i=1}^{n_k} L_k (Z_i^{(k)}, \theta),
\]
for \( k = 1, \ldots, K \), where \( L_k (\cdot, \cdot) \) is some loss function that may differ from source to source. In this case, the probability limit of \( \tilde{\theta}_k \) is the minimum point of \( E[L_k (Z^{(k)}; \theta)] \) under some regularity conditions. Hence here we use \( \theta_k^* \) to denote the minimum point of \( E[L_k (Z^{(k)}; \theta)] \). Let \( \zeta_k (\theta) = L_k (Z^{(k)}; \theta) - E[L_k (Z^{(k)}; \theta)] \). To begin with, we first introduce a commonly used condition in the literature with diverging parameter dimension.

**Condition 6.** There are some constants \( \sigma_1, u_1, b \) independent of \( n \) and some positive definite matrices \( \Phi_k (k = 1, \ldots, K) \) that may depend on \( n \) such that
\[
E \left[ \exp \left( \frac{\gamma^T \nabla \zeta_k (\theta)}{\| \Phi_k \gamma \|^2} \right) \right] \leq \exp \left( \frac{\sigma_1^2 \lambda^2}{2} \right)
\]
and
\[ E[L_k(Z^{(k)}, \theta)] - E[L_k(Z^{(k)}, \theta^*_k)] \geq b\|\Phi_k(\theta - \theta^*_k)\|^2, \]
for all \( \theta, |\lambda| \leq u_1, \|\gamma\| = 1 \) and \( k = 1, \ldots, K \).

See Spokoiny (2012, 2013); Zhou et al. (2018); Chen and Zhou (2020) for further explanations and examples of this condition. The following proposition shows that Condition 6 along with some other conditions implies Condition 3.

**Proposition 2.** Under Condition 6, if (i) for \( k = 1, \ldots, K \), the eigenvalues of \( \Phi_k \) are bounded away from zero; (ii) \( d = O(n^{\nu_0}), K = O(n^{\nu_1}) \) for some positive constants \( \nu_0, \nu_1 \) such that \( \nu_0 + \nu_1 < 1 \) and (iii) \( \tilde{n}_k \geq C^*/K \) for some positive constant \( C^* \), then \( \max_k \|\hat{\theta}_k - \theta^*_k\| = O_P\left(n^{-\left(1-\nu_0-\nu_1\right)/2}\right) \).

**Proof.** For convenience, in this and the following proofs, we let \( C \) be a generic positive constant that may be different in different places. Under Condition 6, according to Theorem 5.2 in Spokoiny (2012), we have
\[ P\left(\|\Phi_k(\hat{\theta}_k - \theta^*_k)\| \geq 6\sigma_1 b^{-1} \sqrt{\frac{3d + t}{n_k}}\right) \leq e^{-t}, \]
for \( t \leq \Delta_k \) with \( \Delta_k = (3b^{-1}\sigma_1^2u_1n_k^{1/2} - 1)^2 - 3d \). Thus, according to (i), we have
\[ P\left(\|\hat{\theta}_k - \theta^*_k\| \geq L \sqrt{\frac{3d + t}{n_k}}\right) \leq e^{-t}, \]
for \( t \leq \Delta_k \) and \( k = 1, \ldots, K \), where \( L = 6\sigma_1 b^{-1}B_L^{-1} \). By Bonferroni inequality, it follows
\[ P\left(\max_k \|\hat{\theta}_k - \theta^*_k\| \geq L \max_k \left\{ \sqrt{\frac{3d + t_n}{n_k}} \right\} \right) \leq K e^{-t}. \]
By (iii) we have \( n_k \geq C^*n/K \). Letting \( t_n = \min\{n^{\nu_0}, \min_k \Delta_k\} \), according to (ii) and (iii), we have
\[ \max_k \left\{ \sqrt{(3d + t_n)/n_k} \right\} \leq \sqrt{K(3d + t_n)/(C^*n)} \leq C \left(n^{-\frac{1-\nu_0-\nu_1}{2}}\right). \]
Thus
\[ P\left(\max_k \|\hat{\theta}_k - \theta^*_k\| \geq \frac{Cn^{-\frac{1-\nu_0-\nu_1}{2}}}{2} \right) \leq K \exp(-t_n) \to 0. \quad (28) \]
This indicates that \( \max_k \|\hat{\theta}_k - \theta^*_k\| = O_P\left(n^{-(1-\nu_0-\nu_1)/2}\right) \).
To establish the uniform asymptotically linear representation, some further conditions on the Hessian of the expected loss function are required. Let $D_k(\theta) = (\nabla^2 E[L_k(Z^{(k)}, \theta)])^{1/2}$ be the Hessian of the expected loss function and let $D_{k*} = D_k(\theta_0^*)$.

