ACCURACY AND ANALYSIS OF GWAS (GENOME WIDE ASSOCIATION STUDIES)

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GWAS BACKGROUND

- GWAS identifies genetic variations associated with diseases
  - Benefits
    - Detection, treatment, prevention
    - Personalized medicine
  - Ethics
    - Prenatal testing
  - Refinement
    - Increase efficiency and decrease cost

1 in 11

Americans have

DIABETES

*American Diabetes Association (2012)

1

million

Americans have PARKINSON'S DISEASE

*Parkinson's Disease Foundation (2015)

1

American dies from **HEART DISEASE** every

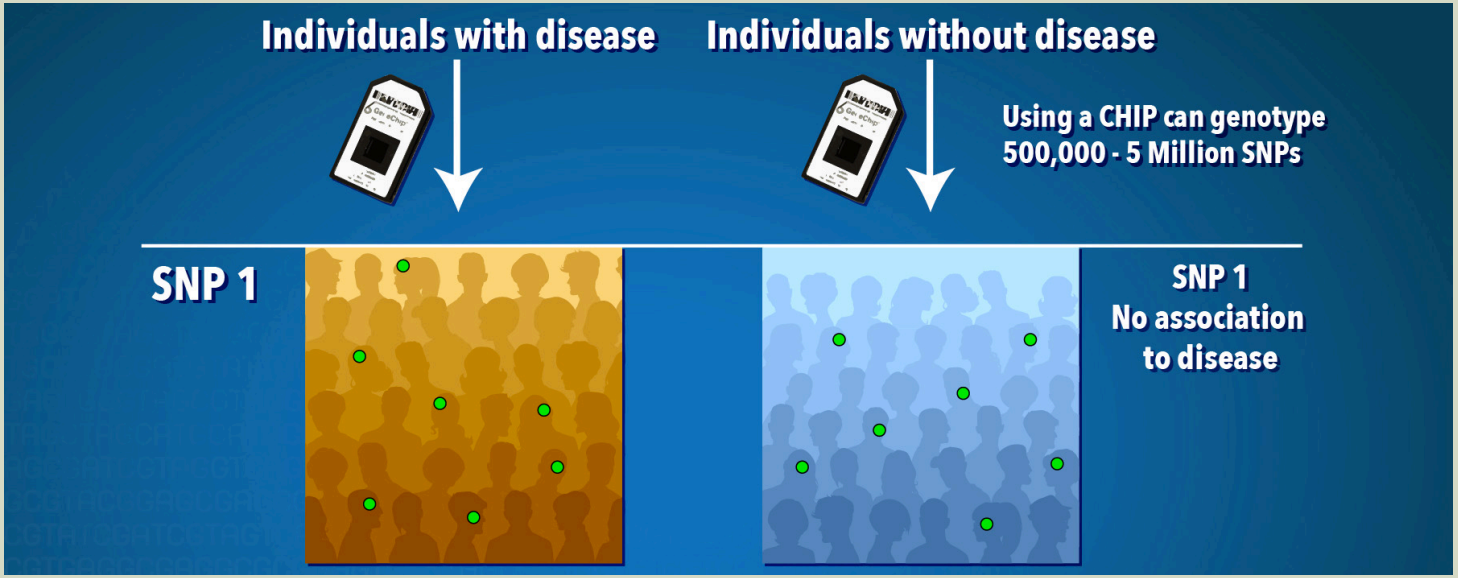
90

seconds

*American Heart Association (2015)

