Instrumental Variable Treatment Effects Estimation: A Comparison of Instrumental Variables and OLS Approaches

MSR132

Pharmaco Evidence
Science-led HEOR & Tech-driven AI

Md. Sameer Mansoori[1], Neha Tripathi[1], Parampal Bajaj[1], Akanksha Sharma[1], Shubhram Pandey[2]

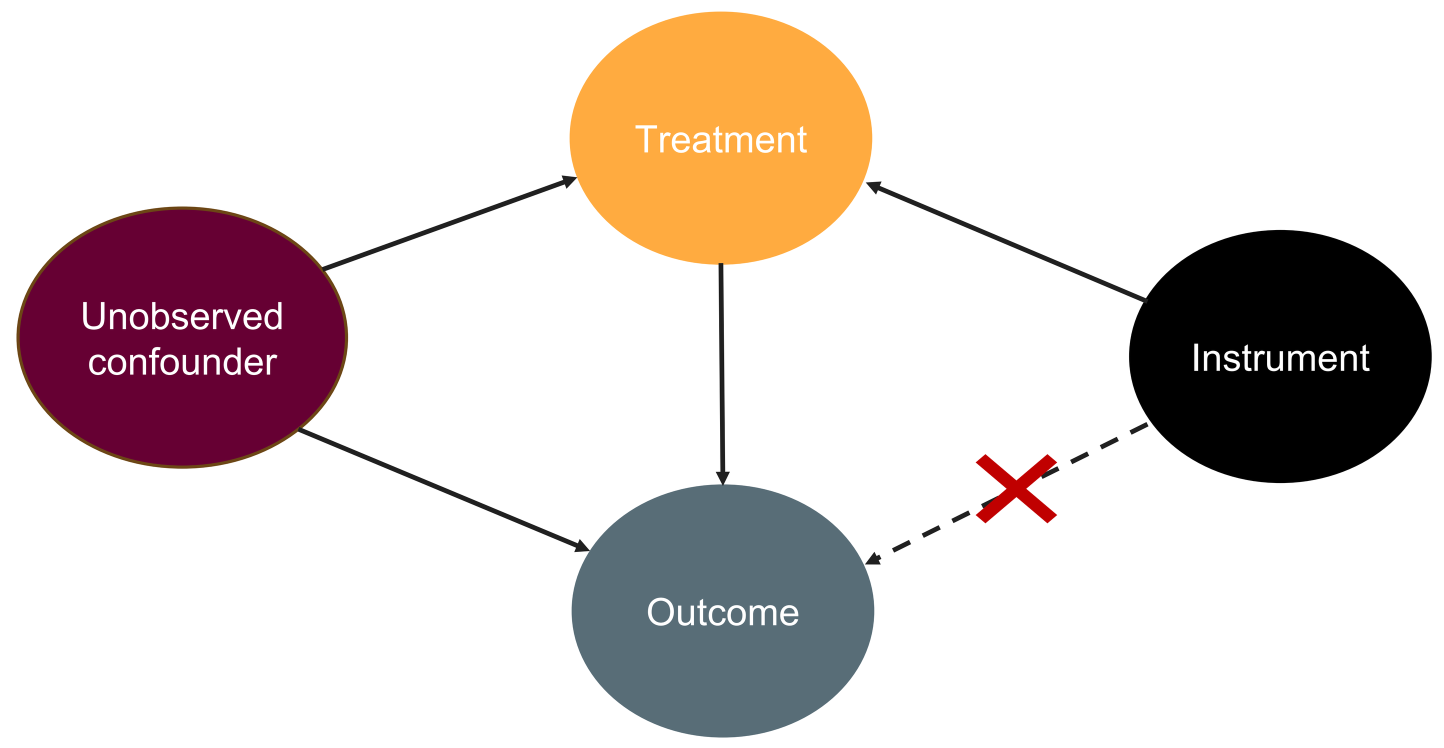
[1]Heorlytics, Mohali, India; [2]Pharmacoevidence, Mohali, India

