

# Introduction to Modern Statistics

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2025 Winter

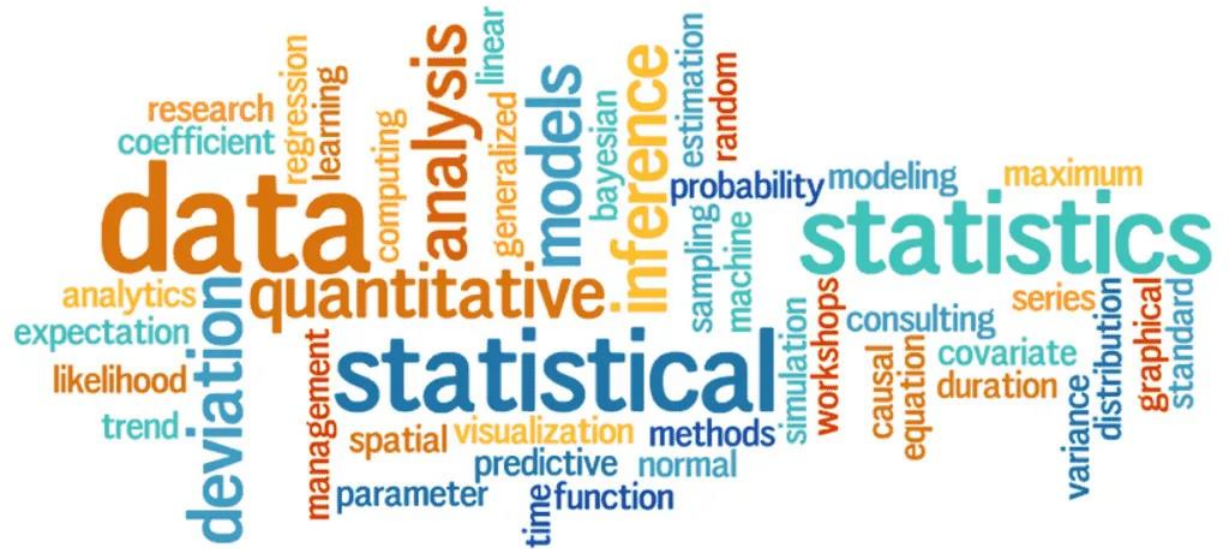
# Notation of the slides

- Code or Pseudo-Code chunk starts with " ➤ ", e.g.  
➤ `print("Hello world!")`
- Link is underlined
- Important terminology is in **bold** font
- Practice comes with



# Agenda

- Day 1: Probability and Statistics basics
  - Uncertainty; Probability; Distribution
  - Descriptive statistics
- Day 2: **Inference**
  - Hypothesis testing and  $p$ -values
  - Permutation test and bootstrap
  - False discovery rate control
- Day 3: **Modeling**
  - Regression techniques
  - Model selection



# Day 2: Statistical inference

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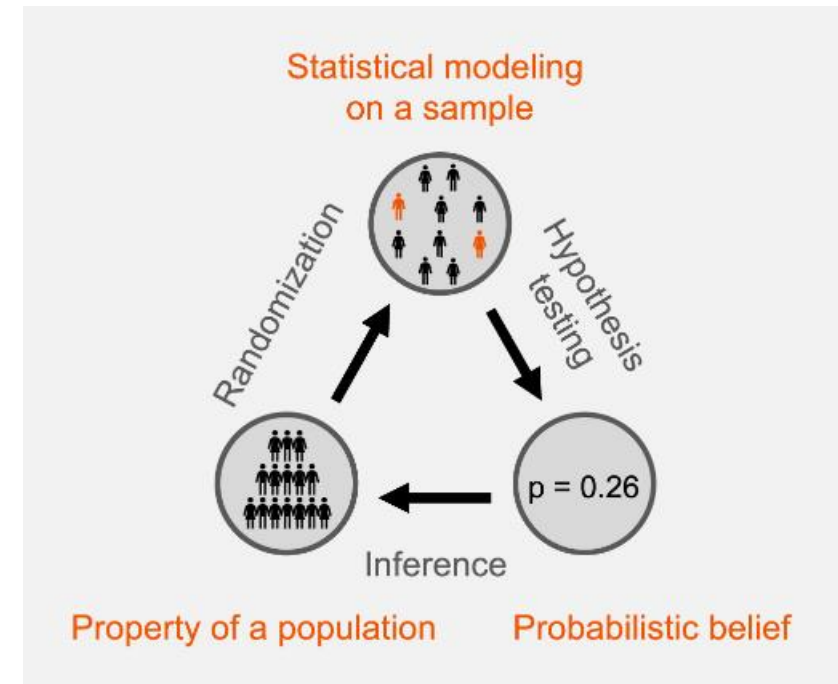
# Overview

## Time

- 2-hour workshop (45min + 45min + practice/Q&A)

## Topics

- ☐ Inferential statistics basics
- ☐ Hypothesis testing
- ☐ Permutation test
- ☐ Bootstrap
- ☐ Multiple test correction



# Summary – Day1

## Introduction to statistics

- ☐ Concept
- ☐ History
- ☐ Importance



## Uncertainty

- ☐ Causes
- ☐ Examples in real life
- ☐ How do we react with it



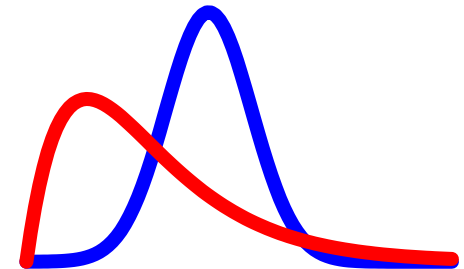
# Summary – Day1

## Probability

- ❑ Events and sample space
- ❑ Probability and its properties  $P(\mathbf{A}) = \frac{|\mathbf{A}|}{|\mathbf{\Omega}|}$
- ❑ Conditional probability  $P(\mathbf{A} \mid \mathbf{B}) = \frac{P(\mathbf{AB})}{P(\mathbf{B})}$
- ❑ Bayes Theorem



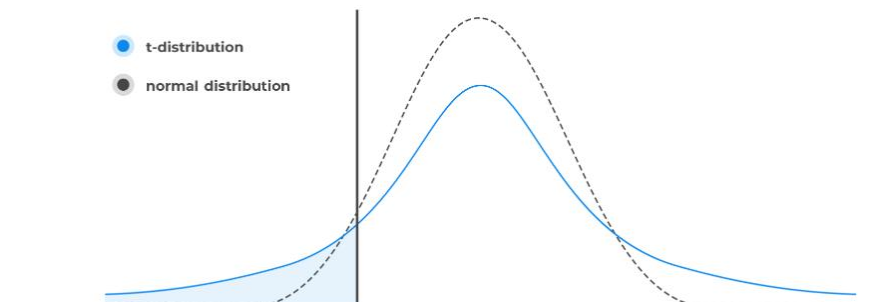
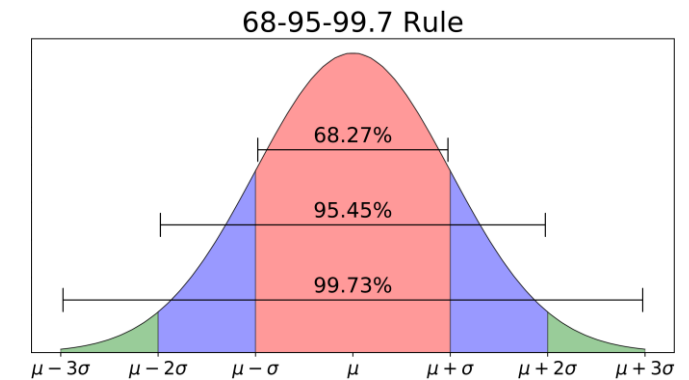
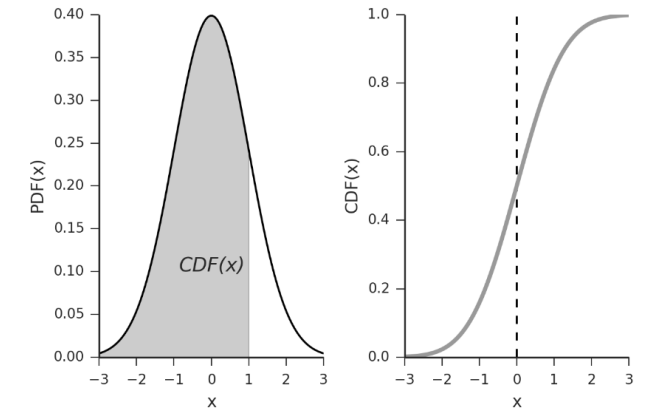
$$P(A|B) = \frac{P(B|A)P(A)}{P(B)}$$



# Summary – Day1

## Distributions

| Category   | Name              | Description  |
|------------|-------------------|--|
| Discrete   | Uniform           | equal probability to every integer between $a$ and $b$   |
|            | Bernoulli         | single trial with two possible outcomes with success rate $p$  |
|            | Binomial          | number of successes in $n$ independent Bernoulli trials  |
|            | Negative Binomial | number of failures before achieving $r$ successes  |
|            | Geometric         | number of trials needed to get the first success in a series of Bernoulli trials   |
|            | Hypergeometric    | the number of successes in a sample of size $n$ drawn without replacement from a population of size $N$ containing $K$ successes |
|            | Poisson           | number of events occurring in a fixed interval of time or space  |
| Continuous | Uniform           | equally probability to every value in an interval $[a,b]$  |
|            | Normal            | bell curve center around mean $\mu$ with standard deviation $\sigma$   |
|            | $t$               | Similar to Normal but with heavier tails   |
|            | Chi-square        | models the sum of the squares of $k$ independent standard normal variables   |
|            | F                 | compare variances between two groups   |
|            | Exponential       | models the time between events in a Poisson process  |
|            | Beta              | model proportions and probabilities  |



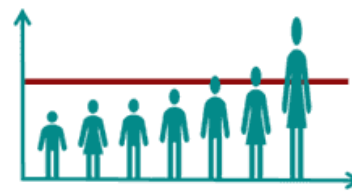


# Summary – Day1

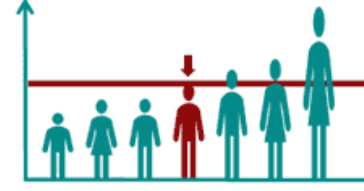
## Descriptive statistics

- Tendency
- Dispersion
- Skewness
- Distribution

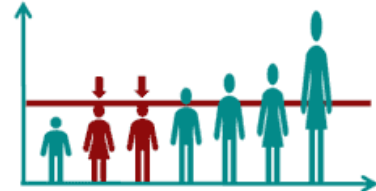
Mean



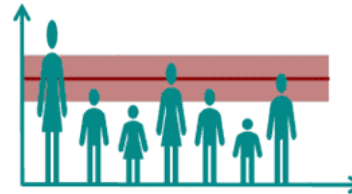
Median



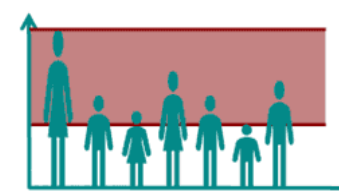
Mode



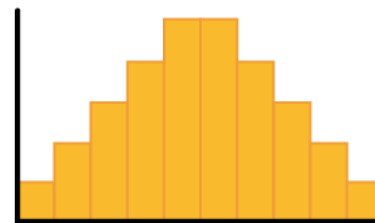
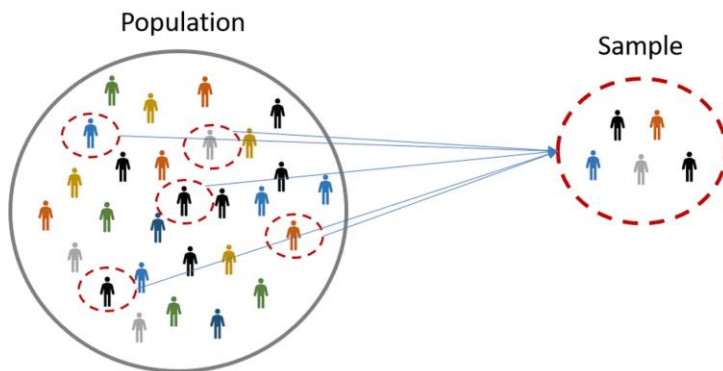
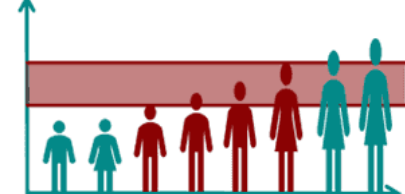
Standard Deviation



