

TF → EGR₁ ← Gene

DNA → mRNA ⇒ proteins

? why / how to know?

GWAS

- variants ??

- "whole bunch" → play role?
(associated)
w/ MH

Sample Size

N ~ 20-50 ← enough?

Does it/OK to assume prevalence equal?

Prevalence

MDD > BPD > SCZ
common

Age of onset

✓ allows inher.

Repro. Dis.

survival
fertility

Heritability

✓ GWAS

✓ Twin Studies

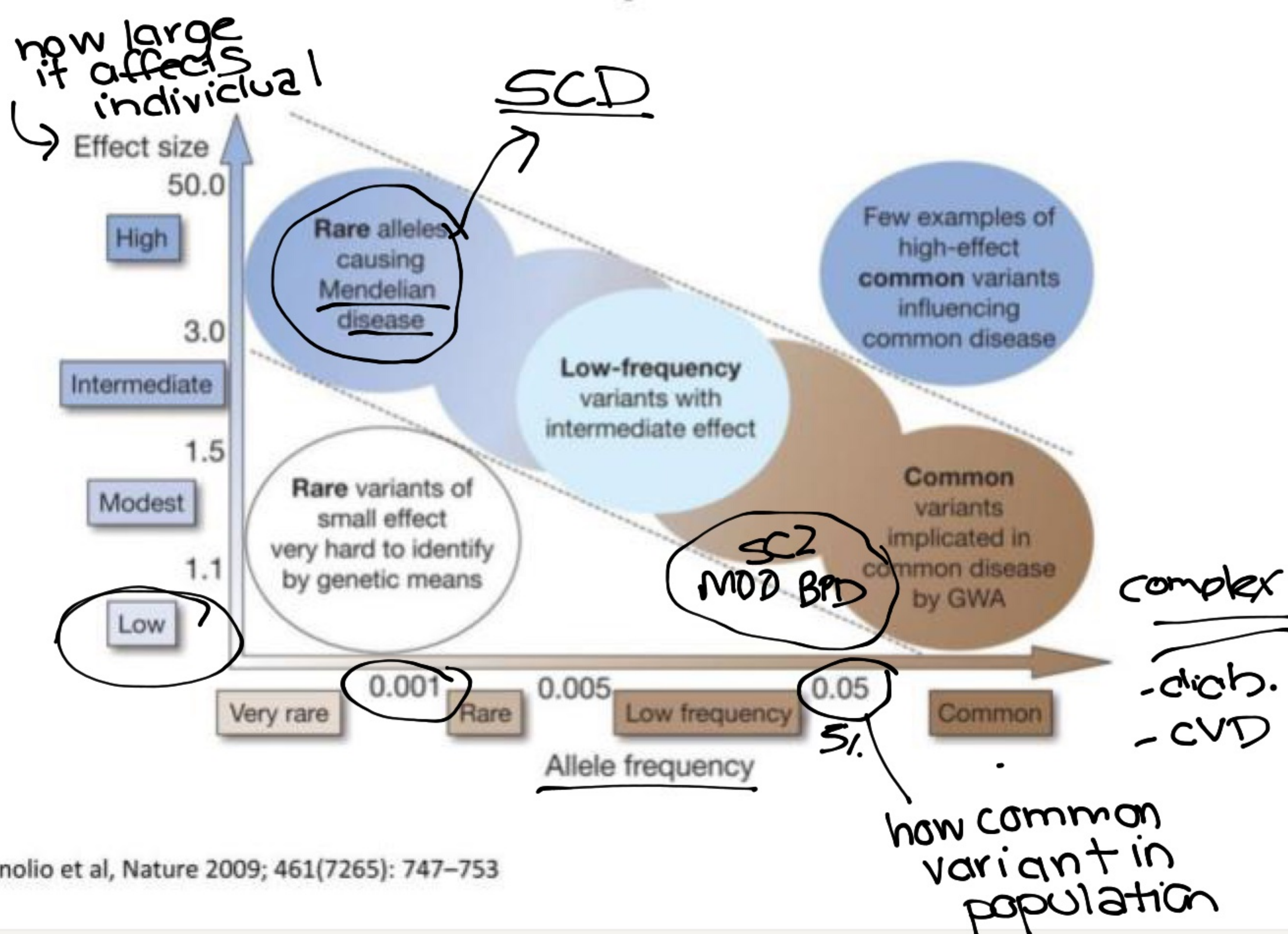
Paternal Age Effects

✓ ♂ > ♀

CDCV Hypothesis

genetics

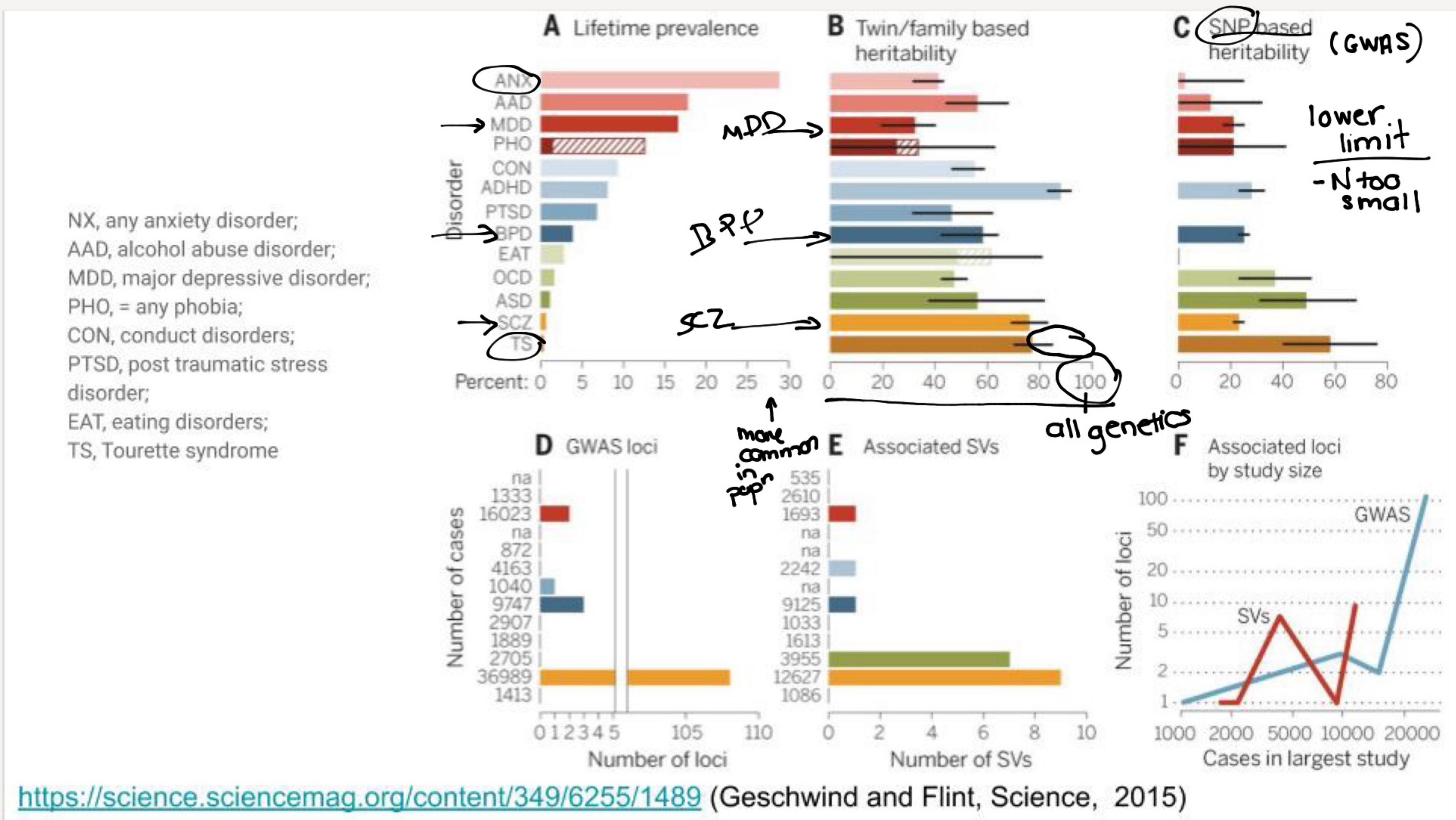
Common alleles usually have small effects...



Manolio et al, Nature 2009; 461(7265): 747-753

*Genetics

*Environment



Twin Studies

MZ (ident) clones > DZ (fraternal) siblings

Twins reared apart (rare)

environmental

Genetic Variations

- SNP ← single base in DNA
- SVs ← changes in chromosome
- CNVs ← diff # of copies

Calculations

Environ

- in utero
- air quality
- food/diet
- life events
-

Maternal vs Paternal Inheritance?

how much?

common variant risk dis
Paternal Effects

- * increased risk
- * accum. mutations
- * "Advanced Pat. Age"

↑ divisions

~ 23/div/year

* Sperm == always replicating
↑

"Adv. Mat Effects"

→ ≥ 35 years

Maternal Effects

~ 23 div / lifetime

* eggs = birth

? lower # variants

single perturb

Down Syndrome
Trisomy 21

XXX

chr. abcl

Applications?

