BASICS OF GENOMICS

Basic Genome-wide Association Studies (GWAS)

After this module you should be able to explain the following terms and ideas.

KEY TERMS

Phenotype, Mendelian randomization, case-control, continuous phenotype, full model, marginal model, covariates, true effect, estimated effect, top hit, GWAS locus (loci)

CONCEPT QUESTIONS

What is the difference between a continuous trait and a case-control trait?

Why is it that a genetic variant can affect a phenotype but a phenotype cannot affect a genetic variant.

You run a GWAS on height and test 2,000 independent genetic variants for association with height. What significance threshold should you use to control the FWER at a 0.05 rate? Why is this necessary?

What is the difference between a true effect size and an estimated effect size? How are they represented?

If a genetic variant has a significant p-value, why is it not right to assume that that genetic variant has a non-zero effect on the phenotype?

What is the difference between a top-GWAS hit and a GWAS locus? Why do GWAS loci exist?

If you don’t account for covariates such as population structure, what risks do you run?

You run a height GWAS in Europeans and in Africans. Do you expect top hits in Europeans to also be top hits in Africans? Why or why not?

Why is it appropriate to call a top GWAS hit a risk/trait associated variant and not causal variant?