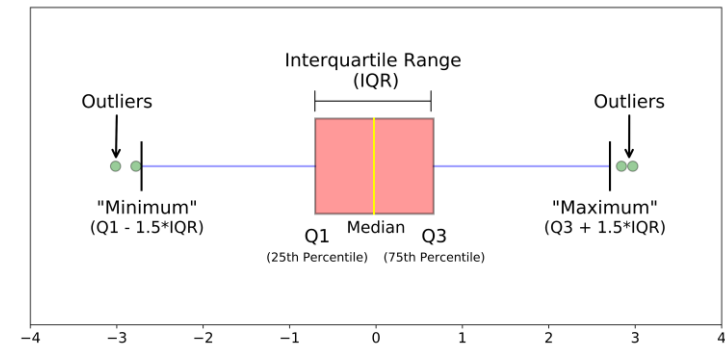
Range

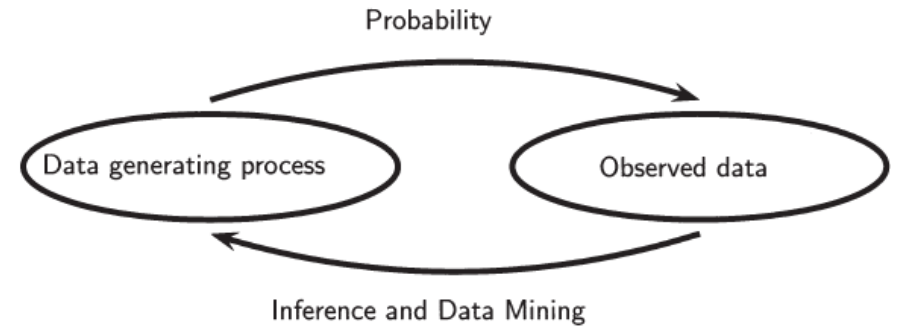


Interquartile Range



**Normal distribution**  
(unimodal, symmetric,  
the “bell curve”)



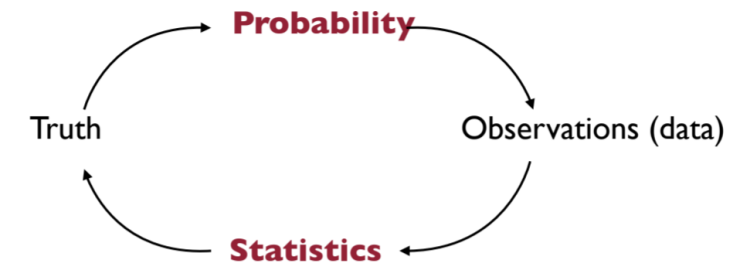
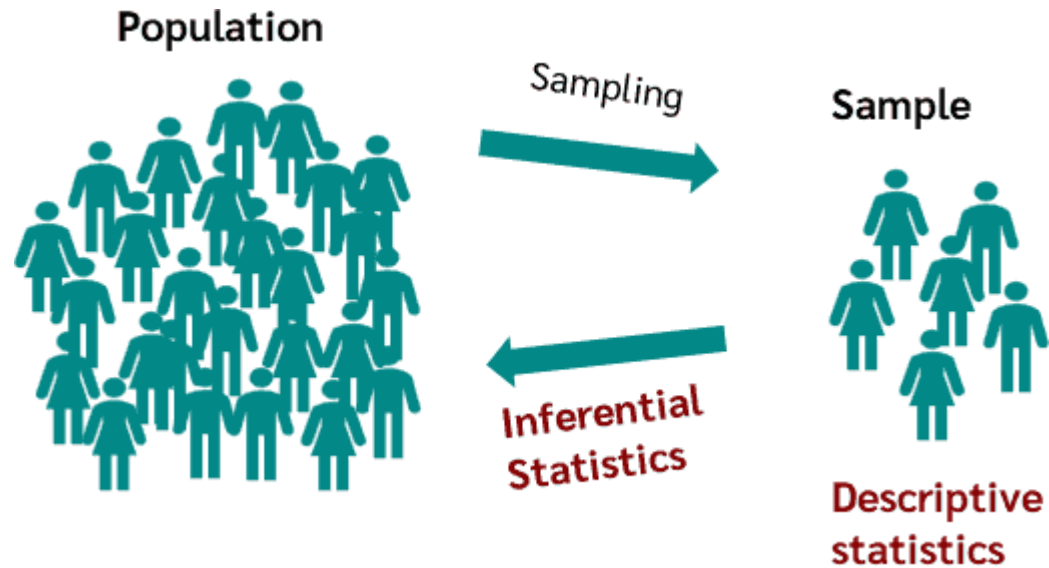


# Inferential statistics

Use the part to learn about the whole

# Inferential statistics

Draw conclusions about the population based on sample data



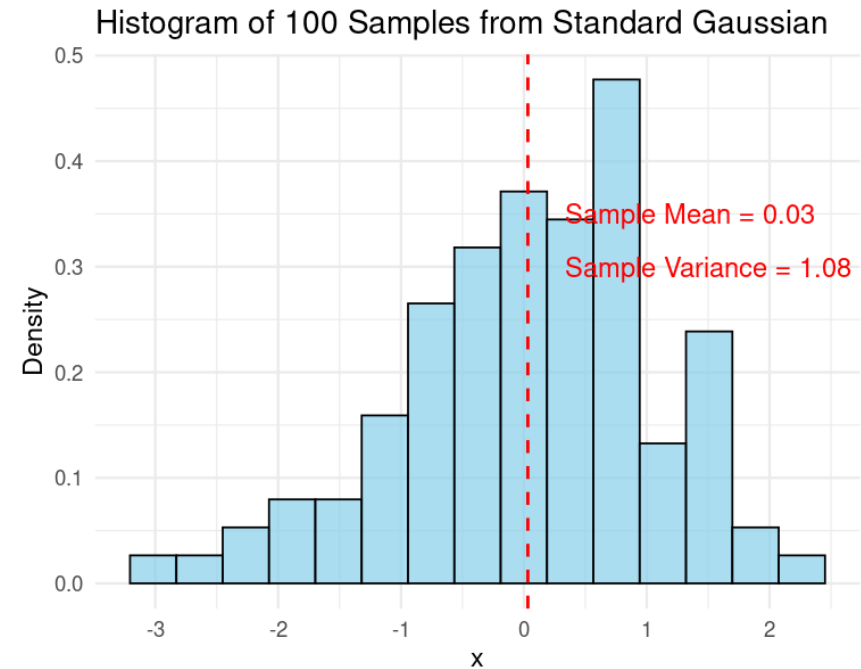
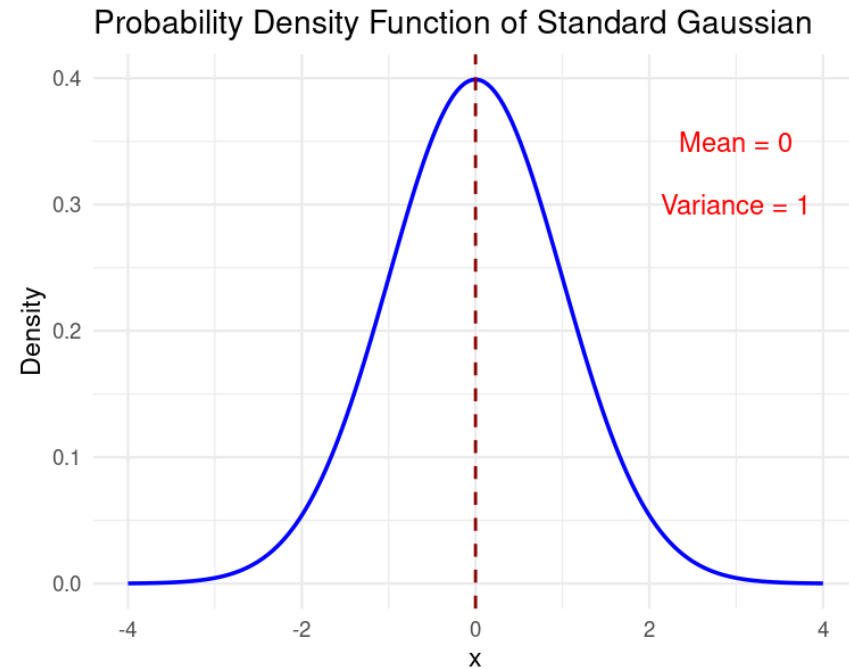
## Typical tasks

- ❑ Parameter **estimation**
- ❑ Hypothesis **testing**

Given a sample  $x_1, \dots, x_n \sim F$ , how do we infer  $F$ ?

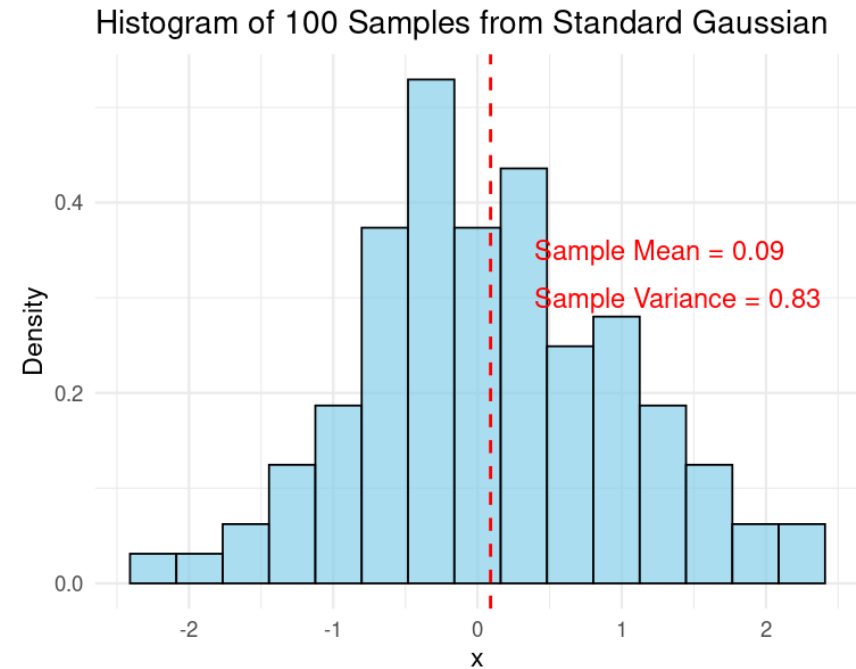
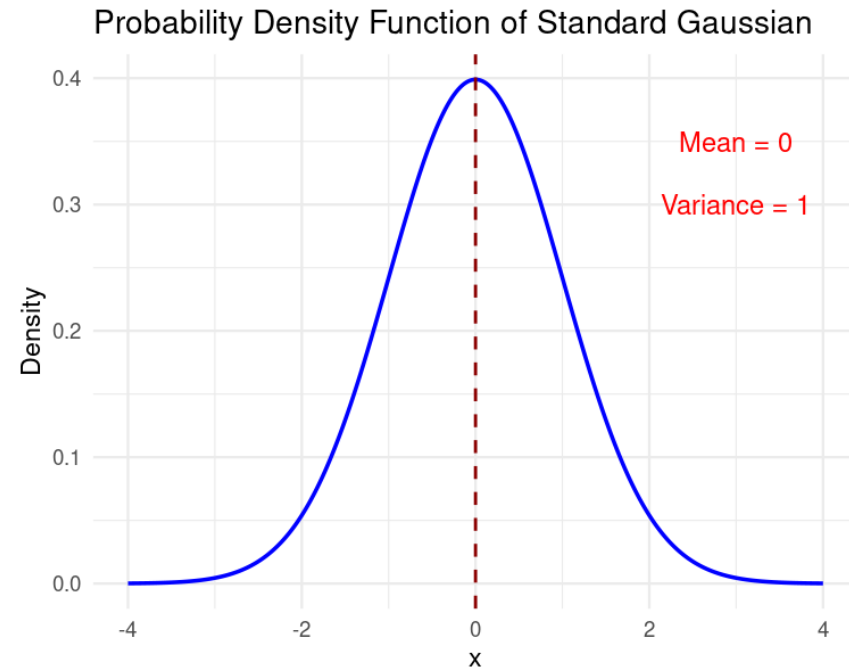
# Population vs samples

Use standard gaussian as an example



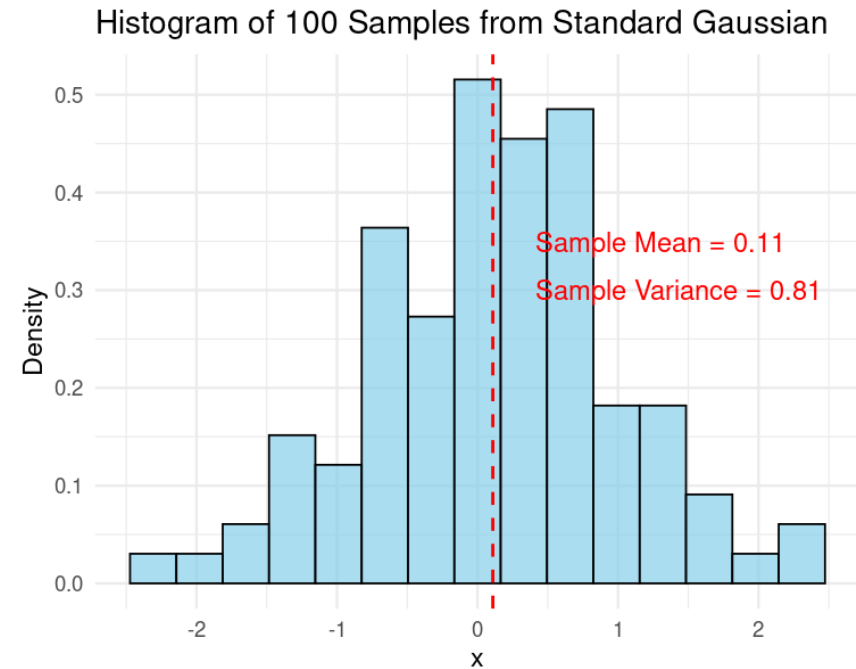
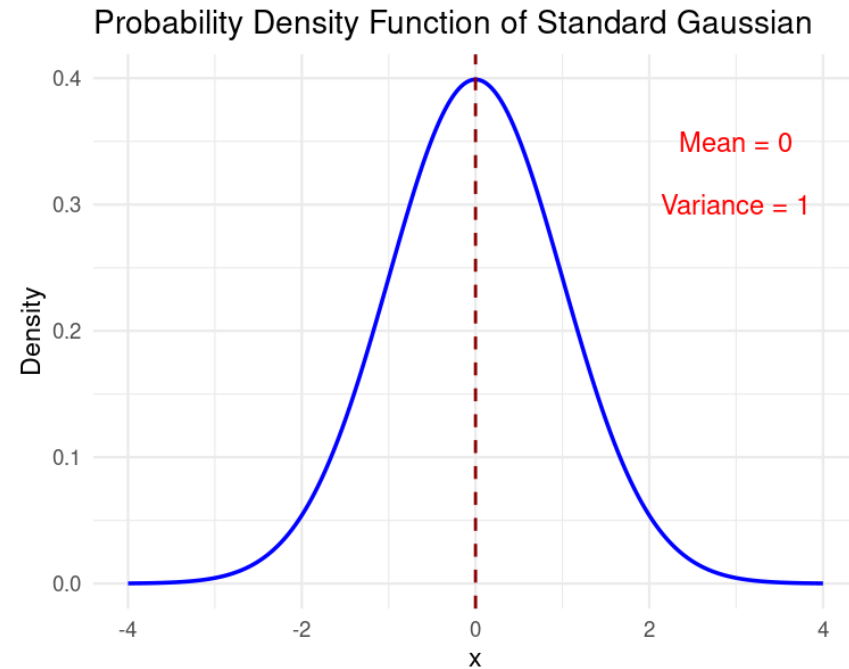
# Population vs samples