**Condition 7.** For $k \in \mathcal{K}_0$, the eigenvalues of $D_{k*}$ are bounded away from zero and infinity, and there is some constant $M_*$ such that $\|D^2_k(\theta) - D^2_{k*}\| \leq M_* \|\theta - \theta_0\|$, for all $\theta$. Moreover, for some constants $\sigma_2$ and $u_2$,

$$E \left[ \exp \left( \frac{\lambda \gamma_1^T \nabla^2 \zeta_k(\theta) \gamma_2}{\|D_{k*} \gamma_1\| \|D_{k*} \gamma_2\|} \right) \right] \leq \exp \left( \frac{\sigma_2^2 \lambda^2}{2} \right)$$

for all $|\lambda| \leq u_2$, $\|\gamma_1\| = 1$, $\|\gamma_2\| = 1$, and $k \in \mathcal{K}_0$.

Under Condition 7 and the conditions of Proposition 2, we establish the uniform asymptotically linear representation (Condition 5).

**Proposition 3.** Under Condition 7 and the conditions of Proposition 2, if $\nu_0 + \nu_1 < 1/2$, then Condition 5 holds with $\Psi_k(Z^{(k)}) = -D_{k*}^{-2} \nabla L(Z^{(k)}, \theta_0)$.

**Proof.** For $k \in \mathcal{K}_0$, according to Condition 7, it is not hard to verify that the Condition $ED_2$ in (Spokoiny, 2013) is satisfied with $g = u_2 \sqrt{m}_k$ and $\omega = 1/\sqrt{m}_k$. Because $B_L \leq \min_k \lambda_{\min}(D_{k*}) \leq \max_k \lambda_{\max}(D_{k*}) \leq B_U$, and $\|D^2_k(\theta) - D^2_{k*}\| \leq M_* \|\theta - \theta_0\|$, we have

$$\|D_{k*}^{-1} D^2_k(\theta) D_{k*}^{-1} - I_d\| \leq \|D_{k*}^{-1}\|^2 \|D^2_k(\theta) - D^2_{k*}\| \leq M_* B_L^{-3} \|D_{k*}(\theta - \theta_0)\|,$$

for $k \in \mathcal{K}_0$, where $I_d$ is the $d \times d$ identity matrix.

Thus Condition $\mathcal{L}$ in Spokoiny (2013) is satisfied with $\delta(r) = M_* B_L^{-3} r$. For $k \in \mathcal{K}_0$, define the event

$$E_{r,t}^{(k)} = \left\{ \sup_{\theta \in \Theta_*(r)} \left| \frac{1}{n_k} \sum_{i=1}^n D_{k*}^{-1} \{ \nabla L(Z_i^{(k)}, \theta) - \nabla L(Z_i^{(k)}, \theta_0) \} - D_{k*}(\theta - \theta_0) \right| \geq \epsilon_{r,t}^{(k)} \right\},$$

where $\Theta_*(r) = \|D_{k*}(\theta - \theta_0)\| \leq r$ and $\epsilon_{r,t}^{(k)} = M_* B_L^3 r^2 + 6\sigma_2 r \sqrt{(4p + 2l)/n_k}$. According to Proposition 3.1 in Spokoiny (2013), we have

