A GWAS for all in the WHI

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The Rationale

• All human traits have a genetic component
• Large numbers needed for genetic discovery
  • Even larger for gene-environment and gene-gene interactions
  • Modest effects (for both common and rare variants)
• Era of large scale molecular epidemiology studies is here!
  • UK Biobank (500K), MVP (>550K), China Kadoorie Biobank (510k)
• Opportunity for more collaborations and to lead studies
• Maximally leverage investment in WHI biobank
• ↓↓ Cost: genotyping ~800k carefully selected polymorphisms: $45-50 / sample.
• Now easy to add ~15M variants (>0.1%) via imputation
The Rationale (con’t)

• Large number and breadth of adjudicated outcomes
  • Cancer, CVD, Linkage to CMS

• Repeated measures of important health related traits:
  • Diet, alcohol, coffee, sleep, psychosocial, osteoporosis, fractures exercise, etc.

• Many other unique phenotypes
  • Bone density, body fat, biomarkers, reproductive, cognition, MRI, mammography, weight loss response to diet....

• About 50,000 participants already have GWAS or Whole Genome Sequencing. Another 96,000 more have genetic (dbGaP) consent.

• Ample blood for multi-omic studies – genetics always the anchor
The Challenge

• ~96k need genotyping, ~45k need DNA extraction

• Total Cost: ~$8M (< 4 R01s)
  • $4.7M genotyping + $2.25M DNA extraction + $1M salaries/computing
  • DNA extraction could drop to $0.8M if done outside academic labs

• Ideally, genotyping all in “Year 1 and 2” to maximize scientific utility, and reduce batch effects

• How to fund?
  • Not possible with a regular R01
  • NIH sponsored Center of Inherited Disease Research?
  • Super R01 (a. >$0.5-1.5M /year, or b. >1.5M)?
  • Industry (e.g. Regeneron-UK Biobank ESP)?