Use standard gaussian as an example



# Population vs samples

Use standard gaussian as an example



Sampling is **random**, so are the summary statistics (sample mean/sample variance)

# Expectation and Variance

## Population

Mean:

$$E(X) = \sum x_i P(x_i) = \int_{-\infty}^{+\infty} x f(x) dx$$

Variance:

$$Var(X) = E[(X - E(X))^2]$$

## Samples

Mean:

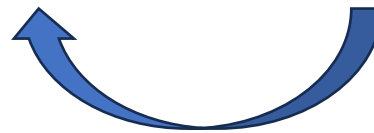
$$\frac{\sum_{i=1}^n x_i}{n}$$

Variance:

$$s^2 = \frac{\sum_{i=1}^n (x_i - \bar{x})^2}{n - 1}$$

**Parameter:** a property of the distribution

**Statistic:** a summary calculated from samples

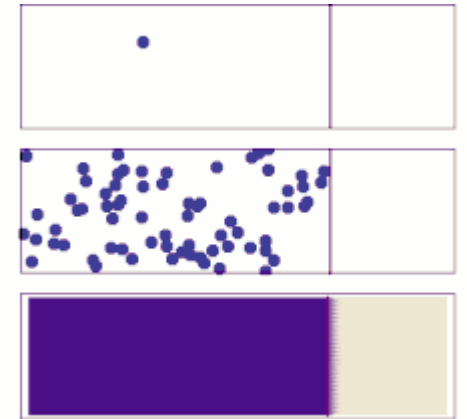


# Law of large numbers (LLN)

**5.6 Theorem** (The Weak Law of Large Numbers (WLLN)).

*If  $X_1, \dots, X_n$  are IID, then  $\bar{X}_n \xrightarrow{P} \mu$ .*

$$\mathbb{P}(|\bar{X}_n - \mu| > \epsilon) \leq \frac{\mathbb{V}(\bar{X}_n)}{\epsilon^2} = \frac{\sigma^2}{n\epsilon^2}$$



Diffusion is an example of the law of large numbers.

In summary:

- Sample mean converges to population mean as sample size increases
- LLN provides Implications for estimation and reliability

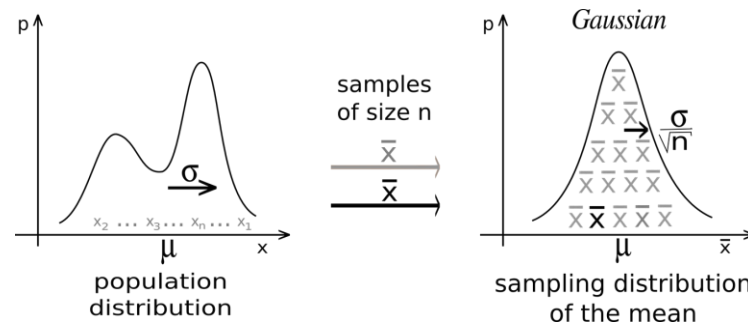


# Central limit theorem (CLT)

**5.8 Theorem** (The Central Limit Theorem (CLT)). *Let  $X_1, \dots, X_n$  be IID with mean  $\mu$  and variance  $\sigma^2$ . Let  $\bar{X}_n = n^{-1} \sum_{i=1}^n X_i$ . Then*

$$Z_n \equiv \frac{\bar{X}_n - \mu}{\sqrt{\mathbb{V}(\bar{X}_n)}} = \frac{\sqrt{n}(\bar{X}_n - \mu)}{\sigma} \rightsquigarrow Z$$

where  $Z \sim N(0, 1)$ . In other words,



In summary:

- Distribution of sample means approaches normal distribution as sample size grows.
- CLT allows for hypothesis testing and constructing confidence interval using normal approximation.

# Let's do some practice!

➤ git clone <https://github.com/wbvguo/qcbio-Intro2ModernStats.git>



# Hypothesis testing

*“To reject or not to reject, that is the question.”*



Wenbin Shakespeare  
A famous nobody

# Hypothesis testing

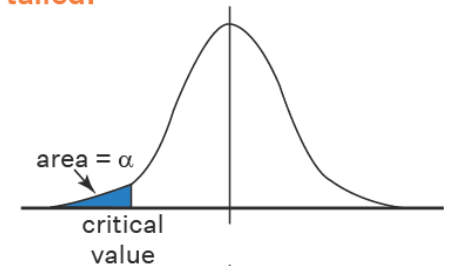
A process to determine if there is enough evidence to **reject** a null hypothesis

## Procedure:

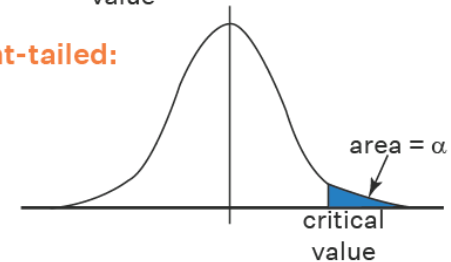
- ❑ Frame the hypothesis
  - Null hypothesis ( $H_0$ ): no difference/effect, ...
  - Alternative hypothesis ( $H_a$  or  $H_1$ ): there is an effect/difference, ...
- ❑ Choose an appropriate Test Statistics
- ❑ Calculate the statistical significance ( $p$ -value)
- ❑ Compare to a significance level ( $\alpha$ )
- ❑ Make decision: reject/not reject

Rejection Region for Null Hypothesis

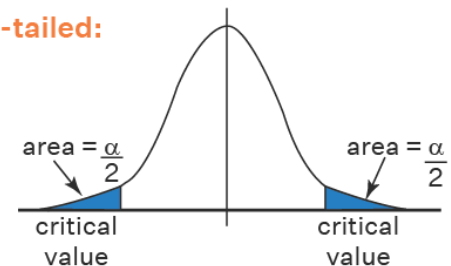
left-tailed:



right-tailed:



two-tailed:



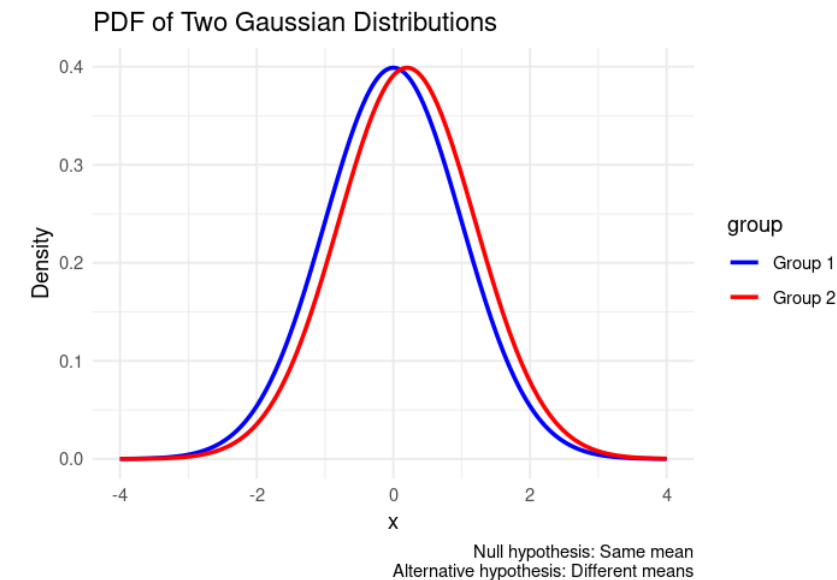
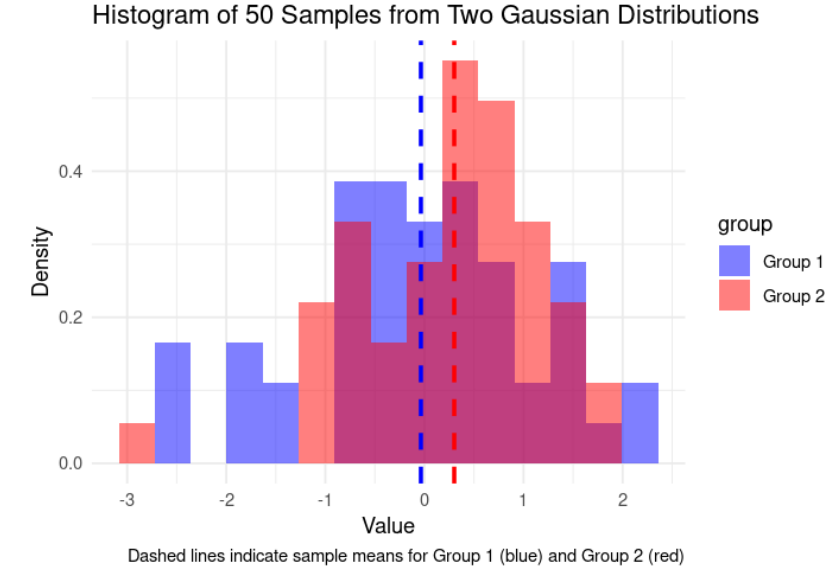
- - Reject  $H_0$
- - Do not reject  $H_0$

# Let's see an example

## Use gaussian distributions as an example

### □ Frame the hypothesis

- Null hypothesis ( $H_0$ ): two group have the same mean
- Alternative hypothesis ( $H_a$ ): two group have the different mean



# Let's see an example

## Use gaussian distributions as an example

### ❑ Frame the hypothesis

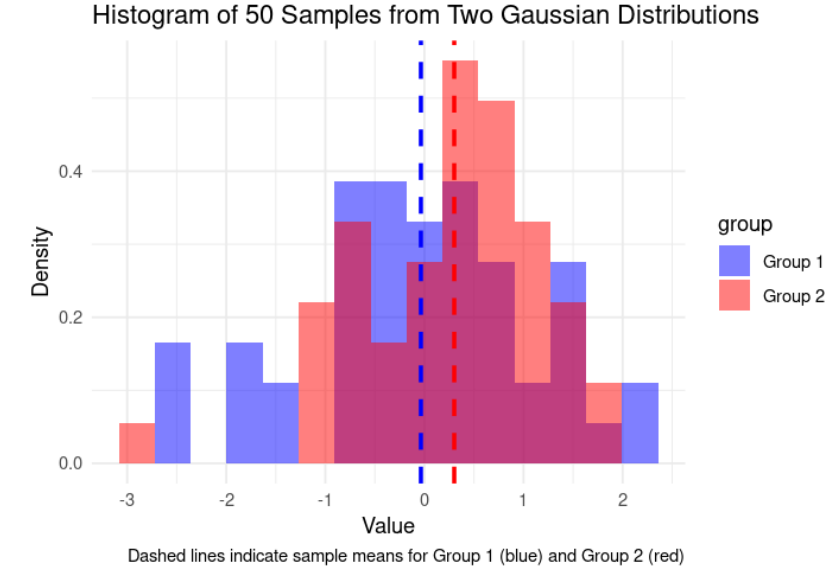
- Null hypothesis ( $H_0$ ): two group have the same mean
- Alternative hypothesis ( $H_a$ ): two group have the different mean

### ❑ Choose an appropriate Test Statistics: t-test

### ❑ Calculate the statistical significance ( $p$ -value)

### ❑ Compare to a significance level ( $\alpha$ )

### ❑ Make decision: reject/not reject



```
{r}  
t.test(samples_group1, samples_group2)
```

Welch Two Sample t-test

```
data: samples_group1 and samples_group2  
t = -1.6104, df = 93.647, p-value = 0.1107  
alternative hypothesis: true difference in means is not equal to 0  
95 percent confidence interval:  
-0.7511248 0.0783784  
sample estimates:  
mean of x mean of y  
-0.03567178 0.30070141
```

# Rethink about hypothesis testing

**Reject:** Why our goal is to reject? not to prove?

- Proving something to be true is difficult, proving something to be false is usually easier, as long as you can find a counter-example.

**Enough evidence:**

- **Presumption of innocence:** any defendant in a criminal trial is assumed to be innocent until they have been proven guilty

In other words, hypothesis testing is **conservative**, we turn to not reject unless we have enough evidence



Better Call Saul

# Fail to reject == the hypothesis is true?

**No**, this is not a binary world

Example: Clinical Trail for new drug

A clinical trial tests whether a new drug reduces blood pressure. The  $p$ -value for the difference between the drug and placebo group is **0.16**—greater than the conventional **0.05** threshold.

- The **absence of evidence** (failing to reject the null hypothesis) **does not prove** that the drug has no effect.
- The trial might have been underpowered (small sample size), lacking the data needed to detect a true effect.

In statistics, **failing to find evidence** does not imply **evidence of no effect**—it may simply reflect study limitations.

