

MODULE 5: What do we know about the genetics of common, complex diseases?

Published Genome-Wide Associations through 12/2012

Published GWA at $p \leq 5 \times 10^{-8}$ for 17 trait categories



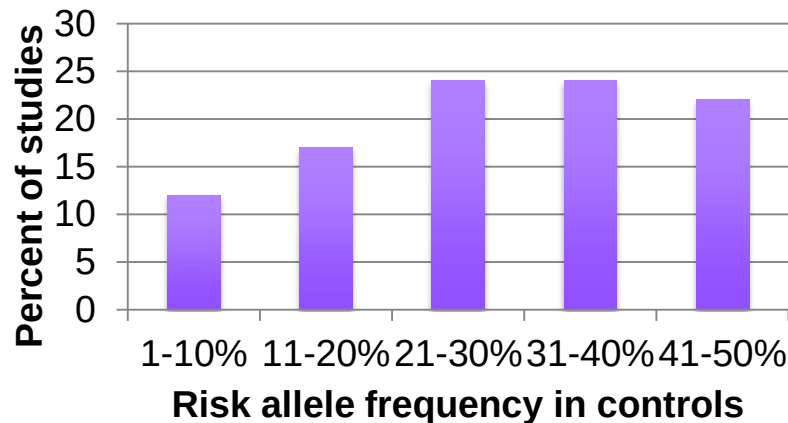
- Digestive system disease
- Cardiovascular disease
- Metabolic disease
- Immune system disease
- Nervous system disease
- Liver enzyme measurement
- Lipid or lipoprotein measurement
- Inflammatory marker measurement
- Hematological measurement
- Body measurement
- Cardiovascular measurement
- Other measurement
- Response to drug
- Biological process
- Cancer
- Other disease
- Other trait

As of 03/13/14, the catalog includes 1836 publications
and 12756 SNPs.

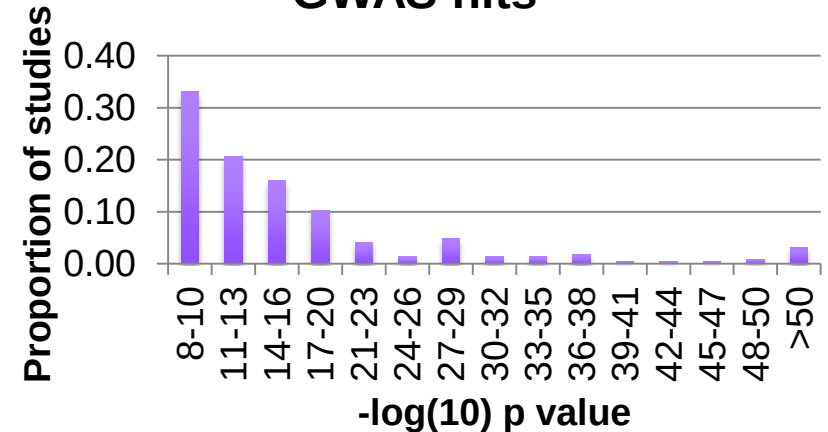
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What are we finding?

Average risk allele frequencies in GWAS

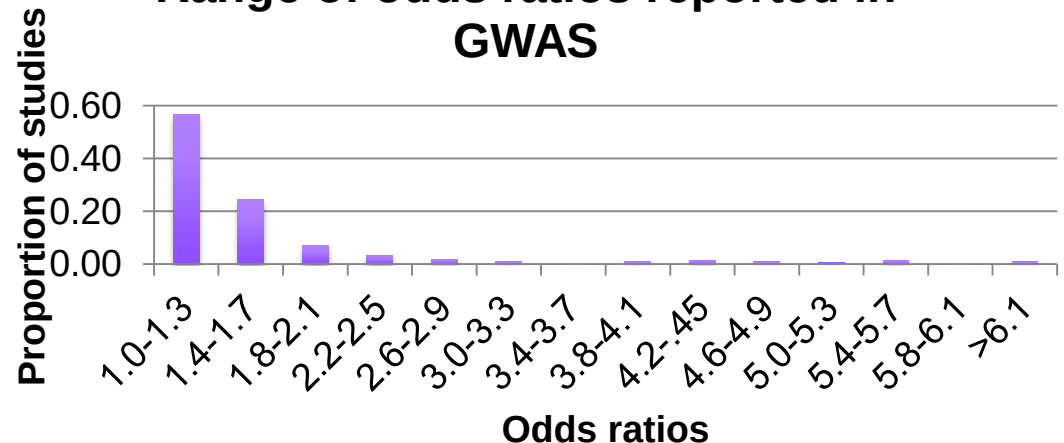


P value distribution among genome-wide significant GWAS hits



- Highly significant associations
- Common SNPs with weak effects... i.e. small increased risk, not diagnostic

Range of odds ratios reported in GWAS



Many SNPs for each disease/trait

Disease/trait	# GWAS loci	% heritability explained
Type 1 diabetes	41	~60%
Fetal hemoglobin	3	~50%
Macular degeneration	3	~50%
Type 2 diabetes	39	20-25%
Crohn's disease	71	20-25%
LDL/HDL levels	95	20-25%
Height	180	~12%

GWAS SNPs explain only a fraction of the heritability

Limitations of GWAS...what we're missing

- Common SNPs not tagged well
- Rare variants
- Other types of variants (CNV, etc)
- Epistatic effects (gene-gene interaction)
- Effects of gene*environment interaction

THE END