Introduction to statistical thinking

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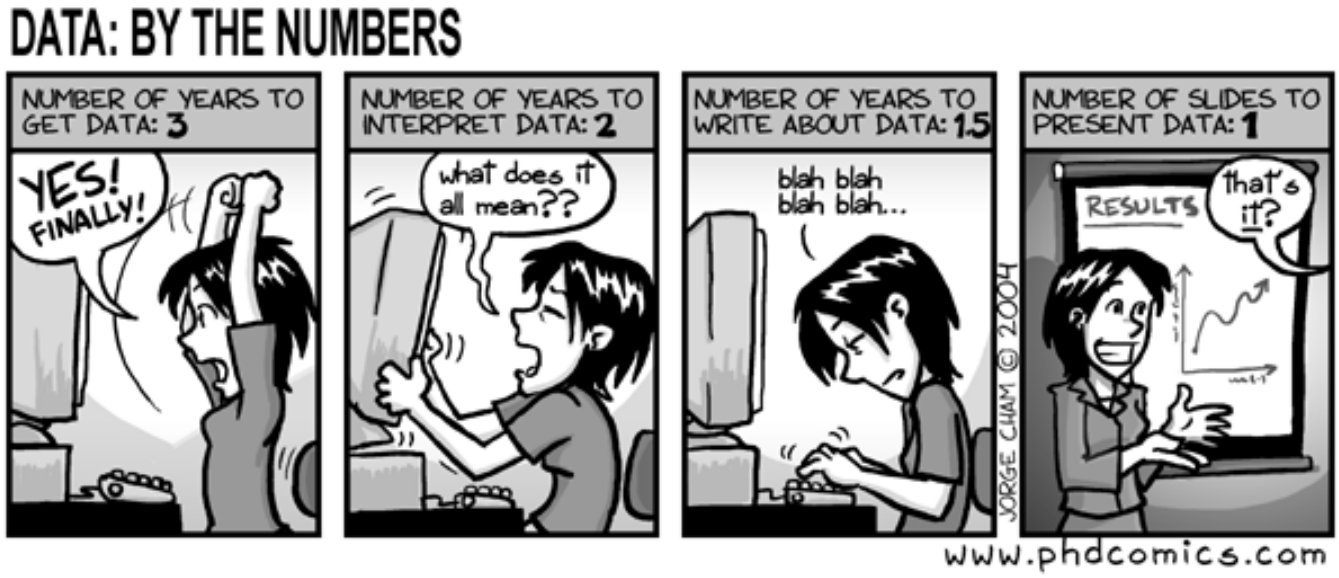
2016-11-17

Why statistics?



Why statistics?

Statistics is at the core of modern research

What is statistics?

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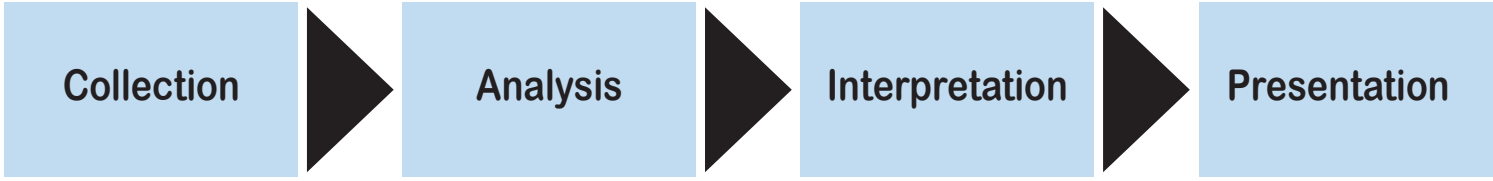
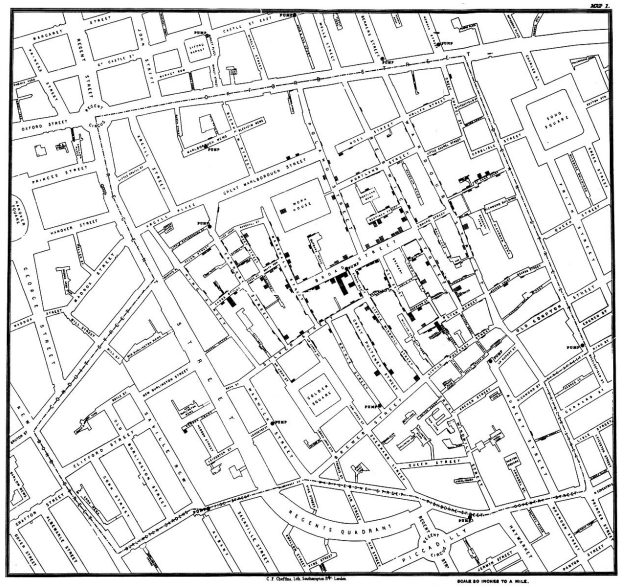


$\rightarrow$ everything from experimental design to figure preparation!

What can we do with statistics?

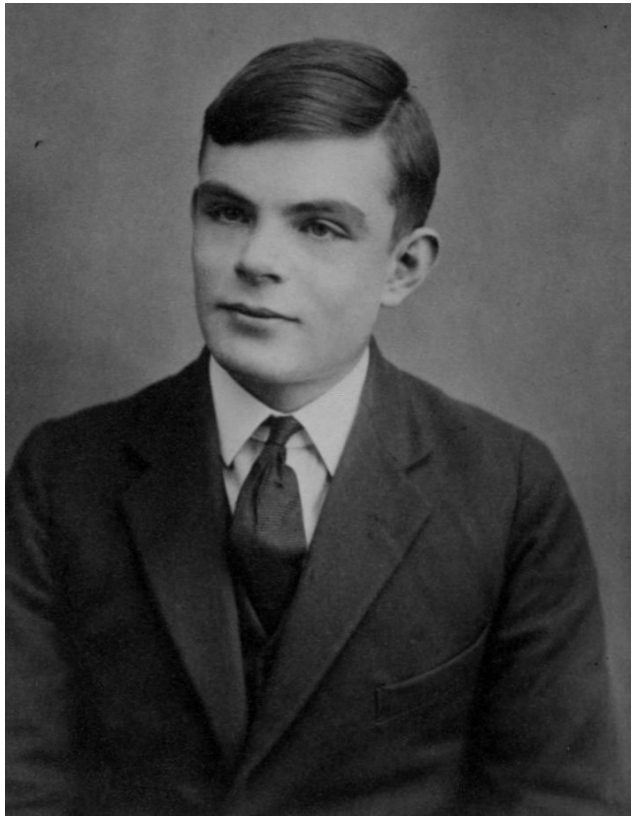


Public domain image

During the Soho cholera outbreak in 1854, John Snow used statistics to find an **association** between the quality of the water source and cholera cases

John Snow is considered one of the fathers of modern epidemiology

What can we do with statistics?



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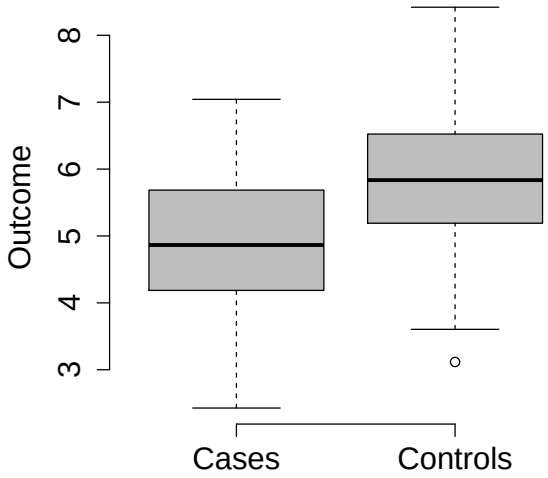
During WWII, Alan Turing used advanced statistics to **predict** the meaning of Enigma messages

Alan Turing is considered one of the fathers of modern computers

What can we do with statistics?

Comparisons between two groups



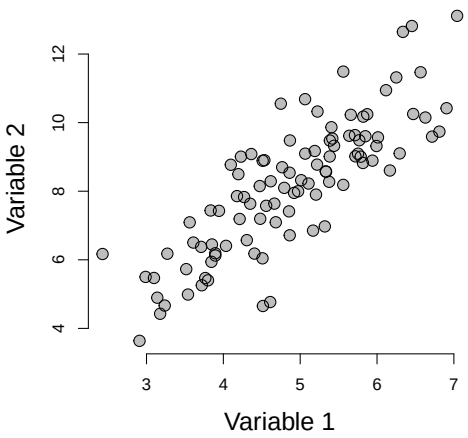
For example,

- Case/control studies
- Differential expression studies

Is this difference *statistically significant*?

What can we do with statistics?

Finding associations between variables



For example,

- Dose level vs survival time
- Association studies (e.g. GWAS)
- Co-expression networks

Is there an association between X and Y?

Which associations are *statistically significant*?

Outline for the course

- **Introduction to statistics**
  - Types of data
  - Descriptive statistics
  - Practical: descriptive statistics in Rmarkdown
  - Statistical inference
- **Hypothesis testing (in R)**
- **Linear regression (in R)**

Introduction to statistics

Types of data

Prior to any analysis, it is important to know what type of data is available

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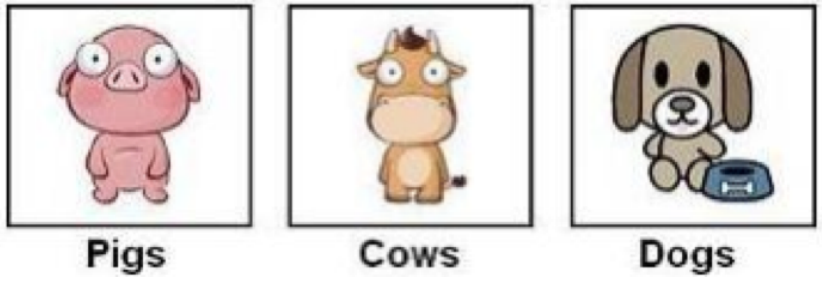
Data can be classified into different **types of variables**:

- Categorical (nominal)
- Categorical (ordinal)
- Discrete
- Continuous

Types of data: categorical (nominal)

To describe categories that cannot be ordered



Source: http://www.restore.ac.uk

Requirements:

- Same value assigned to all the members of level
- Same value not assigned to different levels
- Each observation only assigned to one level

Examples: gender, yes/no answers, surgery type, cancer type, eye colour, dead/alive, ethnicity, etc.

Types of data: categorical (ordinal)

To describe categories that have a logical order

Requirements:

- Mutually exclusive fixed categories
- Implicit order
- Can say one category higher than another (but not how much)

Examples: stress level ($1 =$ low, $\ldots$, $7 =$ high), pain level (low/medium/high), education level (primary, secondary, $\ldots$), etc.