*“Absence of evidence is not evidence of absence”*



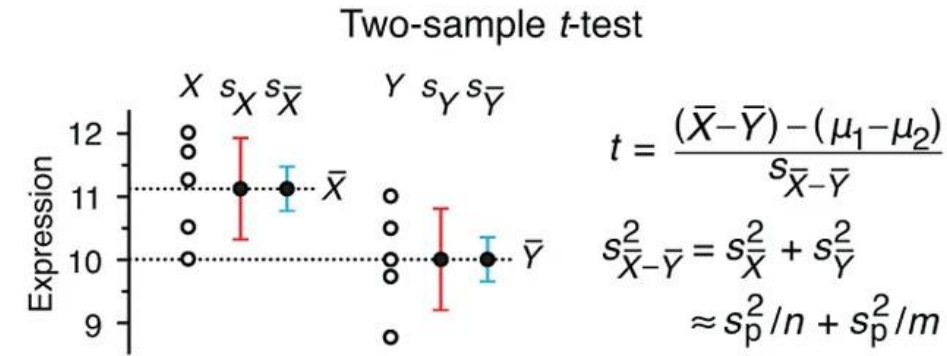
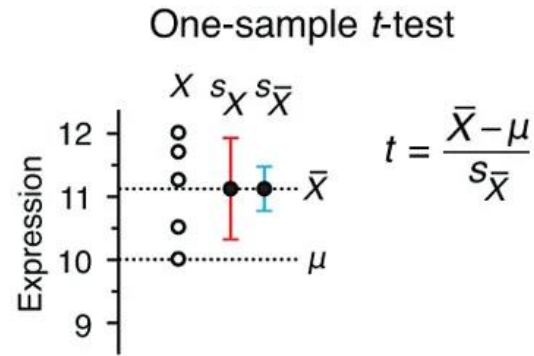
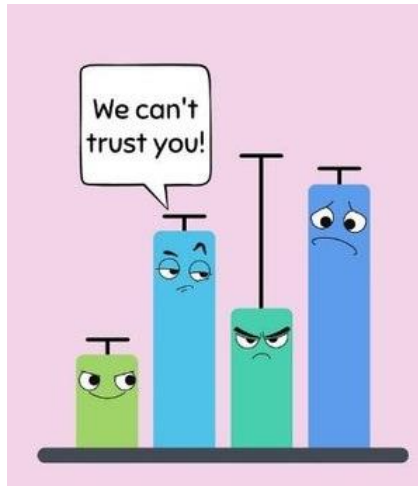
Carl Edward Sagan  
(1934-1996)



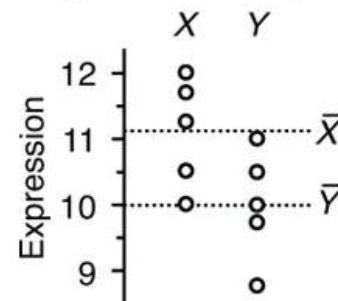
# Statistical tests

- Test mean:

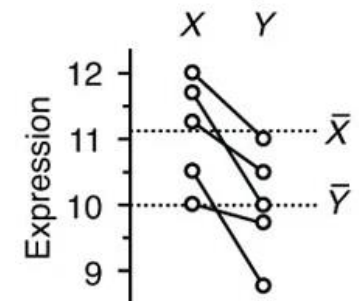
- ☐ One group
- ☐ Two group
- ☐ Paired
- ☐ Multiple group



Independent samples

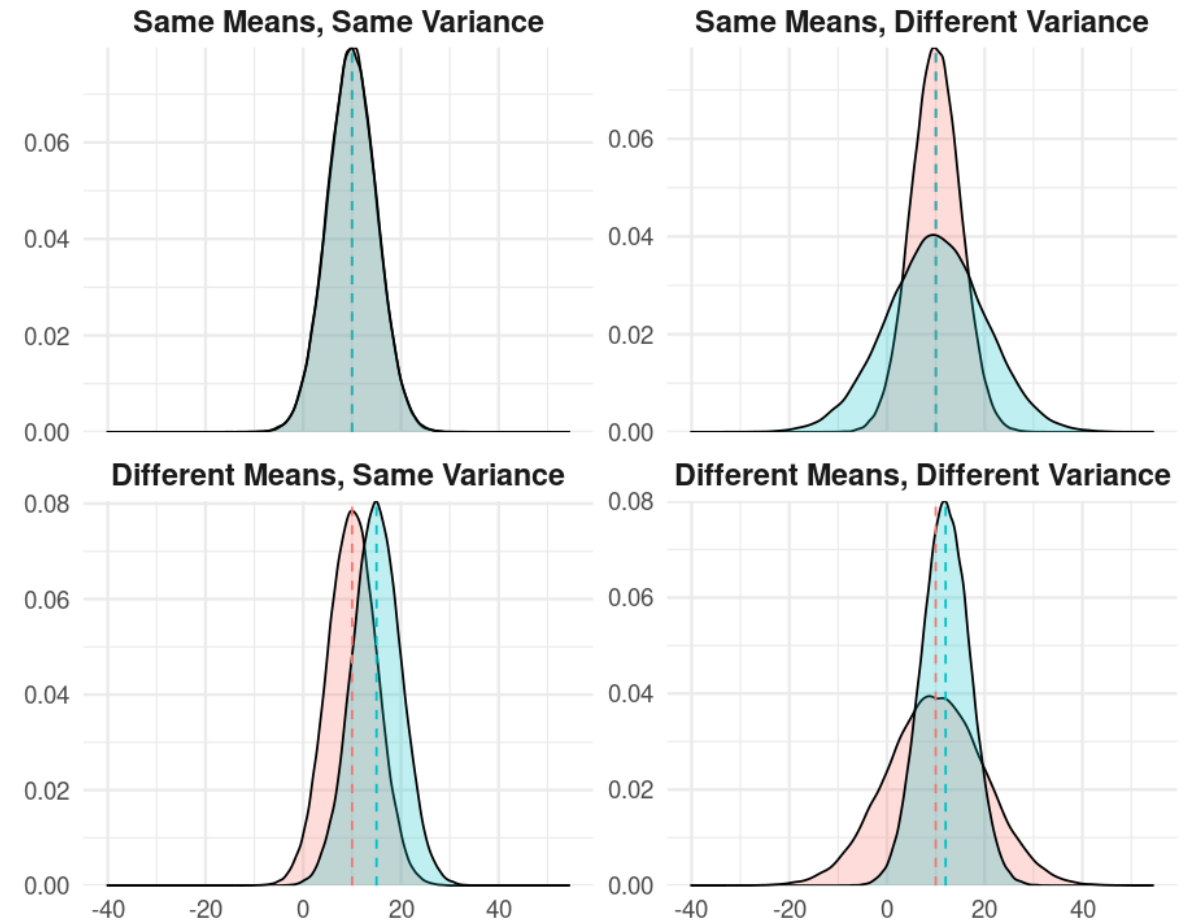


Paired samples



# Statistical tests

- Test mean:
  - ☐ One group
  - ☐ Two group
  - ☐ Paired
  - ☐ Multiple group
- Test variance
- Test distribution



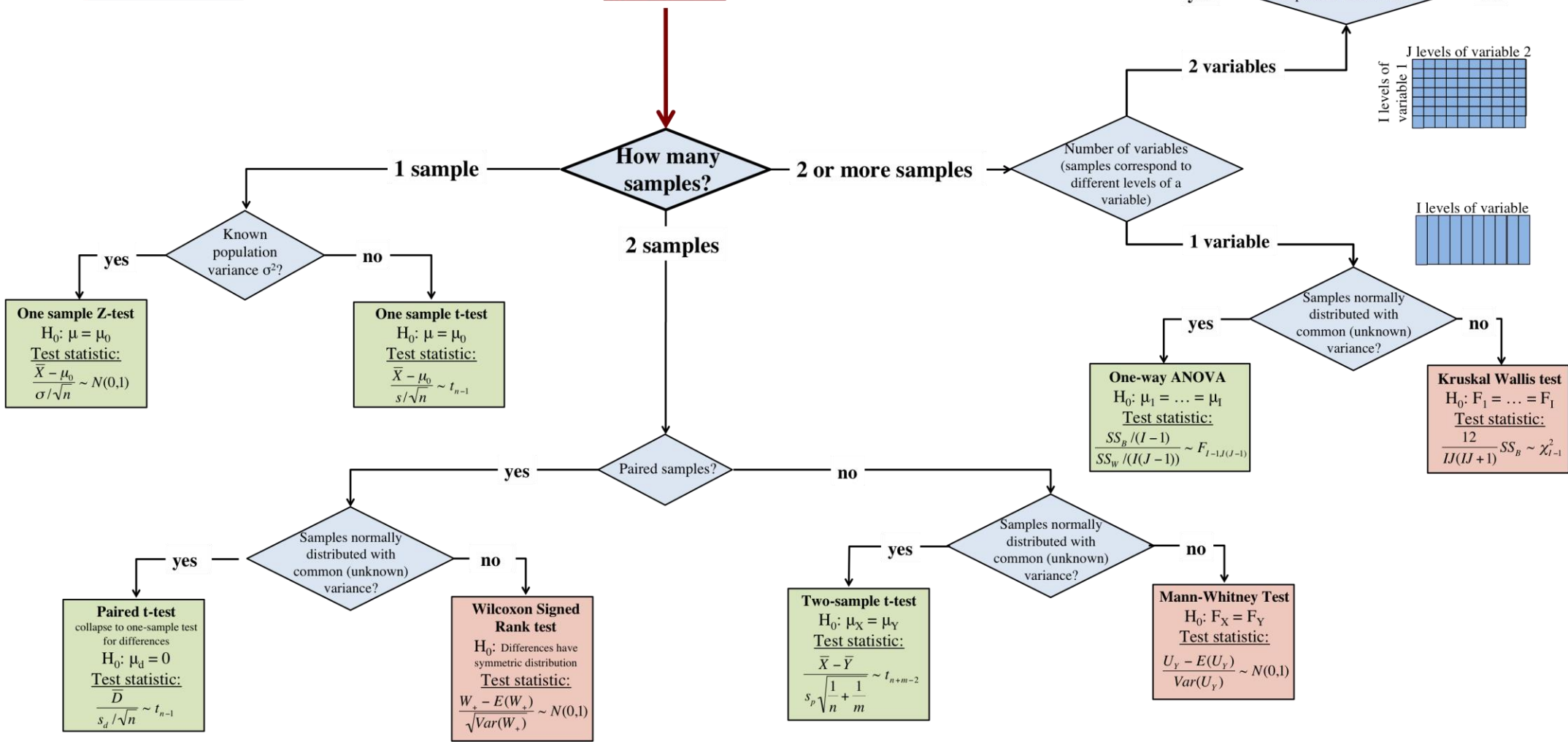
# Which test to use?

Because flow-charts are fun!

Parametric test

Non-Parametric test

## TESTING HYPOTHESES ABOUT THE MEAN



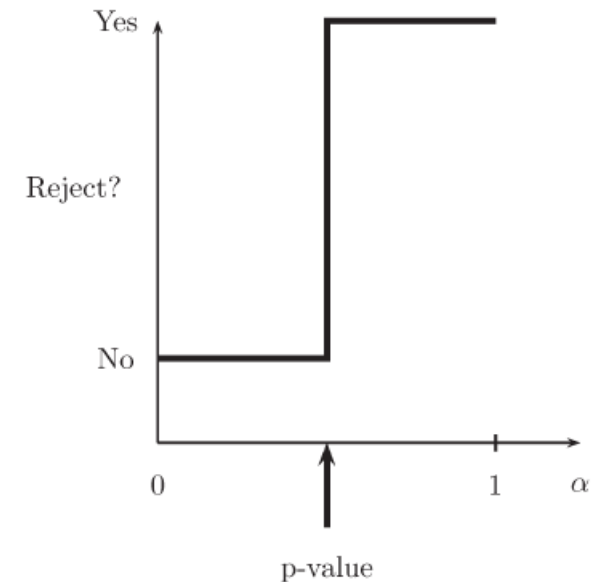
# $p$ -value

The  $p$ -value is the probability (under  $H_0$ ) of observing a value of the test statistic the same as or more extreme than what was actually observed.

- a measure of the evidence against  $H_0$
- the smaller the  $p$ -value, the stronger the evidence against  $H_0$ .

Typically,

| p-value     | evidence                            |
|-------------|-------------------------------------|
| $< .01$     | very strong evidence against $H_0$  |
| $.01 - .05$ | strong evidence against $H_0$       |
| $.05 - .10$ | weak evidence against $H_0$         |
| $> .1$      | little or no evidence against $H_0$ |



# True or false?



- large  $p$ -value is strong evidence in favor of  $H_0$ .
  - False
- The  $p$ -value is the probability that the null hypothesis is true
  - False
- $p = 0.05$  means there's a 95% chance  $H_0$  is true
  - False

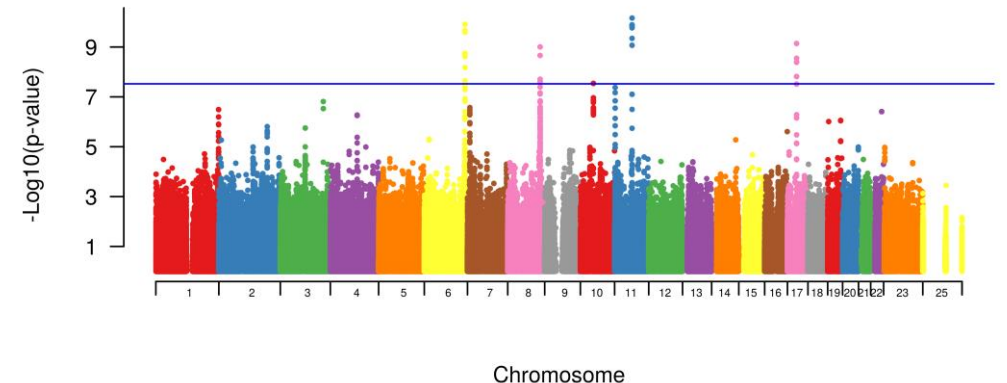
# $p$ -value distribution when $H_0$ is true

$$\begin{aligned} \Pr(P < p) &= \Pr(F^{-1}(P) < F^{-1}(p)) \\ &= \Pr(T < t) \\ &\equiv p; \end{aligned}$$