$$P \left( E_{r,t}^{(k)} \right) \leq \exp(-t) \quad (29)$$

40
for \( k \in K_0 \) and \( t \leq \Delta'_k \) with \( \Delta'_k = -2p + u_2n_k/2 \). By (28), there is some \( C \) such that
\[
P \left( \max_k \| \tilde{\theta}_k - \theta^*_k \| \geq Cn^{-\frac{1-\nu_0-\nu_1}{2}} \right) \to 0.
\]
Let \( r_n = B_U Cn^{-\frac{1-\nu_0-\nu_1}{2}} \). Then we have
\[
\bigcup_{k \in K_0} \left\{ \tilde{\theta}_k \notin \Theta(r_n) \right\} \subset \left\{ \max_k \| \tilde{\theta}_k - \theta^*_k \| \geq Cn^{-\frac{1-\nu_0-\nu_1}{2}} \right\}.
\]
This implies
\[
P \left( \bigcup_{k \in K_0} \left\{ \tilde{\theta}_k \notin \Theta(r_n) \right\} \right) \leq P \left( \max_k \| \tilde{\theta}_k - \theta^*_k \| \geq Cn^{-\frac{1-\nu_0-\nu_1}{2}} \right) \to 0. \tag{30}
\]
Letting \( t_n = \min \{ n^\nu_0, \min_k \Delta'_k \} \), we have
\[
P \left( \bigcup_{k \in K_0} E^{(k)}_{r_n,t_n} \right) \leq K \exp(-t_n) \to 0 \tag{31}
\]
according to (29) and the rate conditions on \( K \). By the definition of \( \tilde{\theta}_k \), we have \( \sum_{i=1}^{n_k} \nabla L(Z_i^{(k)}, \tilde{\theta}_k) / n_k = 0 \). Combining this with (30) and (31), we have
\[
P \left( \max_{k \in K_0} \left\| \frac{1}{n_k} \sum_{i=1}^{n} D^{-1}_{k} \nabla L(Z_i^{(k)}, \theta_0) + D_{k} (\tilde{\theta}_k - \theta_0) \right\| \geq \xi_n \right) \to 0 \tag{32}
\]
where \( \xi_n = M_{\ast} B_U^3 r_n^2 + 6\sigma_2 r_n \sqrt{(4d+2t_n)/n_k} = o(1/\sqrt{n}) \) because \( \nu_0 + \nu_1 < 1/2 \). Thus
\[
\max_{k \in K_0} \left\| \frac{1}{n_k} \sum_{i=1}^{n} D^{-2}_{k} \nabla L(Z_i^{(k)}, \theta_0) + (\tilde{\theta}_k - \theta_0) \right\| = o_P \left( \frac{1}{\sqrt{n}} \right), \tag{33}
\]
and this implies the result of the proposition.

\[\square\]

References

Battey, H., J. Fan, H. Liu, J. Lu, and Z. Zhu (2018). Distributed testing and estimation under sparse high dimensional models. The Annals of Statistics 46(3), 1352.

Berkey, C., D. Hoaglin, A. Antczak-Bouckoms, F. Mosteller, and G. Colditz (1998). Meta-analysis of multiple outcomes by regression with random effects. Statistics in Medicine 17(22), 2537–2550.
Bickel, P. J., C. A. Klaassen, P. J. Bickel, Y. Ritov, J. Klaassen, J. A. Wellner, and Y. Ritov (1993). *Efficient and Adaptive Estimation for Semiparametric Models*, Volume 4. Johns Hopkins University Press Baltimore.

Bowden, J., G. Davey Smith, and S. Burgess (2015). Mendelian randomization with invalid instruments: effect estimation and bias detection through egger regression. *International Journal of Epidemiology* 44(2), 512–525.

Bowden, J., G. Davey Smith, P. C. Haycock, and S. Burgess (2016). Consistent estimation in mendelian randomization with some invalid instruments using a weighted median estimator. *Genetic Epidemiology* 40(4), 304–314.

Burgess, S., C. N. Foley, E. Allara, J. R. Staley, and J. M. Howson (2020). A robust and efficient method for mendelian randomization with hundreds of genetic variants. *Nature Communications* 11(1), 1–11.

Burgess, S. and S. G. Thompson (2015). Multivariable mendelian randomization: the use of pleiotropic genetic variants to estimate causal effects. *American Journal of Epidemiology* 181(4), 251–260.

Chatterjee, N., Y.-H. Chen, P. Maas, and R. J. Carroll (2016). Constrained maximum likelihood estimation for model calibration using summary-level information from external big data sources. *Journal of the American Statistical Association* 111(513), 107–117.

