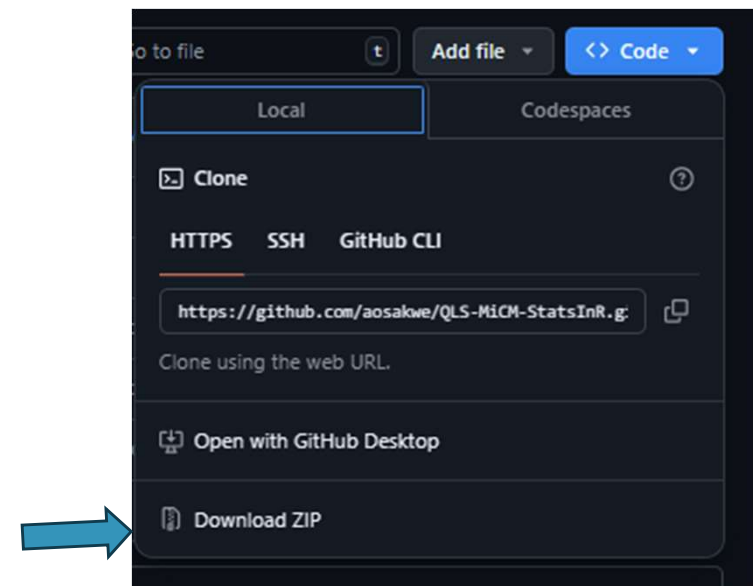
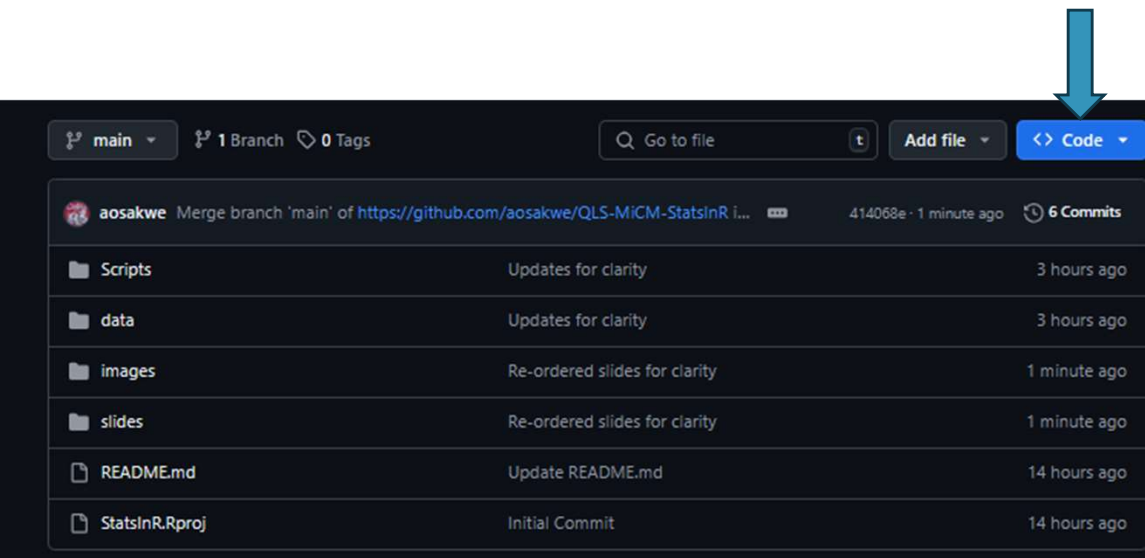


Workshop materials

<https://github.com/aosakwe/QLS-MiCM-StatsInR>

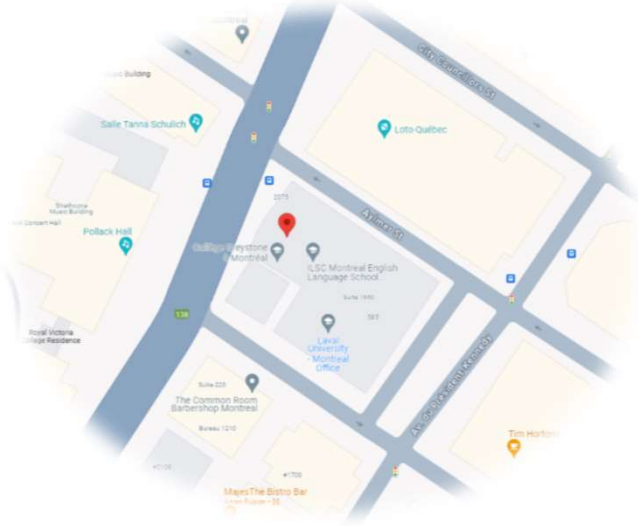
use 'git clone' command OR



Statistical Analysis in R

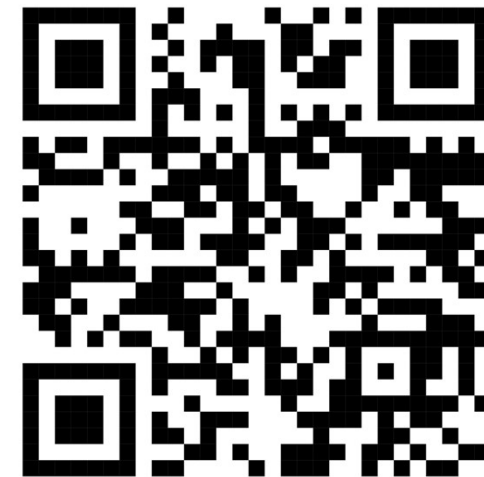
Workshop Lead: Adrien Osakwe
Facilitator: Bangli Cao
February 20, 2025

QLS-MiCM mission statement: deliver quality workshops designed to help biomedical researchers develop the skills they need to succeed.



