Supplement to “Mediation Analysis for Count and Zero-Inflated Count Data Without Sequential Ignorability and Its Application in Dental Studies”

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Summary. This web-based supplementary materials contain three sections. Section 1 presents the technical proofs and discuss the partial verification of Exclusive Restriction assumption; Section 2 presents the discussion on consistency of 2SRI; Section 3 presents the estimating equations for two conditional independent mediators and for the model with interaction between the treatment and the mediator; Section 4 presents extended simulation studies.

1. Proofs and extended discussions

1.1. Proof of natural effect ratio

We first establish the results for the natural effect rate ratio. When the mediator is continuous and $M(z^*) = \alpha_0 + \alpha_z z^* + \alpha_{\mathbf{x}}\mathbf{x} + \alpha_{IV}\mathbf{x}z^* + \alpha_u u + v$ with v independent of z^* and $\mathbf{x}$, we have the conditional expectation of the potential outcome $Y(z, M(z^*))$,

$$\begin{aligned}
&\mathbb{E}_Y\left(Y\left(z, M(z^*)\right)|\mathbf{x}, u\right) \\
&= \exp\left(\beta_0 + \beta_z z + \beta_m\left(\alpha_0 + \alpha_z z^* + \alpha_{\mathbf{x}}\mathbf{x} + \alpha_{IV}\mathbf{x}z^* + \alpha_u u + v\right) + \beta_{\mathbf{x}}\mathbf{x} + \beta_u u\right).
\end{aligned}$$

By integrating with respect to v, we have

$$\begin{aligned}
&\mathbb{E}_{M(z^*)|\mathbf{x},u}\mathbb{E}_Y\left(Y\left(z,M(z^*)\right)|\mathbf{x},u\right)=\exp\left(\log\mathbb{E}(\exp(v))\right)\\
&\times\exp\left(\beta_0+\beta_m\alpha_0+\beta_z z+\beta_m\alpha_z z^*+\beta_m\alpha_{IV}\mathbf{x}z^*+\left(\beta_{\mathbf{x}}+\beta_m\alpha_{\mathbf{x}}\right)\mathbf{x}+\left(\beta_u+\beta_m\alpha_u\right)u\right).
\end{aligned}\tag{1}$$

The natural direct effect rate ratio can be expressed as

$$\frac{\mathbb{E}\left(Y\left(z,M^{z^*}\right)|\mathbf{x},u\right)}{\mathbb{E}\left(Y\left(z^*,M^{z^*}\right)|\mathbf{x},u\right)}=\exp\left(\beta_z(z-z^*)\right),\tag{2}$$

and the natural indirect effect rate ratio is

$$\frac{\mathbb{E}\left(Y\left(z,M^{z}\right)|\mathbf{x},u\right)}{\mathbb{E}\left(Y\left(z,M^{z^*}\right)|\mathbf{x},u\right)}=\exp\left(\beta_m\alpha_z\left(z-z^*\right)+\beta_m\alpha_{IV}\mathbf{x}(z-z^*)\right).\tag{3}$$

In the following, we derive the natural direct ratio for binary mediator.

$$\begin{aligned}
&\frac{\mathbb{E}\left(Y\left(z,M^{z^*}\right)|\mathbf{x},u\right)}{\mathbb{E}\left(Y\left(z^*,M^{z^*}\right)|\mathbf{x},u\right)}\\
=&\frac{P\left(M(z^*)=1|\mathbf{x},u\right)\mathbb{E}\left(y\left(z,M(z^*)=1\right)|\mathbf{x},u\right)+P\left(M(z^*)=0|\mathbf{x},u\right)\mathbb{E}\left(y\left(z,M(z^*)=0\right)|\mathbf{x},u\right)}{P\left(M(z^*)=1|\mathbf{x},u\right)\mathbb{E}\left(y\left(z^*,M(z^*)=1\right)|\mathbf{x},u\right)+P\left(M(z^*)=0|\mathbf{x},u\right)\mathbb{E}\left(y\left(z^*,M(z^*)=0\right)|\mathbf{x},u\right)}\\
=&\frac{\exp\left(\beta_z z\right)\left(P\left(M(z^*)=1|\mathbf{x},u\right)\exp(\beta_m)+P\left(M(z^*)=0|\mathbf{x},u\right)\right)\exp\left(\beta_0+\beta_{\mathbf{x}}\mathbf{x}+\beta_u u\right)}{\exp\left(\beta_z z^*\right)\left(P\left(M(z^*)=1|\mathbf{x},u\right)\exp(\beta_m)+P\left(M(z^*)=0|\mathbf{x},u\right)\right)\exp\left(\beta_0+\beta_{\mathbf{x}}\mathbf{x}+\beta_u u\right)}\\
=&\exp\left(\beta_z(z-z^*)\right).
\end{aligned}\tag{4}$$

The proof of the natural indirect ratio for binary mediator is as follows.

$$\begin{aligned}
&\frac{\mathbb{E}\left(Y\left(z,M^{z}\right)|\mathbf{x},u\right)}{\mathbb{E}\left(Y\left(z,M^{z^*}\right)|\mathbf{x},u\right)}\\
=&\frac{P\left(M(z)=1|\mathbf{x},u\right)\mathbb{E}\left(y\left(z^*,M(z)=1\right)|\mathbf{x},u\right)+P\left(M(z)=0|\mathbf{x},u\right)\mathbb{E}\left(y\left(z^*,M(z)=0\right)|\mathbf{x},u\right)}{P\left(M(z^*)=1|\mathbf{x},u\right)\mathbb{E}\left(y\left(z^*,M(z^*)=1\right)|\mathbf{x},u\right)+P\left(M(z^*)=0|\mathbf{x},u\right)\mathbb{E}\left(y\left(z^*,M(z^*)=0\right)|\mathbf{x},u\right)}\\
=&\frac{\left(P\left(M(z)=1|\mathbf{x},u\right)\exp(\beta_m)+P\left(M(z)=0|\mathbf{x},u\right)\right)\exp\left(\beta_0+\beta_z z^*+\beta_{\mathbf{x}}\mathbf{x}+\beta_u u\right)}{\left(P\left(M(z^*)=1|\mathbf{x},u\right)\exp(\beta_m)+P\left(M(z^*)=0|\mathbf{x},u\right)\right)\exp\left(\beta_0+\beta_z z^*+\beta_{\mathbf{x}}\mathbf{x}+\beta_u u\right)}\\
=&\frac{P\left(M(z)=1|\mathbf{x},u\right)\exp(\beta_m)+P\left(M(z)=0|\mathbf{x},u\right)}{P\left(M(z^*)=1|\mathbf{x},u\right)\exp(\beta_m)+P\left(M(z^*)=0|\mathbf{x},u\right)}.
\end{aligned}\tag{5}$$

