Environment vs Genetics: Predicting Common Disease Risk in the UK

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Phenotype: Type 2 Diabetes, Lung Function, Coronary Artery Disease, Atrial Fibrillation

Genotype: Genetic Variants

Exposures: Pollutants, Physical Activity, Nutrients + Diet, Education Attainment

$P = G + X$
Genotype

Genome Wide Association Studies (GWAS)
- Identify variants associated with phenotype
- Genome wide significance of $p=5 \times 10^{-8}$

GWAS Catalog
- ~4000 publications and >138,000 associations (2019 May)
- [https://www.ebi.ac.uk/gwas/](https://www.ebi.ac.uk/gwas/)

Common disease, Common variant model
- Most common disorders are due to a large number of alleles
Polygenic Risk Scores (PRS)

Combines individual effects of all GWAS variants across the genome to predict risk

Accounts for correlation between variants (linkage disequilibrium)

Theoretically maximizes power of GWAS

Liu and Kiryluk 2018
Identified individuals with greater than threefold increased risk.
Environmental exposure variables can be extracted based on category name.

Only those with <10% missing entries were retained.

Deemed Benjamini-Hochberg False Discovery Rate (FDR) of <0.05 as significant.
Prevalence of disease in each of the 100 groups binned according to the percentile of significant eXposures.

**T2D**: type 2 diabetes

**CAD**: coronary heart disease
### Conclusions:

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<th>Phenotype</th>
<th>Genotype</th>
<th>Exposures</th>
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- Information in large databases like the UKBiobank allows us to study associations between environment and phenotype.

- In addition to genetics, environmental exposures also provide critical information that can help improve clinical care in complex common diseases.
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