Chen, X. and W.-X. Zhou (2020). Robust inference via multiplier bootstrap. *The Annals of Statistics* 48(3), 1665–1691.

Claggett, B., M. Xie, and L. Tian (2014). Meta-analysis with fixed, unknown, study-specific parameters. *Journal of the American Statistical Association* 109(508), 1660–1671.

Fan, J., F. Han, and H. Liu (2014). Challenges of big data analysis. *National Science Review* 1(2), 293–314.
Gormley, M., T. Dudding, E. Sanderson, R. M. Martin, S. Thomas, J. Tyrrell, A. R. Ness, P. Brennan, M. Munafò, M. Pring, et al. (2020). A multivariable mendelian randomization analysis investigating smoking and alcohol consumption in oral and oropharyngeal cancer. Nature Communications 11(1), 1–10.

Guo, Z., H. Kang, T. Tony Cai, and D. S. Small (2018). Confidence intervals for causal effects with invalid instruments by using two-stage hard thresholding with voting. Journal of the Royal Statistical Society: Series B (Statistical Methodology) 80(4), 793–815.

Hample, F. R., E. M. Ronchetti, P. J. Rousseeuw, and W. A. Stahel (2005). Robust Statistics: The Approach Based on Influence Functions. John Wiley & Sons, New York.

Han, C. (2008). Detecting invalid instruments using l1-gmm. Economics Letters 101(3), 285–287.

Hanley, J. A. and G. Thériault (2000). Simpson’s paradox in meta-analysis. Epidemiology 11(5), 613.

Hartwig, F. P., G. Davey Smith, and J. Bowden (2017). Robust inference in summary data mendelian randomization via the zero modal pleiotropy assumption. International Journal of Epidemiology 46(6), 1985–1998.

Jordan, M. I. (2013). On statistics, computation and scalability. Bernoulli 19(4), 1378–1390.

Kang, H., A. Zhang, T. T. Cai, and D. S. Small (2016). Instrumental variables estimation with some invalid instruments and its application to mendelian randomization. Journal of the American Statistical Association 111(513), 132–144.

Katan, M. B. (2004). Commentary: Mendelian randomization, 18 years on. International Journal of Epidemiology 33(1), 10–11.

Kundu, P., R. Tang, and N. Chatterjee (2019). Generalized meta-analysis for multiple regression models across studies with disparate covariate information. Biometrika 106(3), 567–585.
Lamport, L., R. Shostack, and M. Pease (1982). The byzantine generals problem. *ACM Transactions on Programming Languages and Systems* 4(3), 382–401.

Lawlor, D. A., K. Wade, M. C. Borges, T. Palmer, F. P. Hartwig, G. Hemani, and J. Bowden (2019). A mendelian randomization dictionary: Useful definitions and descriptions for undertaking, understanding and interpreting mendelian randomization studies.

Lesseur, C., B. Diergaarde, A. F. Olshan, V. Wünsch-Filho, A. R. Ness, G. Liu, M. Lacko, J. Eluf-Neto, S. Franceschi, P. Lagiou, et al. (2016). Genome-wide association analyses identify new susceptibility loci for oral cavity and pharyngeal cancer. *Nature Genetics* 48(12), 1544–1550.

Lin, D.-Y. and P. F. Sullivan (2009). Meta-analysis of genome-wide association studies with overlapping subjects. *The American Journal of Human Genetics* 85(6), 862–872.

Lin, D.-Y. and D. Zeng (2010). On the relative efficiency of using summary statistics versus individual-level data in meta-analysis. *Biometrika* 97(2), 321–332.

Lin, H.-W. and Y.-H. Chen (2014). Adjustment for missing confounders in studies based on observational databases: 2-stage calibration combining propensity scores from primary and validation data. *American Journal of Epidemiology* 180(3), 308–317.

Lindsay, B. G. (1994). Efficiency versus robustness: the case for minimum hellinger distance and related methods. *The Annals of Statistics* 22(2), 1081–1114.

Liu, D., R. Y. Liu, and M. Xie (2015). Multivariate meta-analysis of heterogeneous studies using only summary statistics: efficiency and robustness. *Journal of the American Statistical Association* 110(509), 326–340.

