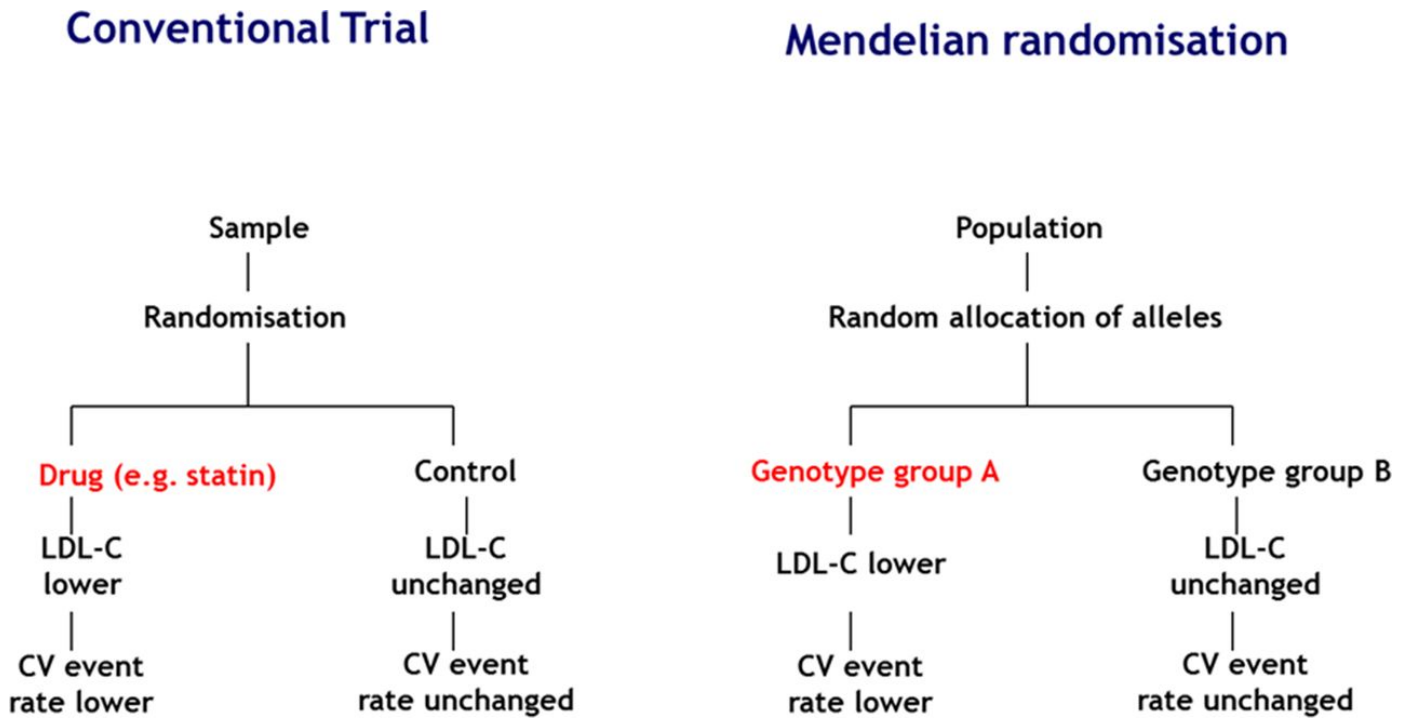
Using genome data to discover medicines

John Whittaker

Why is genetics useful in drug discovery?