Location: 550 Sherbrooke
Street, Montreal, Quebec

Contact: workshop-micm@mcgill.ca



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Workshop Series

Workshop	Date	Location	Registration
How to think in Code	Jan. 28 1PM-3PM	EDUC 133	Closed
Intro to Git & GitHub	Jan. 30 1PM-5PM	EDUC 133	Closed
Intro to Unix	Feb. 6 1PM-5PM	EDUC 133	Closed
Intro to Python (Part 1)	Feb. 11 1PM-5PM	EDUC 133	Closed
Intro to R (Part 1)	Feb. 13 1PM-5PM	EDUC 133	Closed
Exploring MATLAB	Feb. 18 1PM-5PM	EDUC 133	Closed
Statistics in R (Part 2)	Feb. 20 1PM-5PM	EDUC 133	Open
Data Processing in Python	Feb. 25 1PM-5PM	EDUC 133	Open
Intro to Machine Learning	Mar. 13 1PM-5PM	EDUC 133	TBA
Intro to R (Part 1)	TBA	EDUC 133	TBA
Intro to Python (Part 1)	TBA	EDUC 133	TBA

<https://www.mcgill.ca/micm/training/workshops-series>

Outline

1. Data Manipulation/Wrangling
2. Linear Regression Models
3. Logistic Regression Models
4. Statistical Testing
5. Study Design

Acknowledgements

Gerardo Martinez - McGill
Alex Diaz-Papkovich - Brown
Larisa Morales Soto - HMS
Lisa Sullivan BUSPH

Data Wrangling

Learning objectives:

- Become familiar with the dplyr syntax
- Create pipes with the operator %>%
- Perform operations on data frames using dplyr and tidyr functions
- Implement functions from other external packages