Locke, A. E., B. Kahali, S. I. Berndt, A. E. Justice, T. H. Pers, F. R. Day, C. Powell, S. Vedantam, M. L. Buchkovich, J. Yang, et al. (2015). Genetic studies of body mass index yield new insights for obesity biology. *Nature* 518(7538), 197–206.

Mathew, T. and K. Nordstrom (1999). On the equivalence of meta-analysis using literature and using individual patient data. *Biometrics* 55(4), 1221–1223.
Minelli, C., F. Del Greco M, D. A. van der Plaat, J. Bowden, N. A. Sheehan, and J. Thompson (2021). The use of two-sample methods for mendelian randomization analyses on single large datasets. *International Journal of Epidemiology* 50(5), 1651–1659.

Olkin, I. and A. Sampson (1998). Comparison of meta-analysis versus analysis of variance of individual patient data. *Biometrics* 54(1), 317–322.

Qi, G. and N. Chatterjee (2019). Mendelian randomization analysis using mixture models for robust and efficient estimation of causal effects. *Nature Communications* 10(1), 1–10.

Qin, J., H. Zhang, P. Li, D. Albanes, and K. Yu (2015). Using covariate-specific disease prevalence information to increase the power of case-control studies. *Biometrika* 102(1), 169–180.

Rees, J. M., A. M. Wood, and S. Burgess (2017). Extending the mr-egger method for multivariable mendelian randomization to correct for both measured and unmeasured pleiotropy. *Statistics in Medicine* 36(29), 4705–4718.

Sanderson, E., G. Davey Smith, F. Windmeijer, and J. Bowden (2019). An examination of multivariable mendelian randomization in the single-sample and two-sample summary data settings. *International Journal of Epidemiology* 48(3), 713–727.

Shen, J., R. Y. Liu, and M.-g. Xie (2020). ifusion: Individualized fusion learning. *Journal of the American Statistical Association* 115(531), 1251–1267.

Sheng, Y., Y. Sun, D. Deng, and C.-Y. Huang (2020). Censored linear regression in the presence or absence of auxiliary survival information. *Biometrics* 76(3), 734–745.

Silvapulle, M. J. (1981). On the existence of maximum likelihood estimators for the binomial response models. *Journal of the Royal Statistical Society: Series B (Statistical Methodology)* 43(3), 310–313.

Singh, K., M. Xie, and W. E. Strawderman (2005). Combining information from independent sources through confidence distributions. *The Annals of Statistics* 33(1), 159–183.
Spokoiny, V. (2012). Parametric estimation. finite sample theory. *The Annals of Statistics* **40**(6), 2877–2909.

Spokoiny, V. (2013). Bernstein-von mises theorem for growing parameter dimension. *arXiv preprint*.

Sterne, J. A., D. Gavaghan, and M. Egger (2000). Publication and related bias in meta-analysis: power of statistical tests and prevalence in the literature. *Journal of Clinical Epidemiology* **53**(11), 1119–1129.

Tu, J., W. Liu, X. Mao, and X. Chen (2021). Variance reduced median-of-means estimator for byzantine-robust distributed inference. *Journal of Machine Learning Research* **22**(84), 1–67.

Van der Vaart, A. W. (2000). *Asymptotic Statistics*, Volume 3. Cambridge university press.

Vershynin, R. (2018). *High-dimensional Probability: An Introduction with Applications in Data Science*, Volume 47. Cambridge university press, Cambridge.

Wainwright, M. J. (2019). *High-dimensional Statistics: A Non-asymptotic Viewpoint*, Volume 48. Cambridge University Press.

Wang, C., M.-H. Chen, E. Schifano, J. Wu, and J. Yan (2016). Statistical methods and computing for big data. *Statistics and Its Interface* **9**(4), 399.

Windmeijer, F., H. Farbmacher, N. Davies, and G. Davey Smith (2019). On the use of the lasso for instrumental variables estimation with some invalid instruments. *Journal of the American Statistical Association* **114**(527), 1339–1350.