TheoRlytics

INTRODUCTION

- Health technology assessment and reimbursement decisions rely on valid estimates of treatment effects from real-world and observational data
- Mis-estimated treatment effects can distort cost-effectiveness estimates and lead to sub-optimal coverage decisions in HTA submissions
- In many settings, treatment choice is influenced by patient prognosis, clinician preference, or healthcare system factors that are not fully observed
- When such unmeasured factors affect both treatment and outcomes, standard regression approaches (e.g., OLS) yield biased and inconsistent estimates
- Instrumental variable (IV) methods can mitigate this bias by using external variation in treatment that is unrelated to unmeasured confounders
- Endogeneity is a common challenge in observational research, where there is a correlation between exposure and confounding variables that cannot be measured, resulting in a biased OLS regression estimate
- Instrumental Variable (IV) methods offer a robust alternative by leveraging external factors that influence the exposure but are not directly correlated with the outcome. This approach effectively identifies the true causal effects
- Simulating OLS and IV estimation under endogeneity demonstrates the practical implications of endogeneity on causal inference, providing valuable insights for real-world data analysis

Figure 1: Schematic to show when IV variables are needed



- Endogeneity arises when unobserved confounders affect both treatment and outcome then IV methods use instruments, which can affect treatment but is assumed not to directly affect outcome

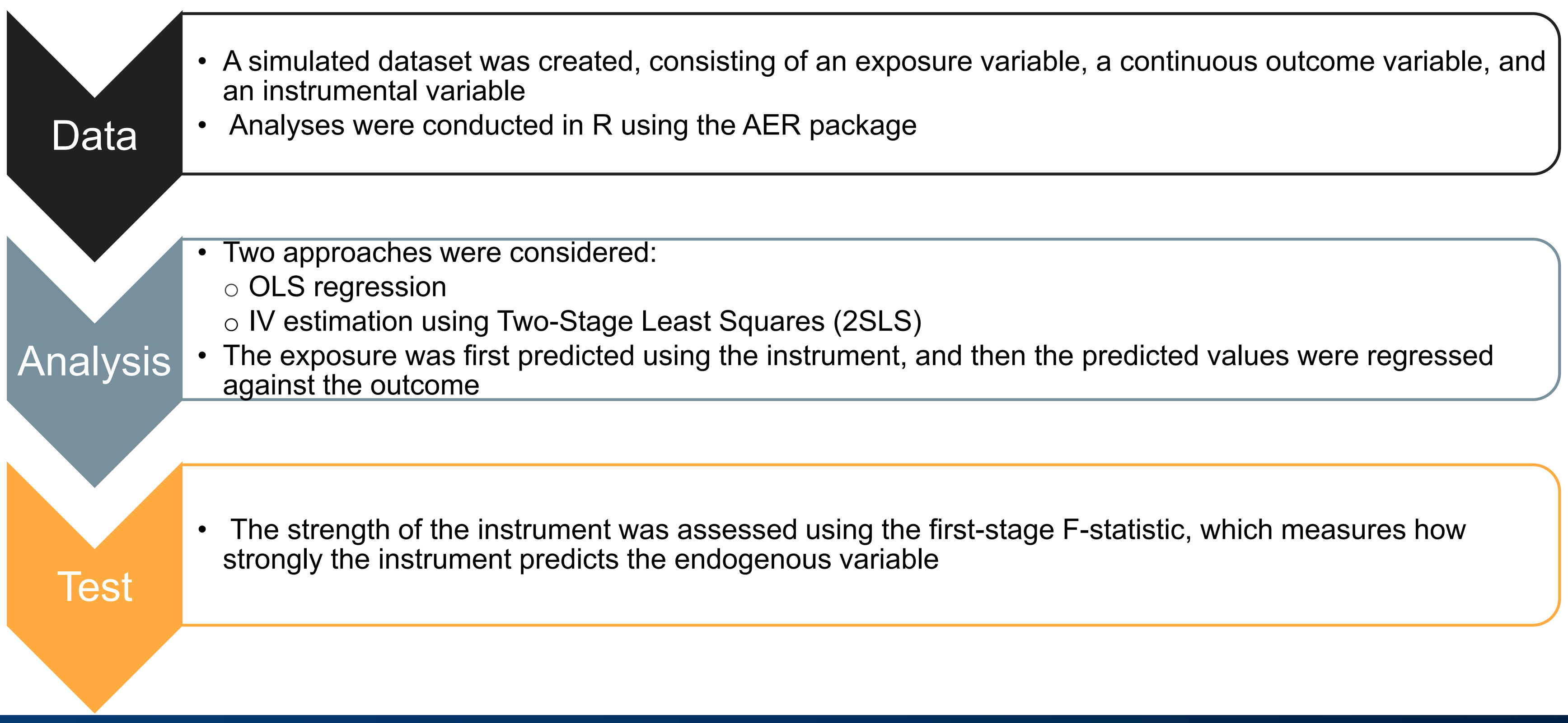
OBJECTIVE

- To evaluate and compare the performance of OLS and IV estimators in the presence of endogeneity using a simulation framework
- To assess how model choice (OLS vs IV) affects the accuracy and credibility of causal treatment effect estimates in observational research

