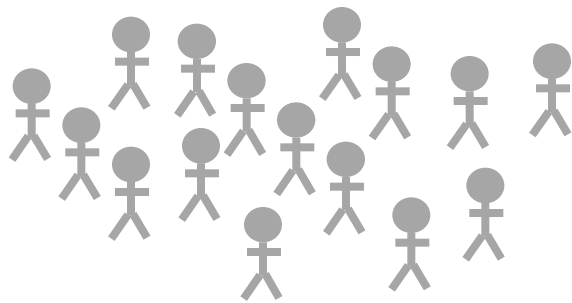


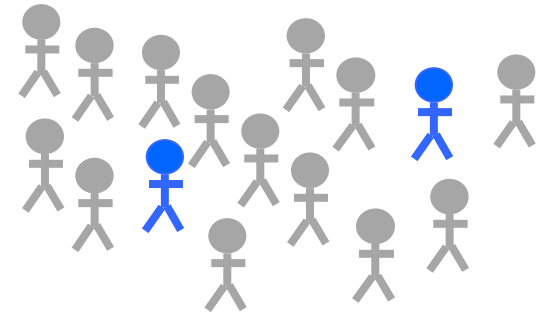
MODULE 4: Genome-wide association study — interpretation

Calculation of risk

- Risk= incidence of disease
- Can be calculated from cohort studies



Disease-free
(n=1005)



How many get disease?
 $105/1005 = 0.10$

Risk of disease is 10%

Calculation of risk for each genotype

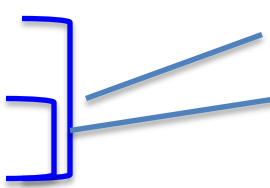
	D+	D-	Total	Risk	Interpretation
All	105	900	1005	$105/1005=0.10$	10% risk of disease
TT	15	84	99	$15/99= 0.15$	15% risk of disease
TC	46	383	429	$46/429= 0.11$	11% risk of disease
CC	44	433	477	$44/477= 0.09$	9% risk of disease

Each is an absolute risk, conveying the likelihood of developing disease if you have a specific genotype

Calculation of a relative risk

Relative risk = ratio of two risks

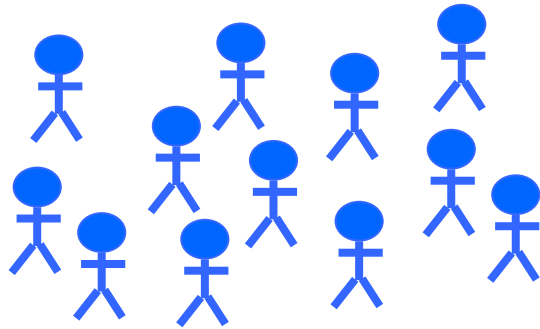
Measures the 'effect' of the variant on risk of disease

	<u>Absolute risk</u>	<u>Relative Risk</u>
TT	0.15	 $0.15/0.09 = 1.7$
TC	0.11	
CC	0.09	
		1.0 (reference)

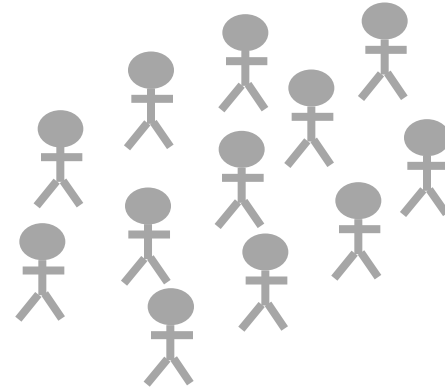
1.7-fold increased risk of disease
70% increased risk of disease

1.2-fold increased risk of disease
20% increased risk of disease

Can we calculate risk (incidence) of disease from a case-control study???



