Choosing a Proper Statistical Method – Part III

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Relationship between odds ratio and relative risk

	Disease developed	No Disease developed	Total
Exposed	a	b	a+b
Not Exposed	c	d	c+d
Total	a+c	b+d	a+b+c+d

$$RR = \frac{\frac{a}{a+b}}{\frac{c}{c+d}}$$

$$OR = \frac{\frac{a}{b}}{\frac{c}{d}}$$

Odds ratio: a good approximation of the relative risk when the disease is rare

ISSUES IN BIOSTATISTICS

Review: Hypotheses and Test Statistics

- Step 1: State hypotheses (H_o and H_a)
- Step 2: Summarize data (and eyeball it)
- Step 3: Think about what data might look like if H_o true ('Under H_o')
- Step 4: Using data, gauge whether H_o true.
  - 4a: Calculate test statistic
  - 4b: p-value: evaluate probability (Test statistic under H_o)
- Step 5: Conclusion

Type I and II errors

Research	Reality	
	H_o is True (No Difference)	H_o is False (Difference)
Accept H_o (Conclusion: No Difference)	Correct Decision	Type II error (β, False Negative)
Reject H_o (Conclusion: Difference)	Type I error (α, False Positive)	Correct Decision

H_o = no statistically significant difference between two groups

Based on the primary objective

SAMPLE SIZE ESTIMATIONS

Sample Size Determination

- Why do we determine sample size
  - To make sure that the results of the *statistical approach align with scientifically useful results* given the constraints of ethics and feasibility
- When is it appropriate to prospectively power a study?
  - Study is prospective
  - When we have information to do it
  - The analysis is sufficiently simple (e.g., bivariate analysis)

Parameters

- Used to determine an appropriate sample size
  - Significant level
  - Desired statistical power
  - Minimal clinical difference
  - Estimated measurement variability

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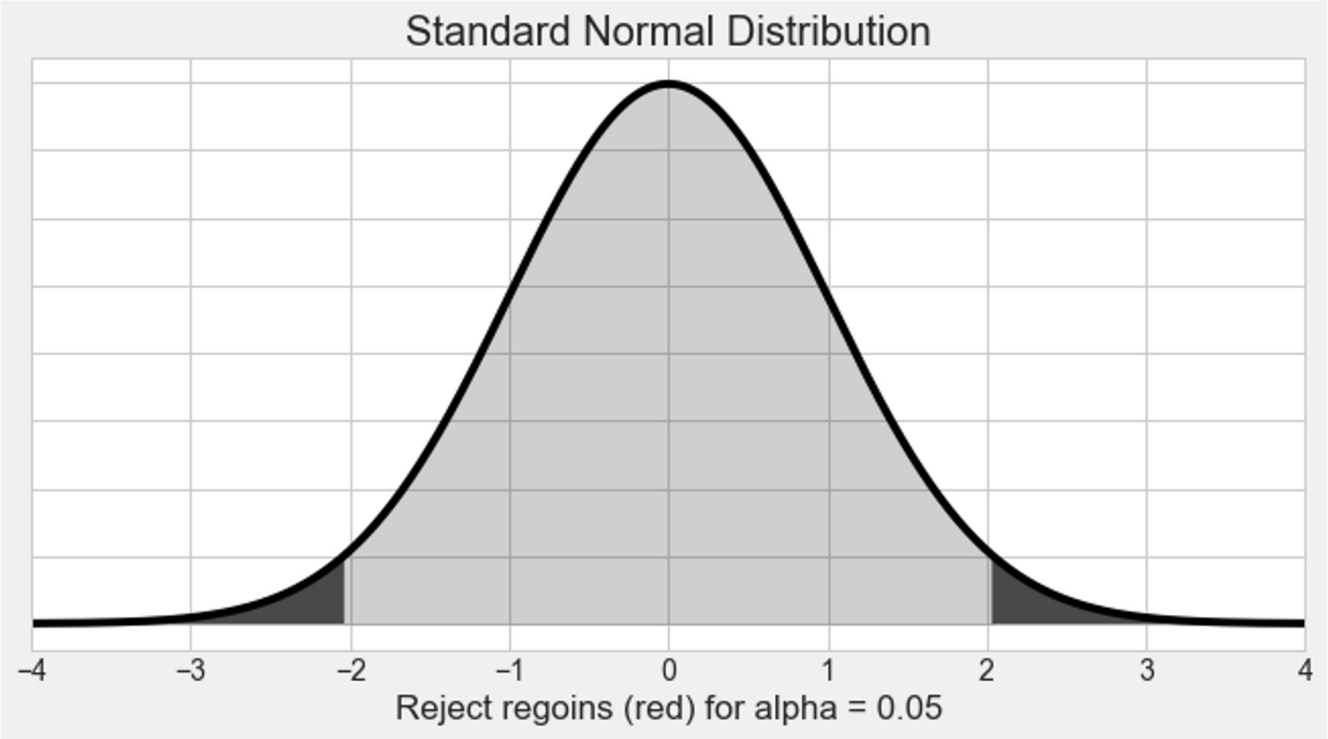
Significance Level