Split-Apply-Combine problem

INPUT

x	y
a	2
a	4
b	0
b	5

SPLIT

x	y
a	2
a	4
b	0
b	5

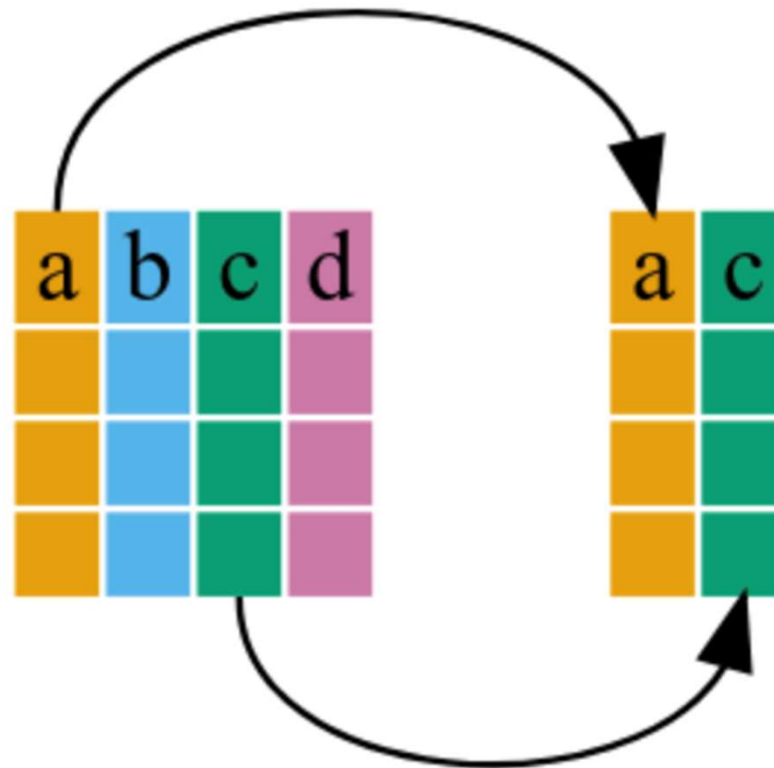
APPLY

x	y
a	3
b	2.5

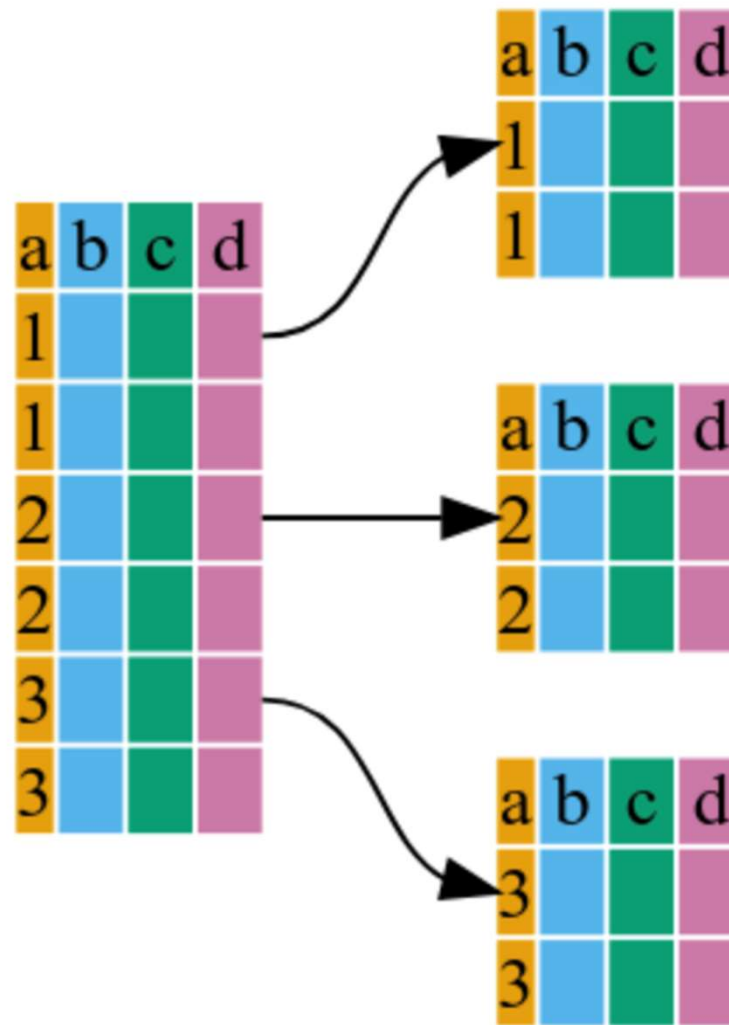
COMBINE

x	y
a	3
b	2.5

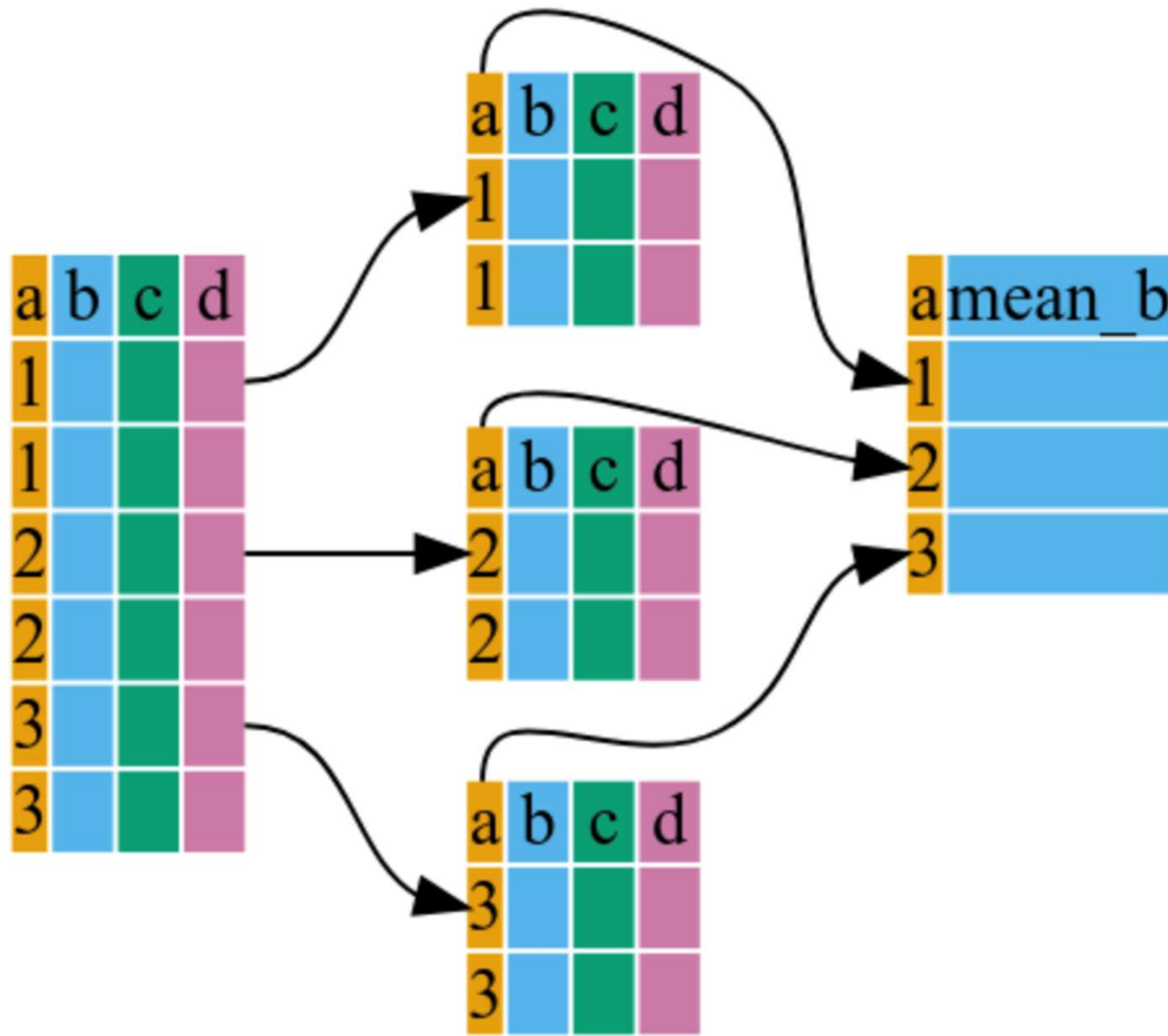
Select



Group by



Summarize



Managing Missing Data

- Most of the time, samples having missing entries
 - Missed medical appointment
 - Error with measuring instruments etc.
 - Represented as *NA* in R