1.2. Proof of the estimating equations

In the following, we derive the estimation equations that we propose in the main paper,

$$\begin{aligned}
&\mathbb{E}\left(\frac{y}{\exp(\beta_0+\beta_z z+\beta_m m+\beta_{\mathbf{x}}\mathbf{x})}-1\right)\\
=&\mathbb{E}\left(\mathbb{E}\left(\frac{y}{\exp(\beta_0+\beta_z z+\beta_m m+\beta_{\mathbf{x}}\mathbf{x})}-1|z,\mathbf{x},m,u\right)\right)\\
=&\mathbb{E}\left(\frac{E\left(y|z,\mathbf{x},m,u\right)}{\exp(\beta_0+\beta_z z+\beta_m m+\beta_{\mathbf{x}}\mathbf{x})}-1\right)\\
=&\mathbb{E}\left(\exp(\beta_u u)-1\right)=0.
\end{aligned}\tag{6}$$

and

$$\begin{aligned}
&\mathbb{E}\left(\left(\frac{y}{\exp(\beta_0+\beta_z z+\beta_m m+\beta_{\mathbf{x}}\mathbf{x})}-1\right)\times \mathbf{x}z\right)\\
=&\mathbb{E}\left(\mathbb{E}\left(\frac{y}{\exp(\beta_0+\beta_z z+\beta_m m+\beta_{\mathbf{x}}\mathbf{x})}-1|z,\mathbf{x},m,u\right)\mathbf{x}z\right)\\
=&\mathbb{E}\left(\left(\frac{\mathbb{E}\left(y|z,\mathbf{x},m,u\right)}{\exp(\beta_0+\beta_z z+\beta_m m+\beta_{\mathbf{x}}\mathbf{x})}-1\right)\mathbf{x}z\right)\\
=&\mathbb{E}\left(\left(\exp(\beta_u u)-1\right)\mathbf{x}z\right)=0,
\end{aligned} \tag{7}$$

where the last equation follows from the randomness of treatment and the assumption that $P(u|\mathbf{x})$ has the same distribution across different $\mathbf{x}$. We also have the following estimating equations,

$$\begin{aligned}
&\mathbb{E}\left(\frac{y}{\exp(\beta_m m)}-\exp(\beta_0+\beta_z z+\beta_{\mathbf{x}}\mathbf{x})\right)\\
=&\mathbb{E}\left(\mathbb{E}\left(\frac{y}{\exp(\beta_m m)}-\exp(\beta_0+\beta_z z+\beta_{\mathbf{x}}\mathbf{x})|z,\mathbf{x},m,u\right)\right)\\
=&\mathbb{E}\left(\frac{\mathbb{E}\left(y|z,\mathbf{x},m,u\right)}{\exp(\beta_m m)}-\exp(\beta_0+\beta_z z+\beta_{\mathbf{x}}\mathbf{x})\right)\\
=&\mathbb{E}\left(\left(\exp(\beta_u u)-1\right)\exp(\beta_0+\beta_z z+\beta_{\mathbf{x}}\mathbf{x})\right)=0,
\end{aligned} \tag{8}$$

where the last equation follows from the randomness of treatment and the assumption that $P(u|\mathbf{x})$ has the same distribution across different $\mathbf{x}$. The proofs of other estimating equations are similar.

1.3. Testing the Exclusion Restriction assumption in the real data analysis

The Exclusion Restriction assumption states that the interaction $Z\times\mathbf{X}^{\text{IV}}$ affects the outcome only through its effect on the mediator M, conditional on $\mathbf{X}$ and Z. The Exclusion Restriction assumption cannot be formally tested. In the following, we will provide a partial test for this assumption. The direct effect of the treatment Z on the outcome Y can be actually through the pathway of some other intermediate variable, $\bar{M}$. Such pathway can be visualized as

$$Z\rightarrow\bar{M}\rightarrow Y \tag{9}$$

For example, in the dental data, Z is the motivational interviewing and $\bar{M}$ can be the kid's dental visit and diet behavior other than the mediator of interest; in the flood data, Z is the flood and $\bar{M}$ can be the mother's health other than the mediator of interest. If the instrument $Z\times\mathbf{X}^{\text{IV}}$ affects $\bar{M}$, conditioning on $Z,\mathbf{X}$, then the instrument $Z\times\mathbf{X}^{\text{IV}}$ can affect Y through the mediator $\bar{M}$, which violates the Exclusion Restriction assumption. Therefore, conditioning on Z and $\mathbf{X}$, we can assess if $Z\times\mathbf{X}^{\text{IV}}$ predicts $\bar{M}$ to evaluate if the Exclusion Restriction assumption of the instrument $Z\times\mathbf{X}^{\text{IV}}$ is potentially violated. Even if $Z\times\mathbf{X}^{\text{IV}}$ does not significantly affect $\bar{M}$, we could not conclude that the Exclusion Restriction assumption is verified. However, we are more confident in the plausibility of the Exclusion Restriction assumption for that it is not violated through the intermediate variable

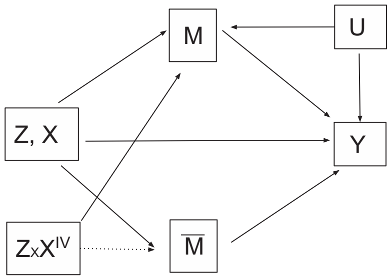

Fig. 1: Causal pathway of testing the Exclusion Restriction assumption

$\bar{M}$. As illustrated in Figure 1, we test whether the dotted arrow exists.

Let h denote the link function for $E\left(\bar{M}^{z*} \mid \mathbf{X}=\mathbf{x}\right)$ and define

$$\gamma = h\left(E\left(\bar{M}^{z*} \mid \mathbf{X}=\mathbf{x}\right)\right) - h\left(E\left(\bar{M}^{z} \mid \mathbf{X}=\mathbf{x}\right)\right). \tag{10}$$

Formally, we test the following null hypothesis

$$H_0 \; : \gamma \text{ is a function which does not depend on } z \times \mathbf{x}^{\mathrm{IV}}. \tag{11}$$

When $\bar{M}$ is continuous and the link function h is identity function with

$$E\left(\bar{M}^{z*} \mid \mathbf{X}=\mathbf{x}\right) = \nu_0 + \nu_z z^* + \nu_{\mathbf{X}}\mathbf{x} + \nu_{IV} z \times \mathbf{x}^{\mathrm{IV}}$$

and hence

$$E\left(\bar{M}^{z*} - \bar{M}^{z} \mid \mathbf{X}=\mathbf{x}\right) = \nu_{IV}\left(z^* - z\right)\mathbf{x}^{\mathrm{IV}}.$$

In this case, we are testing

$$H_0 \; : \nu_{IV} = 0. \tag{12}$$

When $\bar{M}$ is binary and the link function h is logit function with

$$\operatorname{logit}\left(E\left(\bar{M}^{z*} \mid \mathbf{X}=\mathbf{x}\right)\right) = \nu_0 + \nu_z z^* + \nu_{\mathbf{X}}\mathbf{x} + \nu_{IV} z \times \mathbf{x}^{\mathrm{IV}}$$

and hence

$$\operatorname{logit}\left(E\left(\bar{M}^{z*} \mid \mathbf{X}=\mathbf{x}\right)\right) - \operatorname{logit}\left(E\left(\bar{M}^{z*} \mid \mathbf{X}=\mathbf{x}\right)\right) = \nu_{IV}\left(z^* - z\right)\mathbf{x}^{\mathrm{IV}}.$$

In this case, we also test

$$H_0 \; : \nu_{IV} = 0. \tag{13}$$

1.4. *Proof of Proposition 2*

It suffices to verify the following regularity conditions and then an application of Theorem 1 in Qin and Lawless(1994) leads to Proposition 2. $\mathbb{E}\left(g\left(w,\theta_0\right)g^{\mathsf{T}}\left(w,\theta_0\right)\right)$ is positive definite and the rank of

$\mathbb{E}\left(\frac{\partial g(w,\theta)}{\partial\theta}\right)$ is the same as the dimension of θ and $\left\|\frac{\partial^2 g(w,\theta)}{\partial\theta\partial\theta^\intercal}\right\|$ can be bounded by some integrable function $G(w)$ in the neighborhood $\|\theta-\theta_0\|_2 \leq 1$ of the true value θ_0.

