Regression to the mean: ① Random measurement error of the variable because some extreme value
② tendency that more likely to be closer to the mean if the measurement is repeated.

How to deal with it ←
① include a control grp. to see if there is similar decrease
② take several measurements up front.

pretest-posttest intervention study.
(doesn't need base population can recruit all patients). design special case of cross-over study

case-case studies
allow us to test for interaction on multiplicative scale
one factor is genetic and one is environmental
Key Assumption.
Gene Environmental are independent in the pop who give rise to the data

Case-only study design

Affected relative pair
studies of genetic linkage
allow us to search genomes for susceptibility genes
(doesn't need base population but needs several affected relatives)
AKA. genetic Linkage studies.

Adv: Requires no prior knowledge of gene location.

Dis:
① performs poorly when multiple separate genes are important
② extreme sensitive to data errors.

case-parent studies
of genotype-disease association
(doesn't need base population, kids bring controls by themselves)

Rationale

ineffective design when it is rare. Lots of LL

Adv: virtually free of confounding by ethnicity.

Disadv: ① Lower power
② Less practical for Late-onset.
e.g. Alzheimer-patients will not be around.
③ Nothing about Environmental E.

Extreme phenotype association study. (do need base population)

- Examples
- Rationale
- Approach.
- Variants

Consider source of systematic bias.