Types of data: discrete

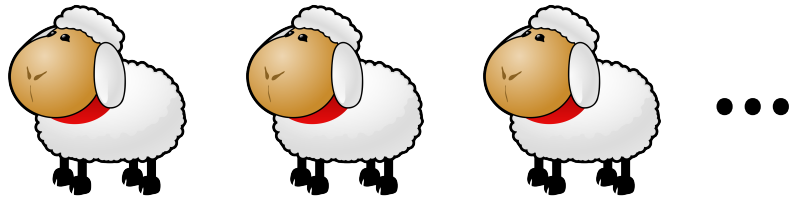


Image modified from Free Stock Photos

Requirements:

- Fixed categories, can only take certain values
- Like ordinal but with well-defined distances
- Basically, anything counted (cardinal): how much?

Examples: number of tumours, hospital admissions, etc.

Sometimes treated as continuous if range is large!

Types of data: continuous

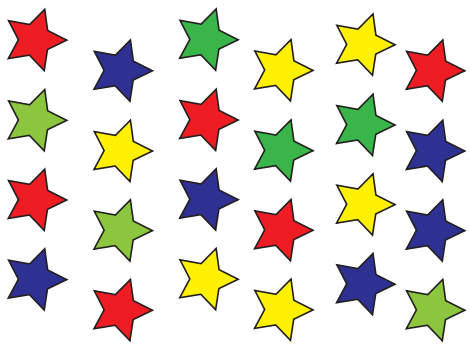
Requirements:

- Observations can take any value
- May have finite or infinite range
- Given any two values, one fits between

Examples: height, weight, blood presure, temperature etc.

Population versus sample

Census records information from every subject within a population



Population

Population versus sample

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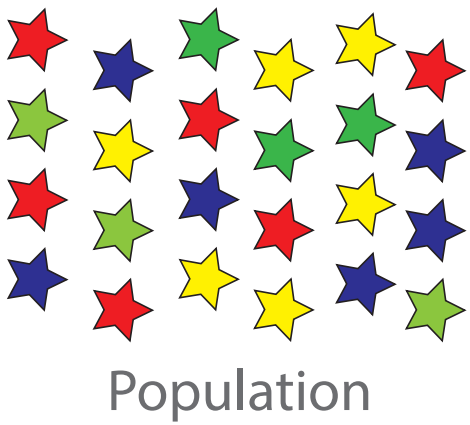
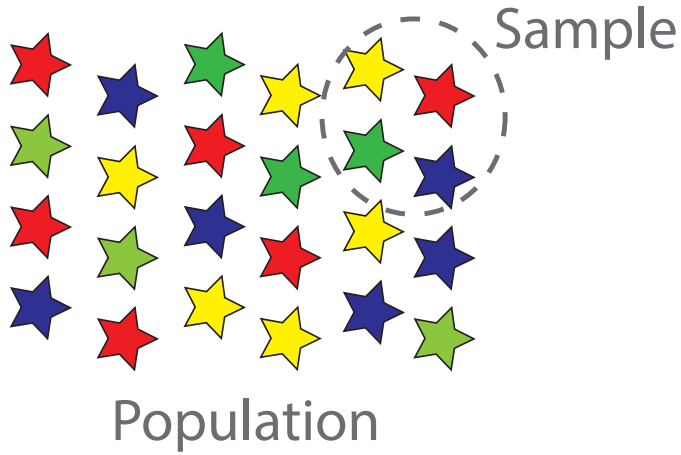


Scientific studies typically rely on a subset of a population



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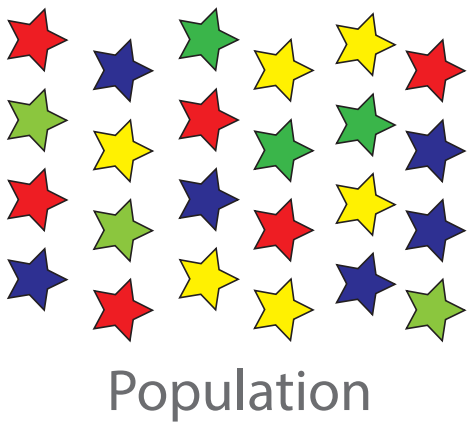
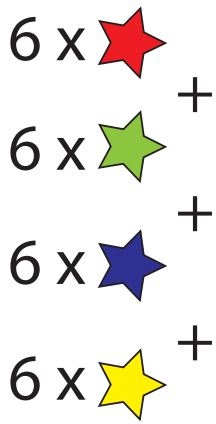


Scientific studies typically rely on a subset of a population

A good sample must be a good representative of the population!

Descriptive statistics versus statistical inference

Descriptive statistics
summarizes the information
available in the data



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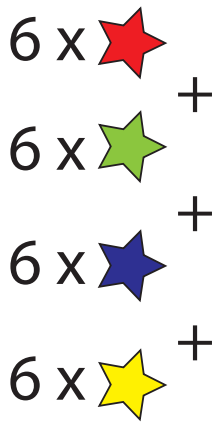
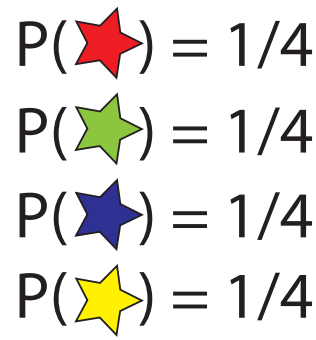


Statistical inference
extrapolates sample information to population level



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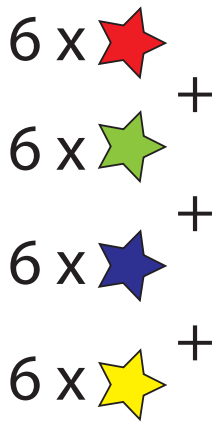

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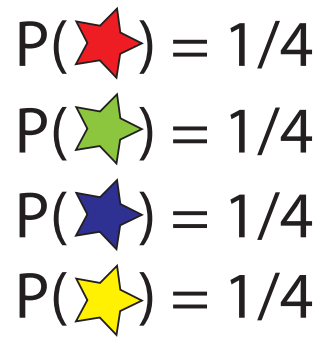

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Descriptive analyses

Descriptive analyses

There are two basic forms of data summary

- Numerical: frequency tables, summary measures, etc
- Graphical: histograms, scatter-plots, boxplots, etc

We need to choose the summary depending on the data type!

Descriptive analyses: categorical variables

Numerical summary

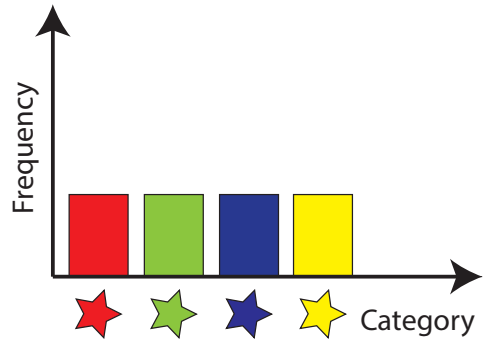
Category	Frequency	Cumulative frequency	Relative frequency	Cum. rel. frequency
	6	6	0.25	0.25
	6	12	0.25	0.50
	6	18	0.25	0.75
	6	24	0.25	1.00

Descriptive analyses: categorical variables

Numerical summary

Category	Frequency	Cumulative frequency	Relative frequency	Cum. rel. frequency
★	6	6	0.25	0.25
★	6	12	0.25	0.50
★	6	18	0.25	0.75
★	6	24	0.25	1.00

Graphical summary



Descriptive analysis: discrete/continuous variables

Frequency tables are not useful
unless we *categorize* the data

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Frequency tables are not useful unless we *categorize* the data

Example:

Birth weight	Rel. freq
Very low ($<$1.5 kg.)	0.05
Low (1.5-2.5 kg.)	0.10
Normal ($\geq$2.5 kg.)	0.85

Descriptive analysis: discrete/continuous variables

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Example:

Birth weight	Rel. freq
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Normal ($\geq$2.5 kg.)	0.85

Instead, we typically prefer *summary measures*

- Mean
- Median
- Mode
- Variance
- Quantiles

Which one?

Descriptive analysis: discrete/continuous variables

Firstly, we can use measures to describe the **location** of the data

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Mean ($\bar{x}$)

$$\bar{x} = \frac{x_1 + x_2 + \cdots + x_n}{n}$$

Median ($x_{50\%}$)

50% of observations lie below $x_{50\%}$

Descriptive analysis: discrete/continuous variables

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Median ($x_{50\%}$)

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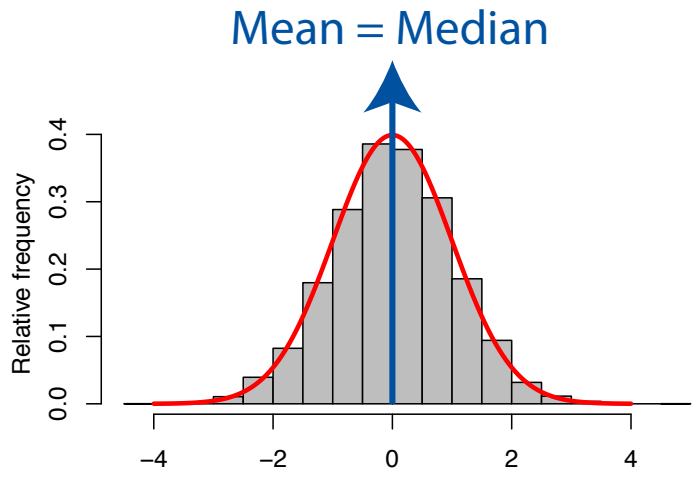
When the data is normal ...



... but that is not always true

Descriptive analysis: example

Suposse we record the number of Facebook friends for 7 colleagues:

$$311, 345, 270, 310, 243, 5300, 11$$

Mean $(\bar{x})$

$$\bar{x} = \frac{x_1 + x_2 + \cdots + x_7}{7} = 970$$

Median $(x_{50\%})$

$$11, 243, 270, 310, 311, 345, 5300 \Rightarrow x_{50\%} = 310$$

Which one provides a better description for the location of the data?

Descriptive analysis: example

Now suppose the data is slighty different:

$$311, 345, 270, 310, 243, 530, 11$$

Mean $(\bar{x})$

$$\bar{x} = \frac{x_1 + x_2 + \cdots + x_7}{7} = 289$$

Median $(x_{50\%})$

$$11, 243, 270, 310, 311, 345, 530 \Rightarrow x_{50\%} = 310$$

What happened?