Simple Solution

- Drop samples with missing observations

More rigorous solutions

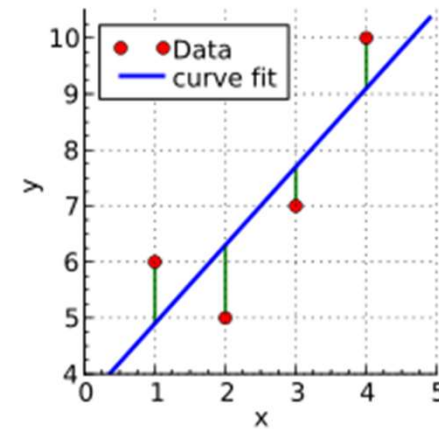
- Fill in with average/median of dataset or condition
- Train a model to 'impute' missing entries based on other features

Linear Regression

Learning objectives:

- Understand the fundamental regression algorithms
- What is a coefficient/effect size

The Linear Model



Credit: Wikipedia

- The fundamental model for statistics & machine learning
- Follows a normal distribution

Imagine a dataset with a dependent variable y and a set of descriptive features x

We want to learn what features in x are good predictors of y (what is their **effect size/coefficient** β)

$$y = \beta x + \varepsilon \quad \varepsilon \sim \text{Normal}(0, \sigma^2)$$

$$y \sim \text{Normal}(\beta x, \sigma^2)$$

Model Assumptions

1. Outcome is **continuous** and a **linear combination of predictors**
2. Outcome is such that $y \sim Normal(\beta x, \sigma^2)$
3. Predictors must not be perfectly correlated (linear combination)
4. For every observation i the error is:
 1. **Normally distributed**
 2. **Mean zero**
 3. **Homoskedastic** (same variance as other observations)
 4. **Independent** (not correlated)

Model Fitting

Probability

- Maximum Likelihood Estimation

Machine Learning

- **Mean Squared Error**

$$y = \beta x + \epsilon$$

$$\hat{y} = \hat{\beta} x$$

$$MSE = \frac{\sum_{i=1}^N (\hat{y}_i - y_i)^2}{N}$$

Extensions

Interaction effects

- Outcomes depend on interactions of (e.g.) age*sex

Different Types of Data

- **Multivariate regression (multiple, correlated outcomes)**
- **Logistic regression (Binary outcomes like healthy vs. disease)**
- Multinomial/Poisson regression (Count data)
- ARIMA (Time series—data correlated over time)

Logistic Regression

Learning objectives:

- What is a logistic function
- How LR extends the linear model
- Cross-Entropy

Working with categories

Linear Regression could be used to predict categories (technically) BUT it has many flaws

- Formulation isn't bounded (0,1)
- Impractical for predicting multiple classes
- Mean-Squared Error is not an optimal objective function

Propose to use the linear equation with a **sigmoid function**

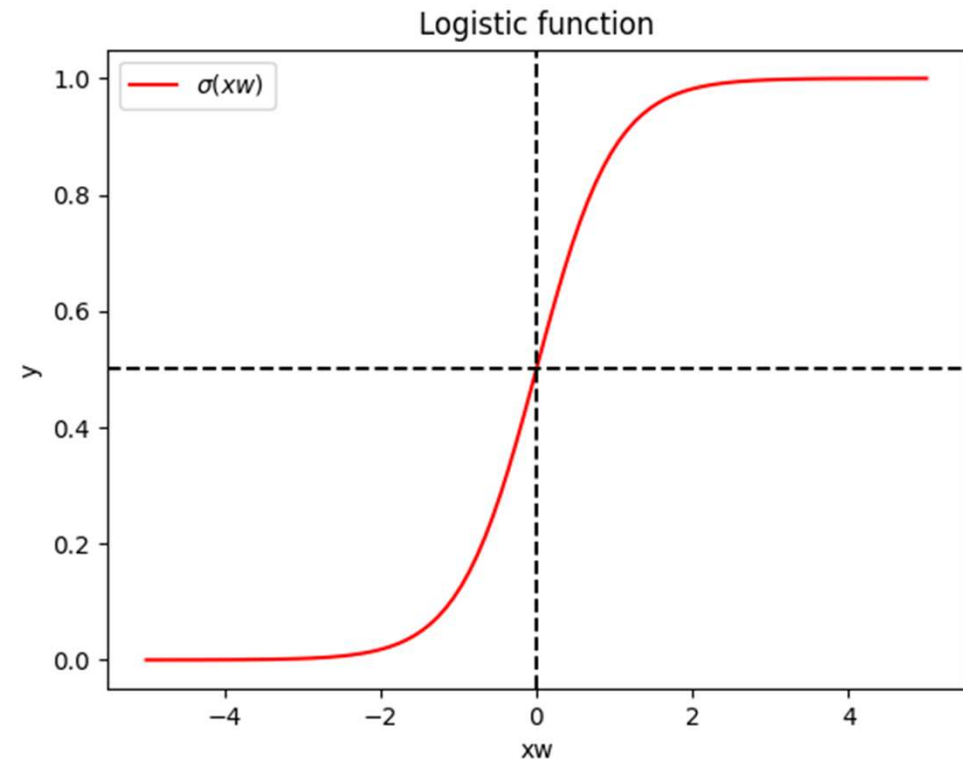
Logistic Regression

- Sigmoid/Logistic function provides us with a bounded output
- Range is also easy to interpret as a probability