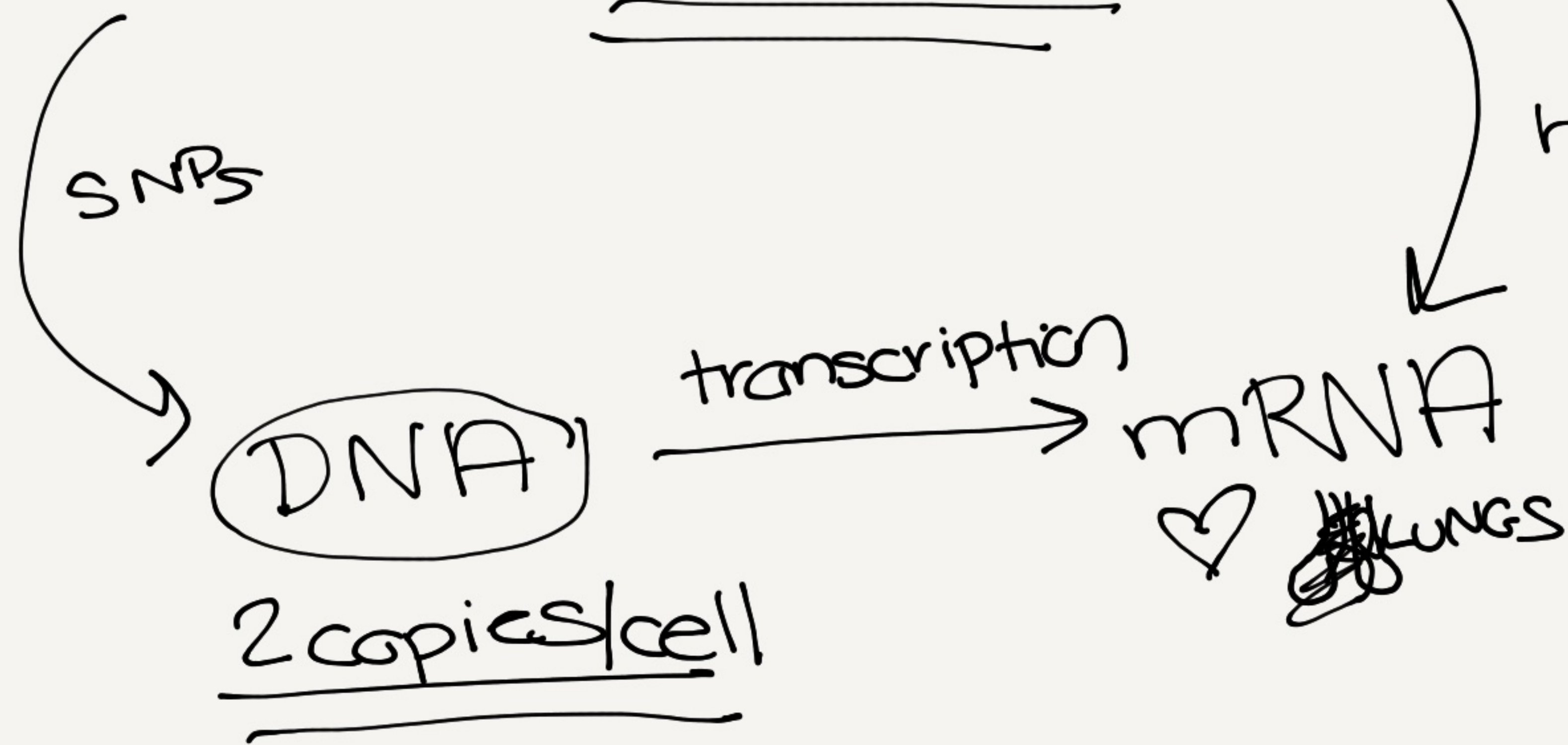
→ GWAS?

→ Framework?

→ Next Steps?

think over
this!
to be discussed
soon!

GWAS vs RNA-Seq?



how much
gene expression
 $\emptyset \rightarrow$ 1000s

RNA-Seq

Differentially Expressed Genes?

cond. vs ctrl/s