- The maximum p value for which a difference is considered statistically significant
- Represents by the symbol α (alpha)
- Type I error (false positive rate)
- Conventionally set at 0.05

Significance Level (cont.)

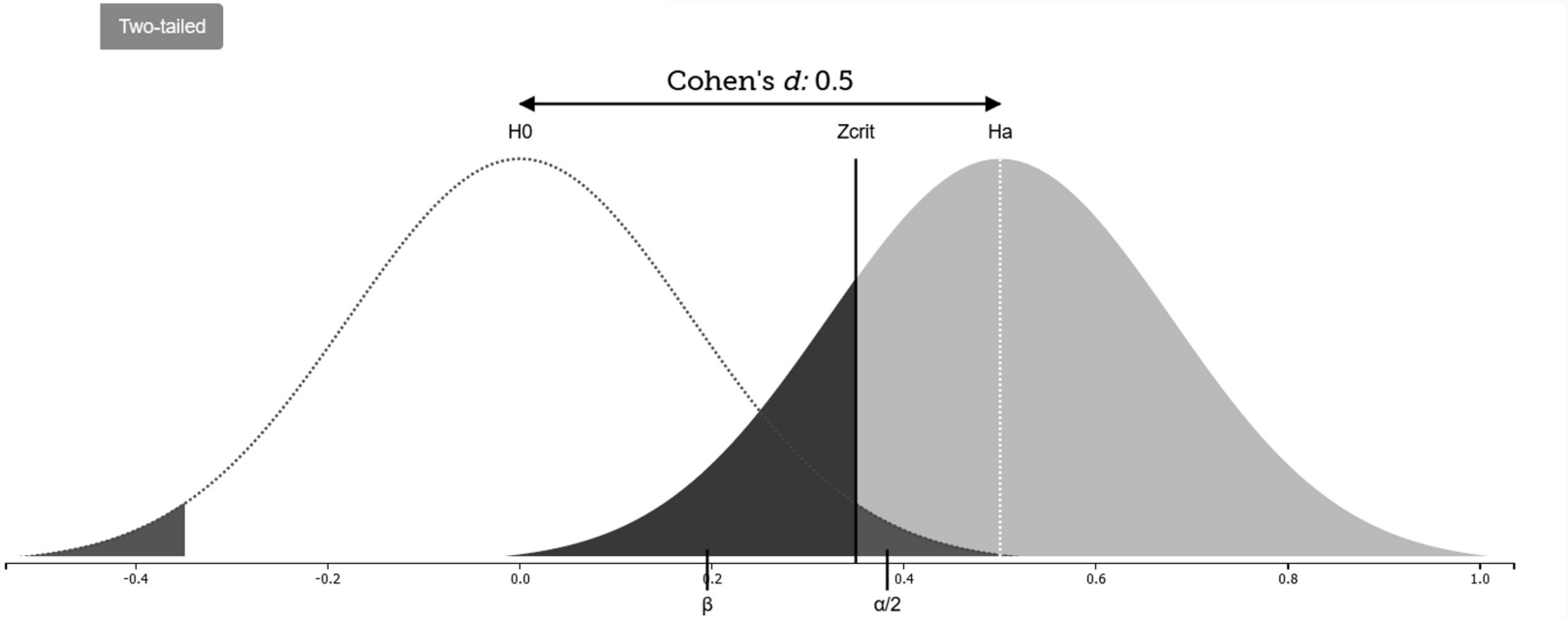


Alpha: Type I error (false positive rate)