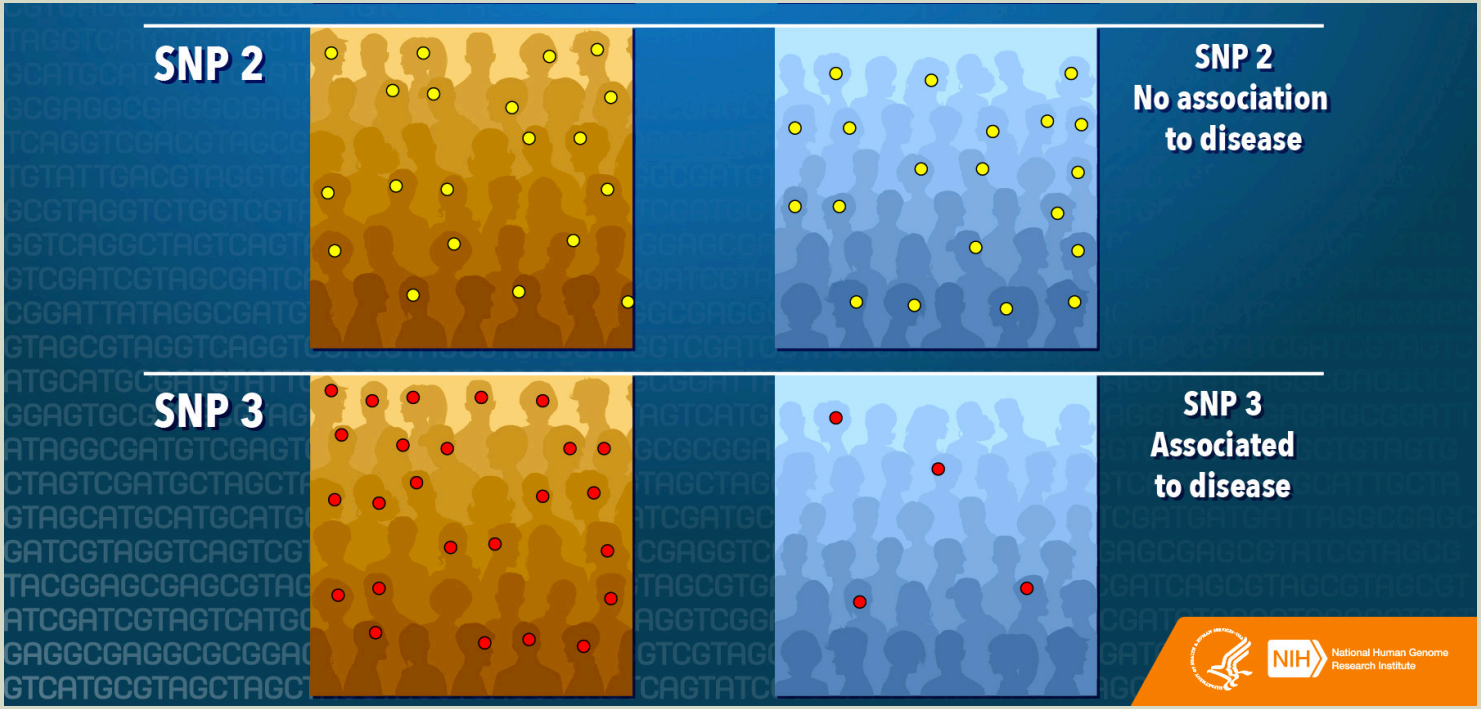
GWAS METHOD

- Compares SNPs between those with and without the disease



GWAS METHOD

- Compares SNPs between those with and without the disease

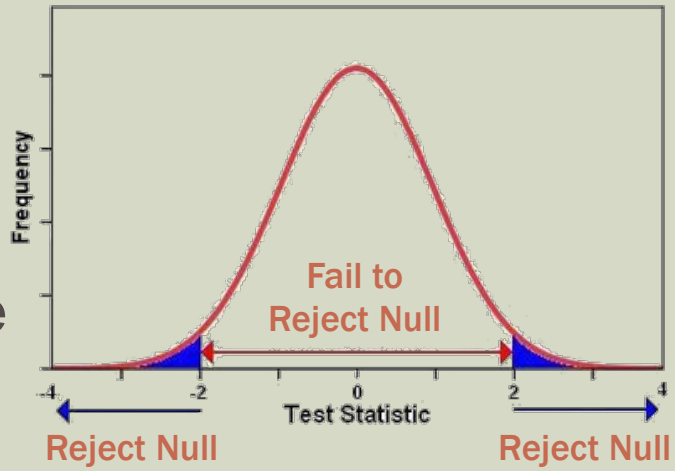


GWAS METHOD

- Compares SNPs between those with and without the disease
- Each disease
  - Many experiments
  - Each experiment
    - Series of associated SNP
      - Each SNP has a p-value