Can also use the **softmax** if working with multiple classes

$$\sigma(\mathbf{z})_i = \frac{e^{\beta z_i}}{\sum_{j=1}^K e^{\beta z_j}}$$

$$\hat{y} = \sigma(\mathbf{xw}) = \frac{1}{1 + \exp(-\mathbf{xw})}$$



Cross-Entropy

$$CE(\hat{y}, y) = -y \log(\hat{y}) - (1 - y) \log(1 - \hat{y})$$

Most commonly used loss function for classification

- More intuitive meaning for classification than MSE
- Faster model convergence than MSE
- Is compatible with a **multi-class dataset** (more than two classifications)

Statistical Testing

Learning objectives:

- Understand the formulation and assumption of standard statistical tests
- Understand the interpretation of a p-value
- Considerations when designing an experiment

Hypothesis Tests

Goal

- Determine if two sets of data are **different**
- Can approach this with **test statistics**
 - Is the difference **significant** or not?

Many Types of Tests

- Parametric tests – **makes an assumption on the data distribution**
 - Z-score vs. t-test
 - ANOVA
- Non-parametric – **does not make an assumption on data dist.**
 - Permutation test

Hypothesis Formulation

Null Hypothesis

- Effect size is 0
- Difference between conditions is 0

Alternative Hypothesis

- Effect size is NOT 0
- Difference between conditions is NOT 0

We accept or reject the null based on the generated p-value (< 0.05)

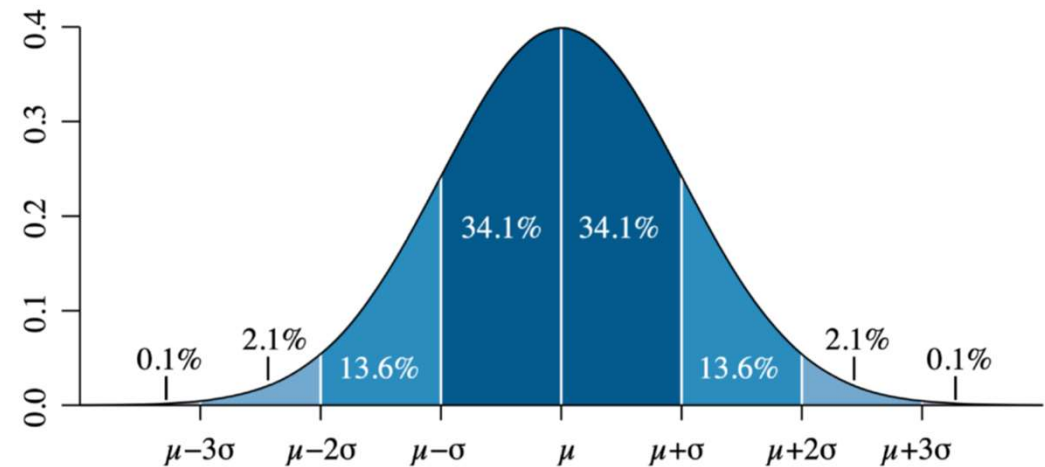
Understanding Significance

Statistical significance **DOES NOT** imply causality

It is a measurement of the likelihood of the observed data happening by chance.

A p-value tells us the probability of seeing the observation **if the null hypothesis is true.**

Z-score Test



Credit: Wikipedia

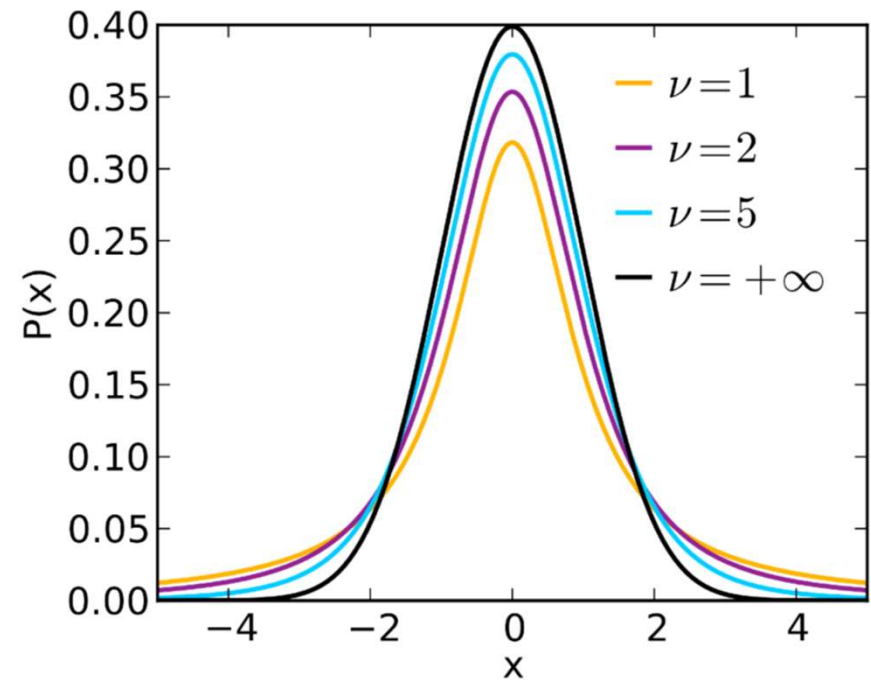
- Based on the Normal Distribution
- Generate a Z-score from our effect size estimate
- Compare to Normal(0,1) distribution
 - One-tail or Two-tail
- Used when we have a **large sample size** (Central Limit Theorem)

$$z = \frac{\beta - \mu}{\sigma} = \frac{\beta}{SE(\beta)}$$

t-test

Based on the student t distribution

- Defined by degrees of freedom (d.f)
 - $n-1$ d.f.
- More appropriate for smaller sample sizes (most cases)
- Use our sample mean \bar{X} and sample s.d $\hat{\sigma}$ to calculate test statistic
- Value of μ depends on your null hypothesis
 - One-Sample
 - Two-sample