Wootton, R. E., R. C. Richmond, B. G. Stuijfzand, R. B. Lawn, H. M. Sallis, G. M. Taylor, G. Hemani, H. J. Jones, S. Zammit, G. D. Smith, et al. (2020). Evidence for causal effects of lifetime smoking on risk for depression and schizophrenia: a mendelian randomisation study. *Psychological Medicine* **50**(14), 2435–2443.
Xie, M., K. Singh, and W. E. Strawderman (2011). Confidence distributions and a unifying framework for meta-analysis. *Journal of the American Statistical Association* 106(493), 320–333.

Yang, S. and P. Ding (2020). Combining multiple observational data sources to estimate causal effects. *Journal of the American Statistical Association* 115(531), 1540–1554.

Ye, T., J. Shao, and H. Kang (2021). Debiased inverse-variance weighted estimator in two-sample summary-data mendelian randomization. *The Annals of statistics* 49(4), 2079–2100.

Yin, D., Y. Chen, R. Kannan, and P. Bartlett (2018). Byzantine-robust distributed learning: Towards optimal statistical rates. In *International Conference on Machine Learning*, pp. 5650–5659. PMLR.

Yuan, M. and Y. Lin (2006). Model selection and estimation in regression with grouped variables. *Journal of the Royal Statistical Society: Series B (Statistical Methodology)* 68(1), 49–67.

Zhai, Y. and P. Han (2022). Data integration with oracle use of external information from heterogeneous populations. *Journal of Computational and Graphical Statistics* 31(4), 1001–1012.

Zhang, H., L. Deng, M. Schiffman, J. Qin, and K. Yu (2020). Generalized integration model for improved statistical inference by leveraging external summary data. *Biometrika* 107(3), 689–703.

Zhang, H., J. Qin, S. I. Berndt, D. Albanes, L. Deng, M. H. Gail, and K. Yu (2019). On mendelian randomization analysis of case-control study. *Biometrics* 76, 380–391.

Zhao, Q., J. Wang, G. Hemani, J. Bowden, and D. S. Small (2020). Statistical inference in two-sample summary-data mendelian randomization using robust adjusted profile score. *The Annals of Statistics* 48(3), 1742–1769.
Zhou, W.-X., K. Bose, J. Fan, and H. Liu (2018). A new perspective on robust m-
estimation: Finite sample theory and applications to dependence-adjusted multiple test-
ing. *The Annals of Statistics* 46(5), 1904.

Zhu, X., F. Li, and H. Wang (2021). Least-square approximation for a distributed system. *Journal of Computational and Graphical Statistics* 30(4), 1004–1018.

Zou, H. (2006). The adaptive lasso and its oracle properties. *Journal of the American Statistical Association* 101(476), 1418–1429.
Table 1: NB and SSE with least squares regression in the presence of biased sources (results are multiplied by 10)

| Estimator | $n_s$ | naive NB | naive SSE | oracle NB | oracle SSE | iFusion NB | iFusion SSE | $\hat{\theta}$ NB | $\hat{\theta}$ SSE | $\dot{\theta}$ NB | $\dot{\theta}$ SSE |
|------------|-----|-----------|-----------|-----------|-----------|-----------|-----------|----------------|----------------|----------------|----------------|
| $d = 3, K = 10$ | 100 | 9.87 | 0.55 | 0.10 | 1.31 | 0.09 | 1.34 | 0.46 | 1.40 | 0.10 | 1.31 |
| | 200 | 9.85 | 0.40 | 0.04 | 0.90 | 0.04 | 0.92 | 0.37 | 0.98 | 0.04 | 0.90 |
| | 500 | 9.85 | 0.24 | 0.02 | 0.54 | 0.02 | 0.54 | 0.21 | 0.62 | 0.02 | 0.54 |
| $d = 3, K = 30$ | 100 | 9.85 | 0.33 | 0.05 | 0.76 | 0.06 | 0.87 | 0.56 | 0.75 | 0.03 | 0.76 |
| | 200 | 9.85 | 0.21 | 0.01 | 0.50 | 0.01 | 0.57 | 0.42 | 0.49 | 0.02 | 0.50 |
| | 500 | 9.84 | 0.14 | 0.01 | 0.32 | 0.01 | 0.33 | 0.26 | 0.35 | 0.01 | 0.32 |
| $d = 18, K = 10$ | 100 | 24.13 | 3.64 | 0.13 | 8.09 | 0.16 | 11.23 | 1.18 | 7.26 | 0.14 | 8.07 |
| | 200 | 24.12 | 2.41 | 0.10 | 5.47 | 0.14 | 7.29 | 0.77 | 5.23 | 0.08 | 5.46 |
| | 500 | 24.13 | 1.50 | 0.05 | 3.29 | 0.06 | 3.81 | 0.50 | 3.27 | 0.07 | 3.29 |
| $d = 18, K = 30$ | 100 | 24.13 | 2.14 | 0.07 | 4.78 | 0.16 | 11.37 | 1.44 | 4.00 | 0.11 | 4.75 |
| | 200 | 24.11 | 1.38 | 0.05 | 3.16 | 0.15 | 7.71 | 1.00 | 2.81 | 0.06 | 3.15 |
| | 500 | 24.13 | 0.87 | 0.03 | 1.89 | 0.07 | 4.51 | 0.66 | 1.76 | 0.04 | 1.89 |
Table 2: NB and SSE with least squares regression and no biased sources (results are multiplied by 10)

