**Childhood and adolescent internalising problems: GWAS of ~250k observations points to heterogeneous genetic architecture**

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**INTRODUCTION**
- Early symptoms of anxiety & depression are associated with the development of mood disorders in later life
- Little is known about the genetic architecture of childhood and adolescent internalising problems

**METHODS**
- 125 univariate GWASes in 22 cohorts of European ancestry, across Europe, Australia, and the US
  - Repeated measurements between ages 3 – 18
  - 5 raters (mother, father, self, teacher, co-twin)
  - 11 measures (most common: CBCL & SDQ)
- N-weighted meta-analysis to adjust for sample overlap due to repeated measurements

**PRELIMINARY RESULTS**
- 71k sample size, 250k observations
- No significant hits, SNP h2 = 0.03 (SE 0.008)

**Genes**
- 3 genes identified: prior associations with depression & antidepressant response

**Genetic correlations**
- Significant r_g with depression, schizophrenia, & wellbeing

**Enrichment**
- Brain areas show most enrichment (but not significant)

**NEXT STEPS**
- Stratify analyses to identify homogenous genetic effects based on age, rater, or instrument
- Based on above, GenomicSEM will be used to run a common factor GWAS to examine if SNP effects act via latent genetic factor(s)
- Gene-set analyses will be performed to gain insight into specific biological pathways

**DISCUSSION**
- Our study provides insight into the etiology of internalising problems
- Phenotypic heterogeneity of internalising problems is likely to underlie the lack of significant hits
- Stratified analyses will shed further light on the genetic architecture

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