Credit: Wikipedia

$$t = \frac{\bar{X} - \mu}{s} = \frac{\bar{X} - \mu}{\hat{\sigma}/\sqrt{n}}$$

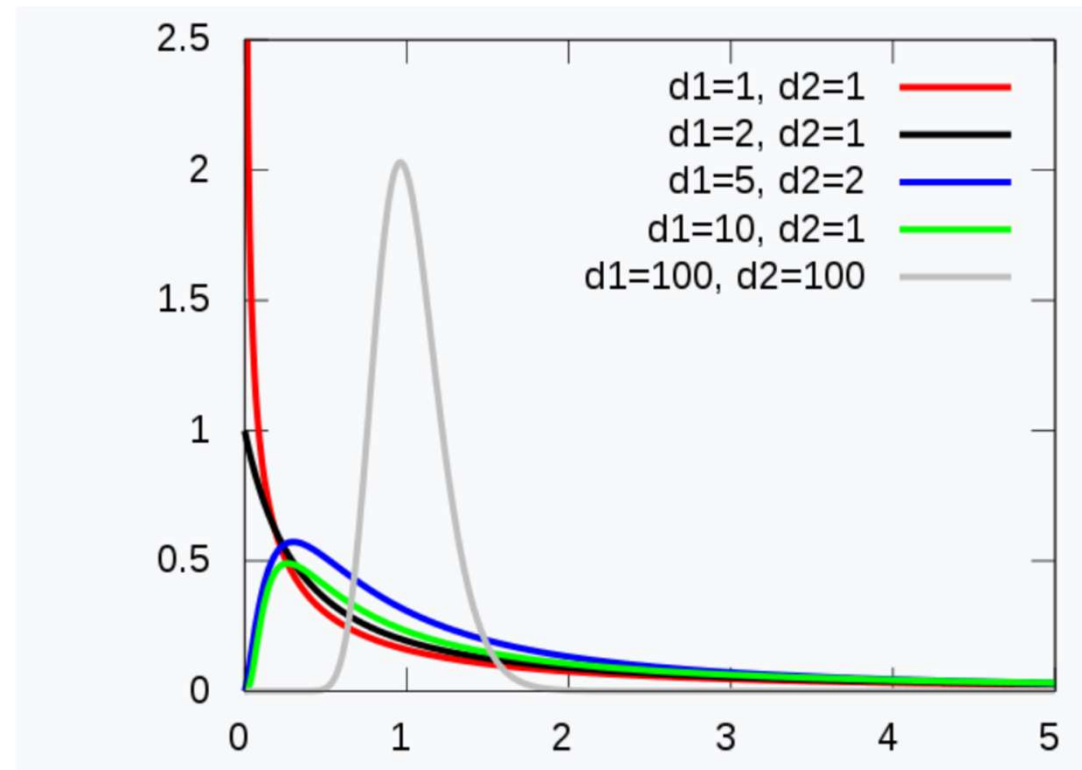
ANOVA

Based on the F-distribution

- Similar to t-statistic
- Statistic is the ratio of two Chi-squareds

Null hypothesis: multiple means are **all** equal

Alternative: At least one group is different



Credit: Wikipedia

ANOVA

How much variation is explained by our treatment condition?

$$SST = \sum_{i=1}^n (y_i - \bar{y})^2$$

Total sum of squares

$$SST = SS(Treatments) + SS(Residuals)$$

Take the ratio of the variance between treatments over the variance within treatments

