

Stanford University

Department of Statistics

DEPARTMENTAL SEMINAR

4:30pm, Tuesday, April 24, 2018
Sloan Mathematics Center Room 380C

Refreshments served at 4pm in Sequoia Lounge.

Speaker: Qingyuan Zhao
*Wharton School of Business,
University of Pennsylvania*

Title: **Statistical inference in Mendelian randomization:
From genetic association to epidemiological causation**

Abstract:

Mendelian randomization (MR) can give unbiased estimate of a confounded causal effect by using genetic variants as instrumental variables (IV). Due to the increasing availability of large-scale genome-wide association studies (GWAS), a particularly attractive proposal is to automate the causal inference using published GWAS summary data. However, existing summary-data MR methods generally lack theoretical grounding. Statistically, there are at least four major challenges: measurement error in the genetic associations, invalid IVs due to pleiotropy, weak IV bias, and selection bias due to screening out weak IVs. To overcome these challenges, I will formulate the summary-data MR problem as a linear errors-in-variables regression problem with overdispersion (systematic pleiotropy) and outliers (idiosyncratic pleiotropy). This model is inspired by our observations in real data and some recent discoveries in genetics. I will present a new approach based on adjusting and robustifying the profile score function, with provable consistency and asymptotic normality when the IVs are collectively strong but may be individually weak. The robustness and efficiency of the proposed methods will be demonstrated using several simulated and real examples.

This talk is based on joint works with Jingshu Wang and Dylan Small (University of Pennsylvania), Jack Bowden and Gibran Hemani (University of Bristol), and Yang Chen (University of Michigan).