- Statins *target* HMG-CoA reductase hence reducing LDL-C and cardiovascular risk
- Genetic variants exist which also reduce HMG-CoA reductase and can mimic a randomised trial of statins

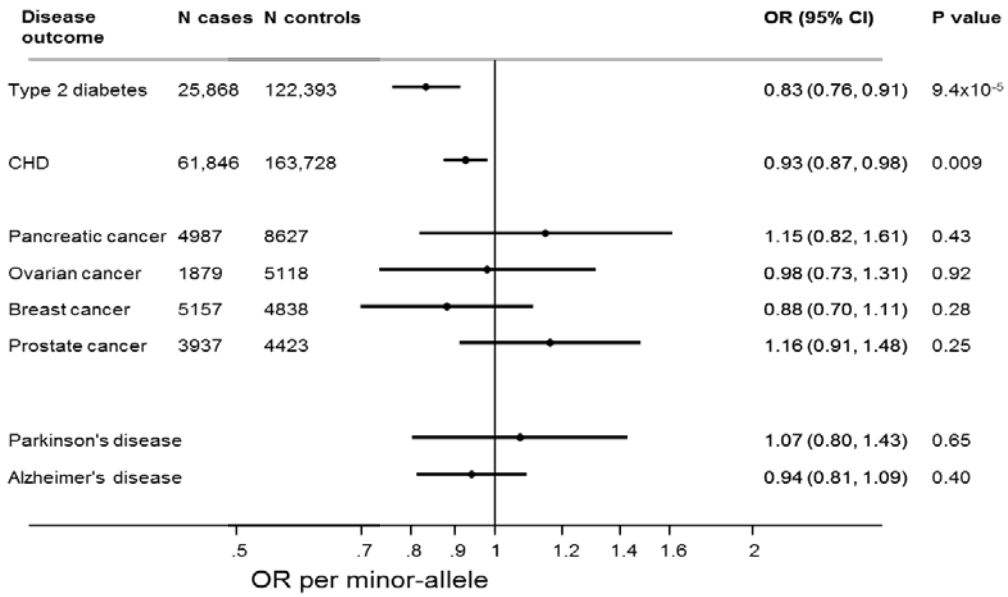


How do we use this?

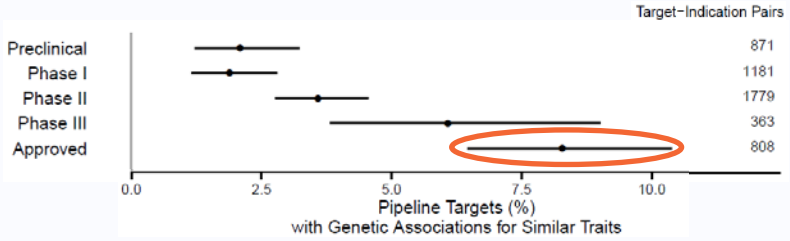
New targets and understanding existing drugs

GLP1R-agonists

- Effective and becoming widely used for T2D
- Cardiovascular risk?
- We found a (rare) variant that mimics drug mechanism of action



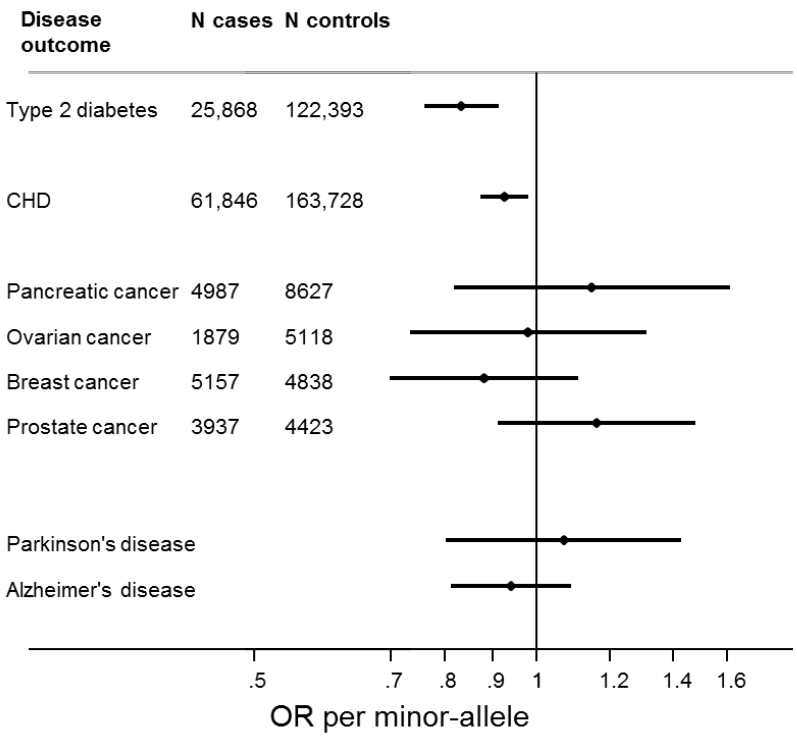
Drugs with human genetic information >2x more likely to be successful