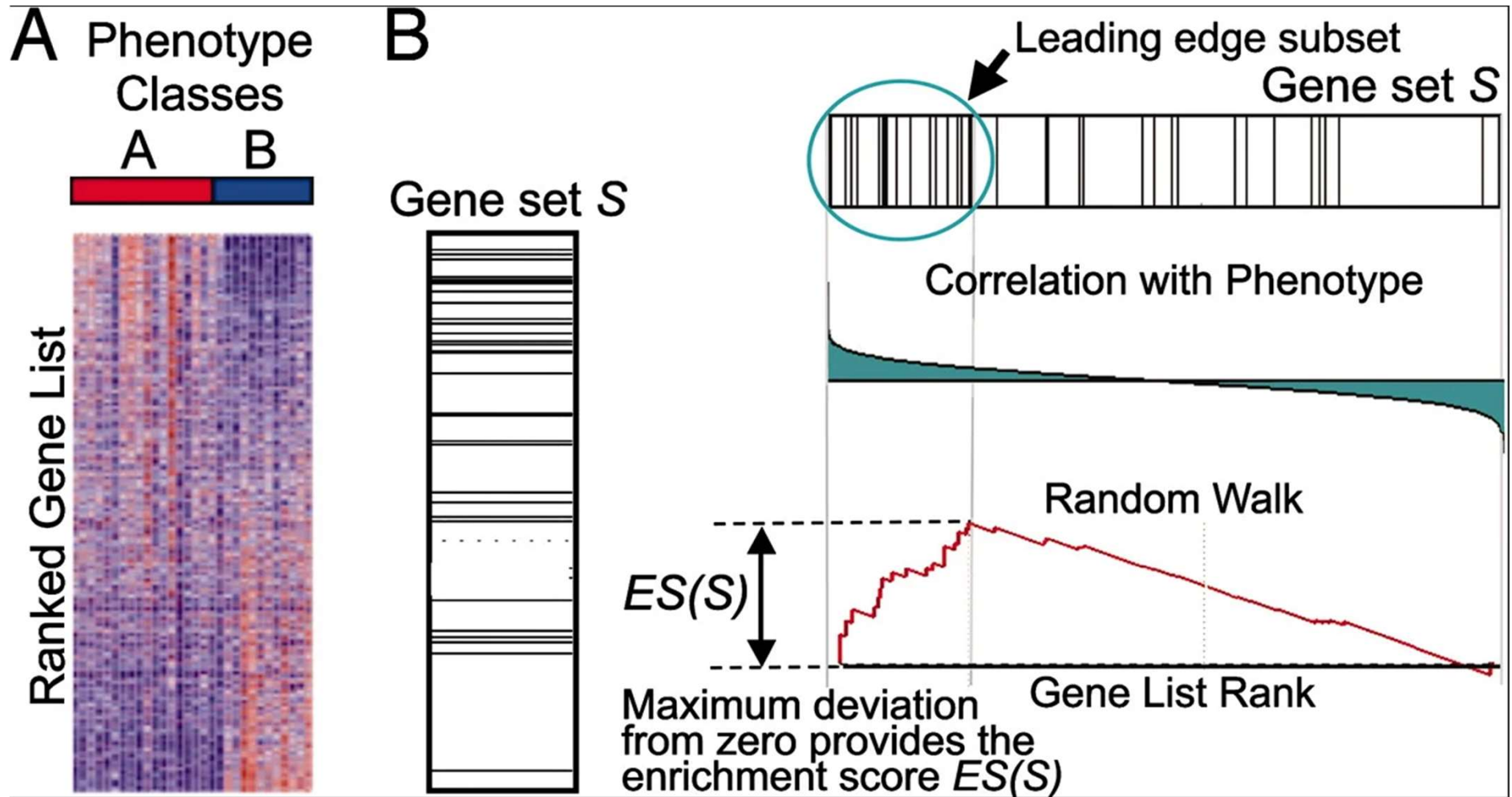
High variance between treatments will give a low p-value

Non-Parametric Test

Similar to what is done for enrichment analyses

- Avoids needing to make assumptions on distributions
 - Can be very **slow**
1. Shuffle labels in your data to generate estimates (random baseline)
 2. See where your true observation lies on this baseline

Gene Set Enrichment



Credit: GSEA

Multiple Testing

- May test multiple hypothesis (example, effect sizes in linear model)
- If null distribution is true, expect a **uniform distribution** of p-values
 - 5% of tests will give a significant result
- Multiple test correction methods are used to address this
 - Bonferonni Correction
 - **Benjamini & Hochberg Correction**
 - Found in results as **FDR, p-adjusted, q-value**

