THE UNIVERSITY OF CHICAGO | DEPARTMENT OF STATISTICS

Master's Thesis Presentation

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"A Comparison of Mendelian Randomization Methods in the Presence of Pleiotropy"

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Abstract

Mendelian randomization is widely used to infer causal effects using genetic variants as instrumental variables, but its validity is often challenged by pleiotropy. In particular, uncorrelated horizontal pleiotropy and correlated horizontal pleiotropy violate core modeling assumptions and lead to unreliable estimation. In this study, we compare several MR methods, including IVW, MR-Egger, cML, BWMR, and MR-Horse, under different pleiotropic scenarios. We evaluate their performance in terms of type I error, power, bias, and coverage, while varying both the proportion of invalid instruments and the total number of instruments. The results show that all methods perform similarly when instrumental variable assumptions are all satisfied. Under pleiotropy, however, performance varies across methods. Increasing the number of instruments primarily reduces variance but does not resolve bias arising from model misspecification. Overall, these findings highlight that both the quality and the quantity of instruments jointly determine the reliability of MR analyses, and that the choice of MR method should be guided by the underlying data characteristics.