By the expression of $g(w,\theta)$, $g(w,\theta)$ and $\frac{\partial g(w,\theta)}{\partial\theta}$ are continuous in a compact neighborhood $\|\theta-\theta_0\|_2 \leq 1$ of the true value θ_0. Hence $\|g(w,\theta)\|^3$ and $\|\frac{\partial g(w,\theta)}{\partial\theta}\|_2$ are bounded in this compact neighborhood $\|\theta-\theta_0\|_2 \leq 1$. $\frac{\partial^2 g(w,\theta)}{\partial\theta\partial\theta^\tau}$ is continuous in θ in a neighborhood $\|\theta-\theta_0\|_2 \leq 1$ of the true value θ_0.

2. Consistency of 2SRI estimator

To see how 2SRI works, we can decompose U into two parts $U = \tau R + \delta$, where R denotes the population residual from the first stage, δ is the population residual and $\mathbb{E}(\delta|R) = 0$. Then for continuous and count outcomes, we respectively have:

$$\begin{aligned}
\mathbb{E}(Y(Z,M)|\mathbf{X},R) &= \int \beta_0+\beta_z Z+\beta_m M+\beta_{\mathbf{x}}\mathbf{X}+\beta_u\tau R+\beta_u\delta dP(\delta|Z,M,\mathbf{X},R) \quad (14)\\
&= \beta_0+\beta_z Z+\beta_m M+\beta_{\mathbf{x}}\mathbf{X}+\beta_u\tau R+\int\beta_u\delta dP(\delta|Z,M,\mathbf{X},R).\\
\mathbb{E}(Y(Z,M)|\mathbf{X},R) &= \int \exp(\beta_0+\beta_z Z+\beta_m M+\beta_{\mathbf{x}}\mathbf{X}+\beta_u\tau R+\beta_u\delta)\,dP(\delta|Z,M,\mathbf{X},R) \quad (15)\\
&= \exp(\beta_0+\beta_z Z+\beta_m M+\beta_{\mathbf{x}}\mathbf{X}+\beta_u\tau R)\int\exp(\beta_u\delta)\,dP(\delta|Z,M,\mathbf{X},R).
\end{aligned}$$

Continuous mediators For a continuous mediator, we consider a linear model:

$$M = \alpha_0+\alpha_z Z+\alpha_{\mathbf{x}}\mathbf{X}+\alpha_{IV}Z\times\mathbf{X}^{IV}+\alpha_u U+V, \quad (16)$$

where V is random error and U is the unmeasured confounder with (V,U) following bivariate normal distribution and is independent of $(\mathbf{X},Z,Z\times\mathbf{X}^{IV})$. 2SRI fits a linear model for M on $Z,\mathbf{X},Z\times\mathbf{X}^{IV}$, and the probability limit α_j^* of first stage estimator is equal to the underlying truth, that is, $\alpha_j^*=\alpha_j$, where $j=0,z,\mathbf{x},IV$. Then the residual is

$$R = M-\left(\alpha_0+\alpha_z Z+\alpha_{\mathbf{x}}\mathbf{X}+\alpha_{IV}Z\times\mathbf{X}^{IV}\right) = \alpha_u U+V.$$

Since $(\alpha_u U+V,U)$ is independent of $(\mathbf{X},Z,Z\times\mathbf{X}^{IV})$, then δ, as the population level residual of regressing U on $R=\alpha_u U+V$, is independent of $(\mathbf{X},Z,Z\times\mathbf{X}^{IV})$. Since δ is independent of R and M is linear combination of $(\mathbf{X},Z,Z\times\mathbf{X}^{IV})$ and R, then δ is independent of R and M, and it is easy to see that the 2SRI estimator is consistent for continuous outcomes with a continuous mediator. For count outcomes, because δ is independent of other variables, $\int\exp(\beta_u\delta)\,dP(\delta|Z,M,\mathbf{X},R)$ in (15) is a constant. Therefore, the 2SRI estimator is also consistent for count outcomes when the mediator is continuous.

Binary mediators For a binary mediator, we consider a logit model:

$$M|\mathbf{X}, Z, U \sim Ber\left(\frac{\exp(\alpha_0 + \alpha_z Z + \alpha_{\mathbf{x}}\mathbf{X} + \alpha_{IV} Z \times \mathbf{X}^{IV} + \alpha_u U)}{1 + \exp(\alpha_0 + \alpha_z Z + \alpha_{\mathbf{x}}\mathbf{X} + \alpha_{IV} Z \times \mathbf{X}^{IV} + \alpha_u U)}\right), \tag{17}$$

2SRI fits a logit model for M on $Z, \mathbf{X}, Z \times \mathbf{X}^{IV}$, and the probability limit α_j^* of the first stage estimators is not equal to the underlying truth α_j, for $j = 0, z, \mathbf{x}, IV$. Then the population residual is

$$R = M - \frac{\exp\left(\alpha_0^* + \alpha_1^* Z + \alpha_2^* \mathbf{X} + \alpha_3^* Z \times \mathbf{X}^{IV}\right)}{1 + \exp\left(\alpha_0^* + \alpha_1^* Z + \alpha_2^* \mathbf{X} + \alpha_3^* Z \times \mathbf{X}^{IV}\right)}.$$

Now $\int \exp(\beta_u \delta)\, dP\,(\delta|Z, M, \mathbf{X}, R)$ is generally not a constant but a function depending on $Z, M, \mathbf{X}, R$, so the 2SRI estimate will typically be biased when both the mediator and outcome models are nonliear.

2.1. The consistency of the 2SRI estimator when the first stage is linear

Consider the following outcome model

$$\mathbb{E}\left(Y(Z, M)|X, U\right) = \exp\left(\beta_0 + \beta_z Z + \beta_m M + \beta_{\mathbf{x}}\mathbf{X} + \beta_u U\right), \tag{18}$$

and the mediator model,

$$M = \alpha_0 + \alpha_z Z + \alpha_{\mathbf{x}}\mathbf{X} + \alpha_{IV} Z \times \mathbf{X} + (\alpha_u U + V), \tag{19}$$

where $\alpha_u U + V$ is the error and U is the unmeasured confounder with $(\alpha_u U + V, U)$ following bivariate normal distribution and is independent of $(\mathbf{X}, Z, Z \times \mathbf{X})$. Let α^* denote the probability limit of the logistic regression estimator $m \sim z + \mathbf{x} + z \times \mathbf{x}$ and $\alpha_j^* = \alpha_j$ for $j = 0, z, x, IV$. In the first stage, the population residual R is defined as

$$R = M - (\alpha_0 + \alpha_z Z + \alpha_{\mathbf{x}}\mathbf{X} + \alpha_{IV} Z \times \mathbf{X}) = \alpha_u U + V,$$

and decompose U into two parts

$$U = \tau R + \delta,$$

where δ is the population residual of the OLS $U \sim R$ and δ is independent of R. Since

$$\mathbb{E}\left(Y(Z, M)|\mathbf{X}, R, \delta\right) = \exp\left(\beta_0 + \beta_z Z + \beta_m M + \beta_{\mathbf{x}}\mathbf{X} + \beta_u \tau R + \beta_u \delta\right),$$

we have

$$\begin{aligned} &\mathbb{E}\left(Y(Z, M)|\mathbf{X}, R\right) \\ &= \int \exp\left(\beta_0 + \beta_z Z + \beta_m M + \beta_{\mathbf{x}}\mathbf{X} + \beta_u \tau R + \beta_u \delta\right) dP\left(\delta|Z, M, \mathbf{X}, R\right), \\ &= \exp\left(\beta_0 + \beta_z Z + \beta_m M + \beta_{\mathbf{x}}\mathbf{X} + \beta_u \tau R\right) \int \exp\left(\beta_u \delta\right) dP\left(\delta|Z, M, \mathbf{X}, R\right). \end{aligned} \tag{20}$$

Since $(\alpha_u U + V, U)$ is independent of $(\mathbf{X}, Z, Z \times \mathbf{X})$, δ is independent of $(\mathbf{X}, Z, Z \times \mathbf{X})$. Since δ is independent of R and M is linear combination of $(\mathbf{X}, Z, Z \times \mathbf{X})$ and R, δ is independent of R and M and hence $\int \exp(\beta_u \delta)\, dP(\delta|Z, M, \mathbf{X}, R)$ is a constant and the 2SRI estimator is consistent. We just show that if we know the error R. Since R is unknown, we need to estimate R by $\hat{R}$ which is the residual of the first stage regression $m \sim z + \mathbf{x} + z \times \mathbf{x}$. Under the identification assumption and the regularity conditions, the 2SRI estimator is consistent even when R is replaced by $\hat{R}$ in the second stage. More detailed and rigorous discussion is referred to section 12.4.1 in Wooldridge(2010).