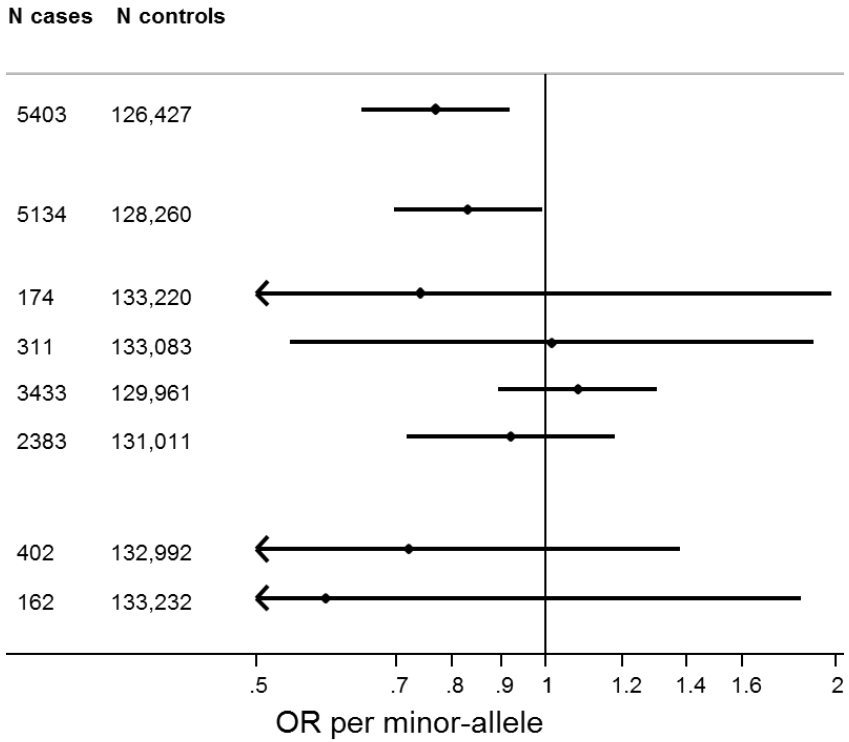
Nelson et al, 2015 Nature Genetics

Why is UK Biobank transformational?

>1.5 years and >1000 emails



1.5 hours and 3 emails



What's next?

The genome

- Exome sequencing: then the whole genome?
- Understanding *how* genetic variants affect disease risk