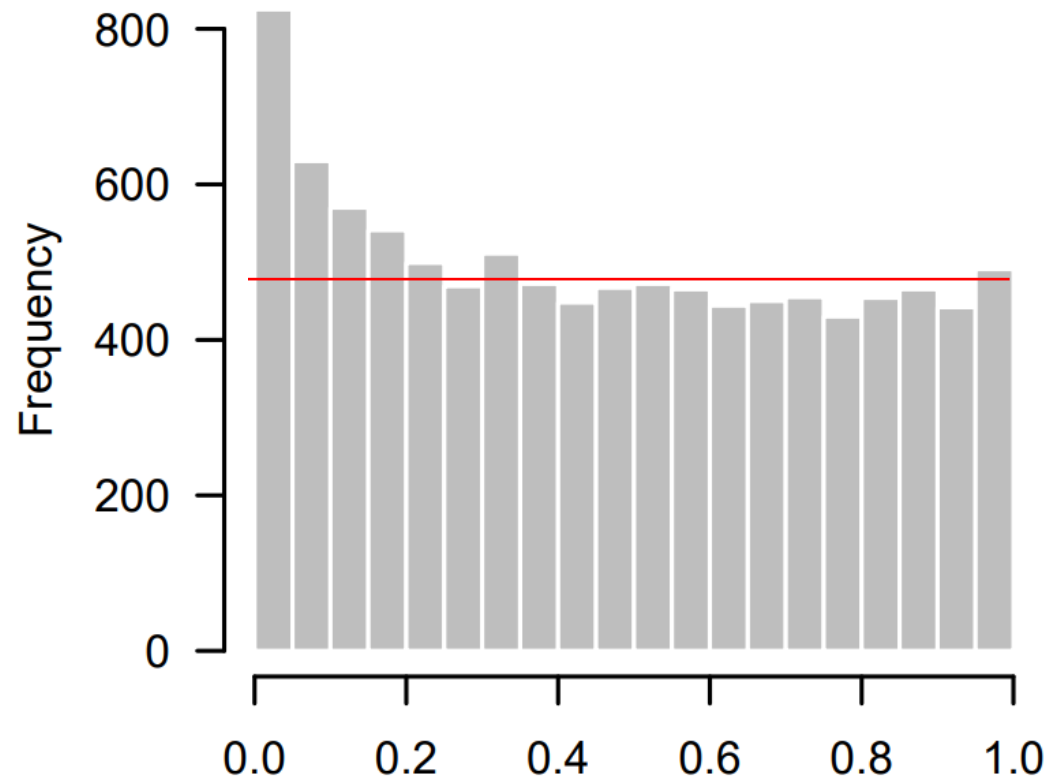
$p$ -value follows **uniform** distribution under the Null

Can use this rationale to diagnostic

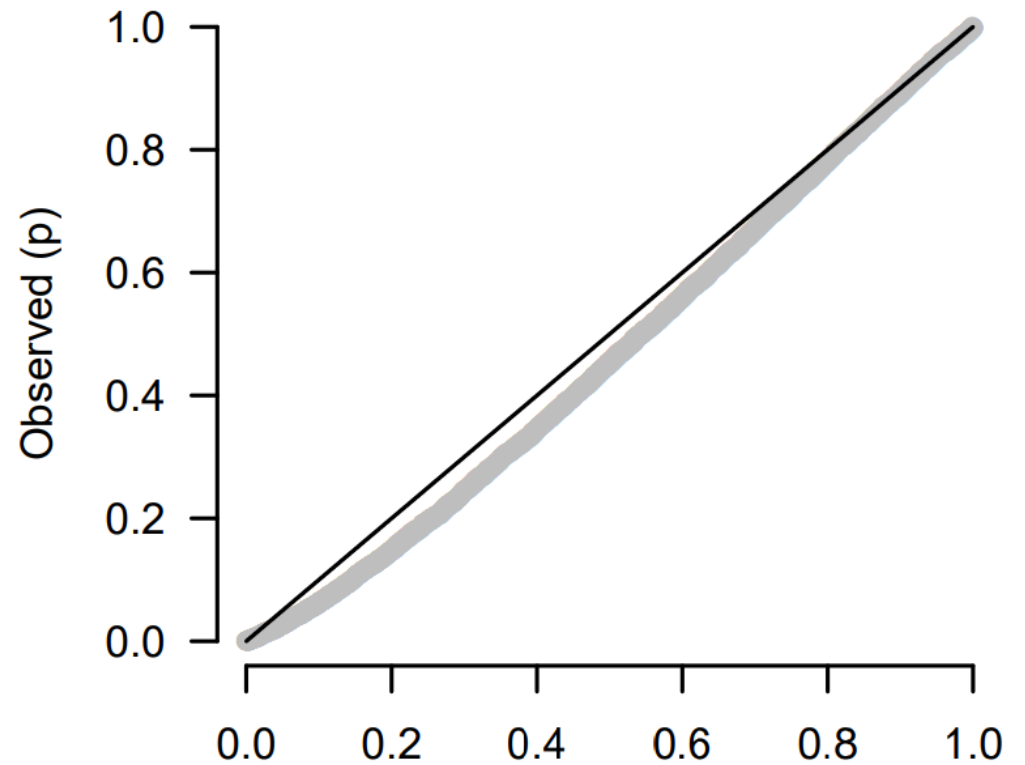
- Histogram of  $p$ -values
- Quantile-Quantile plot (QQ plot)



# Examine $p$ -value distribution



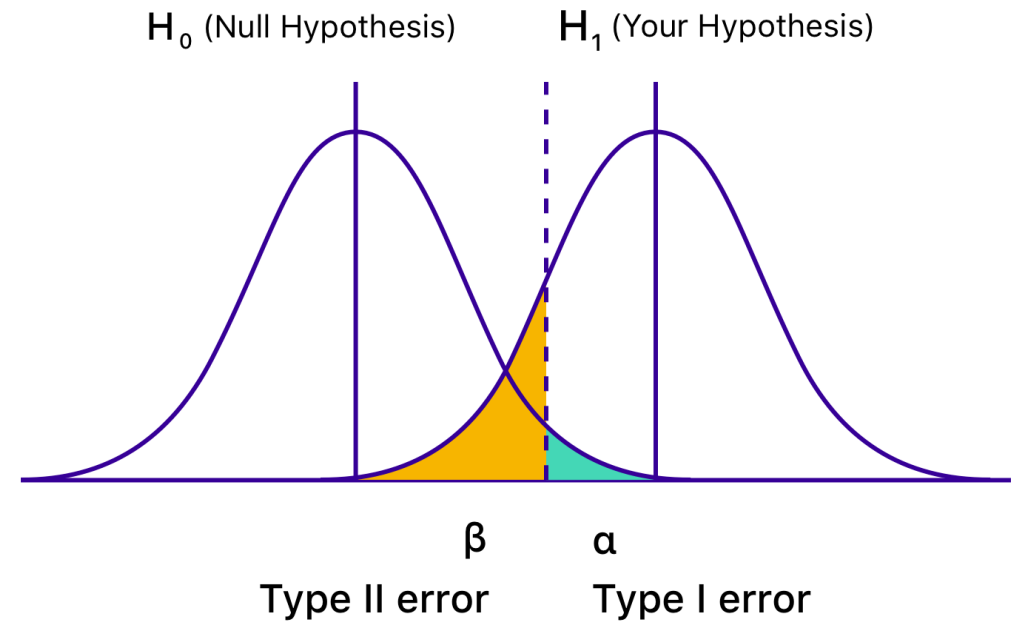
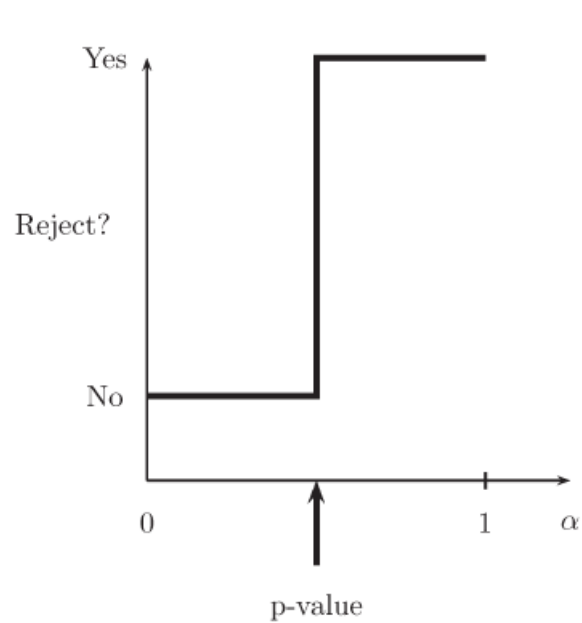
$p$   
Histogram



Expected (p)  
Quantile-Quantile plot

# Decision errors

We use statistics to make decisions

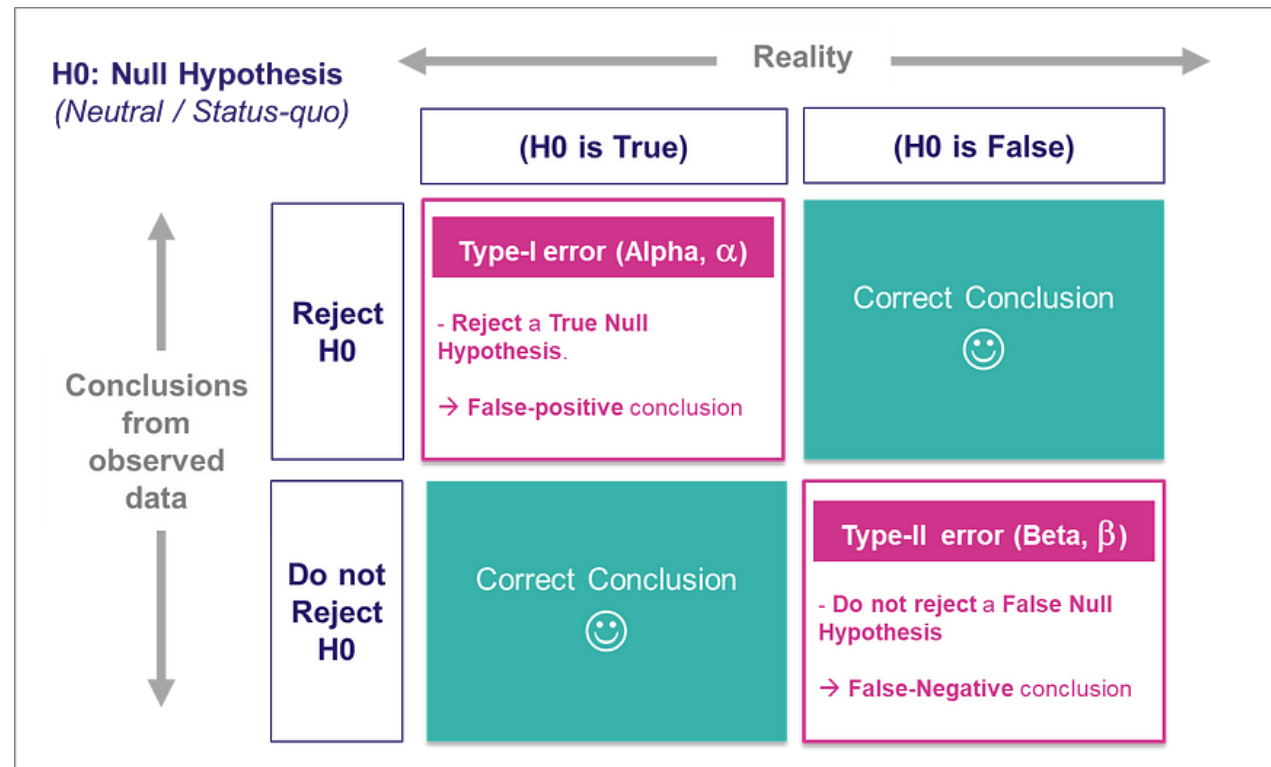




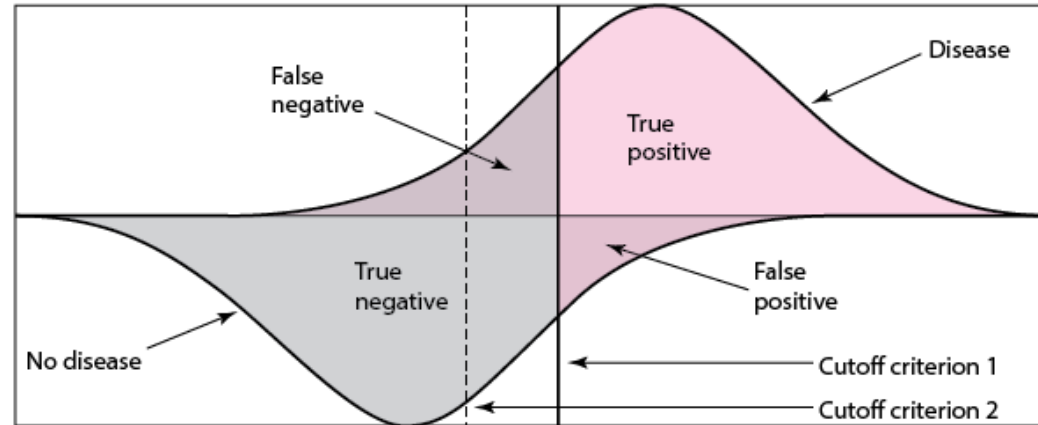
# Decision errors

But the decisions can be wrong...