2.2. *The consistency of the 2SRI estimator when the second stage is linear*

Consider the first stage model

$$M|\mathbf{X}, Z, U \sim Ber\left(\frac{\exp(\alpha_0 + \alpha_z Z + \alpha_{\mathbf{x}}\mathbf{X} + \alpha_{IV} Z \times \mathbf{X} + \alpha_u U)}{1 + \exp(\alpha_0 + \alpha_z Z + \alpha_{\mathbf{x}}\mathbf{X} + \alpha_{IV} Z \times \mathbf{X} + \alpha_u U)}\right), \tag{21}$$

and the following second stage model

$$Y(Z, M) = \beta_0 + \beta_z Z + \beta_m M + \beta_{\mathbf{x}}\mathbf{X} + (\alpha_u U + V), \tag{22}$$

where $\alpha_u U + V$ is the error and U is the unmeasured confounder with $(\alpha_u U + V, U)$ following bivariate normal distribution and is independent of $(\mathbf{X}, Z, Z \times \mathbf{X})$. When the second stage model is linear, then the 2SPS and 2SRI estimators are same. The validity of the instrumental variables will guarantee that the 2SPS and 2SRI estimators are consistent. However, to contrast the argument with the case where the second stage model is Poisson, Negative Binomial and Neyman Type A distribution, we show in the following that the 2SRI estimator is consistent if R is known. When we estimate R by a consistent estimator $\hat{R}$, the 2SRI estimator is still consistent but the proof is omitted here. Let α^* denote the probability limit of the logistic regression estimator $m \sim z + \mathbf{x} + z \times \mathbf{x}$. In the first stage, the residual R is defined as

$$R = M - \frac{\exp(\alpha_0^* + \alpha_z^* Z + \alpha_{\mathbf{x}}^*\mathbf{X} + \alpha_{IV}^* Z \times \mathbf{X})}{1 + \exp\left(\alpha_0^* + \alpha_z^* Z + \alpha_{\mathbf{x}}^*\mathbf{X} + \alpha_{IV}^* Z \times \mathbf{X}\right)},$$

and decompose U into two parts

$$U = \tau R + \delta$$

where δ is the population residue of the OLS $U \sim R$ and $\mathbb{E}(\delta|R) = 0$.

Since

$$\mathbb{E}(Y(Z, M)|\mathbf{X}, R, \delta) = \beta_0 + \beta_z Z + \beta_m M + \beta_{\mathbf{x}}\mathbf{X} + \beta_u \tau R + \beta_u \delta,$$

we have

$$\begin{aligned}\mathbb{E}\left(Y(Z,M)|\mathbf{X},R\right) = &\int \left(\beta_0+\beta_z Z+\beta_m M+\beta_{\mathbf{x}}\mathbf{X}+\beta_u \tau R+\beta_u\delta\right) dP\left(\delta|Z,M,\mathbf{X},R\right),\\ &=\left(\beta_0+\beta_z Z+\beta_m M+\beta_{\mathbf{x}}\mathbf{X}+\beta_u \tau R\right)+\int \left(\beta_u\delta\right) dP\left(\delta|Z,M,\mathbf{X},R\right),\\ &=\left(\beta_0+\beta_z Z+\beta_m M+\beta_{\mathbf{x}}\mathbf{X}+\beta_u \tau R\right)+\beta_u\mathbb{E}\left(\mathbb{E}\left(\delta|R\right)|Z,M,\mathbf{X},R\right),\\ &=\beta_0+\beta_z Z+\beta_m M+\beta_{\mathbf{x}}\mathbf{X}+\beta_u \tau R,\end{aligned} \tag{23}$$

hence the 2SRI estimator is consistent.

3. Estimating equations

In this section, we consider two extensions, where the model is involved with two endogenous mediators (m_1, m_2) and the model is involved with the interaction term between the treatment z and the mediator m.

3.1. Multiple mediators

We consider the mediators (m_1, m_2), where m_1 and m_2 are independent conditioning on $z, \mathbf{x}, u$ and construct the estimating equations in the case of two conditional independent mediators. The outcome model can be written as

$$g\{\mathbb{E}\left(Y(z,m_1,m_2)|z,m_1,m_2,\mathbf{x},u\right)\} = \beta_0+\beta_z z+\beta_{m,1}m_1+\beta_{m,2}m_2+\beta_{\mathbf{x}}\mathbf{x}+\beta_u u. \tag{24}$$

We assume there exist two valid IVs $z\times x_1$ and $z\times x_2$. We will focus on the harder case, binary mediator in this section. With the log link function, the model (24) represents Poisson, Negative Binomial and Neyman Type A distribution,

$$Y|x,z,m,u \sim Poisson\left(\exp\left(\beta_0+\beta_z z+\beta_{m_1}m_1+\beta_{m_2}m_2+\beta_{x_1}x_1+\beta_{x_2}x_2+\beta_u u\right)\right),$$

$$Y|x,z,m,u \sim NegBin\left(\exp\left(\beta_0+\beta_z z+\beta_{m_1}m_1+\beta_{m_2}m_2+\beta_{x_1}x_1+\beta_{x_2}x_2+\beta_u u\right)\right).$$

$$Y=\sum_{k=1}^{N} y_k;$$

where

$$\begin{aligned}&N|x,z,m,u \sim Poisson\left(\exp\left(\gamma_0+\gamma_z z+\gamma_{m_1}m_1+\gamma_{m_2}m_2+\gamma_{x_1}x_1+\gamma_{x_2}x_2+\gamma_u u\right)\right);\\ &y_k|x,z,m,u \sim Poisson\left(\exp\left(\lambda_0+\lambda_z z+\lambda_{m_1}m_1+\lambda_{m_2}m_2+\lambda_{x_1}x_1+\lambda_{x_2}x_2+\lambda_u u\right)\right).\end{aligned}$$

The binary mediators m_1 and m_2 are independent generated as

$$m_1|x,z,u \sim Ber\left(\frac{\exp\left(\alpha_0+\alpha_z z+\alpha_{x_1}x_1+\alpha_{x_2}x_2+\alpha_{IV_1}zx_1+\alpha_{IV_2}zx_2+\alpha_u u\right)}{1+\exp\left(\alpha_0+\alpha_z z+\alpha_{x_1}x_1+\alpha_{x_2}x_2+\alpha_{IV_1}zx_1+\alpha_{IV_2}zx_2+\alpha_u u\right)}\right),$$

$$m_2|x,z,u \sim Ber\left(\frac{\exp\left(\tau_0+\tau_z z+\tau_{x_1}x_1+\tau_{x_2}x_2+\tau_{IV_1}zx_1+\tau_{IV_2}zx_2+\tau_u u\right)}{1+\exp\left(\tau_0+\tau_z z+\tau_{x_1}x_1+\tau_{x_2}x_2+\tau_{IV_1}zx_1+\tau_{IV_2}zx_2+\tau_u u\right)}\right).$$