METHODS

- A simulation framework was developed to model a continuous treatment variable, outcome, and unobserved confounder inducing endogeneity in the treatment–outcome relationship.
- An instrumental variable (Z) was specified that was correlated with treatment but assumed to be independent of the unmeasured confounder and to affect the outcome only through treatment.
- Multiple simulated datasets were generated under predefined data-generating mechanisms, varying the strength of the instrument and the degree of endogeneity.
- For each simulated dataset, treatment effects were estimated using:
  - Ordinary least squares (OLS), and
  - Two-stage least squares (2SLS) instrumental variable (IV) regression.
- Performance metrics included bias, standard error, coverage probability, and the first-stage F-statistic to assess instrument strength.

Figure 2. Workflow for Estimation of Instrumental Variable



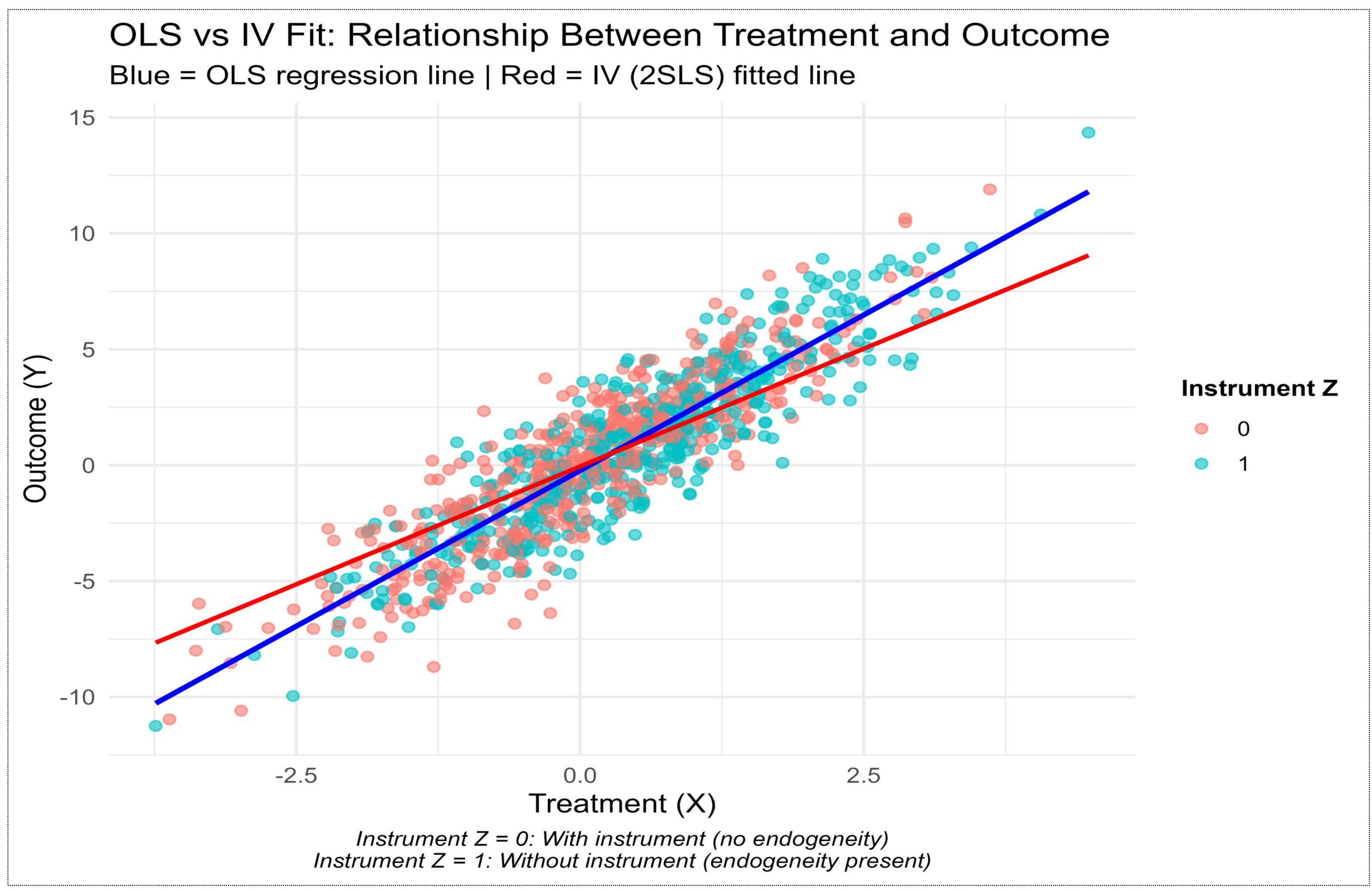
RESULTS

- In the simulated setting, OLS estimated that a one-unit increase in treatment was associated with a ≈2.68-unit increase in the outcome, while the IV estimator yielded a smaller effect of ≈2.03 units (Table 1)

Table 1: Model coefficient estimates

Model	Coefficient Estimates
Ordinary Least Square	2.68
Estimation using Instrumental variable	2.03

Figure 3: OLS vs IV fit



- **Figure 3** shows that the OLS line (blue) is steeper than the IV line (red), indicating that OLS overestimates the treatment effect while IV provides a more conservative estimate after accounting for endogeneity
- Coverage of the 95% confidence interval was closer to nominal for IV, whereas OLS intervals frequently failed to include the true effect when endogeneity was present
- **Figure 4** shows that treatment X values are lower when instrument Z = 0 and higher when instrument Z = 1, indicating a distributional shift that confirms the instrument is effectively generating variation in treatment X required for valid IV estimation