Descriptive analysis: discrete/continuous variables

It is also important to summarize the **spread** of the data

Standard deviation ($\mathrm{sd}(x)$)

$$\mathrm{sd}(x) = \sqrt{\frac{(x_1 - \bar{x})^2 + \cdots + (x_n - \bar{x})^2}{n}}$$

Interquartile range ($\mathrm{IQR}(x)$)

$$\mathrm{IQR}(x) = x_{75\%} - x_{25\%}$$

Descriptive analysis: example

In the first example, we have

Standard deviation $(\mathrm{sd}(x))$

$$\mathrm{sd}(x) = \sqrt{\frac{(x_1 - \bar{x})^2 + \cdots + (x_7 - \bar{x})^2}{7}} = 1912.57$$

Interquartile range $(\mathrm{IQR}(x))$

$$11, 243, 270, 310, 311, 345, 5300 \Rightarrow \mathrm{IQR}(x) = 345 - 243$$

Descriptive analysis: example

In the first example, we have

Standard deviation $(\text{sd}(x))$

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Interquartile range $(\text{IQR}(x))$

$$11, 243, 270, 310, 311, 345, 5300 \Rightarrow \text{IQR}(x) = 345 - 243$$

In the second example, we have

Standard deviation $(\text{sd}(x))$

$$\text{sd}(x) = \sqrt{\frac{(x_1 - \bar{x})^2 + \cdots + (x_7 - \bar{x})^2}{7}} = 153.79$$

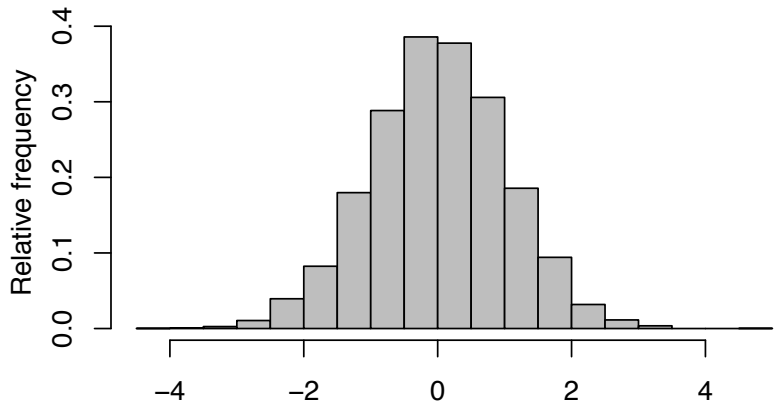
Interquartile range $(\text{IQR}(x))$

$$11, 243, 270, 310, 311, 345, 530 \Rightarrow \text{IQR}(x) = 345 - 243$$

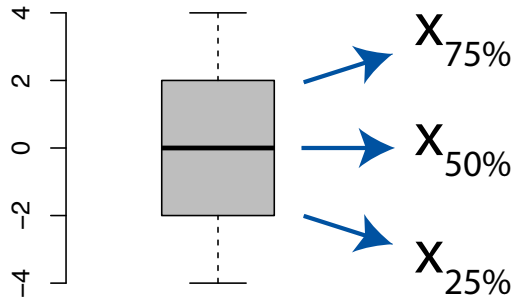
Descriptive analysis: discrete/continuous variables

We can also summarize the distribution of the data **graphically**

Histogram



Boxplot



Link to 'exploration' shiny app

Before we continue: the normal distribution

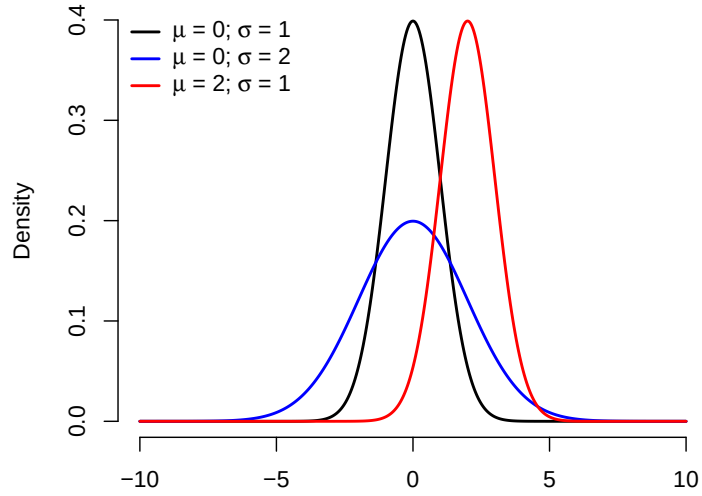
The normal (or Gaussian) distribution is very popular!

Indexed by two parameters:

- $\mu \rightarrow$ location
- σ (or σ^2) $\rightarrow$ spread

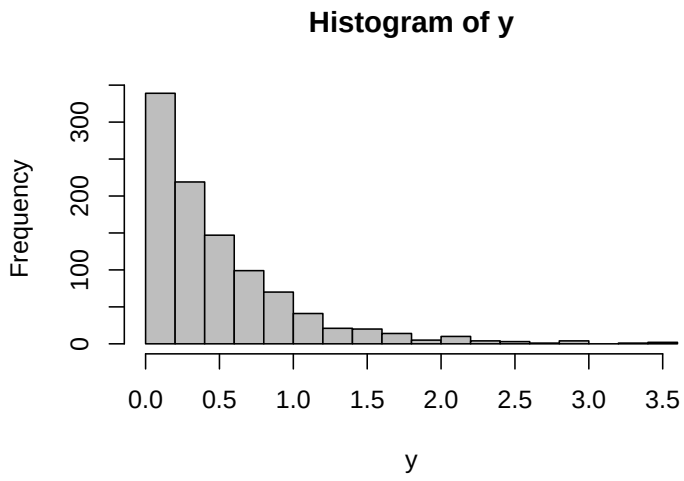
Rule of thumb:

- $\sim$ 95% of the data lies between $(\mu - 2\sigma, \mu + 2\sigma)$
- $\sim$ 99% of the data lies between $(\mu - 3\sigma, \mu + 3\sigma)$



The distribution is symmetric around μ!

Descriptive analysis: is the data normally distributed?



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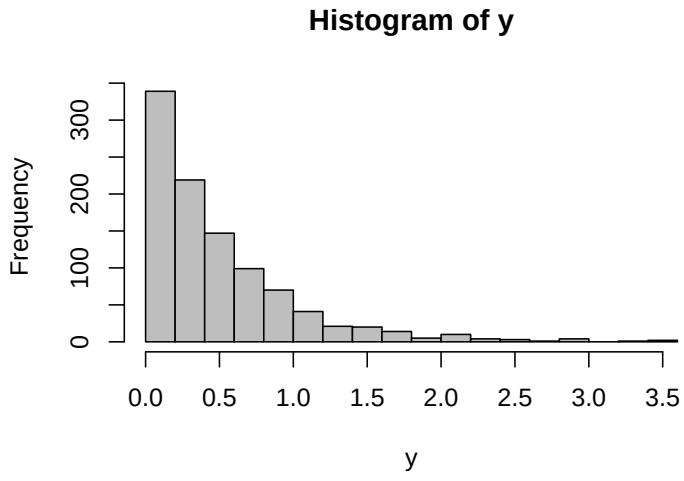

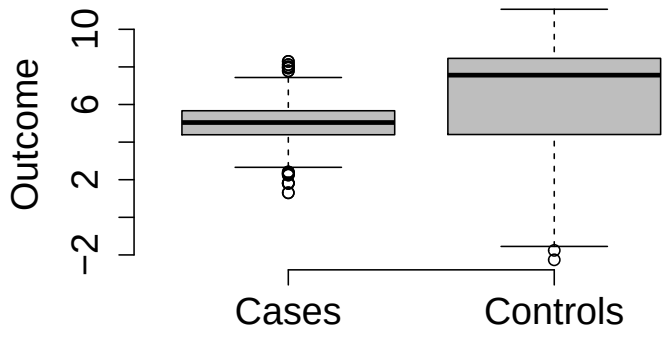

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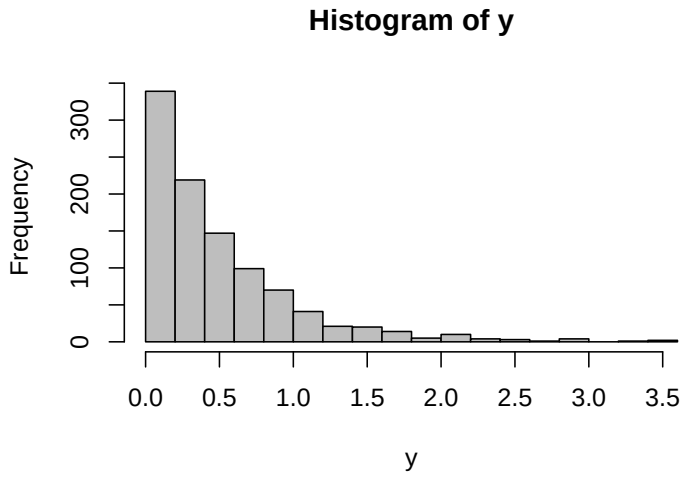