We can establish the following estimating equations,

$$\begin{aligned}
h_1(w,\theta) &= \left(\frac{y}{\exp(\beta_0+\beta_z z+\beta_{m_1}m_1+\beta_{m_2}m_2+\beta_{x_1}x_1+\beta_{x_2}x_2)}-1\right);\\
h_2(w,\theta) &= \left(\frac{y}{\exp(\beta_0+\beta_z z+\beta_{m_1}m_1+\beta_{m_2}m_2+\beta_{x_1}x_1+\beta_{x_2}x_2)}-1\right)z;\\
h_3(w,\theta) &= \left(\frac{y}{\exp(\beta_0+\beta_z z+\beta_{m_1}m_1+\beta_{m_2}m_2+\beta_{x_1}x_1+\beta_{x_2}x_2)}-1\right)x_1;\\
h_4(w,\theta) &= \left(\frac{y}{\exp(\beta_0+\beta_z z+\beta_{m_1}m_1+\beta_{m_2}m_2+\beta_{x_1}x_1+\beta_{x_2}x_2)}-1\right)x_2;\\
h_5(w,\theta) &= \left(\frac{y}{\exp(\beta_0+\beta_z z+\beta_{m_1}m_1+\beta_{m_2}m_2+\beta_{x_1}x_1+\beta_{x_2}x_2)}-1\right)zx_1;\\
h_6(w,\theta) &= \left(\frac{y}{\exp(\beta_0+\beta_z z+\beta_{m_1}m_1+\beta_{m_2}m_2+\beta_{x_1}x_1+\beta_{x_2}x_2)}-1\right)zx_2;\\
h_7(w,\theta) &= \left(\frac{y}{\exp(\beta_{m_1}m_1+\beta_{m_2}m_2)}-\exp(\beta_0+\beta_z z+\beta_{x_1}x_1+\beta_{x_2}x_2)\right);\\
h_8(w,\theta) &= \left(\frac{y}{\exp(\beta_{m_1}m_1+\beta_{m_2}m_2)}-\exp(\beta_0+\beta_z z+\beta_{x_1}x_1+\beta_{x_2}x_2)\right)z;\\
h_9(w,\theta) &= \left(\frac{y}{\exp(\beta_{m_1}m_1+\beta_{m_2}m_2)}-\exp(\beta_0+\beta_z z+\beta_{x_1}x_1+\beta_{x_2}x_2)\right)x_1;\\
h_{10}(w,\theta) &= \left(\frac{y}{\exp(\beta_{m_1}m_1+\beta_{m_2}m_2)}-\exp(\beta_0+\beta_z z+\beta_{x_1}x_1+\beta_{x_2}x_2)\right)x_2;\\
h_{11}(w,\theta) &= \left(\frac{y}{\exp(\beta_{m_1}m_1+\beta_{m_2}m_2)}-\exp(\beta_0+\beta_z z+\beta_{x_1}x_1+\beta_{x_2}x_2)\right)zx_1;\\
h_{12}(w,\theta) &= \left(\frac{y}{\exp(\beta_{m_1}m_1+\beta_{m_2}m_2)}-\exp(\beta_0+\beta_z z+\beta_{x_1}x_1+\beta_{x_2}x_2)\right)zx_2.
\end{aligned} \tag{25}$$

3.2. Model with interaction between treatment and mediator

We consider the outcome model with the interaction term zm,

$$g\{\mathbb{E}\left(Y(z,m)|z,m,\mathbf{x},u\right)\} = \beta_0+\beta_z z+\beta_m m+\beta_{zm}zm+\beta_{\mathbf{x}}\mathbf{x}+\beta_u u. \tag{26}$$

We assume there exist two valid IVs $z\times x_1$ and $z\times x_2$. We will focus on the harder case, binary mediator in this section. With the log link function, the model (26) represents Poisson, Negative

Binomial and Neyman Type A distribution,

$$Y|x,z,m,u \sim Poisson\left(\exp\left(\beta_0+\beta_z z+\beta_m m+\beta_{zm} zm+\beta_{x_1}x_1+\beta_{x_2}x_2+\beta_u u\right)\right),$$

$$Y|x,z,m,u \sim NegBin\left(\exp\left(\beta_0+\beta_z z+\beta_m m+\beta_{zm} zm+\beta_{x_1}x_1+\beta_{x_2}x_2+\beta_u u\right)\right).$$

$$Y=\sum_{k=1}^{N} y_k;$$

where

$$N|x,z,m,u \sim Poisson\left(\exp\left(\gamma_0+\gamma_z z+\gamma_m m+\gamma_{zm} zm+\gamma_{x_1}x_1+\gamma_{x_2}x_2+\gamma_u u\right)\right);$$

$$y_k|x,z,m,u \sim Poisson\left(\exp\left(\lambda_0+\lambda_z z+\lambda_m m+\lambda_{zm} zm+\lambda_{x_1}x_1+\lambda_{x_2}x_2+\lambda_u u\right)\right).$$

The binary mediators m_1 and m_2 are independent generated as

$$m|x,z,u \sim Ber\left(\frac{\exp\left(\alpha_0+\alpha_z z+\alpha_{x_1}x_1+\alpha_{x_2}x_2+\alpha_{IV_1}zx_1+\alpha_{IV_2}zx_2+\alpha_u u\right)}{1+\exp\left(\alpha_0+\alpha_z z+\alpha_{x_1}x_1+\alpha_{x_2}x_2+\alpha_{IV_1}zx_1+\alpha_{IV_2}zx_2+\alpha_u u\right)}\right),$$

We can establish the following estimating equations,

$$\begin{aligned}
h_1(w,\theta) &= \left(\frac{y}{\exp(\beta_0+\beta_z z+\beta_m m+\beta_{zm} zm+\beta_{x_1}x_1+\beta_{x_2}x_2)}-1\right);\\
h_2(w,\theta) &= \left(\frac{y}{\exp(\beta_0+\beta_z z+\beta_m m+\beta_{zm} zm+\beta_{x_1}x_1+\beta_{x_2}x_2)}-1\right)z;\\
h_3(w,\theta) &= \left(\frac{y}{\exp(\beta_0+\beta_z z+\beta_m m+\beta_{zm} zm+\beta_{x_1}x_1+\beta_{x_2}x_2)}-1\right)x_1;\\
h_4(w,\theta) &= \left(\frac{y}{\exp(\beta_0+\beta_z z+\beta_m m+\beta_{zm} zm+\beta_{x_1}x_1+\beta_{x_2}x_2)}-1\right)x_2;\\
h_5(w,\theta) &= \left(\frac{y}{\exp(\beta_0+\beta_z z+\beta_m m+\beta_{zm} zm+\beta_{x_1}x_1+\beta_{x_2}x_2)}-1\right)zx_1;\\
h_6(w,\theta) &= \left(\frac{y}{\exp(\beta_0+\beta_z z+\beta_m m+\beta_{zm} zm+\beta_{x_1}x_1+\beta_{x_2}x_2)}-1\right)zx_2;\\
h_7(w,\theta) &= \left(\frac{y}{\exp(\beta_m m+\beta_{zm} zm)}-\exp(\beta_0+\beta_z z+\beta_{x_1}x_1+\beta_{x_2}x_2)\right);\\
h_8(w,\theta) &= \left(\frac{y}{\exp(\beta_m m+\beta_{zm} zm)}-\exp(\beta_0+\beta_z z+\beta_{x_1}x_1+\beta_{x_2}x_2)\right)z;\\
h_9(w,\theta) &= \left(\frac{y}{\exp(\beta_m m+\beta_{zm} zm)}-\exp(\beta_0+\beta_z z+\beta_{x_1}x_1+\beta_{x_2}x_2)\right)x_1;\\
h_{10}(w,\theta) &= \left(\frac{y}{\exp(\beta_m m+\beta_{zm} zm)}-\exp(\beta_0+\beta_z z+\beta_{x_1}x_1+\beta_{x_2}x_2)\right)x_2;\\
h_{11}(w,\theta) &= \left(\frac{y}{\exp(\beta_m m+\beta_{zm} zm)}-\exp(\beta_0+\beta_z z+\beta_{x_1}x_1+\beta_{x_2}x_2)\right)zx_1;\\
h_{12}(w,\theta) &= \left(\frac{y}{\exp(\beta_m m+\beta_{zm} zm)}-\exp(\beta_0+\beta_z z+\beta_{x_1}x_1+\beta_{x_2}x_2)\right)zx_2.
\end{aligned} \tag{27}$$