Statistical Power

- The probability that a statistical test will indicate a significant difference when, in reality, there is one.
- Analogous to the sensitivity of a diagnostic test
- The definition of sensitivity:
  - True positive rate
  - Ability of a diagnostic test to correctly diagnose the disease

Statistical Power (cont.)



Statistical power: 1-β

Minimal Clinical Difference (MCD)

- Sometime called
  - Minimum expected difference
  - Effect size
- Represent
  - Scientifically meaningful difference
  - Smallest difference between comparison groups that the investigator deems clinically significant
- Based on clinical judgement and experience with the issue of interest

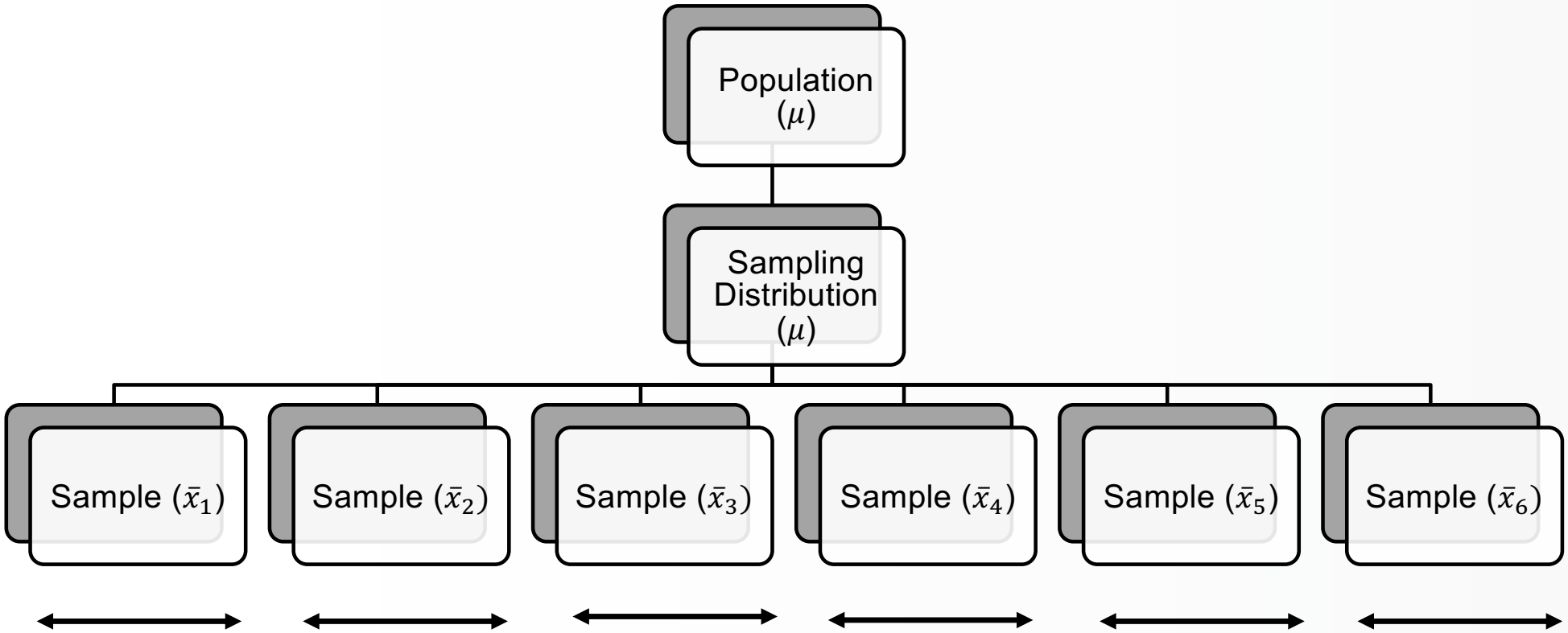
Estimated Variability

- Expected standard deviation of the outcome or measurements
- Can be determined from
  - Review literature of the same research topic in the similar study population

What’s the difference?