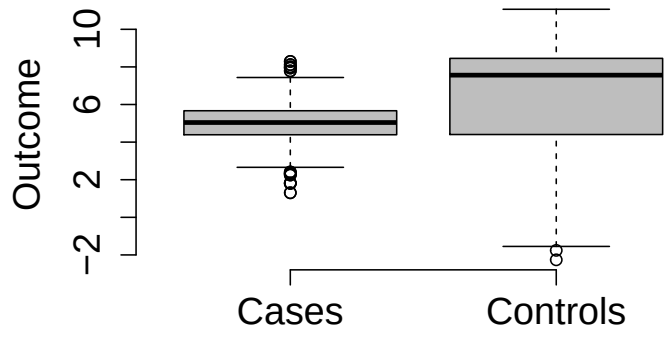

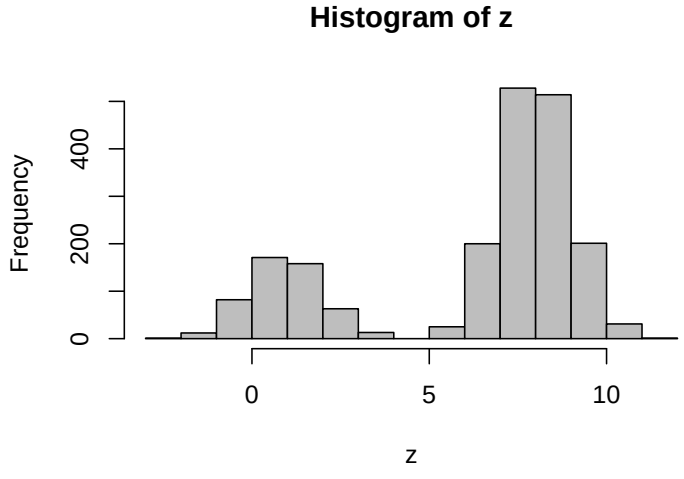

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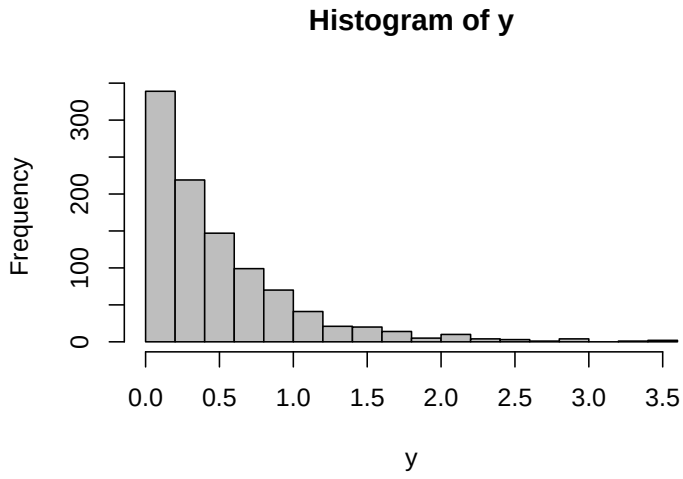
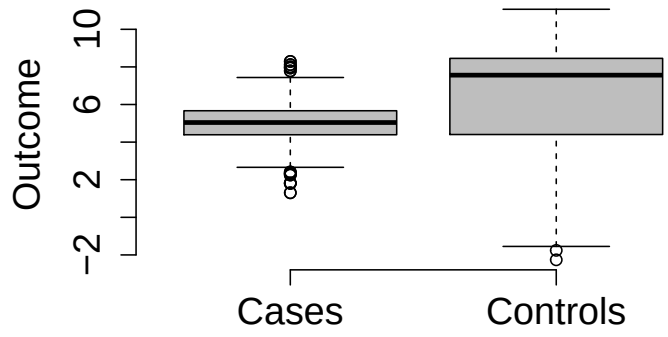
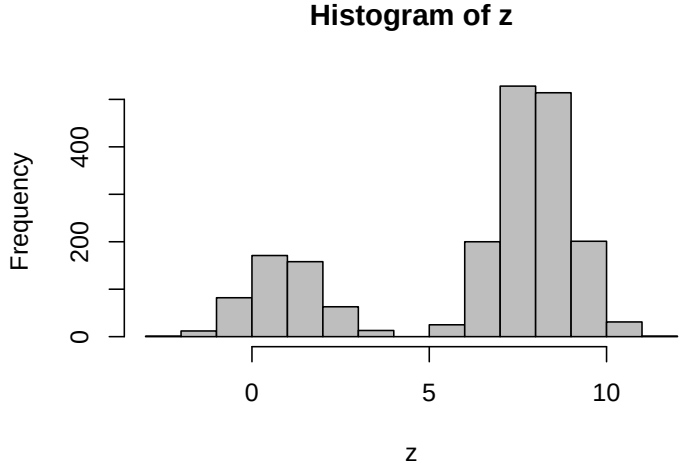
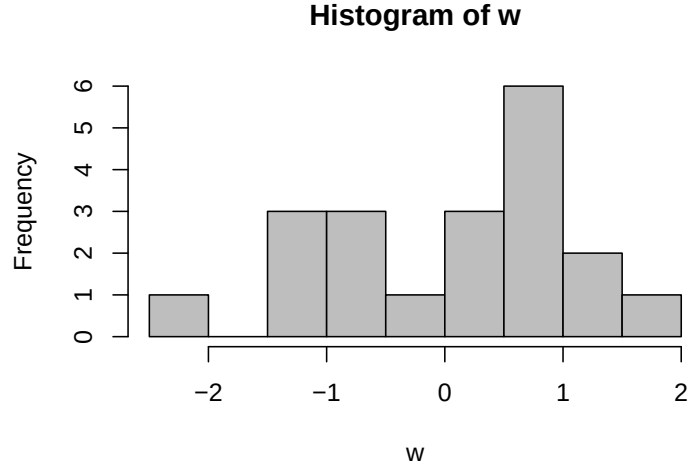




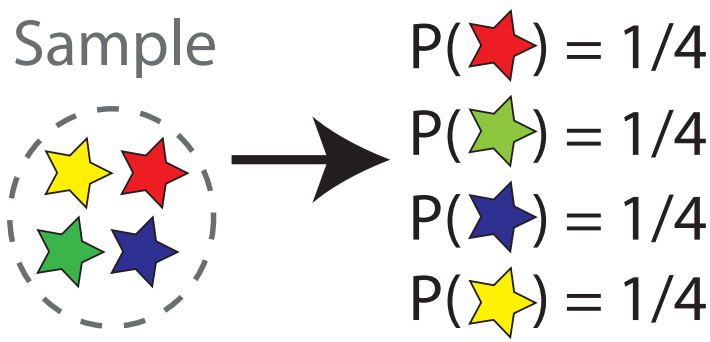




Statistical inference

Statistical inference: estimation

Statistical inference
extrapolates sample information
to population level



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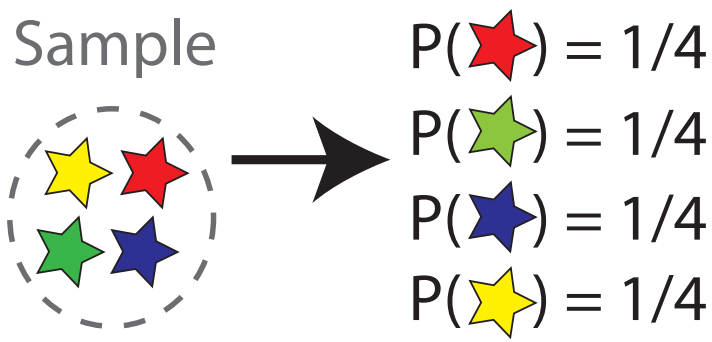

In this example, we want to **estimate** the proportion of red, green, blue and yellow stars in the population based on the observed data

Statistical inference: estimation

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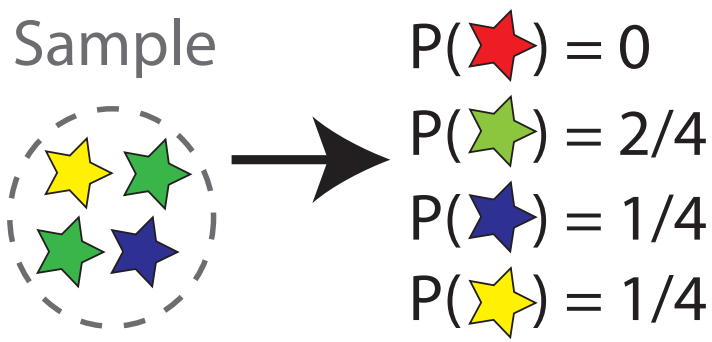
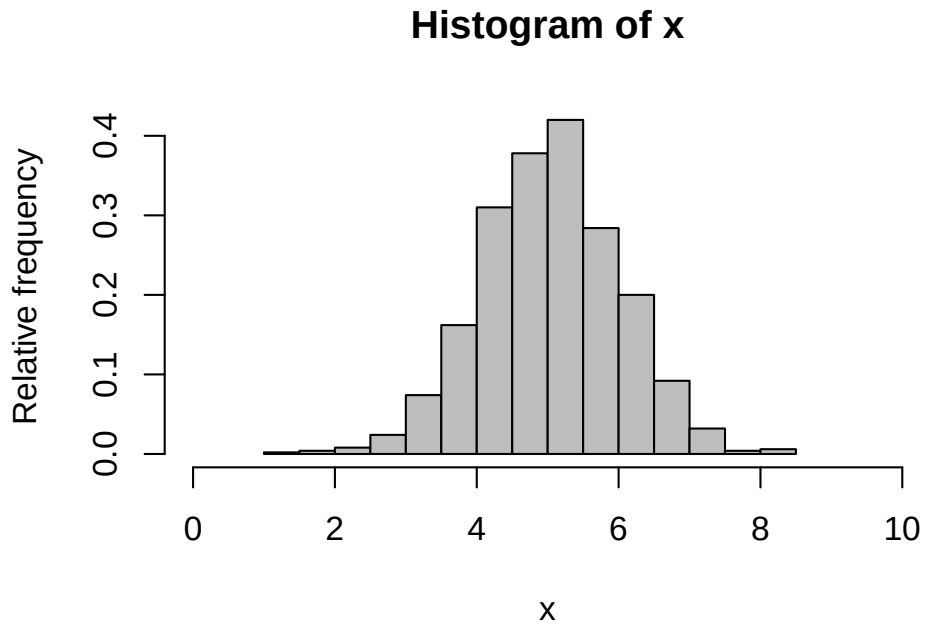


If we observe a different sample,
we obtain different results

Note: in this sample we didn't
observe red stars!

Statistical inference: estimation

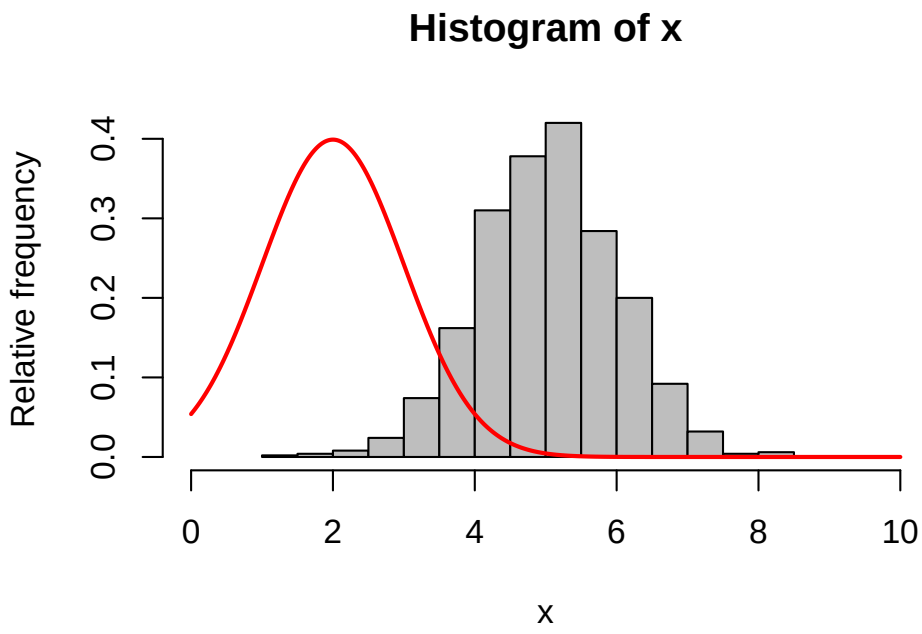
To model the data (e.g. expression of a gene across samples) as being normally distributed with mean μ and standard deviation 1.



The aim here is to estimate the value of μ!