STATISTICS BACKGROUND

- Hypothesis testing
  - Null hypothesis
    - Observations are due to chance
  - Alternative hypothesis
    - Observations are influenced
  - Test statistic
    - Standardized value calculated from sample
  - P-value
    - Pr(observing the test statistic, assuming H_0 is true)



WHAT DOES THE DATA MEAN?

- Accuracy
  1) How accurate were the studies compared to each other?
- Analysis
  1) Given a SNP:
     - What disease(s) are associated with it?
  2) Given a disease:
     - Which SNP(s) are associated with it?
     - Which chromosome(s) are more associated with it?

DETERMINING ACCURACY OF GWAS DATA

- Consolidate SNPs from all studies and filter out >0.05 p-values

[First experiment]

DETERMINING ACCURACY OF GWAS DATA

- Consolidate SNPs from all studies and filter out >0.05 p-values

Data set HGVRS3891

Top **35** associations for Coronary Artery Disease (HGVPM3648) from data set HGVRS3891(35 in database)

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Experiment: Association analysis experiment for coronary artery disease (HGVE3733)
Data set: Coronary artery disease analysis (HGVRS3891)

Rank	Identifier	Accession	Region	p-value	-log p-value	Effect size	Risk allele	Related data	Links
1	HGVM1880766	rs1558902	chr16:53803574..53803574	0.04317	1.365	Not supplied	Not supplied	Details	Not supplied
2	HGVM5089460	rs12444979	chr16:19933600..19933600	0.06869	1.163	Not supplied	Not supplied	Details	Not supplied
3	HGVM3473352	rs10767664	chr11:27725986..27725986	0.1325	0.878	Not supplied	Not supplied	Details	Not supplied
4	HGVM1405127	rs2531995	chr16:4013467..4013467	0.1373	0.862	Not supplied	Not supplied	Details	Not supplied
5	HGVM118737	rs887912	chr2:59302877..59302877	0.1735	0.761	Not supplied	Not supplied	Details	Not supplied
6	HGVM2862188	rs4929949	chr11:8604593..8604593	0.1765	0.753	Not supplied	Not supplied	Details	Not supplied
7	HGVM1872195	rs1514175	chr1:74991644..74991644	0.1856	0.731	Not supplied	Not supplied	Details	Not supplied
8	HGVM759097	rs543874	chr1:177889480..177889480	0.2111	0.676	Not supplied	Not supplied	Details	Not supplied
9	HGVM3675423	rs10968576	chr9:28414339..28414339	0.2118	0.674	Not supplied	Not supplied	Details	Not supplied
10	HGVM498801	rs571312	chr18:57839769..57839769	0.2363	0.627	Not supplied	Not supplied	Details	Not supplied

DETERMINING ACCURACY OF GWAS DATA

- Consolidate SNPs from all studies and filter out >0.05 p-values

[Second experiment]

DETERMINING ACCURACY OF GWAS DATA

- Consolidate SNPs from all studies and filter out >0.05 p-values

Data set HGVRS3892

Top **35** associations for Coronary Artery Disease (HGVPM3648) from data set HGVRS3892(35 in database)

