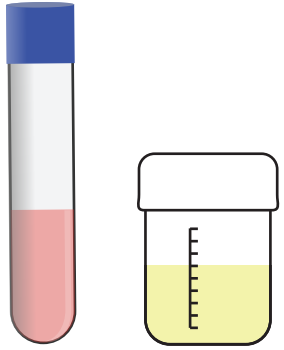
STUDY COHORT

- **UK Biobank**
  363,228 individuals
  35 serum and urine labs
  Genome array, imputation,
  HLA, and Copy number variants



ASSESSING GENETIC ASSOCIATION

A GWAS

- 5792 independent loci
- 28 rare protein-truncating variants
- 192 rare protein-altering variants
- 31 HLA allelotypes
- 10 CNVs
- 28 aggregate rare CNV loci

B Heritability

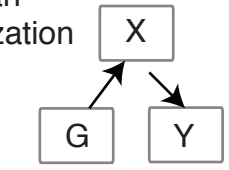
- Up to 57% heritability explained

C PheWAS

- 57 associations across 26 phenotypes for 33 LD independent coding variants

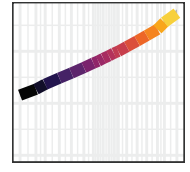
CAUSAL INFERENCE AND PREDICTION

A Mendelian randomization



- 51 causal relationships across 14 diseases & 3 quantitative traits

B PRS & PheWAS



- 70/10/20% training/validation/test
- PRS with R^2 up to 0.51
- median up to 0.24
- 139 associations $p < 10^{-4}$

C multi-PRS

- Improves prediction of complex disease;
  renal failure, cirrhosis, gout, t2d, and heart failure