

Polygenic score construction with mean field  
variational inference to model gene-gene  
interactions

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# Polygenic score

- ▶ Uses genome-wide SNP minor allele counts to produce a number that summarizes genetic risk for a disease of interest, like coronary artery disease
- ▶ Polygenic scores typically rely on SNP effect estimates from genome-wide association studies
- ▶ The polygenic score doesn't correspond directly to a numerical probability of disease
- ▶ Current uses include risk stratification for preventive interventions

# Constructing polygenic scores

- ▶ Existing Bayesian statistical approaches use sampling methods, like Markov chain monte carlo, to draw samples from the posterior distribution
- ▶ Such methods are time-consuming and computationally intensive
- ▶ We propose to use mean field variational methods to fit Bayesian statistical models for allele effects
- ▶ Variational inference involves using analytical solutions to approximations to the posterior distribution
- ▶ Requires less time and fewer computing resources

## Gene-gene interactions

- ▶ Existing polygenic score construction methods consider only SNP main effects and neglect SNP-SNP interactions
- ▶ We hypothesize that our variational inference methods, and the associated reduction in computing requirements, will enable construction of polygenic risk scores that model SNP-SNP interactions
- ▶ We expect polygenic risk scores that model SNP-SNP interactions (and include SNP main effects) to outperform current methods in predictive accuracy