Cases (with disease)
(n=500)



Controls (disease-free)
(n=500)

NO!

of cases in study is pre-selected
 $500/1000 \neq$ disease incidence

We CAN calculate the ODDS of disease

Odds = disease (cases) : no disease (controls)

	<u>Cases</u>	<u>Controls</u>	<u>Total</u>	<u>Odds of disease</u>
All	500	500	1000	$500/500=1.0$
TT	160	108	268	$160/108=1.5$
TC	160	121	281	$160/121=1.3$
CC	180	271	451	$180/271=0.7$

Odds of 1.0 = 50:50 chance of disease

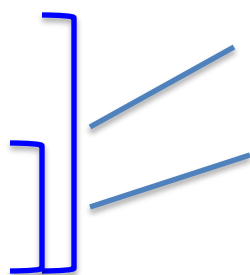
Odds >1 = chance of disease greater than no disease

Odds <1 = chance of disease less than no disease

Calculation of an odds ratio

Odds ratio = ratio of two odds

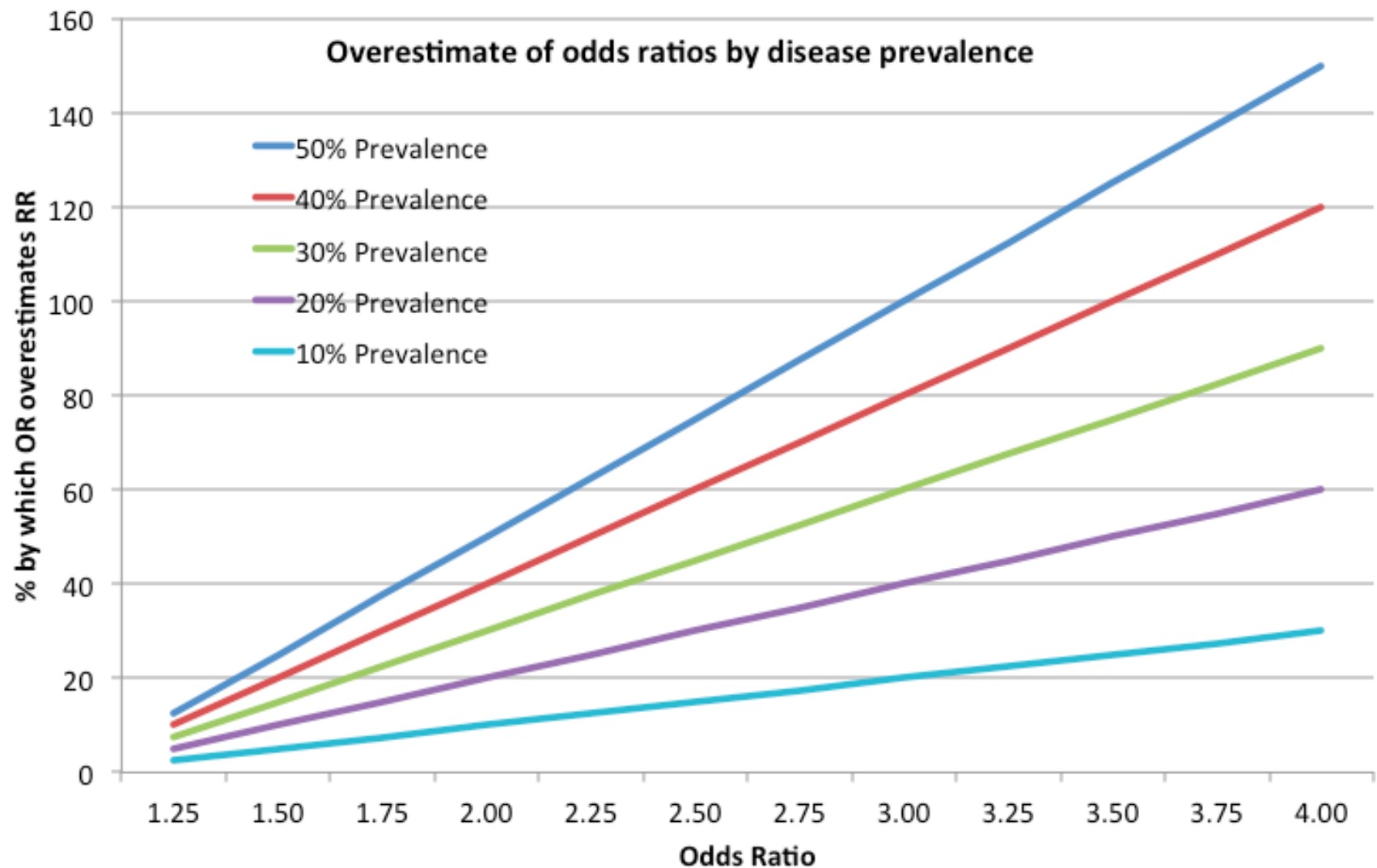
	<u>Odds</u>	<u>Odds ratio (OR)</u>
TT	1.5	$1.5/0.7 = 2.1$
TC	1.3	$1.3/0.7 = 1.9$
CC	0.7	1.0 (ref.)