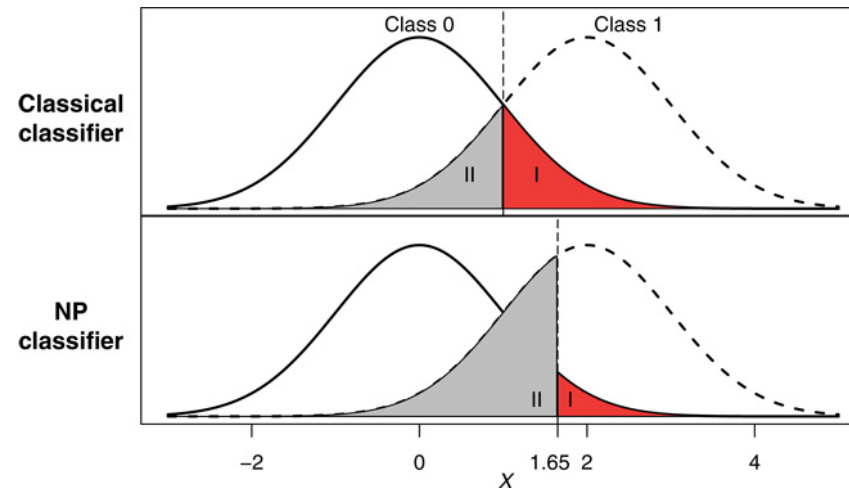
- ❑ Reject the null when it's true
- ❑ Fail to reject the null when it's not true



# Decision errors and asymmetry classification



Put one type of error under control while minimizing the other one



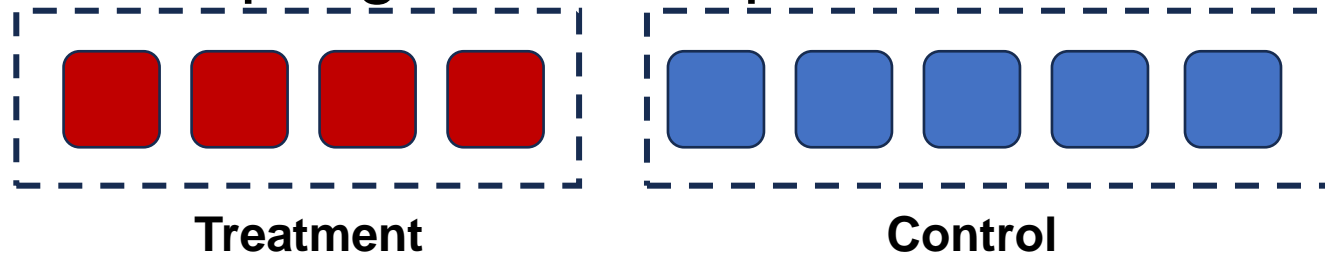


# Permutation and Bootstrap

Computer Age Statistical Inference

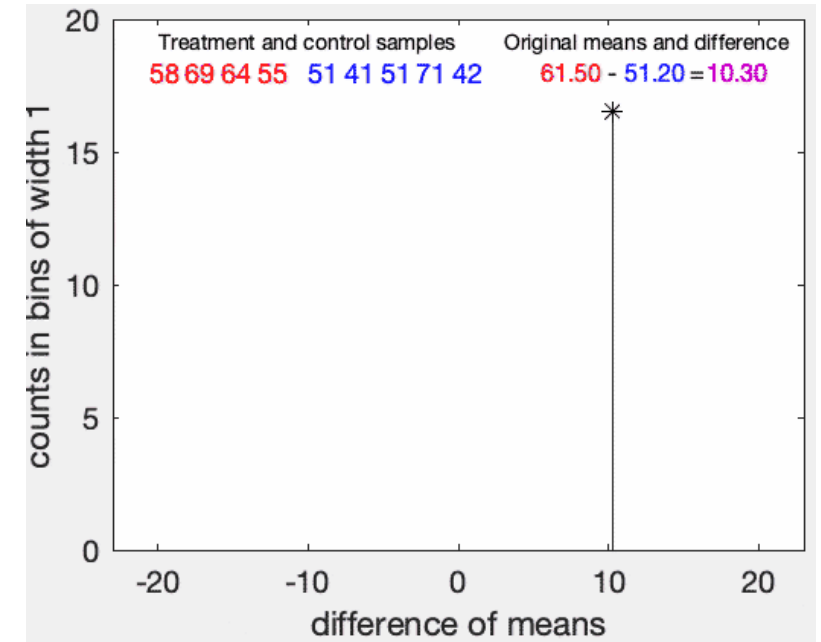
# Permutation test

## Resampling without replacement



## Procedure

- ❑ Define the hypothesis
- ❑ Define the test statistics
- ❑ Randomly permute the data
- ❑ Calculate the test statistics for each permutation
- ❑ Compare the observed test statistics with the permuted test statistic distribution



$$p = \frac{\sum_{i=1}^B I(\Delta\theta^{(i)} > t)}{B}$$

# Permutation test

Take sex\_discrimination data as an example

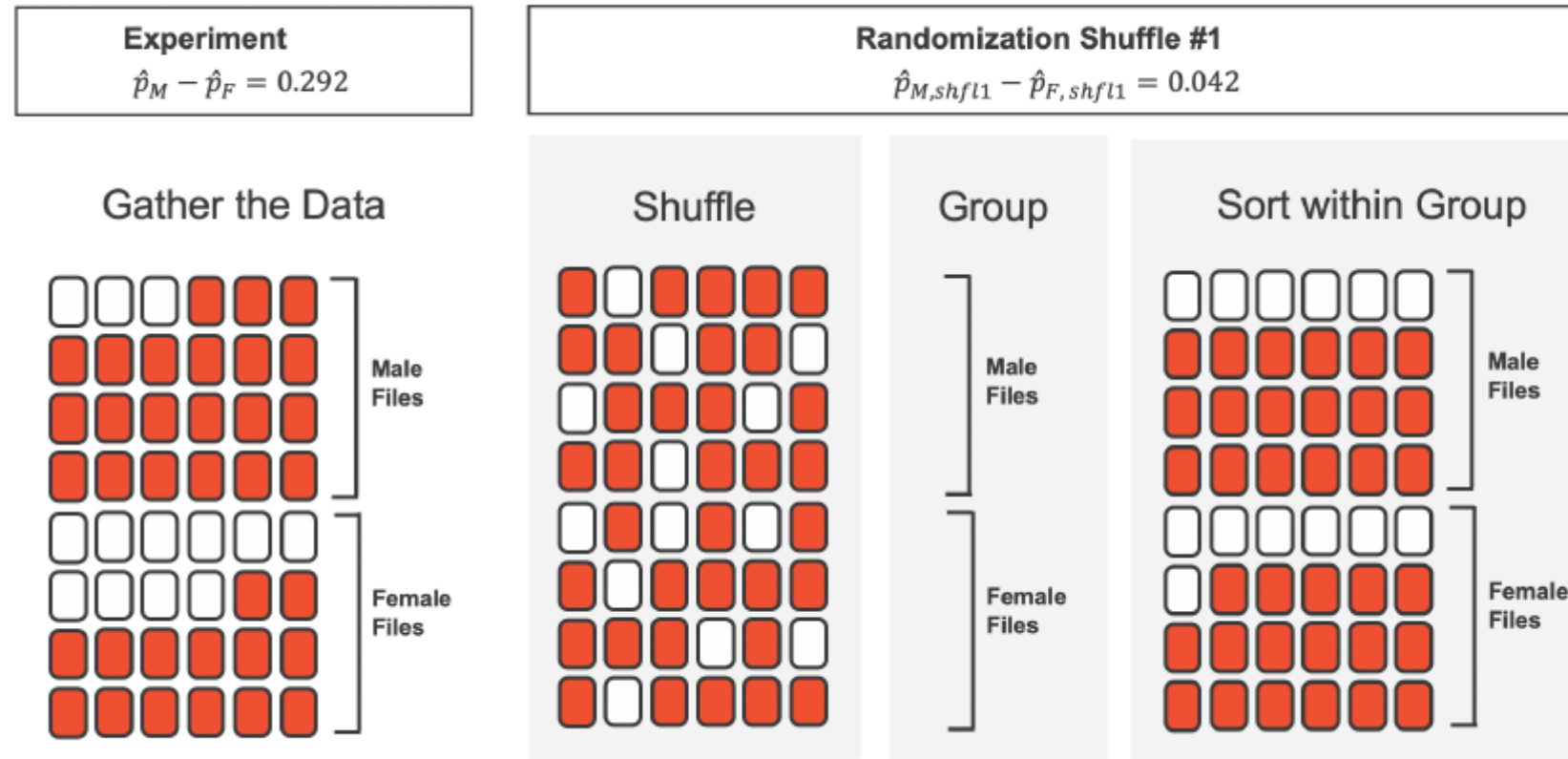
Table 11.1: Summary results for the sex discrimination study.

| sex    | decision |              | Total |
|--------|----------|--------------|-------|
|        | promoted | not promoted |       |
| male   | 21       | 3            | 24    |
| female | 14       | 10           | 24    |
| Total  | 35       | 13           | 48    |

We can clearly see that %promotion is higher in male population, but how to get the significance?

# Permutation test

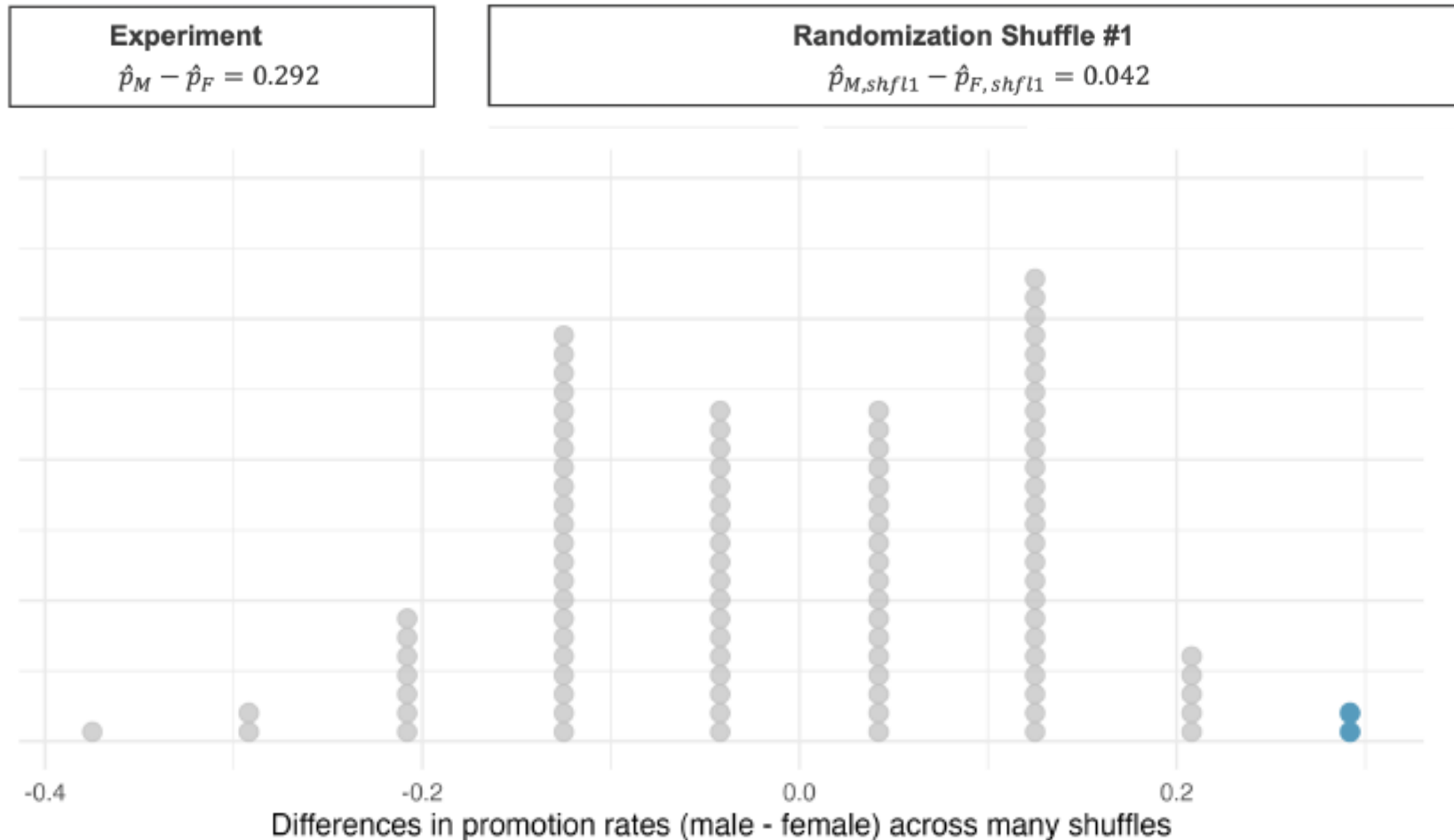
Take sex\_discrimination data as an example



Repeat the shuffling many times

# Permutation test

Take sex\_discrimination data as an example



**Observed statistic**  
**vs.**  
**null statistics**

$$p = \frac{\sum_{i=1}^B I(\Delta\theta^{(i)} > t)}{B}$$

# Permutation test

## Pros:

- ❑ **Distribution-free:** No assumptions about data distribution (non-parametric); Works well with skewed or non-normal data.
- ❑ **Flexible:** Applicable to a wide range of test statistics (mean, median, correlation, etc.).
- ❑ **Easy to implement:** Simple concept based on resampling.