Phenotypes

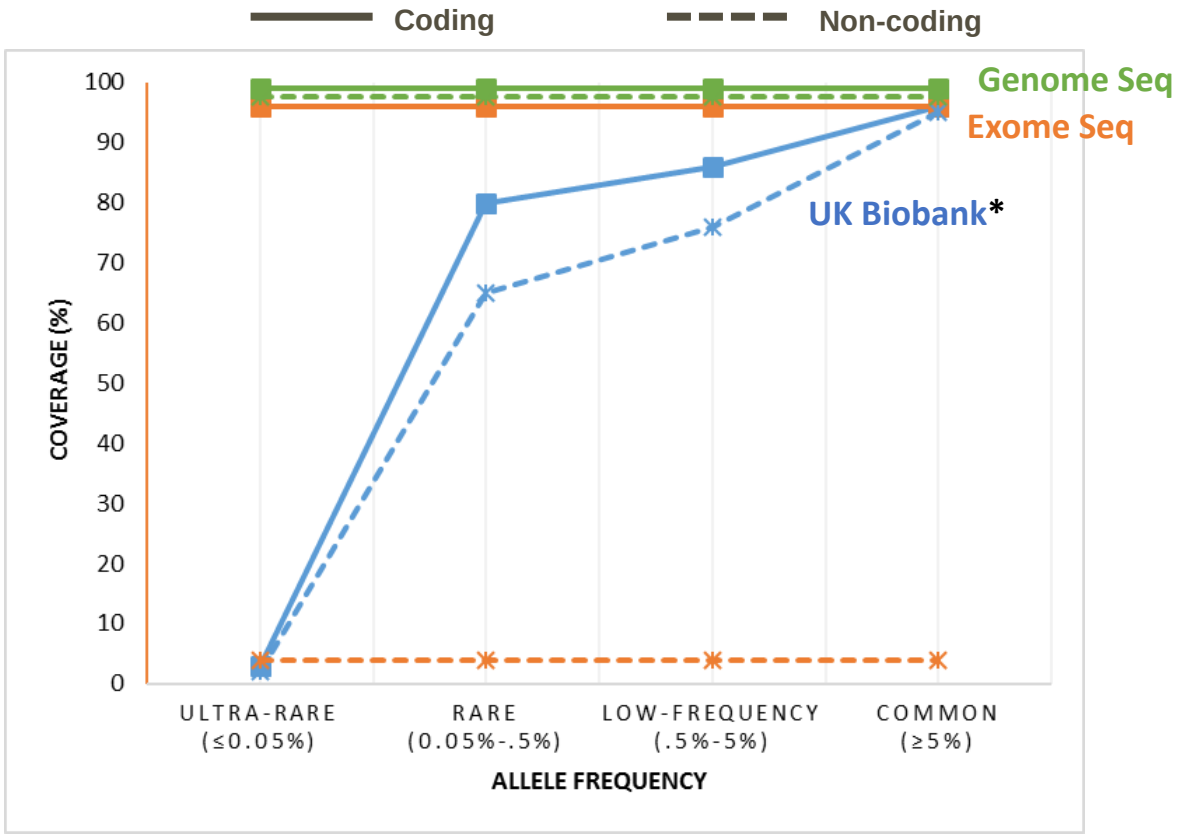
- Blood biomarkers, imaging, etc
- Disease time course: emphasis on progression

Size

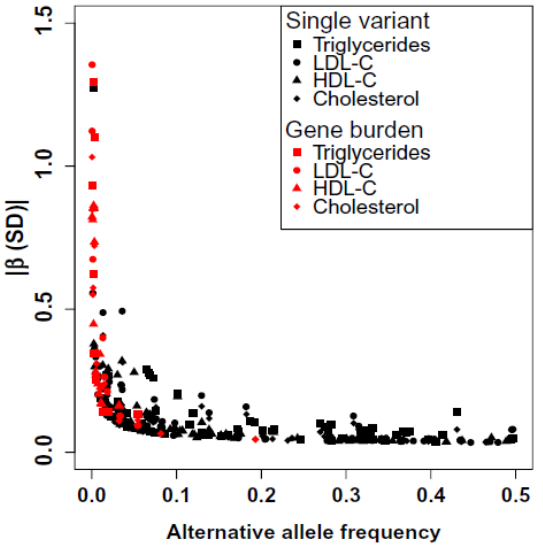
- Federated analysis across multiple biobanks/cohorts?
- Routine collection of DNA in healthcare?

backup

Comparison of genotyping options



*Coverage reported as imputation quality (r^2)



Dewey et al. (2016) Science 354:aaf6814