Statistical inference: estimation

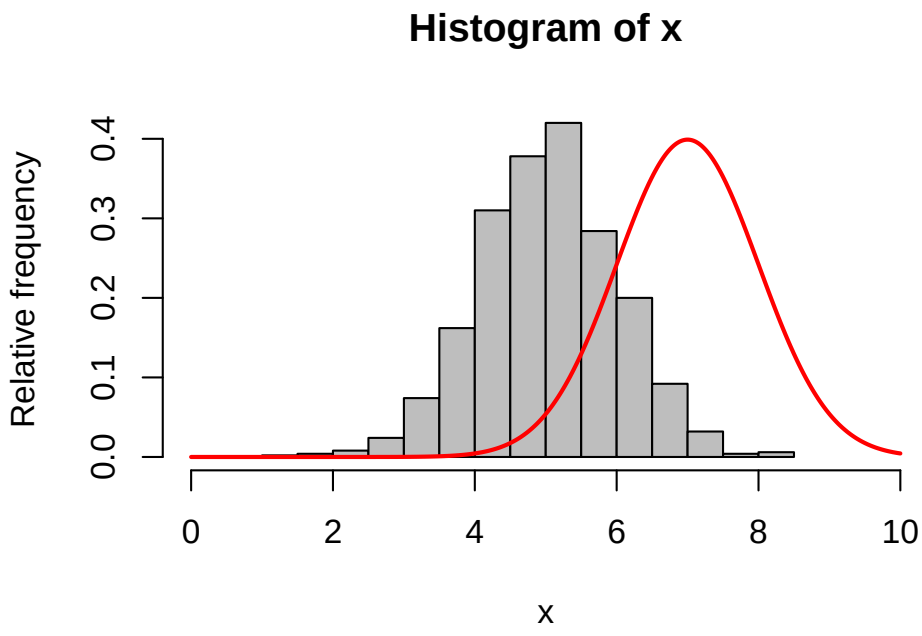
To model the data (e.g. expression of a gene across samples) as being normally distributed with mean μ and standard deviation 1.



$\mu = 2$?

Statistical inference: estimation

To model the data (e.g. expression of a gene across samples) as being normally distributed with mean μ and standard deviation 1.



$\mu = 7$?

Statistical inference: estimation

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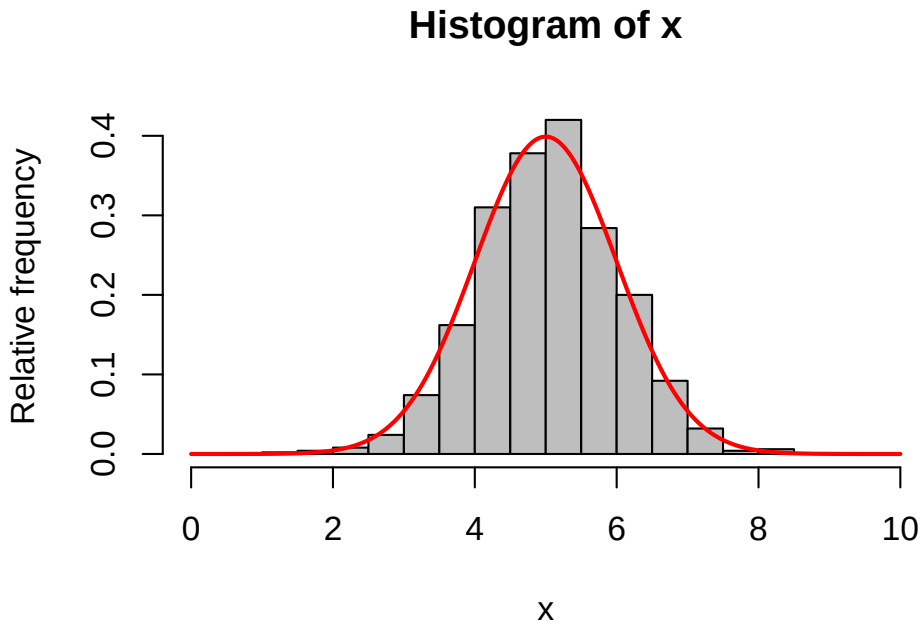

$\mu = 5$?

Statistical inference: estimation

We can estimate μ using the observed data through

$$\bar{x} = \frac{x_1 + \ldots + x_n}{n}$$

Link to 'estimation' shiny app

Statistical inference: estimation

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Estimates of μ that are based on a **finite sample** are not exact:

- The larger the sample size, $\bar{x}$ gets closer to μ
- The smaller σ, the faster $\bar{x}$ gets closer to μ

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Variability in the estimation quantified through the **standard error**:

$$\text{S.E.} = \sigma/\sqrt{n}$$

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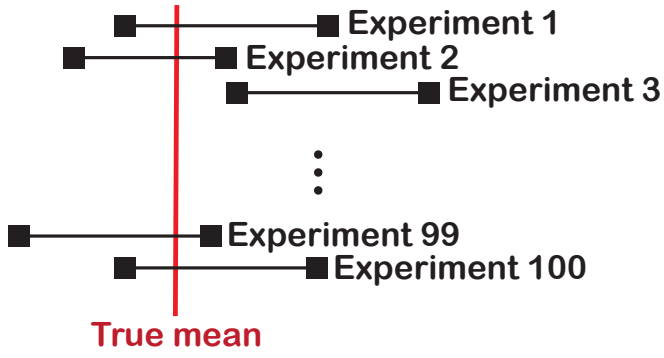
We need to provide a measure of uncertainty every time we provide an estimation!

Statistical inference: confidence intervals

A confidence interval (CI) is a *random* interval

In repeated experiments ...
95% of the time CI covers the *true* mean



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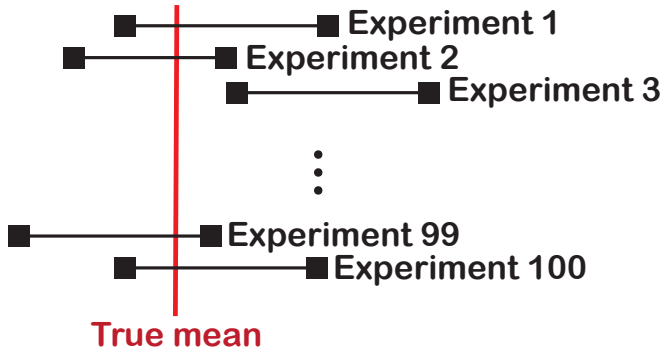

For the mean, the 95% CI is given by

$$(\bar{x} - 1.96 \text{ S.E.}, \bar{x} + 1.96 \text{ S.E.})$$

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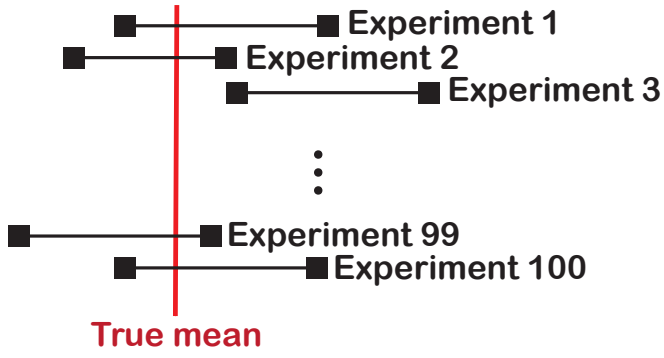

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This assumes the data is **normally distributed**. What if not?

Statistical inference: central Limit Theorem

If the data is not normally distributed, the **Central Limit Theorem** guarantees this result is still valid, provided the sample size is large

Link to 'clt' shiny app

Statistical inference: hypothesis testing

Often, the aim of the analysis is not only **estimation**.

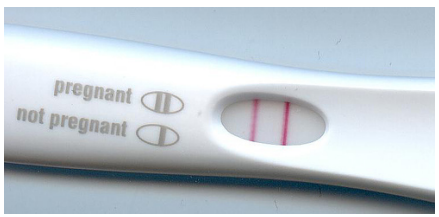
For example,

- *Is the treatment effective?*
- *Is a gene differentially expressed?*
- *Is there an association between genotype and phenotype?*

These questions can be translated as **hypothesis testing** problems

Comic taken from Significance Magazine, December 2008.

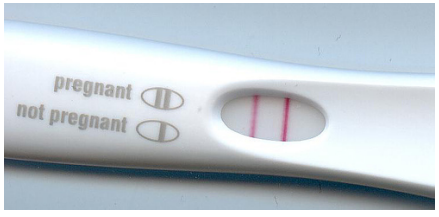
Statistical inference: hypothesis testing



Am I pregnant?

Disclaimer: this image was downloaded from the internet and does not reflect the life of the instructors!

Statistical inference: hypothesis testing



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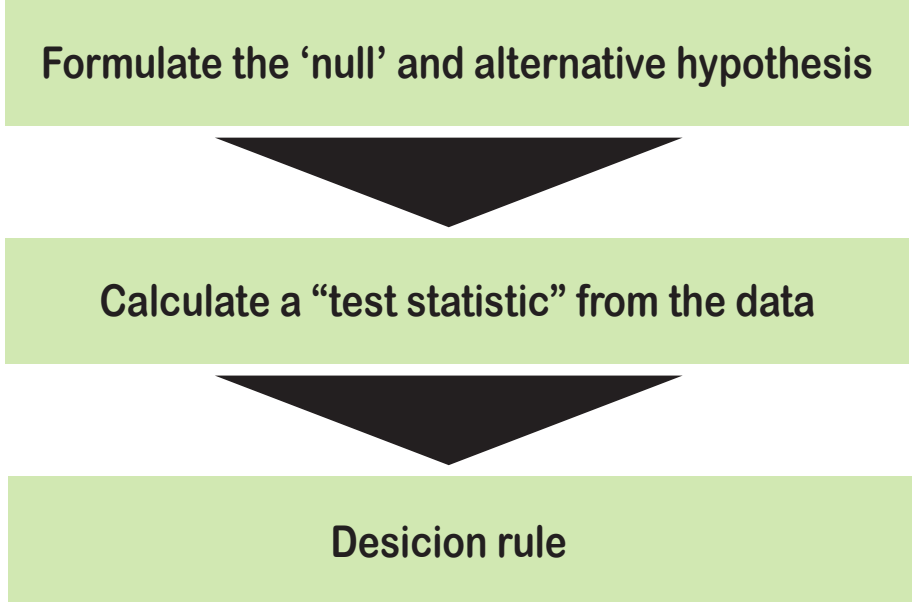
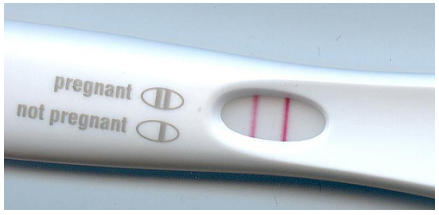
Basic setup



Statistical inference: hypothesis testing



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Basic setup (example)

Formulate the 'null' and alternative hypothesis

e.g. H_o: Not pregnant vs H_1: Pregnant

Calculate a "test statistic" from the data

e.g. summary measure based on hormonal levels

Desicion rule

e.g. is the data more extreme than what is expected by chance (for a non-pregnant woman)?