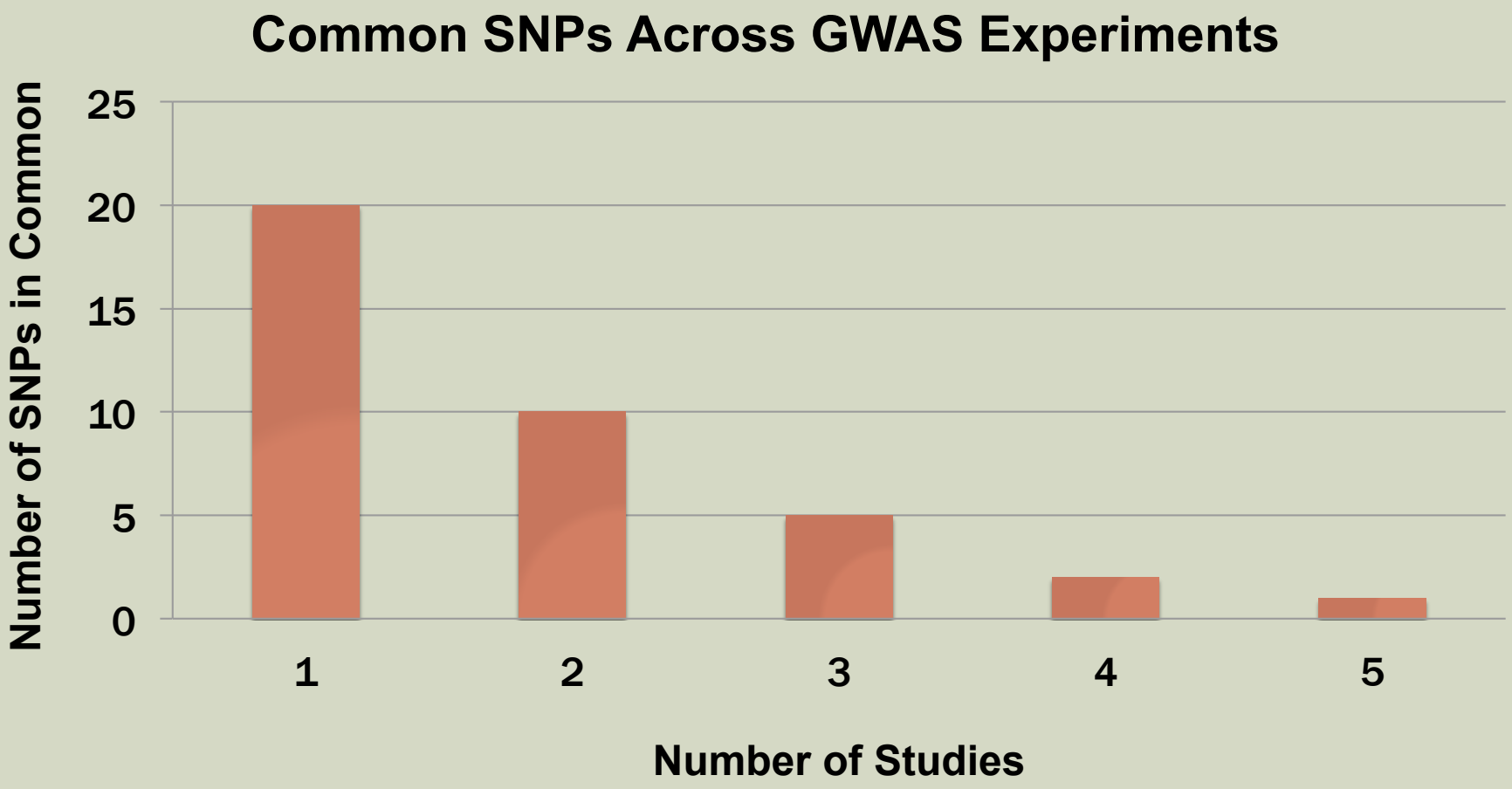
Export as --choose a format -- Go

Experiment: Association analysis experiment for BMI (HGVE3734)
Data set: BMI analysis (HGVRS3892)