STANDARD ERROR VS STANDARD DEVIATION

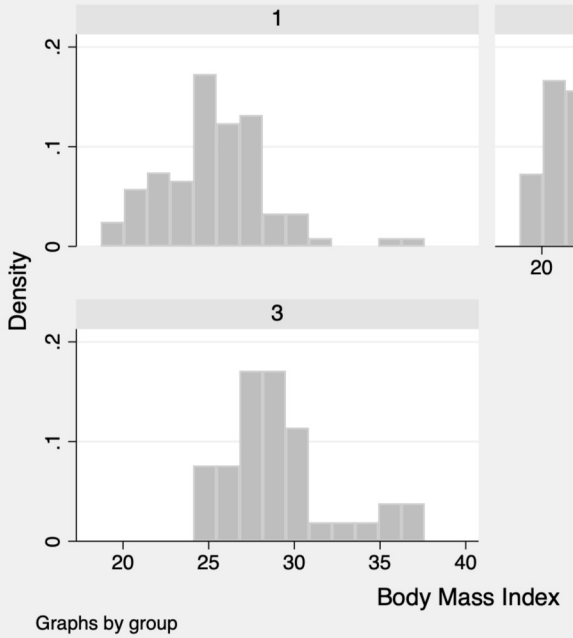
Standard Error: variability across samples