Statistical inference: hypothesis testing

No test is exact:

	Null hypothesis does not hold	**Null hypothesis holds**
Reject null hypothesis	Correct True positive	Wrong False positive
Do not reject null hypothesis	Wrong False negative	Correct True negative

Statistical inference: hypothesis testing

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Error rates depend on e.g. sample size ... what else?

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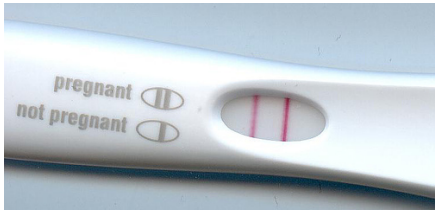
Beware of multiple testing correction issues!

Statistical inference: hypothesis testing



Am I pregnant?

Suppose that 100 women take the test

- 70 of them were trully pregnant
- the test was positive for 75 women
- the result was wrong for 10 non-pregnant women

Complete the table:

	Null hypothesis does not hold	Null hypothesis holds
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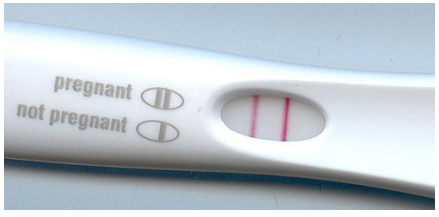
Statistical inference: hypothesis testing



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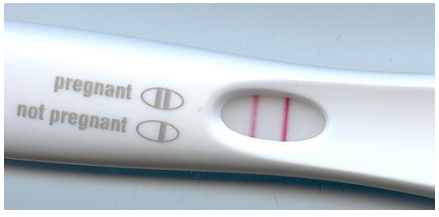

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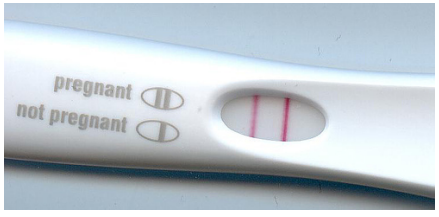

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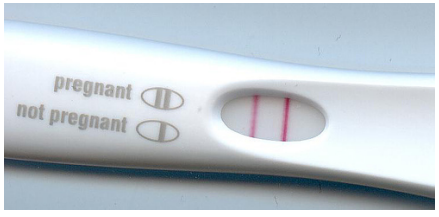
Statistical inference: hypothesis testing



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Statistical inference: hypothesis testing

Typically, two types of error are of main interest:

- Type I error

$$\alpha = p(\text{Reject } H_0 \text{ when } H_0 \text{ is true})$$

- Type II error

$$\beta = p(\text{Do not reject } H_0 \text{ when } H_0 \text{ is false})$$

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Most hypothesis tests are designed to control type I error!

Statistical inference: hypothesis testing

In terms of this table

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- What is the **significance level** of the test?

- What is the **power** of the test?

Statistical inference: hypothesis testing

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  - Type I error (α), i.e. $10/30 = 0.33$
- What is the **power** of the test?
  - 1 - type II error ($1 - \beta$), i.e. $65/70 = 0.93$

Statistical inference: hypothesis testing

In terms of this table

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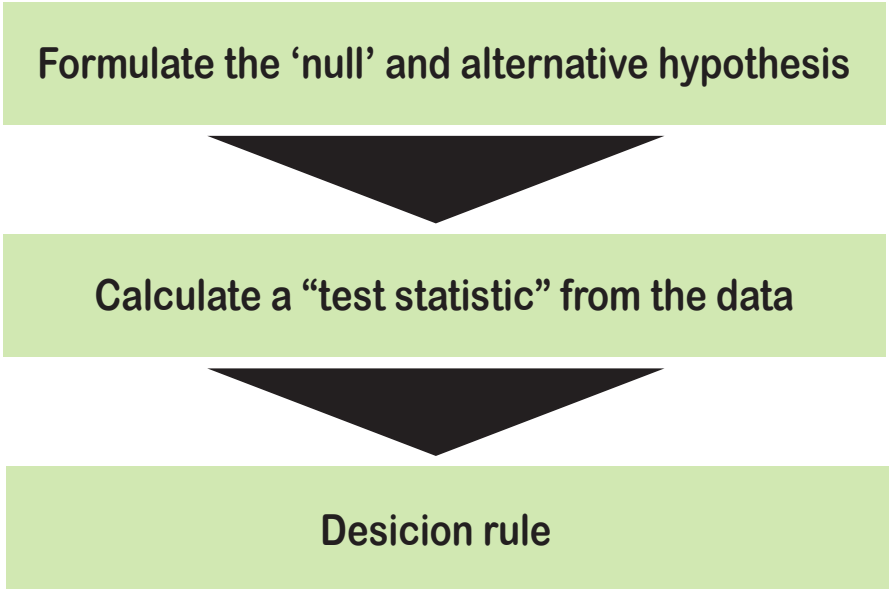
- What is the **sensitivity** of the test?
  - True positive rate, i.e. $65/70 = 0.93$
- What is the **specificity** of the test?
  - True negative rate, i.e. $20/30 = 0.67$

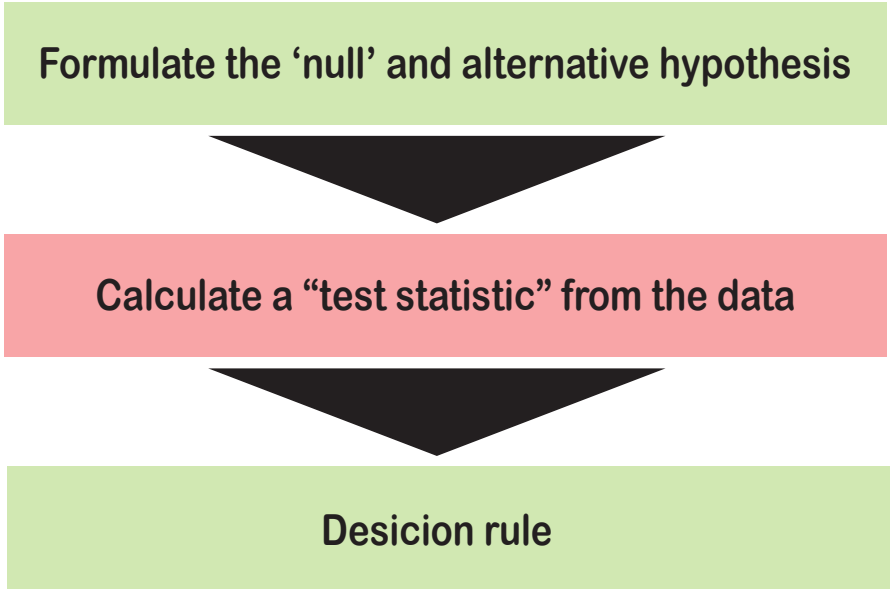
Statistical inference: hypothesis testing

Recall: basic setup



Statistical inference: hypothesis testing

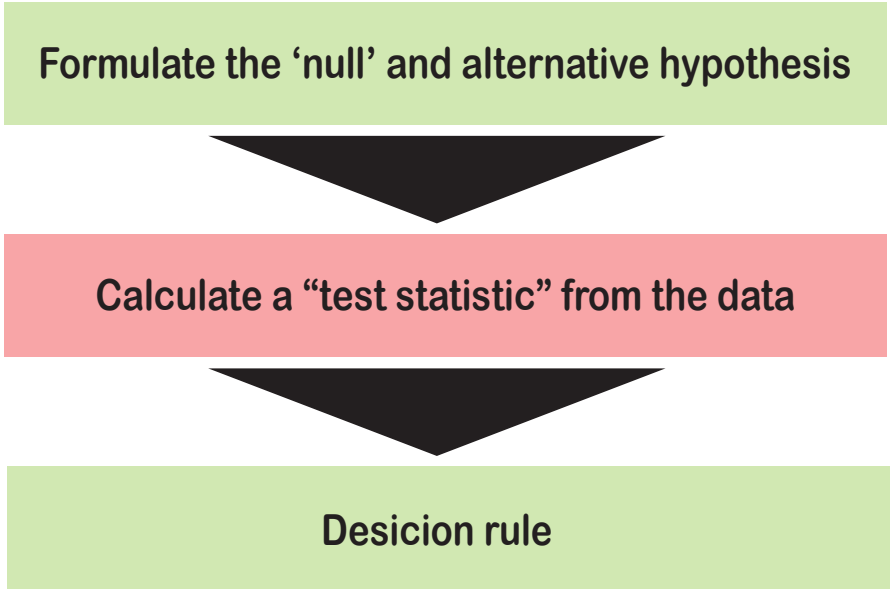
Recall: basic setup



A **test statistic** is a summary calculated from the data whose distribution is known (if H_0 is true)

Statistical inference: hypothesis testing

Recall: basic setup

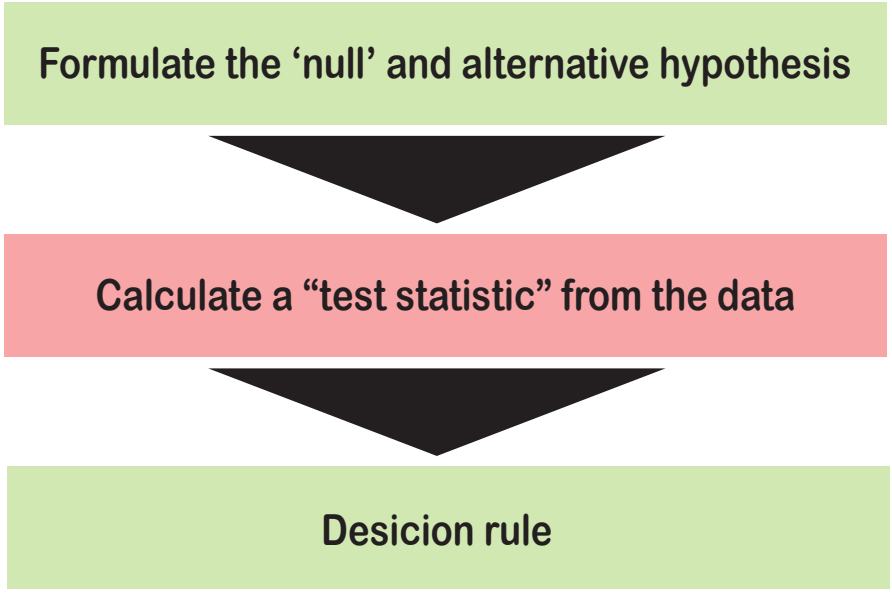


A **test statistic** is a summary calculated from the data whose distribution is known (if H_0 is true)

