GWAS on educational attainment

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Progress

- Established connections with
  - Over 50 GWAS cohorts
  - Major social science data providers (HRS, PSID, WLS)
- Database of available social science phenotypes
- Infrastructure and experience to facilitate large scale GWAS efforts
- Qualified meta-analysts
- http://www.ssgac.org

Progress

- Educational attainment:
  - Widely measured
  - Measures can be harmonized (ISCED)
  - Relevant in medicine and social sciences
  - Moderately heritable
    - Taubman 1976; Miller, Mulvey and Martin 2001
  - However, it's biologically distal
- Analysis plan distributed in Feb 2011
- Deadline for uploading results was Jul 2011
- 5 conference calls
- 42 cohorts uploaded (N ~ 105,000)

Meta-analysis

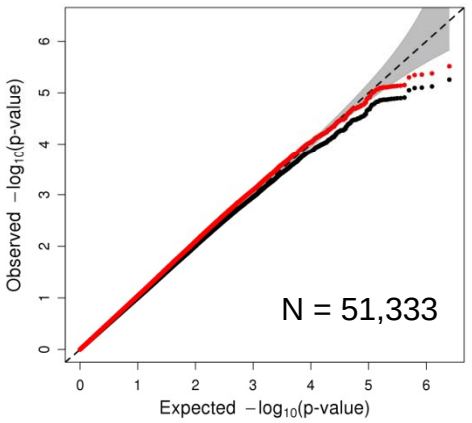
- Analysts:
  - Niels Rietveld (Economics, Erasmus U Rotterdam)
  - Nico Martin (Queensland Institute of Medical Research)
  - Jamie Derringer (Psychology, U Minnesota)
- Methodological advise:
  - Sarah Medland (Queensland Institute of Medical Research)
- Quality control:
  - *MAF* > 1%
  - Imputation quality R^2 > 40% (MACH and Impute)
  - Lambda < 1.05
  - Cohort-specific QQ and Manhattan plots

Issues

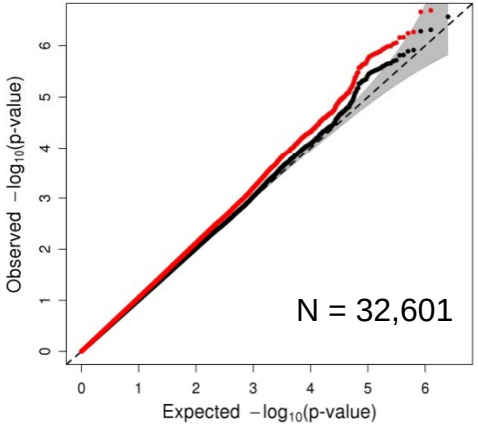
- A lot of follow-up work
- ¼ of the uploaded results looked unreasonable or indicated problems
  - Duplicate SNPs with different *p*-values
  - Inflated QQ plots (often small cohorts & low MAF)
  - Extremely low *p*-values for some SNPs in only one or two studies
- Results are preliminary and based on 80% of all cohorts (N ~ 85,000)
- Two model specifications
  - OLS on educational attainment in US schooling years (ISCED)
  - Logit on college degree

QQ plots educational attainment

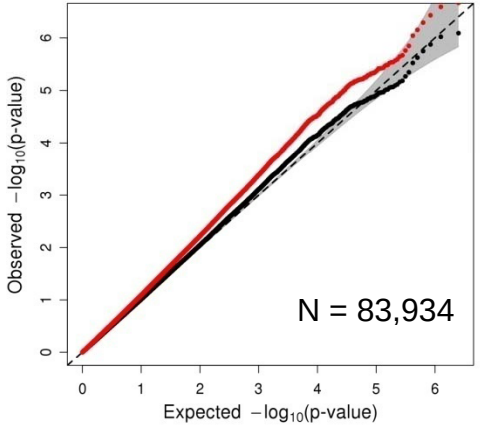
females (edu_years)



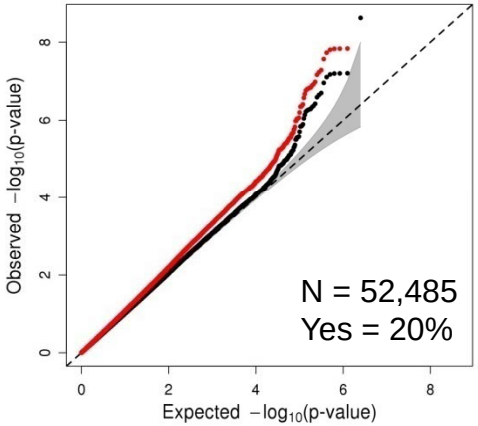
males (edu_years)



