

**University of California, Irvine
Statistics Seminar**

A More Credible Approach to Multivariable Mendelian Randomization

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**4-5 p.m., Thursday, Feb. 20, 2025
6011 Donald Bren Hall**

Multivariable Mendelian randomization (MVMR) uses genetic variants as instrumental variables to infer the direct effects of multiple exposures on an outcome. However, unlike univariable MR, MVMR often faces greater challenges with many weak instruments, which can lead to bias not necessarily toward zero and inflation of type I errors. In this work, we introduce a new asymptotic regime that allows exposures to have different degrees of instrument strength, providing a more credible theoretical framework for studying MVMR estimators. Our analysis of the widely used multivariable inverse-variance weighted method shows that it is often biased and tends to produce misleadingly narrow confidence intervals in the presence of many weak instruments. To address this, we propose a spectral regularized estimator and show that the estimator is consistent and asymptotically normal under many weak instruments. We demonstrate through simulations and real applications that our proposed estimator would bring more credibility to MVMR analysis.

- **Bio:** Ting Ye is an Assistant Professor in Biostatistics at the University of Washington (UW). Her research aims to accelerate human health advances through data-driven discovery, development, and delivery of clinical, medical, and scientific breakthroughs, spanning the design and analysis of complex innovative clinical trials, causal inference in biomedical big data, and quantitative medical research. Prior to joining UW, Ting completed a PhD in Statistics at the University of Wisconsin-Madison in 2019 and a postdoctoral fellowship in Statistics at the University of Pennsylvania in 2021.