We will explore some example test statistics later today

Statistical inference: hypothesis testing

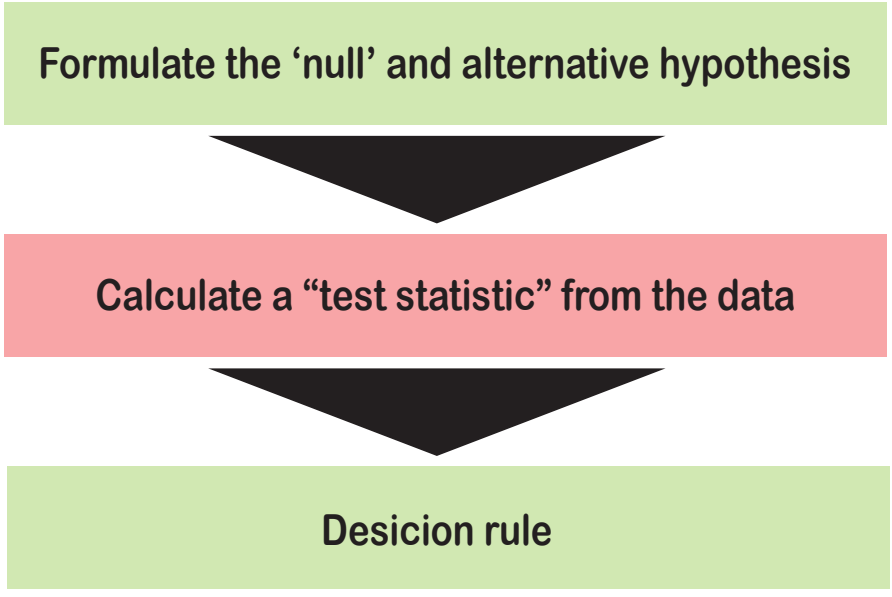
Recall: basic setup



We can also use a
p-value

Statistical inference: hypothesis testing

Recall: basic setup



We can also use a **p-value**

What is a p-value?

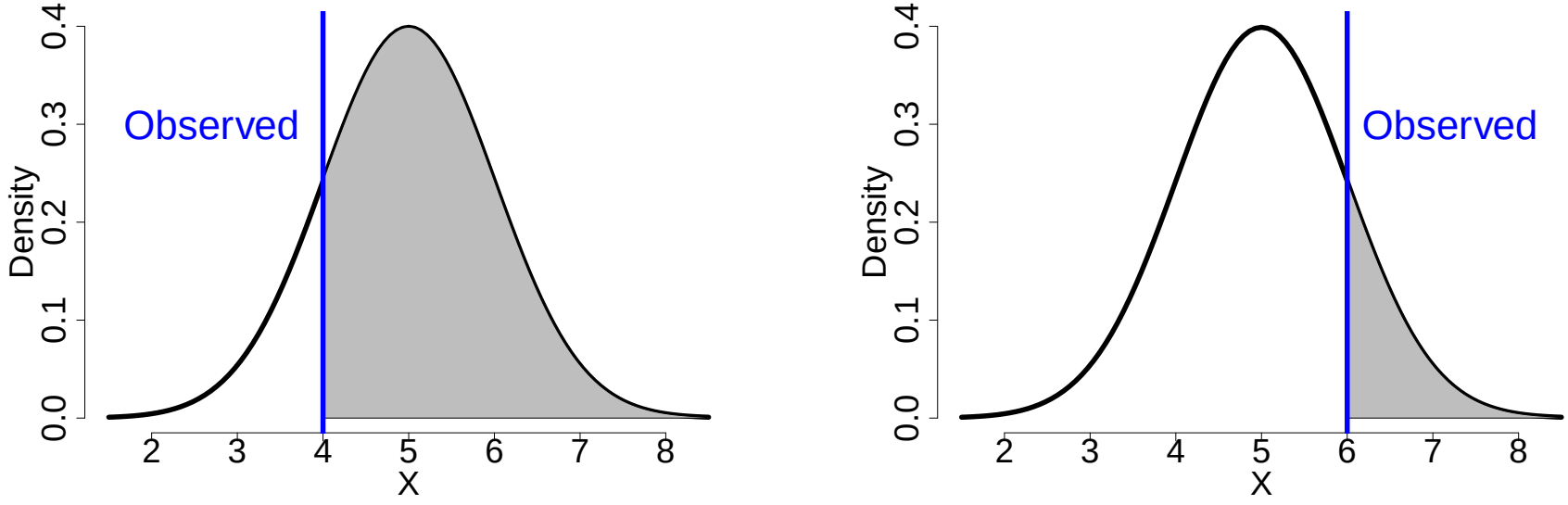
Statistical inference: what is a p-value?

A **p-value** is the probability of observing the current data (or more extreme) given than H_0 is true.

Statistical inference: what is a p-value?

A **p-value** is the probability of observing the current data (or more extreme) given than H_0 is true. For example

$$H_0 : \mu \leq 5 \text{ vs } H_1 : \mu > 5$$



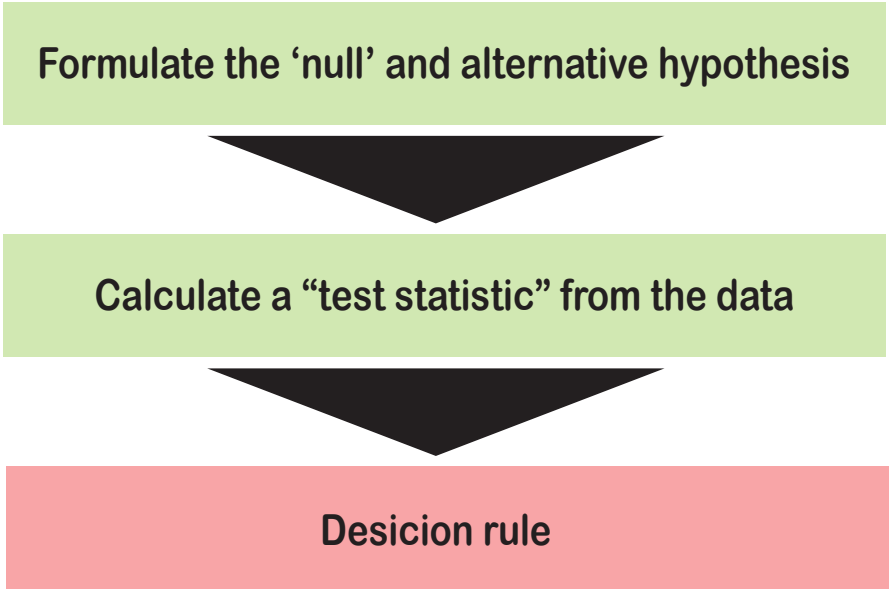
The p-value is equal to the gray area

The smaller p-value, the stronger the evidence against H_0

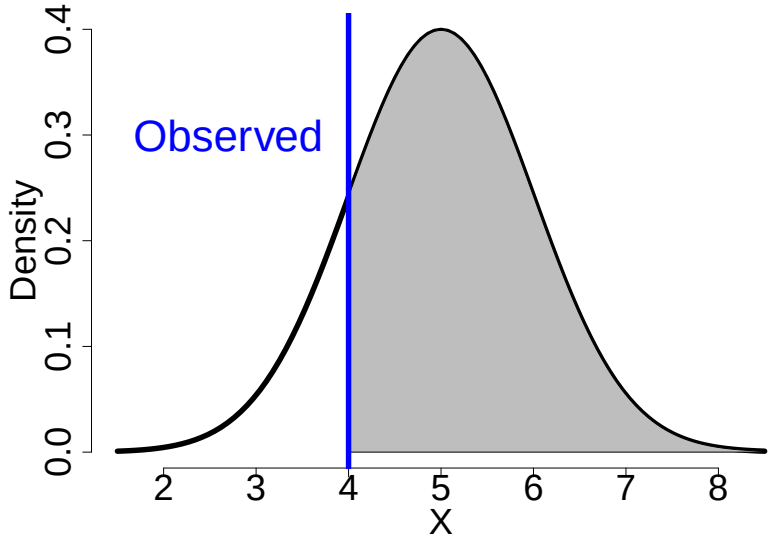
Link to 'pvalue' shiny app

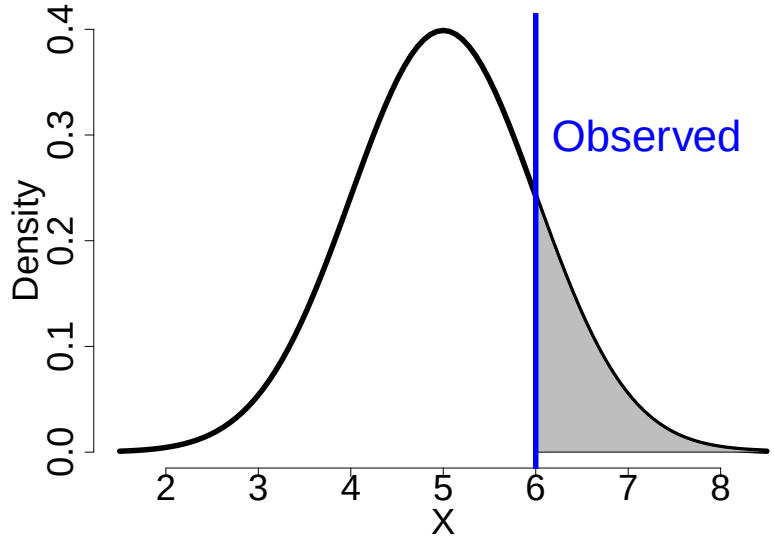
Statistical inference: decision rule of an hypothesis test