		Direct			Indirect		
		EL	2SRI	Reg	EL	2SRI	Reg
Out	n	Med.	Med.	Med.	Med.	Med.	Med.
		(MAD)	(MAD)	(MAD)	(MAD)	(MAD)	(MAD)
Poi	500	0.484	0.478	0.388	0.527	0.592	0.971
		(0.169)	(0.198)	(0.117)	(0.868)	(0.671)	(0.115)
Poi	1000	0.506	0.483	0.385	0.466	0.598	0.965
		(0.131)	(0.148)	(0.079)	(0.611)	(0.514)	(0.078)
Poi	5000	0.506	0.502	0.389	0.494	0.548	0.962
		(0.050)	(0.064)	(0.036)	(0.265)	(0.253)	(0.035)
NB	500	0.497	0.485	0.415	0.525	0.569	0.952
		(0.213)	(0.187)	(0.126)	(1.019)	(0.685)	(0.132)
NB	1000	0.491	0.494	0.413	0.491	0.524	0.951
		(0.153)	(0.122)	(0.081)	(0.773)	(0.510)	(0.089)
NB	5000	0.499	0.493	0.414	0.542	0.541	0.955
		(0.064)	(0.058)	(0.038)	(0.309)	(0.235)	(0.042)
NTA	500	0.526	0.342	0.367	0.285	1.029	1.003
		(0.336)	(0.813)	(0.260)	(1.817)	(2.262)	(0.236)
NTA	1000	0.512	0.337	0.358	0.463	1.112	1.010
		(0.280)	(0.616)	(0.197)	(1.451)	(1.643)	(0.181)
NTA	5000	0.506	0.425	0.368	0.477	0.809	0.995
		(0.145)	(0.407)	(0.092)	(0.651)	(1.147)	(0.091)

Table 1: EL estimate (with Multi-starting values) and 2SRI estimate for the direct effect parameter (β_z) and the indirect effect parameter (β_m) with two instrumental variables. The median (out of parenthesis) and the MAD (inside parenthesis) are reported. EL denotes the Empirical Likelihood estimate, 2SRI denotes the 2SRI estimates and Reg denotes the ordinary (Poisson or Negative Binomial) regression estimate. n stands for sample size; Out stands for the outcome distribution, Poi stands for Poisson distribution, NB stands for Negative Binomial outcome distribution and NTA stands for Neyman Type A distribution outcome. The simulation time is 1000 and the true coefficients are 0.5. The size of negative binomial model is 3.

4. Extended simulation studies

In this section, we discuss the extended simulation results.

4.1. Single Mediator with Two Instrumental Variables

The results are summarized in Table 1.

4.2. More simulation results for Continuous Mediator

The results are summarized in Table 2.

4.3. Simulation results for sensitivity analysis

The results are summarized in Table 3.

4.4. A larger proportion of zeros for Poisson and Negative Binomial

We simulate the Poisson and Negative Binomial outcome model with a larger proportion of zero.

$$y|x, z, m, u \sim Poisson\left(\exp\left(-0.5 + 0.5z + 0.5m + 0.5x + u\right)\right). \tag{28}$$

$$y|x, z, m, u \sim NegBin\left(\exp\left(-0.5 + 0.5z + 0.5m + 0.5x + u\right)\right). \tag{29}$$

The proportion of zeros for poisson increases from 20% to 50% and for Negative Binomial from 25% to 55%. The results are summarized in Table 4.

4.5. Robust to the outcome distribution

It is necessary to know the outcome model for 2SRI second stage regression, which is another challenge for applying 2SRI to real data analysis. In Table 5, we generate the data by Negative Binomial Outcome model while fitting the second stage with Poisson Outcome. Table 5 shows that the proposed estimating equation approach consistently estimates the treatment and mediation effects while 2SRI estimates have a large bias, which illustrates that our method does not rely on the distribution of outcome model.

4.6. Comparison of Two Estimating Equation Methods

The results are summarized in Table 6.

4.7. Comparison of 2SPS and 2SRI

The results are summarized in Table 7 and Table 8.

References

Wooldridge, J. M. (2010). Econometric analysis of cross section and panel data, MIT press.

			Direct			Indirect		
			EL	2SRI	Reg	EL	2SRI	Reg
Out	Str.	n	Med.	Med.	Med.	Med.	Med.	Med.
			(MAD)	(MAD)	(MAD)	(MAD)	(MAD)	(MAD)
Poi	S	500	0.498	0.519	0.146	0.502	0.478	0.771
			(0.151)	(0.212)	(0.143)	(0.136)	(0.190)	(0.079)
Poi	S	1000	0.505	0.515	0.153	0.494	0.492	0.772
			(0.107)	(0.154)	(0.107)	(0.093)	(0.140)	(0.056)
Poi	S	5000	0.499	0.507	0.146	0.500	0.497	0.778
			(0.047)	(0.083)	(0.050)	(0.043)	(0.067)	(0.031)
Poi	W	500	0.498	0.506	0.235	0.498	0.488	0.803
			(0.191)	(0.249)	(0.131)	(0.243)	(0.328)	(0.064)
Poi	W	1000	0.498	0.495	0.230	0.503	0.495	0.803
			(0.130)	(0.192)	(0.093)	(0.170)	(0.242)	(0.051)
Poi	W	5000	0.498	0.506	0.232	0.497	0.494	0.800
			(0.060)	(0.090)	(0.044)	(0.079)	(0.118)	(0.027)
NB	S	500	0.501	0.504	0.261	0.501	0.499	0.822
			(0.168)	(0.166)	(0.135)	(0.151)	(0.142)	(0.052)
NB	S	1000	0.493	0.493	0.249	0.505	0.500	0.820
			(0.122)	(0.110)	(0.094)	(0.105)	(0.096)	(0.039)
NB	S	5000	0.500	0.501	0.258	0.502	0.496	0.821
			(0.053)	(0.053)	(0.040)	(0.048)	(0.044)	(0.016)
NB	W	500	0.508	0.508	0.285	0.510	0.492	0.863
			(0.221)	(0.214)	(0.131)	(0.310)	(0.304)	(0.060)
NB	W	1000	0.491	0.494	0.276	0.514	0.503	0.865
			(0.156)	(0.145)	(0.096)	(0.208)	(0.195)	(0.042)
NB	W	5000	0.500	0.499	0.275	0.500	0.495	0.863
			(0.067)	(0.063)	(0.041)	(0.093)	(0.091)	(0.017)
NTA	S	500	0.509	0.535	-0.086	0.482	0.481	0.786
			(0.464)	(0.572)	(0.330)	(0.421)	(0.345)	(0.139)
NTA	S	1000	0.495	0.550	-0.100	0.510	0.495	0.786
			(0.343)	(0.514)	(0.254)	(0.315)	(0.311)	(0.113)
NTA	S	5000	0.489	0.532	-0.124	0.503	0.490	0.785
			(0.154)	(0.315)	(0.172)	(0.138)	(0.168)	(0.069)
NTA	W	500	0.521	0.508	0.104	0.473	0.481	0.808
			(0.556)	(0.707)	(0.268)	(0.748)	(0.690)	(0.124)
NTA	W	1000	0.493	0.531	0.090	0.511	0.472	0.803
			(0.417)	(0.544)	(0.195)	(0.572)	(0.513)	(0.095)
NTA	W	5000	0.517	0.521	0.091	0.484	0.491	0.804
			(0.225)	(0.341)	(0.118)	(0.280)	(0.313)	(0.060)