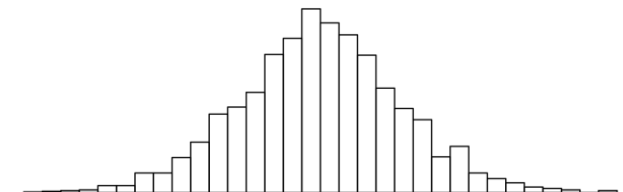
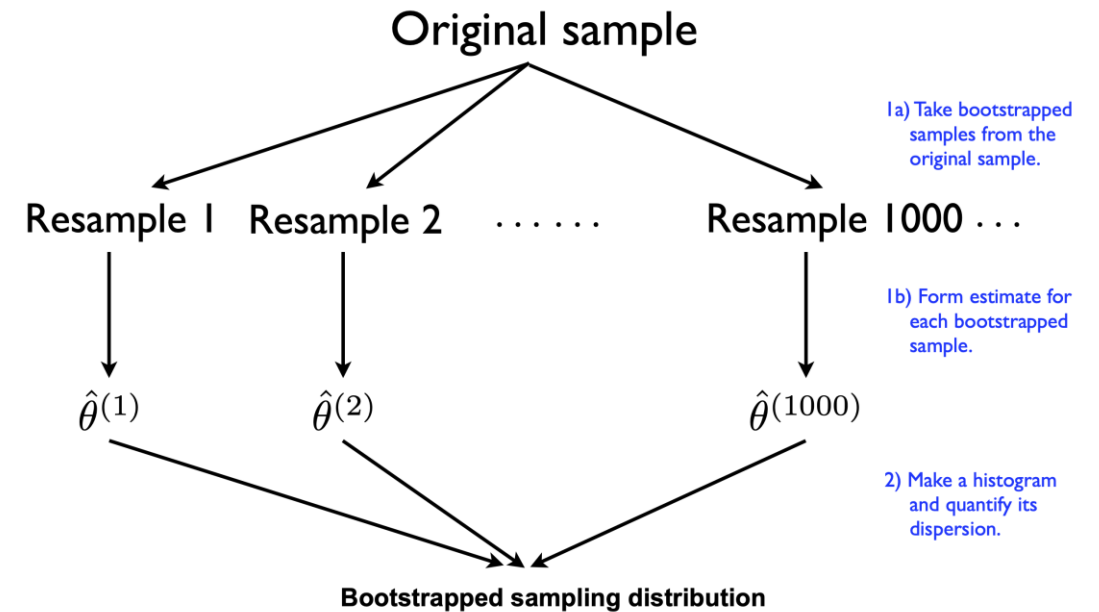
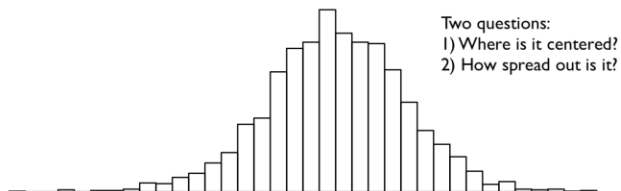
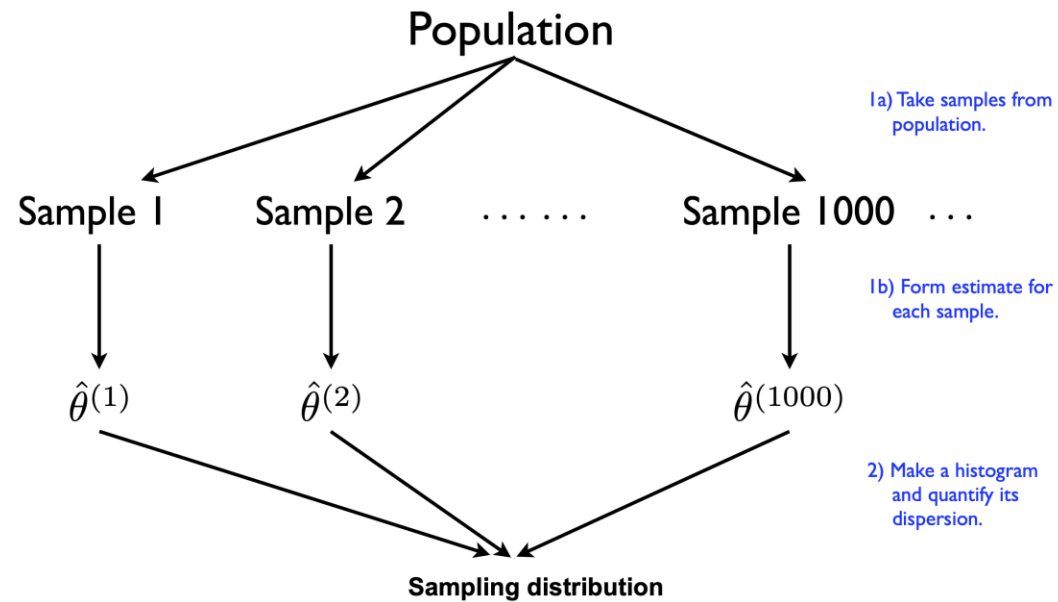
## Cons:

- ❑ **Computationally intensive:** Requires a large number of resamples for accurate  $p$ -values, especially with large datasets.
- ❑ **Randomization required:** Assumes data can be randomly shuffled
- ❑ **Limited interpretability:**  $p$ -values are purely empirical, with no direct parameter estimation