Recall: basic setup



Statistical inference: decision rule of an hypothesis test

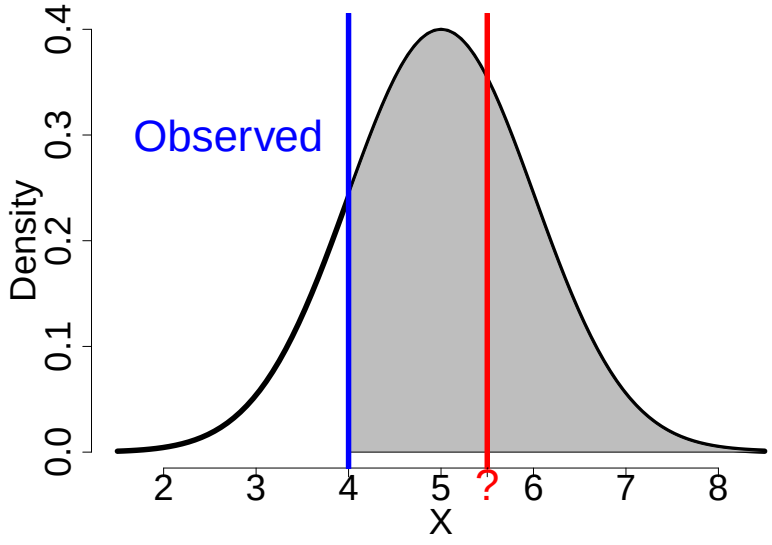


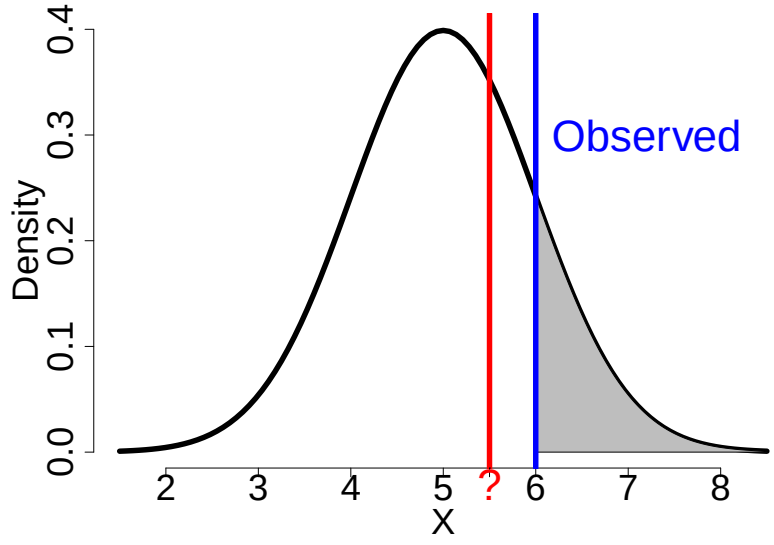


- If the p-value is **large**, the data seems to support H_0.
- If the p-value is **small**, the data does not seem to support H_0.

Where to place the cut-off?

Statistical inference: decision rule of an hypothesis test





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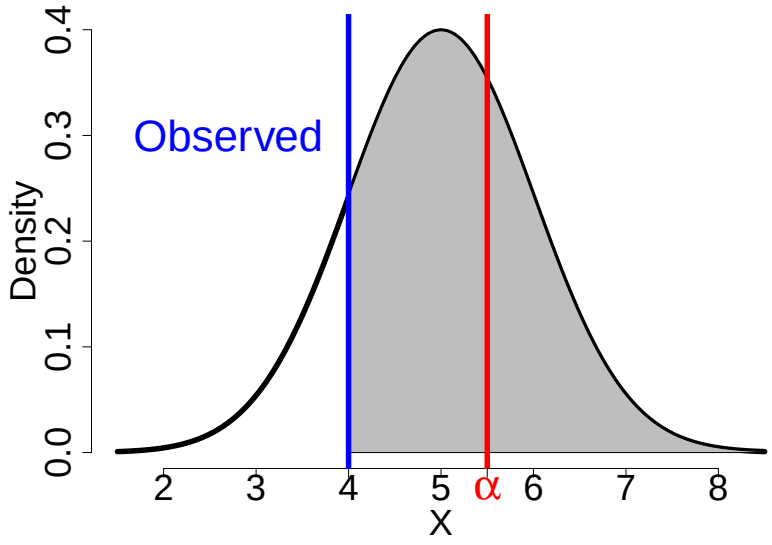
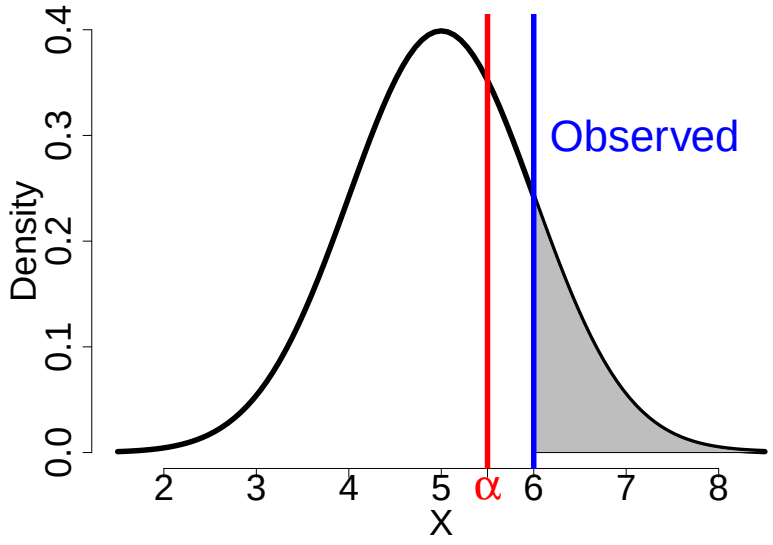
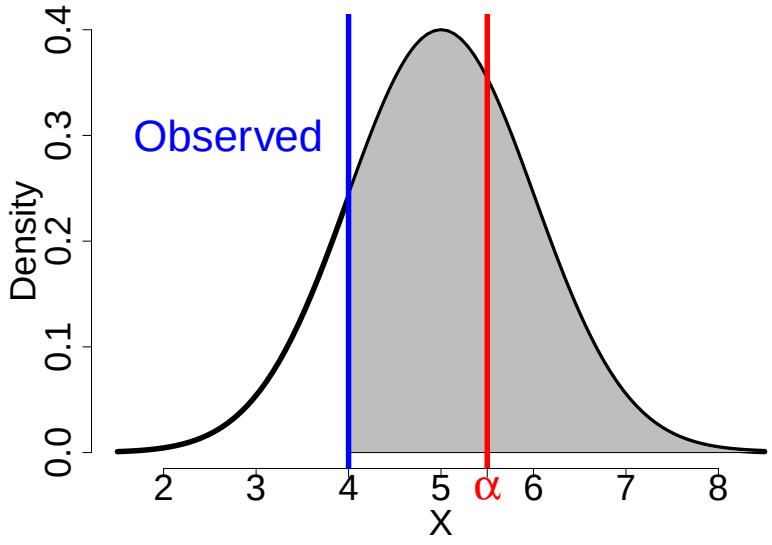
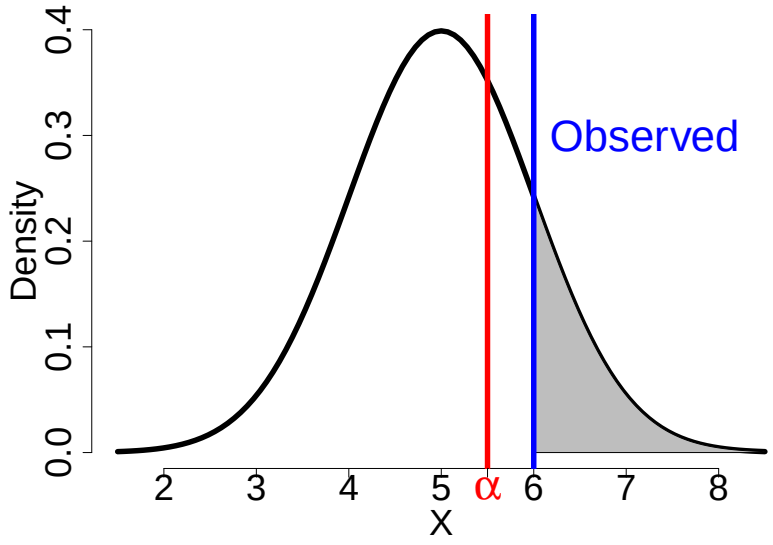




The cut-off is typically set to control **type I error**

Statistical inference: decision rule of an hypothesis test





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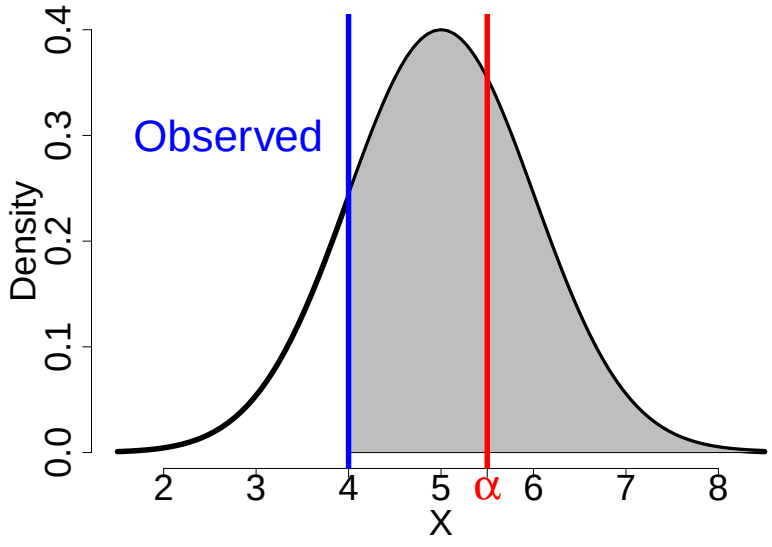
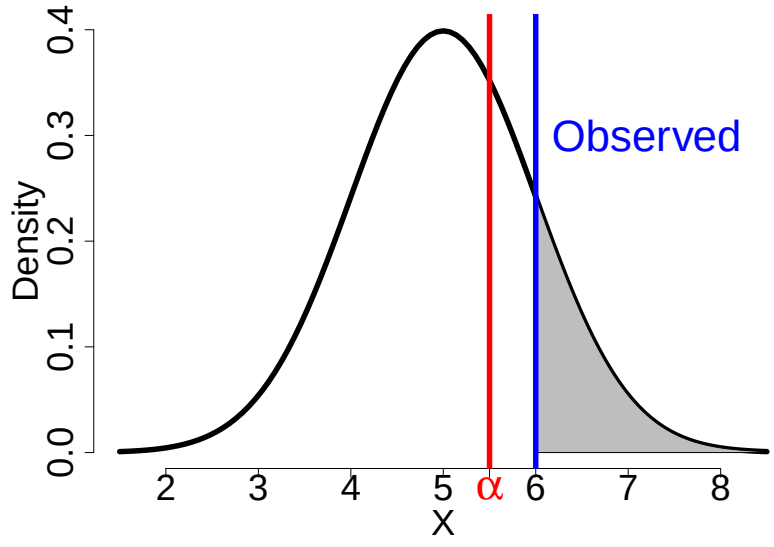
$$\alpha = \text{P (Reject } H_0 \text{ when } H_0 \text{ is true)}$$

Popular choice: $\alpha = 0.05$

Statistical inference: decision rule of an hypothesis test





The cut-off is typically set to control **type I error**

$$\alpha = \text{P (Reject } H_0 \text{ when } H_0 \text{ is true)}$$

Popular choice: $\alpha = 0.05$

Cut-off must be set before running the test!

Statistical inference: what test to use?

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- What type of data is available?
- What is the relevant hypothesis?
- What assumptions underlie the test?

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We will explore some examples in detail this afternoon ...

Acknowledgements

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