Table 2: Continuous Mediator: EL estimate (with Multi-starting values),2SRI estimate and Regression estimate without IV (Reg) for the direct effect parameter (β_z) and the indirect effect parameter (β_m) with one instrumental variable.

			Direct			Indirect		
			EL	2SRI	Reg	EL	2SRI	Reg
Out	θ	n	Med. (MAD)	Med. (MAD)	Med. (MAD)	Med. (MAD)	Med. (MAD)	Med. (MAD)
Poi	$\eta = +0.1$	1000	0.507	0.501	0.415	0.495	0.559	0.954
			(0.099)	(0.119)	(0.079)	(0.512)	(0.494)	(0.075)
Poi	$\eta = -0.1$	1000	0.501	0.496	0.412	0.477	0.566	0.952
			(0.090)	(0.105)	(0.079)	(0.510)	(0.495)	(0.080)
Poi	$\eta = +0.5$	1000	0.492	0.494	0.419	0.525	0.558	0.950
			(0.104)	(0.113)	(0.081)	(0.560)	(0.532)	(0.081)
Poi	$\eta = -0.5$	1000	0.498	0.501	0.417	0.512	0.570	0.952
			(0.093)	(0.112)	(0.082)	(0.478)	(0.485)	(0.077)
Poi	$\eta = +1.0$	1000	0.488	0.495	0.412	0.552	0.564	0.952
			(0.110)	(0.108)	(0.080)	(0.615)	(0.480)	(0.080)
Poi	$\eta = -1.0$	1000	0.504	0.492	0.417	0.490	0.560	0.950
			(0.092)	(0.115)	(0.081)	(0.524)	(0.531)	(0.084)
NegB	$\eta = +0.1$	1000	0.488	0.500	0.446	0.541	0.564	0.949
			(0.119)	(0.121)	(0.091)	(0.574)	(0.521)	(0.096)
NegB	$\eta = -0.1$	1000	0.492	0.496	0.440	0.494	0.511	0.944
			(0.113)	(0.114)	(0.088)	(0.612)	(0.535)	(0.091)
NegB	$\eta = +0.5$	1000	0.494	0.500	0.442	0.510	0.504	0.943
			(0.117)	(0.113)	(0.088)	(0.609)	(0.515)	(0.098)
NegB	$\eta = -0.5$	1000	0.502	0.504	0.449	0.487	0.514	0.939
			(0.116)	(0.117)	(0.085)	(0.643)	(0.561)	(0.096)
NegB	$\eta = +1.0$	1000	0.488	0.500	0.448	0.562	0.517	0.947
			(0.133)	(0.120)	(0.094)	(0.749)	(0.558)	(0.098)
NegB	$\eta = -1.0$	1000	0.494	0.501	0.445	0.511	0.528	0.941
			(0.116)	(0.119)	(0.090)	(0.643)	(0.548)	(0.101)
NTA	$\eta_1 = 0.05$	1000	0.486	0.415	0.362	0.505	0.843	0.991
	$\eta_2 = 0.05$		(0.234)	(0.389)	(0.177)	(1.313)	(1.363)	(0.161)
NTA	$\eta_1 = 0.05$	5000	0.503	0.457	0.368	0.497	0.684	0.984
	$\eta_2 = 0.05$		(0.117)	(0.249)	(0.081)	(0.684)	(0.746)	(0.072)
NTA	$\eta_1 = 0.10$	1000	0.495	0.459	0.370	0.489	0.619	0.983
	$\eta_2 = 0.10$		(0.225)	(0.429)	(0.183)	(1.295)	(1.374)	(0.165)
NTA	$\eta_1 = 0.10$	5000	0.502	0.468	0.366	0.493	0.665	0.983
	$\eta_2 = 0.10$		(0.123)	(0.235)	(0.091)	(0.701)	(0.700)	(0.073)
NTA	$\eta_1 = 0.25$	1000	0.482	0.422	0.370	0.616	0.832	0.987
	$\eta_2 = 0.25$		(0.270)	(0.428)	(0.172)	(1.450)	(1.447)	(0.151)
NTA	$\eta_1 = 0.25$	5000	0.491	0.470	0.378	0.571	0.653	0.979
	$\eta_2 = 0.25$		(0.136)	(0.236)	(0.091)	(0.743)	(0.791)	(0.074)

Table 3: Sensitivity Analysis: EL estimate (with Multi-starting values),2SRI estimate and Regression estimate without IV (Reg) for the direct effect parameter (β_z) and the indirect effect parameter (β_m) with one instrumental variable. Poisson with strong IV and NTA with weak IV.

			Direct				Indirect			
			EL		2SRI		EL		2SRI	
Out	Str.	n	Med.	MAD	Med.	MAD	Med.	MAD	Med.	MAD
Poi	S	500	0.489	(0.188)	0.489	(0.185)	0.492	(1.009)	0.566	(0.830)
Poi	S	1000	0.494	(0.132)	0.494	(0.126)	0.500	(0.692)	0.540	(0.597)
Poi	S	5000	0.501	(0.062)	0.504	(0.062)	0.501	(0.328)	0.537	(0.270)
Poi	W	500	0.487	(0.205)	0.485	(0.234)	0.642	(1.397)	0.686	(1.403)
Poi	W	1000	0.495	(0.170)	0.488	(0.162)	0.514	(1.145)	0.650	(1.010)
Poi	W	5000	0.500	(0.081)	0.497	(0.077)	0.487	(0.553)	0.547	(0.478)
NB	S	500	0.497	(0.200)	0.519	(0.187)	0.503	(1.116)	0.521	(0.841)
NB	S	1000	0.487	(0.151)	0.493	(0.142)	0.530	(0.780)	0.579	(0.635)
NB	S	5000	0.500	(0.066)	0.504	(0.059)	0.495	(0.363)	0.519	(0.277)
NB	W	500	0.477	(0.229)	0.480	(0.251)	0.539	(1.579)	0.595	(1.427)
NB	W	1000	0.485	(0.165)	0.489	(0.180)	0.470	(1.200)	0.535	(1.054)
NB	W	5000	0.491	(0.089)	0.498	(0.081)	0.547	(0.604)	0.538	(0.487)

Table 4: EL estimate (with Multi-starting values) and 2SRI estimate for the direct effect parameter (β_z) and the indirect effect parameter (β_m) with one instrumental variable. We report the median and the MAD of the estimates. The column indexed with EL denotes the corresponding Empirical Likelihood estimate while the column indexed with 2S denotes the corresponding 2SRI estimates. The column indexed with n stands for sample size; the column indexed with $Dis.$ represents the conditional distribution of the outcome, where Poi stands for Poisson distribution, NB stands for Negative Binomial outcome distribution and NTA stands for Neyman Type A distribution outcome. The column indexed with $Str.$ represents the strength of instrumental variables, where S stands for stronger IV (setting 1) while W stands for relatively weaker IV (setting 2). The simulation time is 1000 and the true coefficients are 0.5. The size of negative binomial model is 3.

