

Meta Analysis

GWAS is performed on millions of SNPs. Because of multiple testing, we use very stringent thresholds for statistical significance. This can greatly reduce power and may not be sufficient to detect associated SNPs. Combining information across studies will improve power.

The objective of meta-analysis is to combine results from multiple studies to improve power and get more precise effect estimates.

Limitations of Pooling Raw Data

- May not be possible because of confidentiality restrictions
- May not be desirable because of heterogeneity
 - Differences in population, study design, underlying risk, measurements, etc.

Originally meta-analysis was used to combine results from published studies with small samples to improve power. This is subject to **publication bias**, only studies with significant p-values are chosen so we are more likely to see a positive effect. Not an issue in GWAS meta-analysis since ALL results are included regardless of significance.

Meta-Analysis of a Single SNP

Collection of K studies to test the same null hypothesis. Each study provides an estimate, $\hat{\beta}$, of the effect size and a p-value for testing the null hypothesis.

The key assumption is independence of study results, no subjects should appear in more than one study.

The first step in a meta-analysis is to identify a consistent measure from each study to be summarized (OR, regression coefficient and SE, p-value from chi-square association).

We can use Fisher's method or Stouffer's method, and that's all the information I need for now.

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