Figure 4: Distribution of treatment by instrument

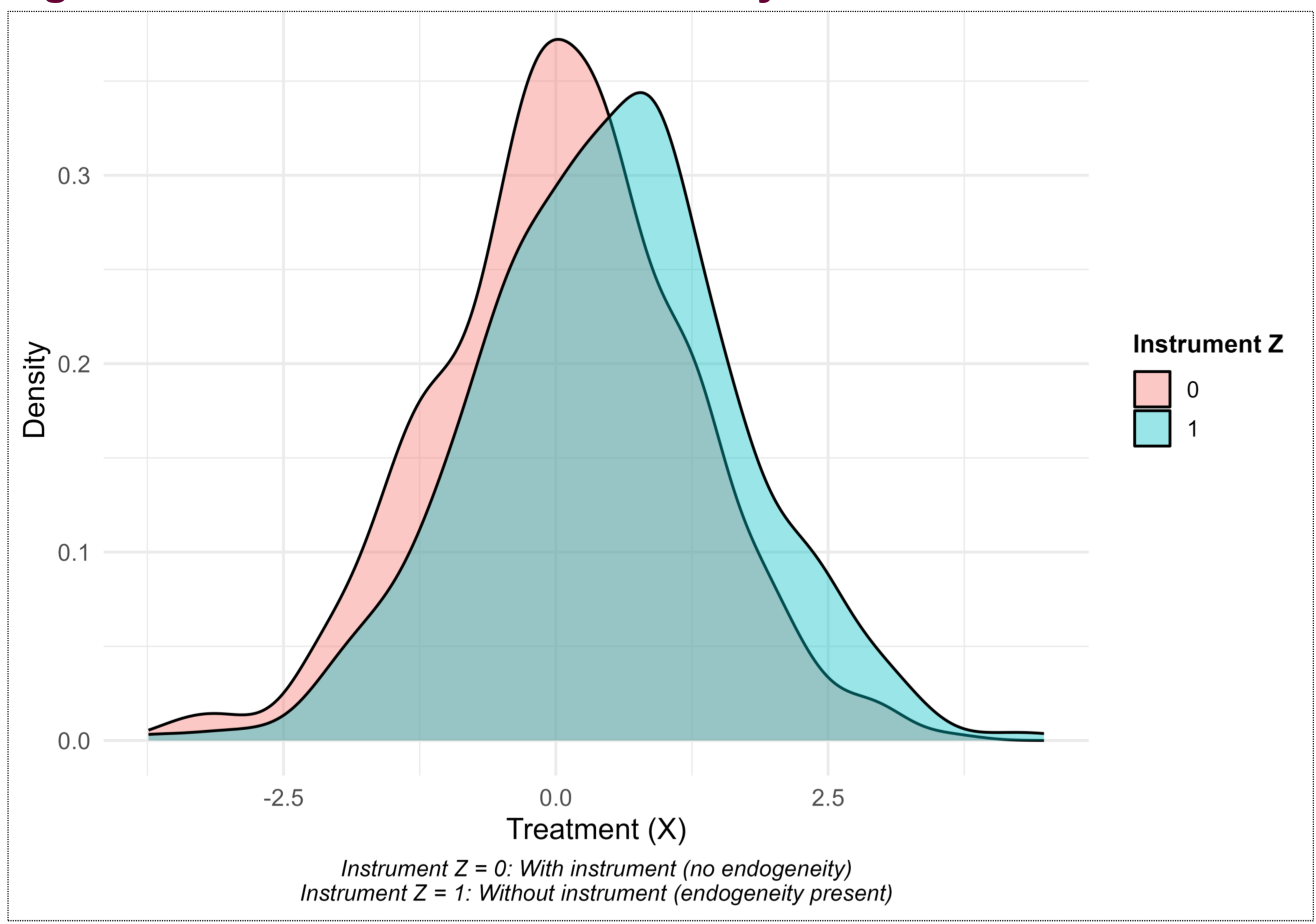
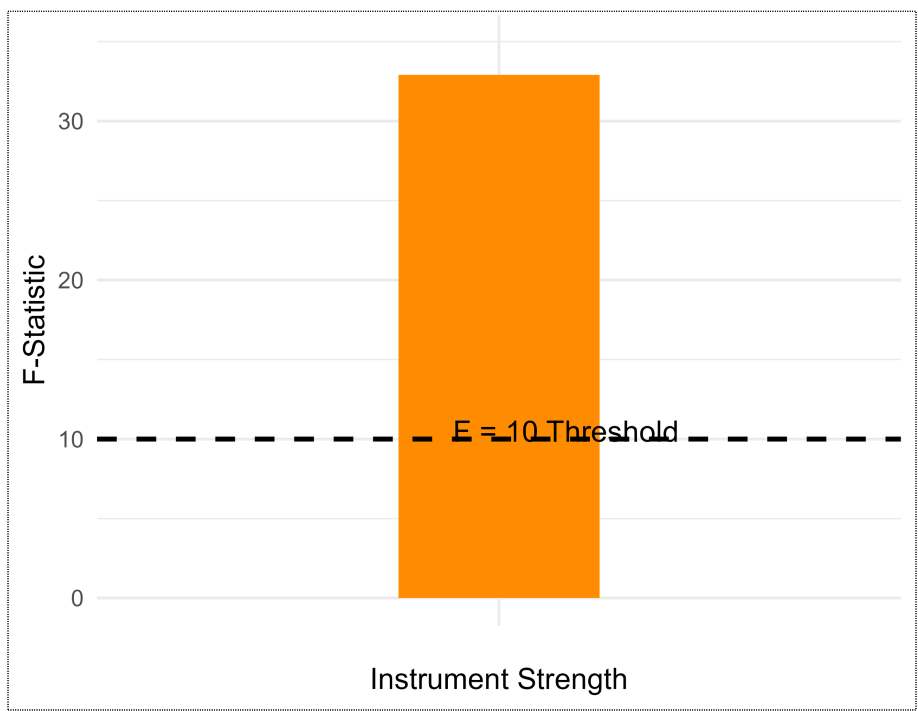


Figure 5: First-stage partial F-statistic



- The high first-stage F-statistic (~33) suggests that most of the variation in treatment is explained by the instrument rather than random noise, supporting the robustness and stability of the IV-based treatment effect estimates (Figure 5)
- Across repeated simulations, IV estimators showed reduced bias compared with OLS, particularly when endogeneity and instrument strength were substantial.

CONCLUSION

Accurate estimation of causal treatment effects is essential for healthcare decision-making and reimbursement policies. When endogeneity is present, OLS regression can yield biased and inconsistent estimates, whereas instrumental variable methods, given a valid and sufficiently strong instrument, can reduce this bias and support more credible causal inferences for HEOR and HTA decisions

References

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Correspondence: shubhram.pandey@pharmacoevidence.com

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