J. Jedediah Smith

Week 2 Paper Questions

BIFX 504-1

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1. As you read through the article, define these terms **IN YOUR OWN WORDS** (Give an example if you are having trouble explaining what you mean).

Linkage Analysis: Searching for disease genes by using genetic markers.

Heterozygosity: Having two different alleles for the same gene, or the part of a population that is heterozygous.

Fine-Scale Mapping: Technique dependent on functional analysis and experimentation. Can be used to help identify causal variants.

Imputation: The insertion of new information, like adding sequence-level variants into samples genotyped by SNP-arrays.

Heritability: How likely a trait is to be passed on to the next generation.

Polygenic Risk Scores (PGS): Uses GWAS data and other information about the effects of multiple genetic variants to help predict someone’s trait value.

Indirect Genetic Effect: When a genetic variant effects phenotype via the environment. For example, a variant that causes increased educational attainment as a direct effect may have an additional indirect effects through parental nurture.

Pleiotropy: Uses genetic effects to help contribute to the associations between traits. Basically, if a variant is already associated with one trait, it is more likely to be associated with another.

Assortative Mating: Non-random mating that results in a trait variant with casual effects becoming correlated with other variants that have casual effects.

Principal Component (PC) Adjustment: Helps account for some of the GWAS confounding effects by removing direct effects that are associated with environmental confounding.

LD Score Regression (LDSR): Used to help differentiate between confounding and causal effects on GWAS test statistics by estimating population stratification.

Mendelian Randomization (MR): Used to help enhance causal inference through genetic data. If one trait predicts a second, and that second predicts a third, then the relationship between this first and third trait can be used to potentially rule out other confounding effects.

Gene-by-Environment Interactions: When the effect of a genetic variant changes depending on the environment. One example is the relationship of FTO variants and the effects of physical activity on BMI.

1. Identify three important concepts from the article and write an exam question that tests understanding of each concept. Answer all three questions.

Concept 1: Basics of GWAS

* Q: What is the typical aim of Genome-Wide Associated Studies (GWAS)?
* A: To sequence a genome and test each single-nucleotide polymorphism (SNP) for association with a particular phenotype.

Concept 2: GWAS Confounding Effects

* Q: Why is assortative mating considered a confounding effect of GWAS?
* A: The non-random mating results in trait variants with casual effects becoming correlated with other variants that have casual effects. This association then makes it difficult to distinguish between the two variants and effects.

Concept 3: Adjusting for GWAS Confounding Effects

* Q: How might a scientist adjust for the different confounding effects of GWAS?
* A: They could use Principal Component (PC) Adjustment, which helps remove direct effects related to identified confounding effects. Alternatively, they could use Fitting Linear Mixed Models (LMMs) which involves a regression of SNPs with their effects modelled as random.