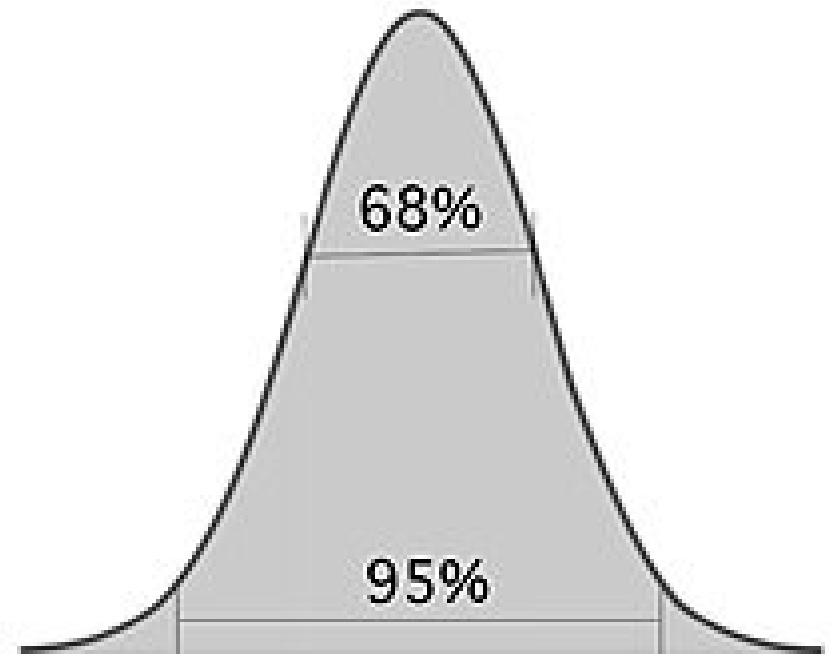
Confidence Intervals

- We may want to attribute a range to our estimate

- Can be calculated with the **margin of error**

$$E = Z \frac{\sigma}{\sqrt{n}}$$

- Where Z is the z-score that defines our confidence level

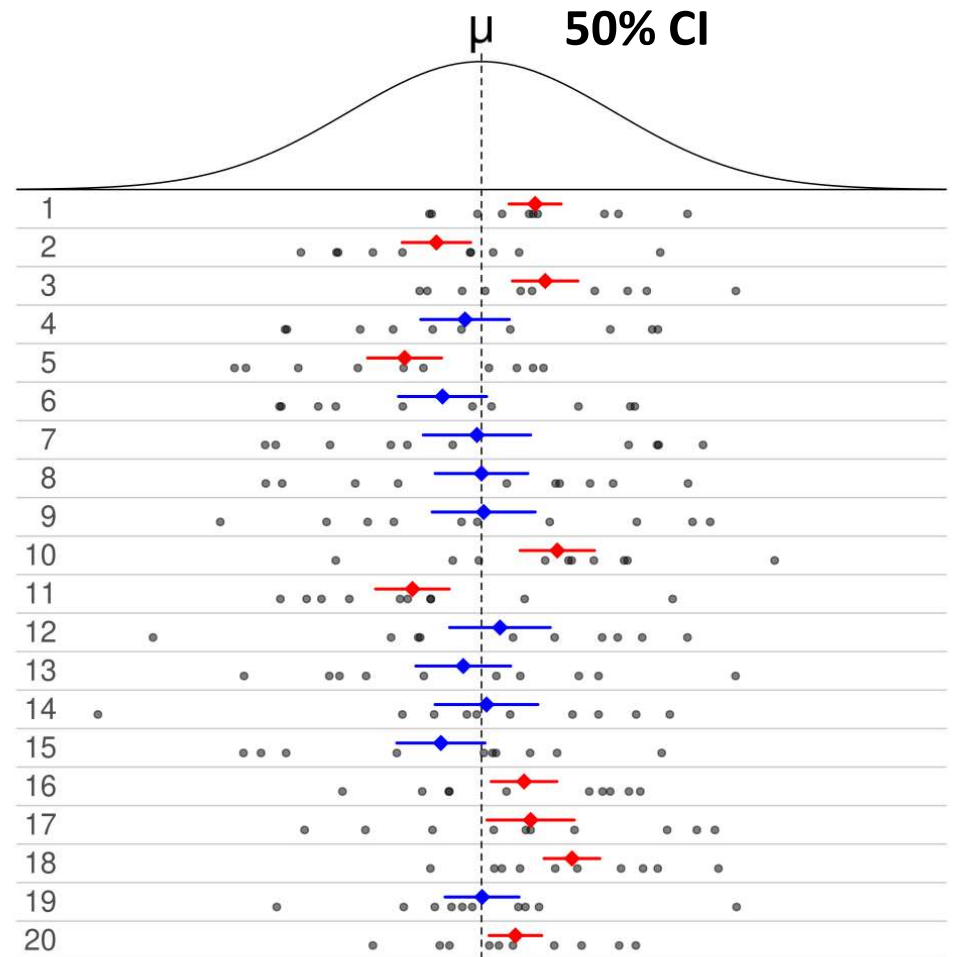


PSA: Confidence Intervals

A 95% CI **DOES NOT** mean there is a 95% chance the true value is in that range

For multiple experiments, 95% of CIs will overlap with the true value

Consider a Bayesian formulation instead (beyond scope)



Study Design

Learning objectives:

- Understand how simulations can be used to help with study design
- How to determine the required sample size

Study Design

Data collection can be expensive and time-consuming

Need to ensure that the collected data has enough **power** to avoid false negatives (type II error)

Can simulate data to help decide on the statistical test used and determine the appropriate **sample size**

Determining sample size

- Statistical test results depend on multiple factors
 - Difference in Samples
 - **Sample Size**
- We want to make sure we have enough samples to avoid False Negatives (type II errors)
- Can leverage the assumptions used for our statistical test to determine sample size

Confidence Intervals

In practice you will want your CI to cover a small range to be informative.
Can achieve this by solving for the **margin of error E**

$$E = Z \frac{\sigma}{\sqrt{n}}$$

$$n = \left(\frac{Z\sigma}{E} \right)^2$$

Note that we may not have a value for σ

- Use estimate from past study
- Make an assumptive guess
- Run a small pilot study

Sample Comparison

$$n_i = 2 \left(\frac{Z_{1-\frac{\alpha}{2}} + Z_{1-\beta}}{ES} \right)^2$$

$$\text{Effect Size (ES)} = \frac{|\mu_1 - \mu_2|}{\sigma}$$

$\alpha \rightarrow$ Significance Level

Probability of rejecting null when it is true

$1-\beta \rightarrow$ Power

Probability of rejecting null when it is false

To summarize

- ✓ Basics for data manipulation & cleaning
- ✓ Explored basic linear modeling for regression & classification
- ✓ Explored statistical testing and intuition behind study design

Now you are ready to:

- Use dplyr to facilitate reproducible data manipulation
- Apply and interpret linear model results
- Interpret confidence intervals and p-values
- Explore more complex models and tests!

Future Statistics Workshops

- Dimension Reduction
- **Bayesian Inference**
- Time-series Analysis
- And more...

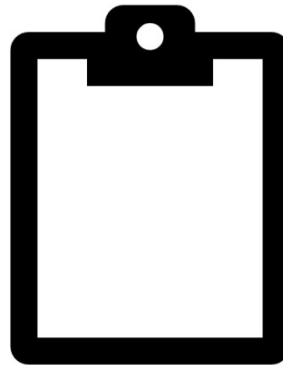
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