| Estimator | $n_*$ | oracle | $\tilde{\theta}$ | $\hat{\theta}$ |
|-----------|-------|--------|----------------|----------------|
|           | NB    | SSE    | NB   | SSE    | NB    | SSE    | NB    | SSE   |
| $d = 3, K = 10$ |       |        |      |       |       |        |       |       |
| 100       | 0.03  | 0.55   | 0.03 | 0.56   | 0.03  | 0.60   | 0.03  | 0.55  |
| 200       | 0.01  | 0.40   | 0.01 | 0.40   | 0.01  | 0.44   | 0.01  | 0.40  |
| 500       | 0.00  | 0.24   | 0.00 | 0.24   | 0.00  | 0.26   | 0.00  | 0.24  |
| $d = 3, K = 30$ |       |        |      |       |       |        |       |       |
| 100       | 0.01  | 0.33   | 0.02 | 0.46   | 0.01  | 0.35   | 0.01  | 0.33  |
| 200       | 0.01  | 0.21   | 0.01 | 0.29   | 0.01  | 0.23   | 0.01  | 0.21  |
| 500       | 0.01  | 0.14   | 0.00 | 0.15   | 0.01  | 0.15   | 0.01  | 0.14  |
| $d = 18, K = 10$ |       |        |      |       |       |        |       |       |
| 100       | 0.05  | 3.64   | 0.16 | 10.13  | 0.05  | 3.66   | 0.05  | 3.64  |
| 200       | 0.04  | 2.41   | 0.09 | 5.05   | 0.04  | 2.44   | 0.04  | 2.41  |
| 500       | 0.02  | 1.50   | 0.03 | 1.91   | 0.03  | 1.52   | 0.02  | 1.50  |
| $d = 18, K = 30$ |       |        |      |       |       |        |       |       |
| 100       | 0.03  | 2.14   | 0.16 | 11.33  | 0.03  | 2.15   | 0.03  | 2.14  |
| 200       | 0.03  | 1.38   | 0.14 | 7.49   | 0.03  | 1.39   | 0.03  | 1.38  |
| 500       | 0.02  | 0.87   | 0.05 | 3.75   | 0.02  | 0.88   | 0.02  | 0.87  |
Table 3: NB and SSE with logistic regression in the presence of biased sources (results are multiplied by 10)