			Direct				Indirect			
			EL		2SRI		EL		2SRI	
Out	Str.	n	Med.	MAD	Med.	MAD	Med.	MAD	Med.	MAD
NB	S	500	0.487	(0.163)	0.491	(0.181)	0.539	(0.939)	0.574	(0.940)
NB	S	1000	0.493	(0.112)	0.494	(0.127)	0.491	(0.655)	0.532	(0.630)
NB	S	5000	0.500	(0.049)	0.498	(0.059)	0.492	(0.257)	0.548	(0.284)
NB	W	500	0.481	(0.177)	0.494	(0.225)	0.585	(1.224)	0.545	(1.485)
NB	W	1000	0.484	(0.146)	0.487	(0.177)	0.560	(1.003)	0.594	(1.131)
NB	W	5000	0.500	(0.064)	0.496	(0.073)	0.490	(0.445)	0.564	(0.476)

Table 5: Fit the second stage with a wrong model. The outcome follows Negative Binomial outcome while we fit the second stage model with Poisson outcome. We report the median and MAD of the estimates. The sample size n is 500,1000 or 5000.

	EE-EL1	EE-EL2	2SRI	Reg	EE-EL1	EE-EL2	2SRI	Reg
Poisson with Sample size 5000								
Median	0.501	0.499	0.499	0.416	0.497	0.508	0.544	0.950
MAD	0.042	0.040	0.047	0.037	0.231	0.213	0.241	0.031
NB with Sample size 5000								
Median	0.497	0.496	0.500	0.445	0.498	0.516	0.514	0.942
MAD	0.049	0.046	0.050	0.038	0.274	0.253	0.233	0.041
NTA with Sample size 5000 (1000 simulation)								
Median	0.496	0.495	0.462	0.375	0.521	0.545	0.678	0.981
MAD	0.116	0.110	0.245	0.088	0.683	0.510	0.787	0.074

Table 6: Two EL estimators (EE-EL1 and EE-EL2),2SRI estimate and Regression estimate without IV (Reg) for the direct effect parameter (β_z) and the indirect effect parameter (β_m) with one instrumental variable.

			Direct		Indirect	
			2SRI	2SPS	2SRI	2SPS
Outcome	IV	n	Med.	Med.	Med.	Med.
			(MAD)	(MAD)	(MAD)	(MAD)
Poi	S	500	0.487	0.478	0.609	0.463
			(0.149)	(0.151)	(0.660)	(0.694)
Poi	S	1000	0.492	0.484	0.570	0.458
			(0.099)	(0.100)	(0.500)	(0.498)
Poi	S	5000	0.500	0.493	0.552	0.431
			(0.047)	(0.047)	(0.229)	(0.226)
Poi	W	500	0.483	0.490	0.692	0.528
			(0.181)	(0.181)	(1.146)	(1.138)
Poi	W	1000	0.495	0.501	0.582	0.425
			(0.137)	(0.141)	(0.897)	(0.888)
Poi	W	5000	0.497	0.509	0.539	0.362
			(0.064)	(0.066)	(0.395)	(0.404)
NB	S	500	0.500	0.500	0.543	0.460
			(0.161)	(0.160)	(0.735)	(0.771)
NB	S	1000	0.496	0.489	0.570	0.488
			(0.105)	(0.109)	(0.504)	(0.506)
NB	S	5000	0.503	0.494	0.499	0.432
			(0.051)	(0.053)	(0.236)	(0.239)
NB	W	500	0.496	0.513	0.423	0.355
			(0.197)	(0.211)	(1.256)	(1.228)
NB	W	1000	0.489	0.493	0.591	0.443
			(0.130)	(0.134)	(0.840)	(0.849)
NB	W	5000	0.492	0.505	0.551	0.438
			(0.059)	(0.059)	(0.378)	(0.391)
NTA	S	500	0.393	0.394	0.786	0.619
			(0.501)	(0.497)	(1.789)	(1.817)
NTA	S	1000	0.413	0.404	0.812	0.641
			(0.398)	(0.413)	(1.308)	(1.355)
NTA	S	5000	0.465	0.455	0.653	0.500
			(0.260)	(0.261)	(0.821)	(0.800)
NTA	W	500	0.411	0.390	1.028	0.918
			(0.599)	(0.614)	(3.045)	(3.314)
NTA	W	1000	0.422	0.421	0.899	0.793
			(0.495)	(0.504)	(2.338)	(2.377)
NTA	W	5000	0.442	0.431	0.834	0.687
			(0.292)	(0.298)	(1.349)	(1.371)

Table 7: Count outcome and binary mediator: Comparison of 2SPS estimate and 2SRI estimate for the direct effect parameter (β_z) and the indirect effect parameter (β_m) with one instrumental variable.

			Direct		Indirect	
			2SRI	2SPS	2SRI	2SPS
Outcome	IV	n	Med.	Med.	Med.	Med.
			(MAD)	(MAD)	(MAD)	(MAD)
Poi	S	500	0.508	0.523	0.496	0.477
			(0.207)	(0.272)	(0.171)	(0.243)
Poi	S	1000	0.515	0.533	0.497	0.476
			(0.157)	(0.202)	(0.131)	(0.168)
Poi	S	5000	0.507	0.516	0.498	0.493
			(0.086)	(0.113)	(0.070)	(0.095)
Poi	W	500	0.511	0.509	0.497	0.469
			(0.249)	(0.314)	(0.321)	(0.377)
Poi	W	1000	0.521	0.532	0.484	0.479
			(0.185)	(0.233)	(0.238)	(0.300)
Poi	W	5000	0.500	0.500	0.501	0.501
			(0.088)	(0.118)	(0.115)	(0.154)
NB	S	500	0.505	0.493	0.497	0.498
			(0.166)	(0.196)	(0.143)	(0.163)
NB	S	1000	0.503	0.496	0.496	0.508
			(0.115)	(0.132)	(0.105)	(0.112)
NB	S	5000	0.499	0.499	0.498	0.500
			(0.056)	(0.062)	(0.043)	(0.052)
NB	W	500	0.505	0.515	0.469	0.493
			(0.224)	(0.262)	(0.273)	(0.324)
NB	W	1000	0.496	0.499	0.508	0.505
			(0.146)	(0.163)	(0.188)	(0.235)
NB	W	5000	0.499	0.503	0.496	0.504
			(0.067)	(0.079)	(0.090)	(0.103)
NTA	S	500	0.535	0.654	0.475	0.405
			(0.540)	(0.771)	(0.340)	(0.480)
NTA	S	1000	0.558	0.640	0.479	0.445
			(0.459)	(0.707)	(0.284)	(0.411)
NTA	S	5000	0.546	0.609	0.480	0.453
			(0.341)	(0.401)	(0.175)	(0.226)
NTA	W	500	0.550	0.584	0.463	0.475
			(0.669)	(0.881)	(0.641)	(0.835)
NTA	W	1000	0.513	0.599	0.495	0.410
			(0.553)	(0.800)	(0.516)	(0.761)
NTA	W	5000	0.484	0.547	0.518	0.466
			(0.348)	(0.482)	(0.308)	(0.448)

Table 8: Count outcome and normal mediator: Comparison of 2SPS estimate and 2SRI estimate for the direct effect parameter (β_z) and the indirect effect parameter (β_m) with one instrumental variable.