Causal exposures
Heritable factors
Biochemical GWAS
Lung function GWAS
LDSC
Druggable biological pathway
Latent causal variable (LCV)
Polygenic score in pathway
Mendelian randomisation
Transcriptome-wide association
$\chi^2 = Z_{Trait\ 1} * Z_{Trait\ 2}$
Chi square
LD score
$r_g > 0$
$\hat{\beta}_1, \hat{\beta}_2, \hat{\beta}_3, \hat{\beta}_4, \ldots, \hat{\beta}_k$
Effect size of SNPs in biological pathway (m) on lung function
$\frac{q_2^2}{q_1^2} = (r_g^2)^{GCP}$
$q_2 < q_1 < 1$
q_2 (LCV effect on lung function)
q_1 (LCV effect on exposure)
Lung function
Exposure
G
LCV
β_2
β_1
q_2
q_1
$PES_i = \sum_{i=1}^{m} \hat{\beta}_j G_{ij}$
Density
Pharmagenic enrichment score [PES]
Confounder
IV
γ
Exposure
Γ
Lung function
$\beta_{Exposure \rightarrow Lung\ function} = \Gamma/\gamma$
Z score
Chromosome
Antagonist
Agonist
↓ expression
↑ lung function
↑ expression
↑ lung function