| Estimator    | $n_s$ | naive | oracle | iFusion | $\hat{\theta}$ | $\hat{\theta}$ |
|--------------|------|-------|--------|---------|---------------|---------------|
|              | NB   | SSE   | NB     | SSE     | NB            | SSE           |
| $d = 3, K = 10$ |      |       |        |         |               |               |
| 100          | 4.79 | 2.32  | 0.24   | 2.73    | 0.24          | 3.80          |
| 200          | 5.89 | 1.89  | 0.13   | 1.83    | 0.18          | 2.34          |
| 500          | 7.36 | 1.62  | 0.02   | 1.10    | 0.05          | 1.35          |
| $d = 3, K = 30$ |      |       |        |         |               |               |
| 100          | 4.77 | 1.34  | 0.22   | 1.62    | 0.28          | 3.86          |
| 200          | 5.88 | 1.11  | 0.10   | 1.08    | 0.16          | 2.21          |
| 500          | 7.37 | 0.84  | 0.06   | 0.65    | 0.03          | 1.20          |
| $d = 18, K = 10$ |      |       |        |         |               |               |
| 100          | 6.19 | 16.47 | 1.97   | 24.68   | 1.90          | 35.18         |
| 200          | 7.12 | 11.91 | 0.82   | 13.70   | 0.93          | 19.59         |
| 500          | 9.11 | 8.13  | 0.28   | 8.04    | 0.31          | 11.34         |
| $d = 18, K = 30$ |      |       |        |         |               |               |
| 100          | 6.24 | 9.63  | 1.86   | 14.24   | 1.90          | 35.18         |
| 200          | 7.15 | 6.96  | 0.78   | 8.03    | 0.93          | 19.59         |
| 500          | 9.12 | 4.62  | 0.29   | 4.59    | 0.31          | 11.34         |
Table 4: NB and SSE with logistic regression and no biased sources (results are multiplied by 10)

| Estimator | $n_*$ | oracle | $iFusion$ | $\hat{\theta}$ | $\hat{\theta}$ |
|-----------|-------|--------|-----------|-----------------|----------------|
|           | NB    | SSE    | NB        | SSE             | NB            | SSE          |
| $d = 3, K = 10$ | 100   | 0.16   | 1.17      | 0.22            | 2.84          | 0.10         | 1.28         | 0.09         | 1.24         |
|           | 200   | 0.08   | 0.81      | 0.09            | 1.46          | 0.07         | 0.86         | 0.06         | 0.81         |
|           | 500   | 0.04   | 0.50      | 0.03            | 0.71          | 0.03         | 0.55         | 0.04         | 0.50         |
| $d = 3, K = 30$ | 100   | 0.14   | 0.70      | 0.19            | 3.28          | 0.10         | 0.76         | 0.11         | 0.71         |
|           | 200   | 0.07   | 0.48      | 0.13            | 1.76          | 0.05         | 0.52         | 0.06         | 0.48         |
|           | 500   | 0.04   | 0.31      | 0.03            | 0.87          | 0.03         | 0.34         | 0.04         | 0.31         |
| $d = 18, K = 10$ | 100   | 1.88   | 11.06     | 1.90            | 35.18         | 1.61         | 10.67        | 1.39         | 11.08        |
|           | 200   | 0.76   | 6.10      | 0.93            | 19.59         | 0.69         | 6.07         | 0.75         | 6.09         |
|           | 500   | 0.28   | 3.50      | 0.31            | 11.34         | 0.25         | 3.54         | 0.28         | 3.50         |
| $d = 18, K = 30$ | 100   | 1.84   | 6.43      | 1.90            | 35.18         | 1.55         | 6.16         | 1.55         | 6.28         |
|           | 200   | 0.74   | 3.53      | 0.93            | 19.59         | 0.65         | 3.51         | 0.74         | 3.53         |
|           | 500   | 0.27   | 2.02      | 0.31            | 11.34         | 0.24         | 2.03         | 0.27         | 2.02         |

Table 5: Bias and SE in Mendelian randomization with invalid instruments (results are multiplied by 10)

| Estimator | MR-Egger | Weighted Median | IVW | Weighted Mode | RAPS | $\hat{\theta}$ | $\hat{\theta}$ |
|-----------|----------|-----------------|-----|----------------|------|----------------|----------------|
| Bias      | 6.48     | -2.05           | 14.44 | -1.30         | 16.95 | 0.71         | -0.26         |
| SE        | 4.79     | 1.09            | 1.73 | 82.14         | 2.34 | 1.79         | 1.17         |
(a) IVW estimation using all datasources for treatment effect in PD: red solid line; estimation for treatment effect in PD produced by $\hat{\theta}$: green dashed line; estimation for treatment effect in PD produced by $\tilde{\theta}$: blue dotted line.

(b) IVW estimation using all data sources for treatment effect in AL: red solid line; estimation for treatment effect in AL produced by $\hat{\theta}$: green dashed line; estimation for treatment effect in AL produced by $\tilde{\theta}$: blue dotted line.

Figure 1: Estimation results under different $t$. 