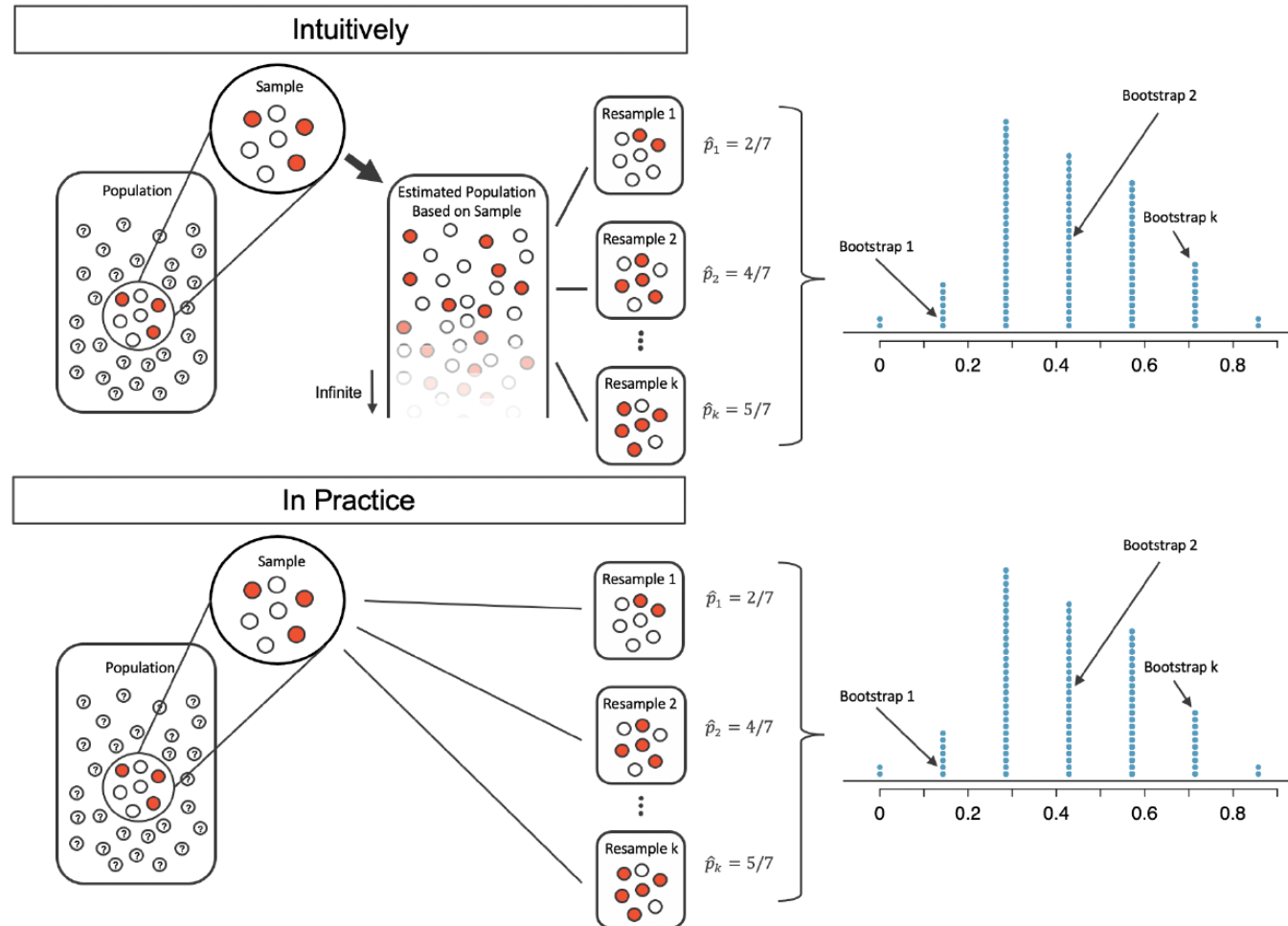
# Bootstrap

## Resampling with replacement



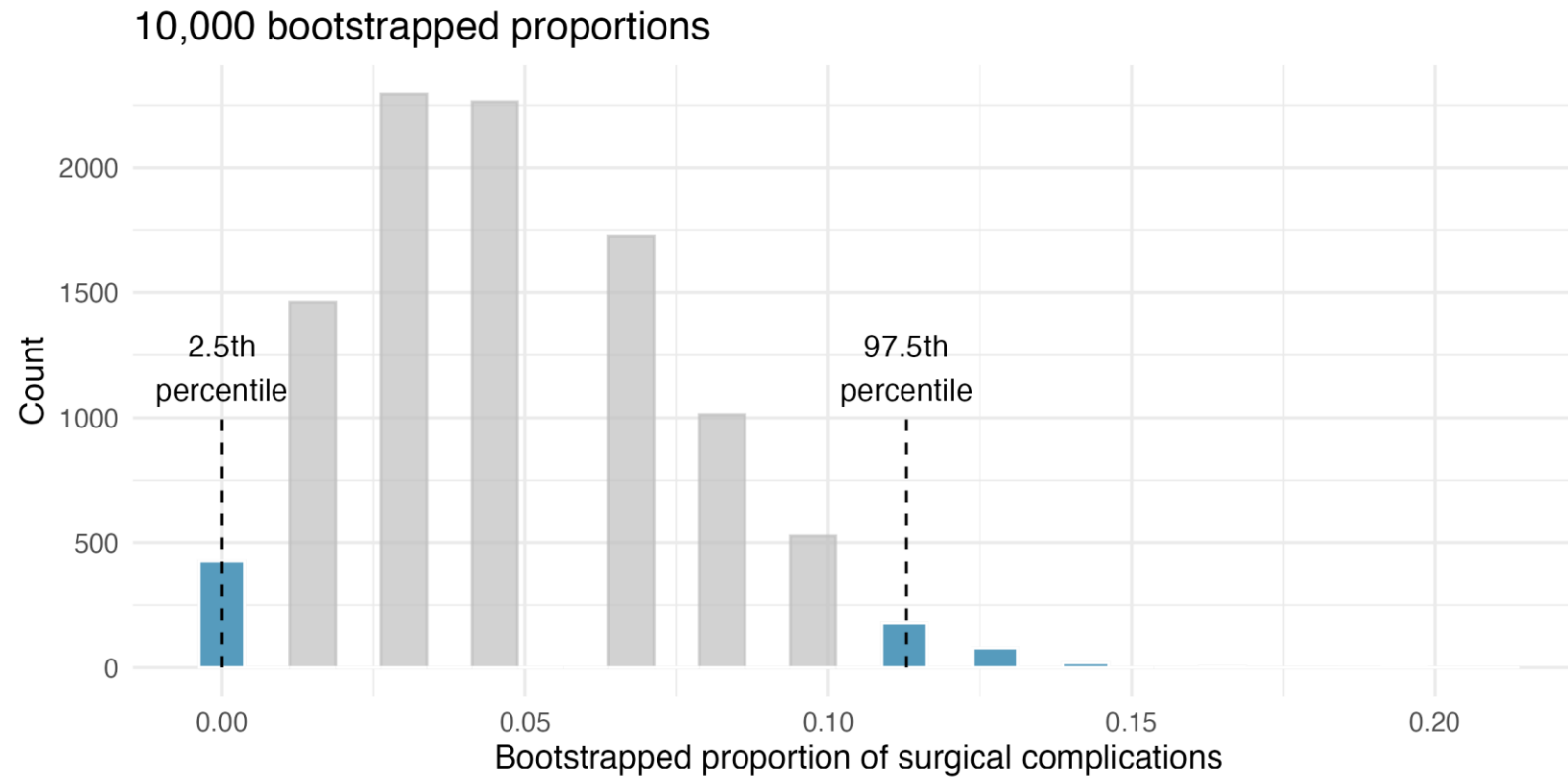
# Bootstrap

## One-sample bootstrap



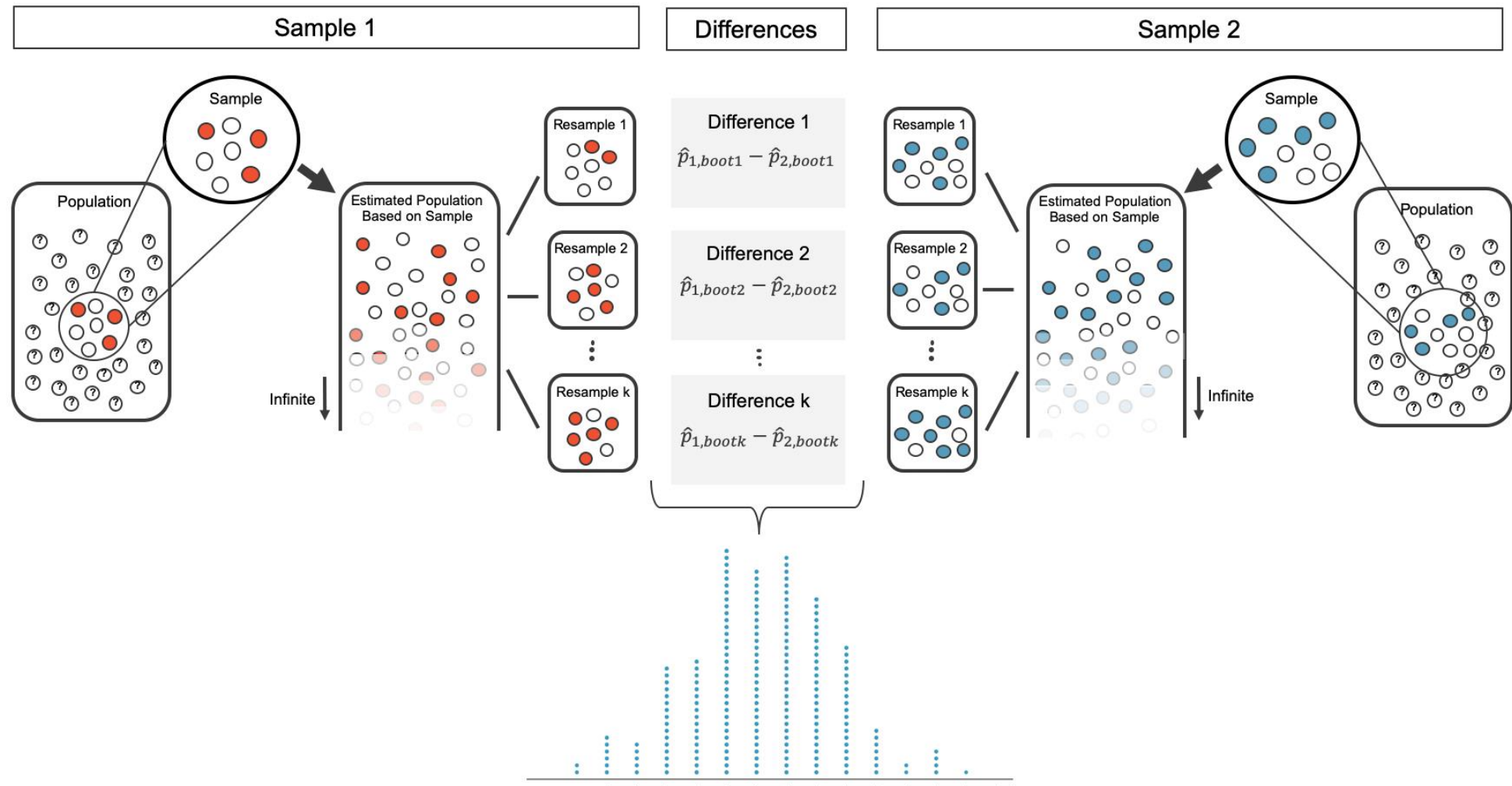
# Bootstrap

## Confidence interval with bootstrapping



# Bootstrap

## Two-sample bootstrap



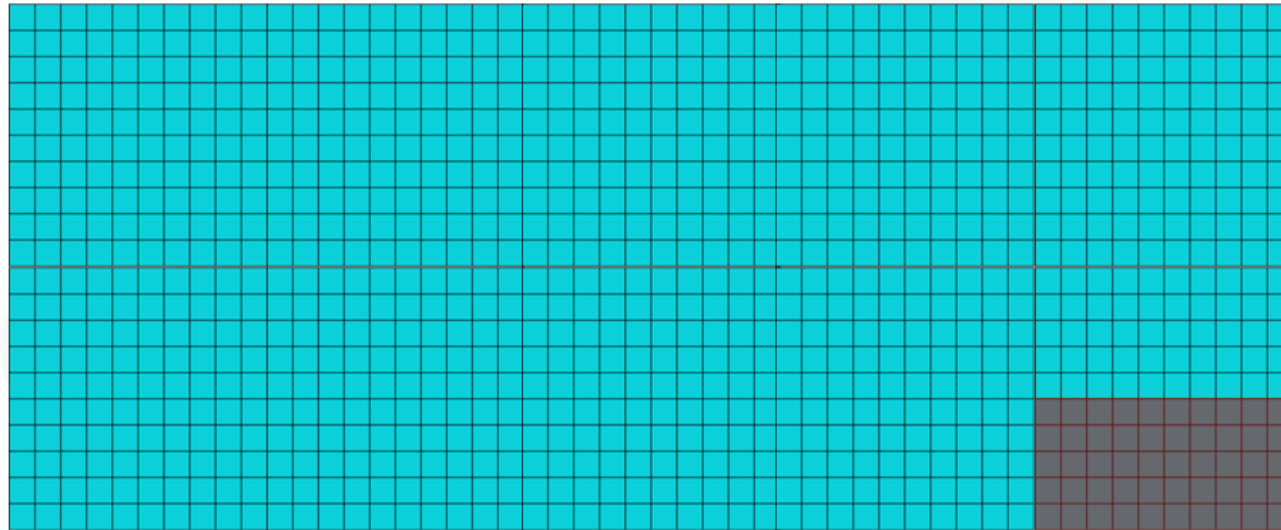


# Multiple testing correction

False positives are a nightmare; false negatives are a tragedy.

# Threshold on $p$ -values for significant discoveries

$p\text{-value} < 0.05$        $= 5\%$  chance of false positive



Remember that  $p$ -value is uniform distributed under the null,  
small  $p$ -values can arise due to chance

# False discovery rate





















$$\text{FDR} = \frac{\text{False positives}}{\text{All significant results}}$$

Genes with p-value < 0.05 which are actually not significant, it was just by chance that they got p-value < 0.05

All significant genes  
(p-value < 0.05)



**THE FALSE DISCOVERY RATE (FDR) IS THE PROPORTION OF FALSE POSITIVES AMONG ALL SIGNIFICANT RESULTS**

# Toy example

|   |   |   |  |   |   |   |   |   |   |
|---|---|---|--|---|---|---|---|---|---|
|  |  |  |  |  |  |  |  |  |  |
| 0.00001   | 0.00005   | 0.0003  | 0.00036  | 0.0003  | 0.000325  | 0.000024  | 0.000044  | 0.000544  | 0.0000459   |
|  |  |  |  |  |  |  |  |  |  |
| 0.000025  | 0.0027  | 0.003   | 0.00036  | 0.0003  | 0.049   | 0.4   | 0.13  | 0.24  | 0.6   |

Significance threshold:  
 $p\text{-value} < 0.05$





















Association with the beach

 Significant  
 Not significant

Test 20 objects to see if they are associated with beach



# Toy example



|   |   |   |  |   |   |   |   |   |   |
|---|---|---|--|---|---|---|---|---|---|
|  |  |  |  |  |  |  |  |  |  |
| 0.00001   | 0.00005   | 0.0003  | 0.00036  | 0.0003  | 0.000325  | 0.000024  | 0.000044  | 0.000544  | 0.0000459   |
|  |  |  |  |  |  |  |  |  |  |
| 0.000025  | 0.0027  | 0.003   | 0.00036  | 0.0003  | 0.049   | 0.4   | 0.13  | 0.24  | 0.6   |

Significance threshold:  
 $p\text{-value} < 0.05$

Association with the beach

- Significant
- Not significant
- False positive

# Toy example

|   |   |   |  |   |   |   |   |   |   |
|---|---|---|--|---|---|---|---|---|---|
|  |  |  |  |  |  |  |  |  |  |
| 0.00001   | 0.00005   | 0.0003  | 0.00036  | 0.0003  | 0.000325  | 0.000024  | 0.000044  | 0.000544  | 0.0000459   |
|  |  |  |  |  |  |  |  |  |  |
| 0.000025  | 0.0027  | 0.003   | 0.00036  | 0.0003  | 0.049   | 0.4   | 0.13  | 0.24  | 0.6   |

Significance threshold:  
 $p\text{-value} < 0.05$

Association with the beach

- Significant
- Not significant
- False positive

$$\text{FDR} = \frac{\text{False positives}}{\text{All significant findings}} = \frac{1}{16} = 6.25\%$$

# $p$ -value adjustment method

- Bonferroni correction: reject  $H_0$  if  $p_i \leq \frac{\alpha}{m}$
- Benjamini-Hochberg procedure (one of the most cited stats paper, ~114k)

Step 1: Considering we have  $m$  p-values, each obtained from a single test:  $p_1, p_2, \dots, p_m$ , we order the p-values in increasing order:

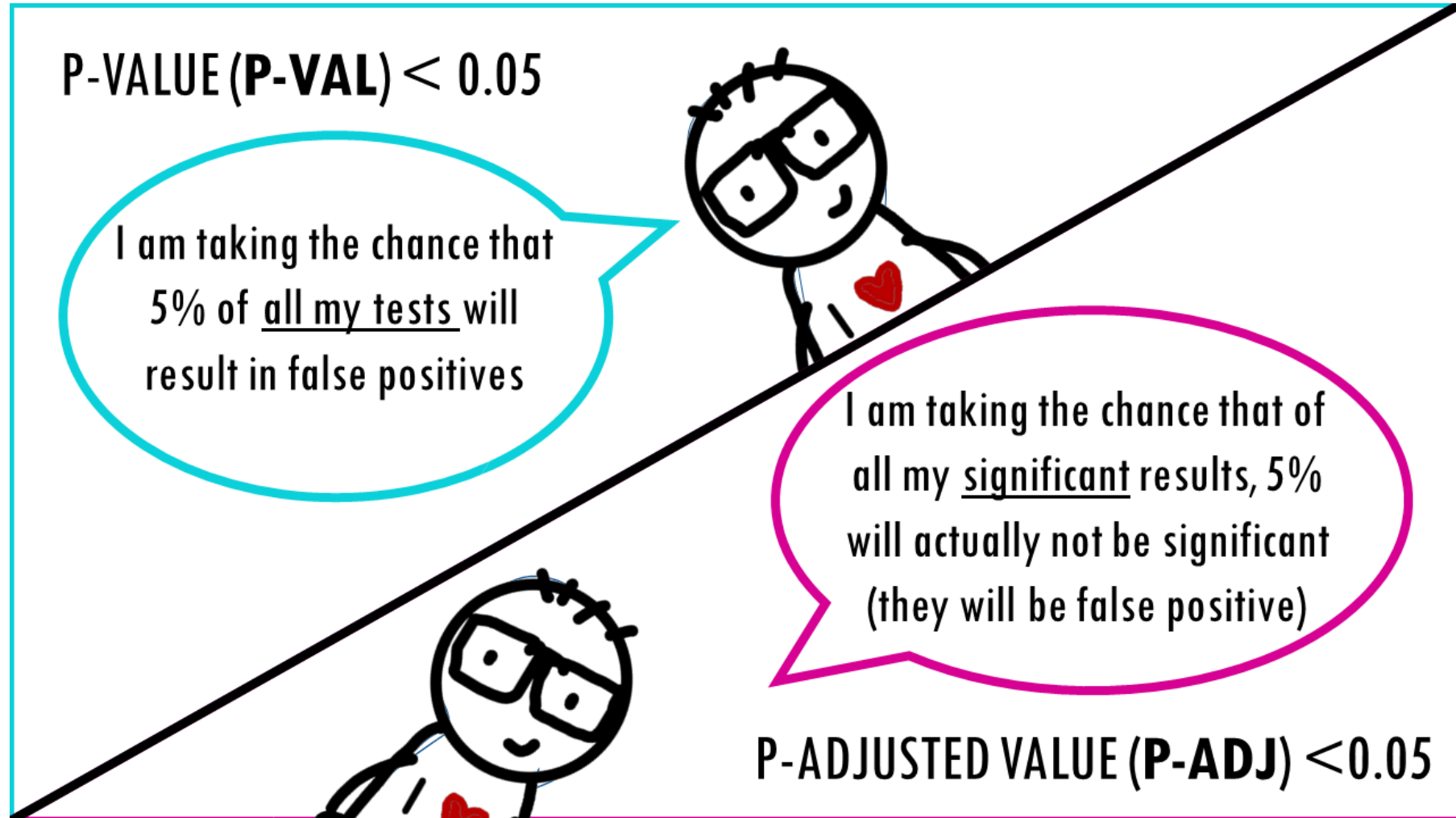
$$p_{(1)} \leq p_{(2)} \leq \dots \leq p_{(m-1)} \leq p_{(m)}$$

and denote their corresponding null hypotheses as:





















$$H_{(1)}, H_{(2)}, \dots, H_{(m-1)}, H_{(m)}$$

Step 2: Find integer  $k$  as the largest  $i$  such that:  $p_{(i)} \leq \frac{i}{m}\alpha$ . Then we reject all  $H_{(i)}$  for which  $i \leq k$ .

# Comparison



# Toy example




|   |   |   |  |   |   |   |   |   |   |
|---|---|---|--|---|---|---|---|---|---|
|  |  |  |  |  |  |  |  |  |  |
| 0.00001   | 0.00005   | 0.0003  | 0.00036  | 0.0003  | 0.000325  | 0.000024  | 0.000044  | 0.000544  | 0.0000459   |
|  |  |  |  |  |  |  |  |  |  |
| 0.000025  | 0.0027  | 0.003   | 0.00036  | 0.0003  | 0.049   | 0.4   | 0.13  | 0.24  | 0.6   |

Significance threshold:





















$p\text{-value} < 0.05$

→  $p\text{-value} < 0.0025$  (Bonferroni correction)

Association with the beach

-  Significant
-  Not significant
-  False positive

# Toy example




|       |   |   |   |  |   |   |   |   |   |   |
|-------|---|---|---|--|---|---|---|---|---|---|
|       |  |  |  |  |  |  |  |  |  |  |
| p-val | 0.00001   | 0.00005   | 0.0003  | 0.00036  | 0.0003  | 0.000325  | 0.000024  | 0.000044  | 0.000544  | 0.0000459   |
| p-adj | 0.0005  | 0.000075  | 0.00083   | 0.0008   | 0.0009  | 0.00084   | 0.0005  | 0.00094   | 0.008   | 0.00046   |
|       |  |  |  |  |  |  |  |  |  |  |
| p-val | 0.000025  | 0.0027  | 0.003   | 0.00036  | 0.0003  | 0.049   | 0.4   | 0.13  | 0.24  | 0.6   |
| p-adj | 0.0004  | 0.0055  | 0.02  | 0.0046   | 0.004   | 0.053   | 0.6   | 0.28  | 0.45  | 0.7   |

Significance threshold:  
**p-adj < 0.05**



$0.05 * 15 = 0.75$  objects  
 falsely significant (falsely  
 associated with the beach)

Association with the beach

-  Significant
-  Not significant
-  False positive

# Let's do some practice!



# Thanks

Q & A