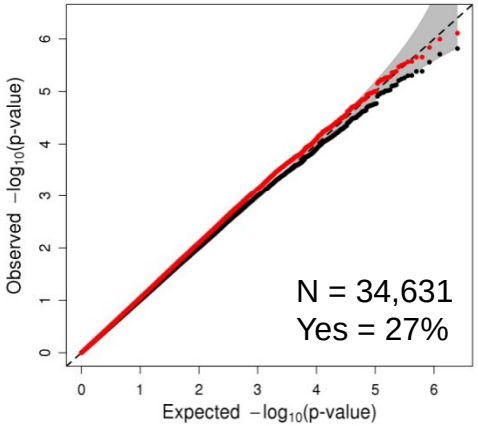
pooled (edu_years)



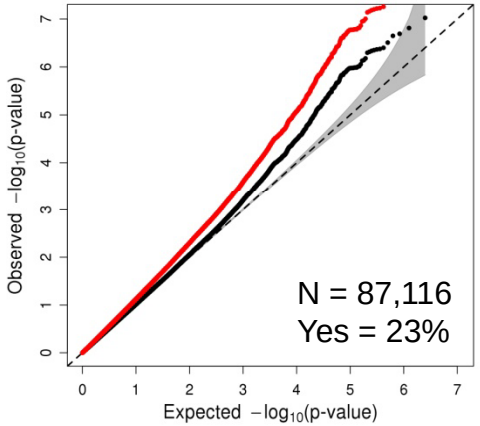
females (college)



males (college)



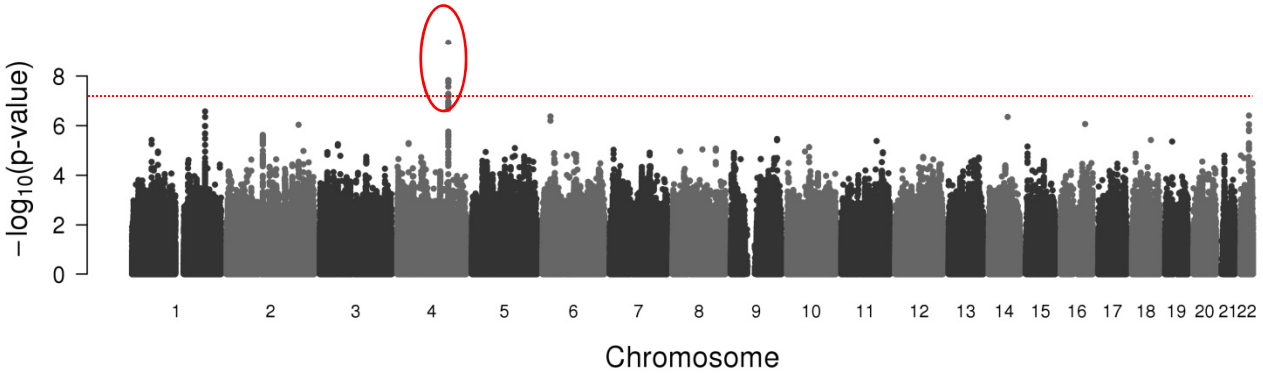
pooled (college)