2.1-fold increased odds of disease

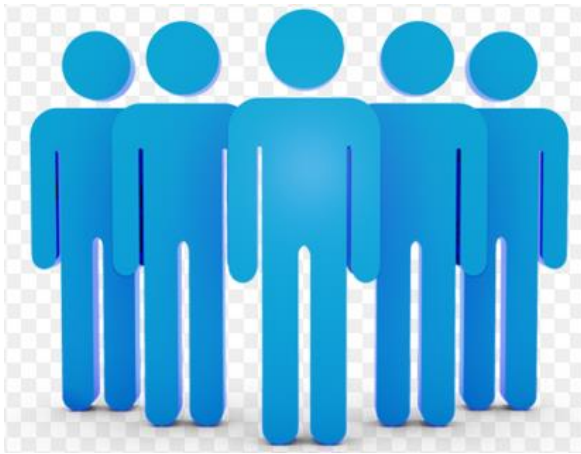
1.9-fold increased odds of disease

Odds ratios overestimate relative risks



Generalizability (external validity)

- How well does the study population represent the general population to which the results are being applied?

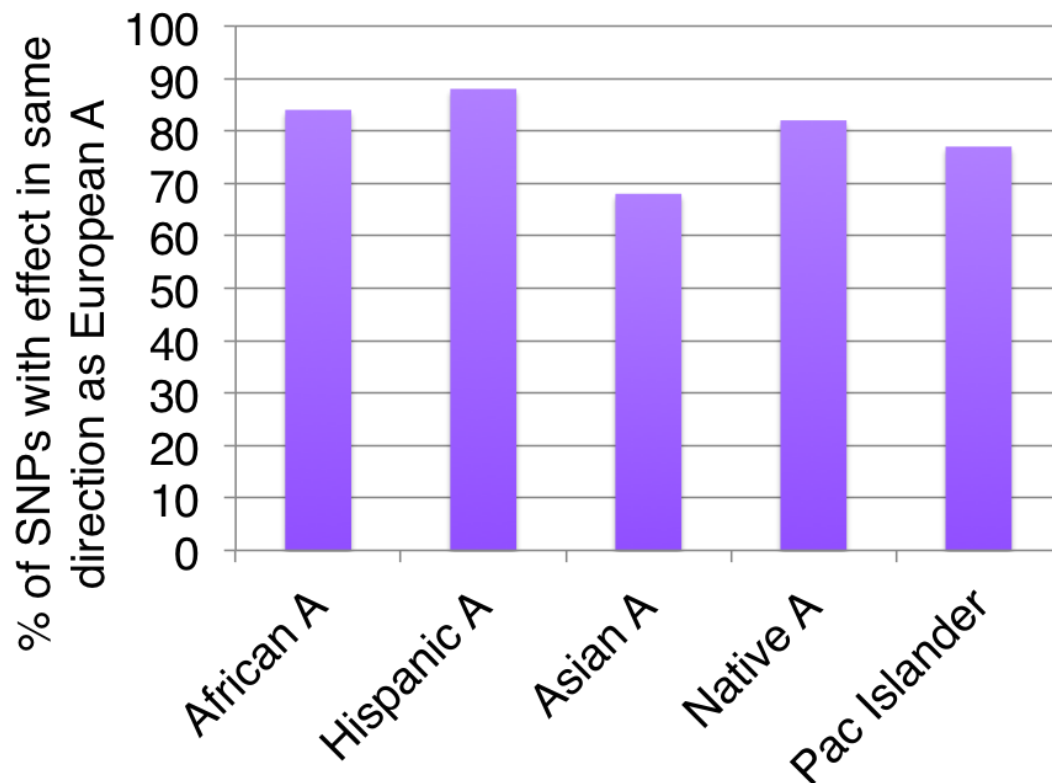


Study population



General population

Generalizability of GWAS results across race



Most GWAS done in Europeans

Most associations generalize from European to non-European populations, but effect sizes usually differ, especially for African Americans.

Question

A relative risk can be measured directly from which study design(s)?

- A. Case – control
- B. Cohort
- C. Both

Answer

B. Relative risks can be calculated directly from cohort studies, not case control studies.

Odds ratios can be calculated from case-control studies.

Odds ratios and relative risks are not the same thing, especially for common diseases where ORs overestimate RRs.