Abstract:
Most complex diseases are the result of environmental variables, genetic factors, and their interaction. In building risk models, it is important to account for each of these components to enable estimation of risk and identification of high-risk subgroups. Historically, research into the genetic determinants of disease has largely focused on the role of individual variants. However, this endeavor is complicated by the fact that most diseases are highly polygenic and result from the combined effect of many variants, each with small effect. A great deal of attention has been paid recently to polygenic risk scores, which represents the total genetic burden of a given trait. Here, I present recent work on utilizing polygenic risk scores in risk models, alongside environmental risk factors. This includes an efficient case-only method for using polygenic risk scores to identify gene-environment interactions and an expansive analysis of the combined utility of polygenic risk scores for specific diseases and mortality risk factors in predicting survival in the UK Biobank, a large cohort study. I will also touch on possibilities for future work in this area, including the use of polygenic risk scores in treatment selection.