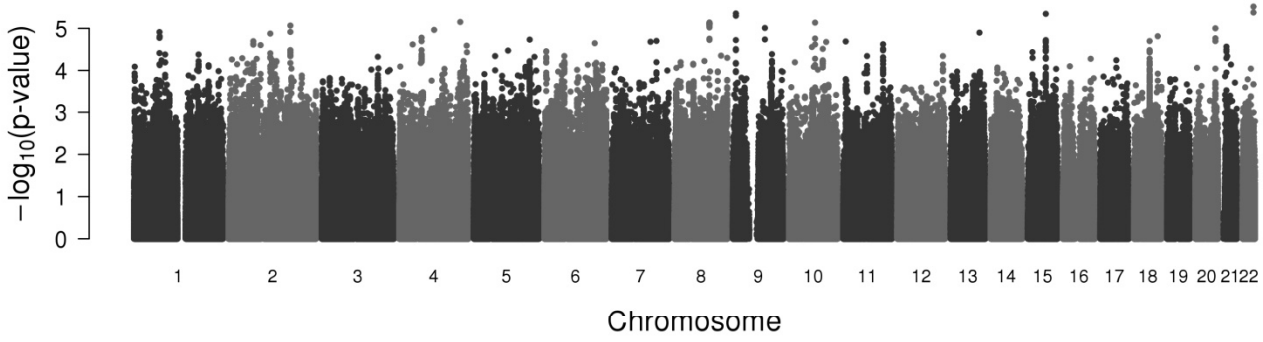
Manhattan plots females

females (college), single GC, N = 52,485:

Genome-wide significance >7.3



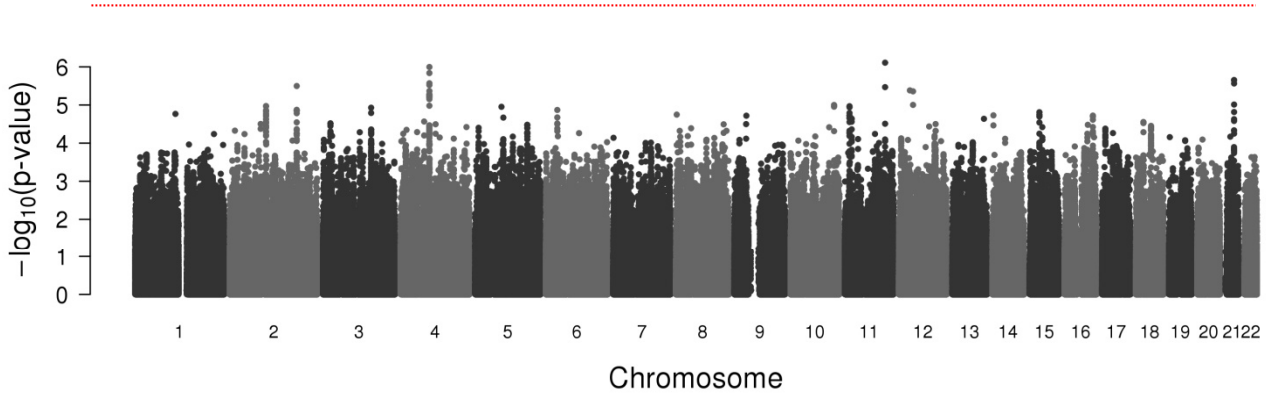
females (edu_years), single GC, N = 51,333:



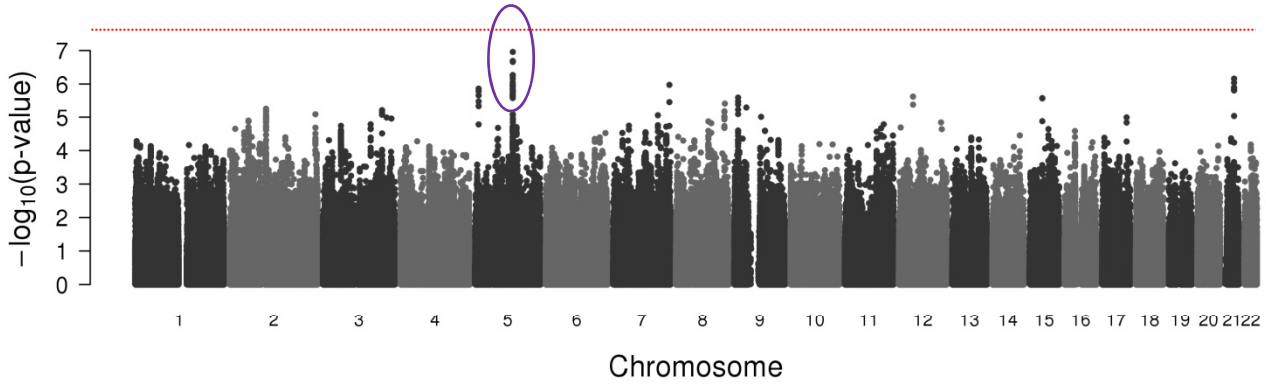
Manhattan plots males

males (college), single GC, N = 34,631:

Genome-wide significance >7.3



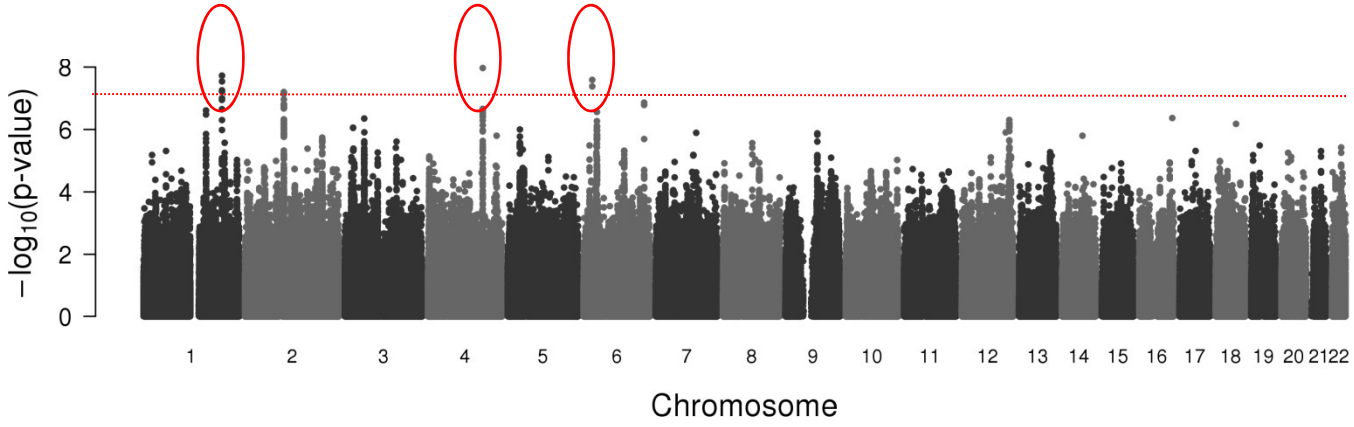
males (edu_years), single GC, N = 32,601:



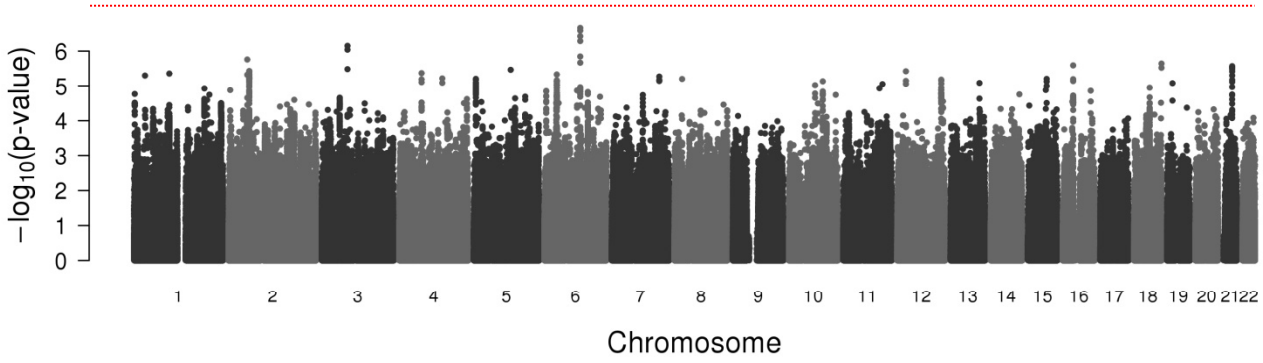
Manhattan plots pooled

pooled (college), single GC, N = 87,116:

Genome-wide significance >7.3



pooled (edu_years), single GC, N = 83,934:



Next steps

- Continue follow-up and QC
- Invite cohorts for replication stage
  - First in-silico
  - Then maybe wet-lab, if something replicates
  - Goal: N > 30,000 replication samples
- Additional analyses

Lessons learnt

- Effect sizes of common SNPs are very small
  - Top hits odds ratios: 0.9; 1.1
- Large *N* and phenotype harmonization are important
- Looking at different proxies of the same phenotype and the tails of the phenotype distribution is a good idea
- QC, follow-up and logistic management take a lot of time

80% power calculations for college, given phenotype distribution and *N*