**Option 1**

Aims

* Identify GxG effects on biomarker concentration to inform future drug development and identify subgroup effects for existing therapies
* Improve prediction of biomarker concentration using interaction terms

Results

* vGWAS QC
* GxG testing to identify interaction effects
* Association of GxG effects with disease (MI, heart failure, CKD, LD, T2D, Gout, )
* For disease associated GxG perform colocalization with eQTL data
* Replication of disease interaction effects (? independent cohort) + sibs
* Improvements in variance explained by use of gxg variants
* GxE – colocalize main effect on gene with eQTL data. MVMR to estimate GxE effect?
* Describe the occurrence of vQTLs at lipid drug target loci and compare results with RCT evidence
* Colocalize lipid vQTLs with e/pQTL data and discuss findings in relation to drug development

Discussion

* Comparison with OSCA
  + Tool can use continuous genotype dosages values unlike OSCA
  + OSCA uses Levene test which should give high T1E with skew and kurtosis (this is what we saw with B-F). Need to compare T1E & power.
  + OSCA tool does not report mean effect only variance effect which is then require additional linear model
  + OSCA effect size is not accurate, snp effect is non-linear

Supplementary

* Trait distributions
* Power and T1E simulations
* Rank normal transformation induces mean-variance effect leading to T1E
* Log scale

Supplementary Figure. Histogram of biomarker distribution

Diagram

Description automatically generated

SD units.

Supplementary Figure. QQ plot of biomarker distribution

A picture containing shape

Description automatically generated

SD units.