Rank	Identifier	Accession	Region	p-value	-log p-value	Effect size	Risk allele	Related data	Links
1	HGVM498801	rs571312	chr18:57839769..57839769	0.0002495	3.603	Not supplied	Not supplied	Details	Not supplied
2	HGVM1405127	rs2531995	chr16:4013467..4013467	0.002647	2.577	Not supplied	Not supplied	Details	Not supplied
3	HGVM1880766	rs1558902	chr16:53803574..53803574	0.002729	2.564	Not supplied	Not supplied	Details	Not supplied
4	HGVM1682064	rs2867125	chr2:622827..622827	0.00452	2.345	Not supplied	Not supplied	Details	Not supplied
5	HGVM673226	rs987237	chr6:50803050..50803050	0.005968	2.224	Not supplied	Not supplied	Details	Not supplied
10	HGVM498801	rs571312	chr18:57839769..57839769	0.2363	0.627	Not supplied	Not supplied	Details	Not supplied

- Compute frequency of same SNPs

EXPECTED ACCURACY OF GWAS DATA



ANALYZING GWAS DATA

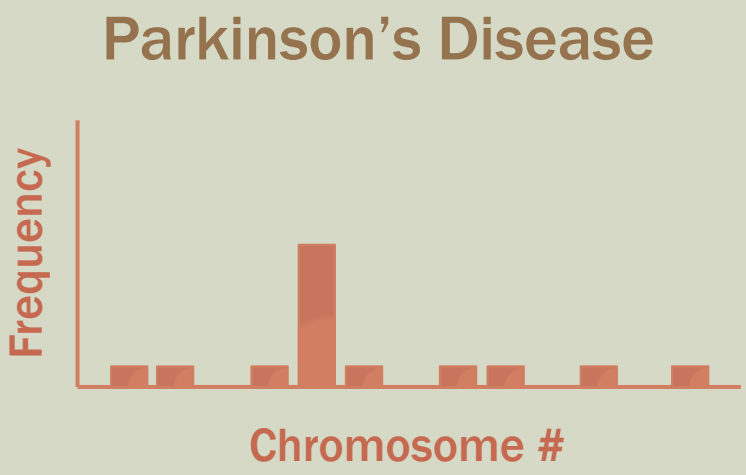
- Given a SNP, what disease(s) are associated with it?
- Hash Table
  - <KEY>,<VALUE>
    - Example: dictionary with <word>, <definition>
    - O(1) retrieval and insertion
  - Question
    - <SNP#>,<DISEASE(S)>

ANALYZING GWAS DATA

- Given a disease, which SNP(s) are associated with it?
  - Hash Table
    - <DISEASE>,<SNP#(s)>
- Given a disease, which chromosome(s) are more associated with it?
  - Hash Table
    - <DISEASE>,<CHROMOSOME#(s)>

EXTENSIONS

- Use R to plot the results visually
  - For particular disease
    - Look at the frequency of SNPs on each chromosome



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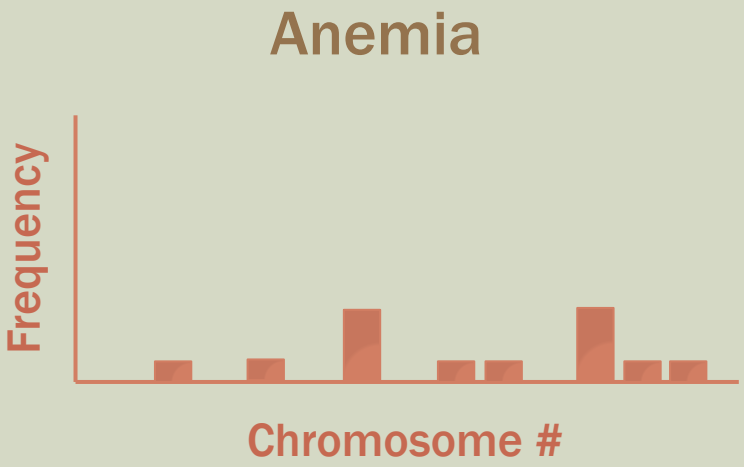

EXTENSIONS

- Explore more diseases
  - Anorexia
  - Sickle Cell Anemia
  - Parkinson's
  - Schizophrenia
  - and more!

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THANK YOU!

Questions/
Comments?