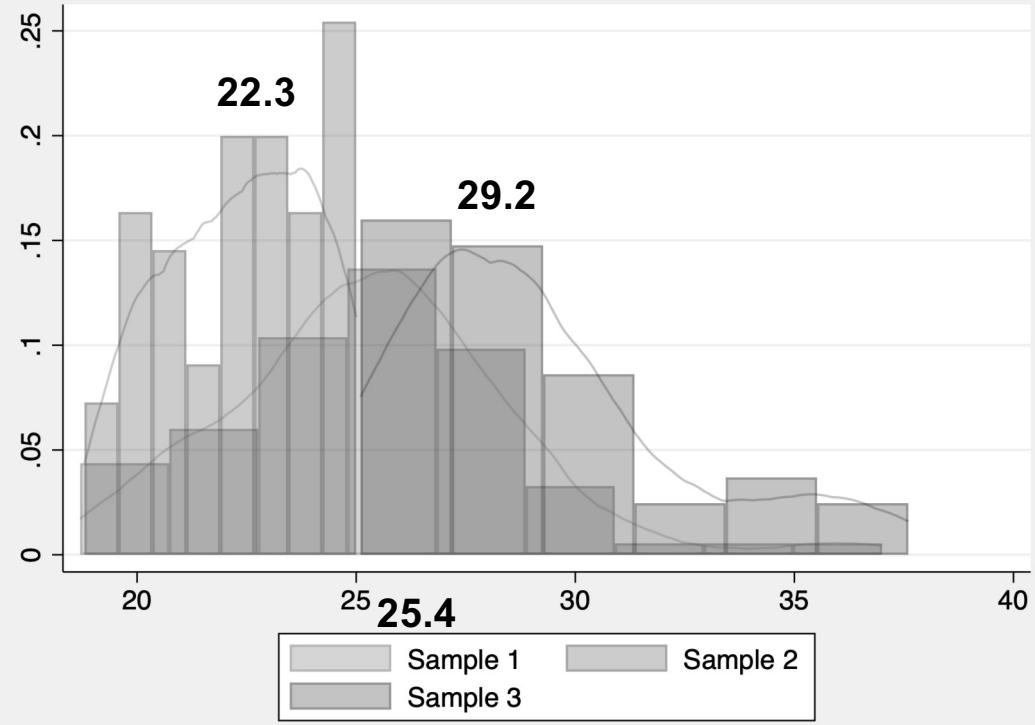


Standard Deviation: variability within a sample

Standard Deviation

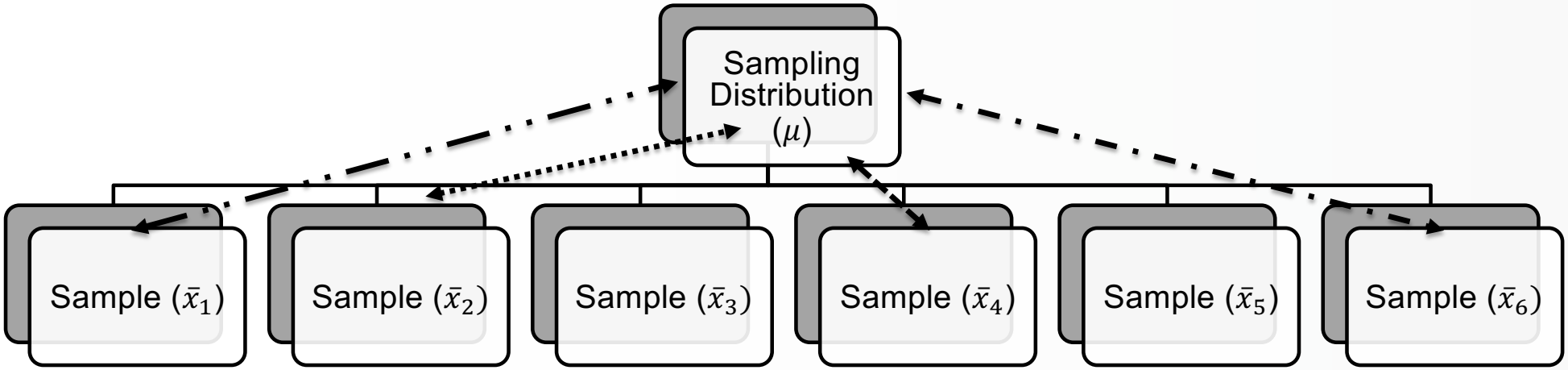
- Standard deviation for each sample
- $s_1 = \sqrt{\frac{\sum_{i=1}^{n}(x_i - \bar{x}_1)^2}{n-1}}$
- Measure of the spread of values within a set of data


1
2
3
Density
0
.1
.2
20
25
30
35
40
Body Mass Index
Graphs by group


22.3
29.2
25.4
0
.05
.1
.15
.2
.25
20
25
30
35
40
Sample 1
Sample 2
Sample 3

Standar Error

- $SE_{\mu_x} = \frac{s}{\sqrt{n}}$
- The standard deviation of its sampling distribution (a sample distribution)
- A sample mean deviates from the actual mean of a population; this deviation is the standard error of the mean



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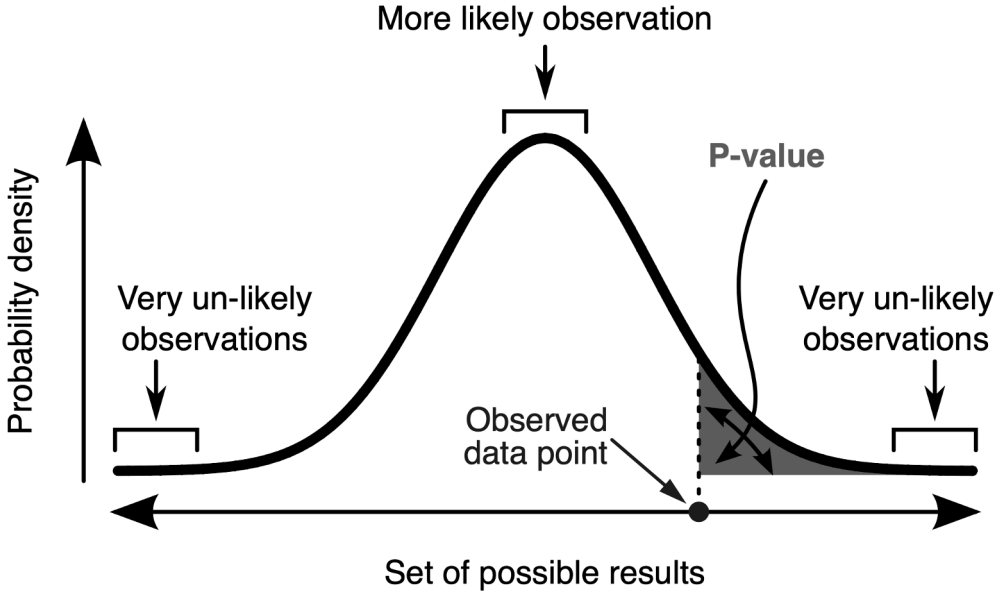
P-VALUE AND CONFIDENCE INTERVAL

Definition of P-value

- The P-value represents *the chance of seeing a statistic* (e.g., a mean difference or an odds ratio) *as extreme, by random chance alone, given the null hypothesis is true*
- By convention, if this chance is less than 1/20 ($p < 0.05$), we throw the null hypothesis away (conclude treatment works)
  - i.e., reject the null hypothesis and accept the alternative hypothesis



Confidence Intervals

- How precise is our estimate in terms of the population? To gauge this, we can use ***confidence intervals***
- A common misinterpretation of the 95% confidence interval (for example) is an interval that has a 95% chance of containing the true population value
- However, operationally, we can view the confidence interval as *an estimate of the range of plausible values for the population parameter*. It is this way that we can use confidence intervals for hypothesis testing

Statistical Significance ≠ Clinical Significance

- Statistical significance: the probability or likelihood that there is a difference
- Clinical significance or clinical importance: decided by judgment whether the observed difference is important enough for you to act (e.g., to start treating patients with a treatment)

One dependent variable and at least one independent variable(s)

REGRESSION

Regression models

- Most used methods in Biostatistics
  - General linear models: linear regression and analysis of variance
  - Generalized linear models: logistic regression, Poisson regression
  - Survival analysis method: Cox proportional hazard regression
  - Methods for longitudinal (panel) data: linear mixed models, generalized estimating equations, generalized linear mixed model
- Choosing models depends on the dependent variable (types of measurement)

Regression model

- A mathematical representation of the relation between an outcome variable and a set of explanatory variables.

$$y = f(x_1, x_2, x_3, x_4, .., x_n) + e$$

- $Cure\ from\ infection =$
  $f(ABX\ used, type\ of\ organism, immune\ system) + residual$
- $Cholesterol\ level = f(\ diet, body\ weight, genetic) + residual$

Steps in regression analysis

- Fit the regression model, and obtain estimates of β_s, (Using Statistical Software)
- Assess model adequacy (Question: is it the 'right' model?)
  - Model significance: Overall model significance, Xs significance
  - Explanatory power: How good is the model?
  - Model validity: Does it work properly? Are any assumptions violated?

Steps in regression analysis (cont.)

- Prediction: Sometimes the model is ‘good’ enough to predict the response variable from values of the explanatory variable (rarely case in an 'observational' setting)

Regression Usage

- RCT: baseline adjustments
- Non-Randomized Studies
  - Cohort study
  - Case-control study
  - Cross-sectional study

Choice of Model

Type of Outcome Variable	Regression Model
Continous	Linear regression
Binary	Logistic regression
Categorical	Ordinal, nominal logistic regression
Count	Poisson regression
Time-to-event	Cox-proportional hazard model

One outcome, measured once

Linear Regression and ANOVA

	ANOVA	Linear Regression
Outcome variable	Continuous	Continuous
Independent variables	At least one **categorical** variables	One or more **continuous** variables
Analysis	Present differences in means of outcome between categories	Estimate regression coefficients
Note	Is a special case of regression	

Both ANOVA and linear regression can be used for one continuous outcome, two independent variables (one continuous and one categorical variables)

Indicator (Dummy) variables

- An indicator variable or proxy variable takes value of 0 or 1 to indicate the absence or presence of some categorical effect
- Number of dummy variables = number of categories - 1
- Categorical variable: severity status (mild, moderate, severe), 2 dummy variables, mild is a reference group

	Dummy 1 (sev1)	Dummy 2 (sev2)
Mild	0	0
Moderate	1	0
Severe	0	1