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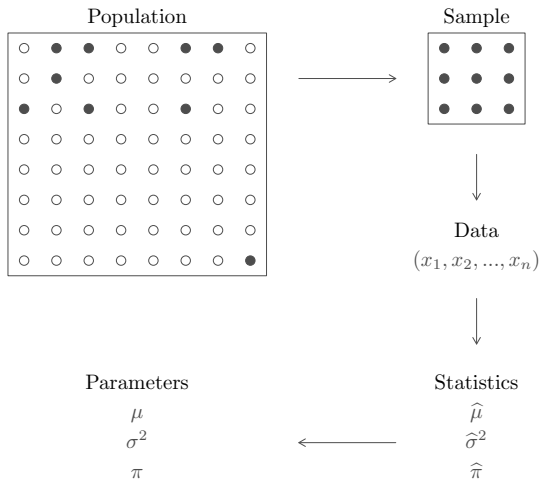
UNIVERSITY OF  
CAMBRIDGE

## Introduction to Statistical Analysis

Cancer Research UK – 23<sup>rd</sup> of February 2022

D.-L. Couturier, M. Eldridge & M. Fernandes (Bioinformatics core)

# Grand Picture of Statistics



# Data Types

|                              | $x_1$ | $x_2$        | $x_3$        | $\dots$ | $x_n$ |
|------------------------------|-------|--------------|--------------|---------|-------|
| Cancer status                | C     | <del>C</del> | <del>C</del> | $\dots$ | C     |
| Nucleic acid sequence        | C     | T            | T            | $\dots$ | A     |
| 5-level pain score           | 3     | 1            | 5            | $\dots$ | 4     |
| # of daily admissions at A&E | 16    | 23           | 12           | $\dots$ | 17    |
| Gene expression intensity    | 882.1 | 379.5        | 528.3        | $\dots$ | 120.9 |

# Summary statistics and plots for qualitative data

5-level answers of 21 patients to the question

"How much did pain due to your ureteric stones interfere with your day to day activities ?":

3, 1, 5, 3, 1, 1, 1, 5, 1, 3, 4, 1, 1, 4, 5, 5, 5, 5, 5, 4, 4,

where

- ▶ 1 = "Not at all",
- ▶ 2 = "A little bit",
- ▶ 3 = "Somewhat",
- ▶ 4 = "Quite a bit",
- ▶ 5 = "Very much".

# Summary statistics and plots for qualitative data

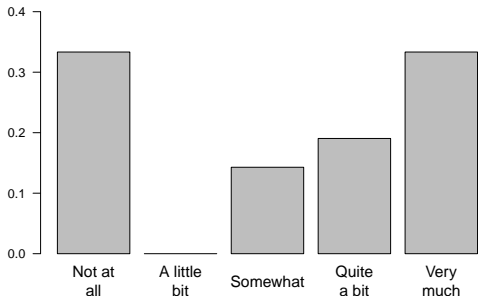
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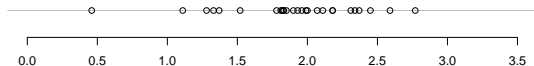
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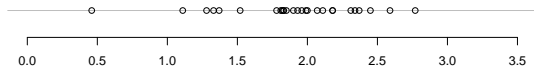
# Summary statistics and plots for quantitative data



Gene expression values of gene “CCND3 Cyclin D3” from 27 patients diagnosed with acute lymphoblastic leukaemia:

|            |            |            |            |            |            |            |            |            |
|------------|------------|------------|------------|------------|------------|------------|------------|------------|
| $x_{(1)}$  | $x_{(2)}$  | $x_{(3)}$  | $x_{(4)}$  | $x_{(5)}$  | $x_{(6)}$  | $x_{(7)}$  | $x_{(8)}$  | $x_{(9)}$  |
| 0.46       | 1.11       | 1.28       | 1.33       | 1.37       | 1.52       | 1.78       | 1.81       | 1.82       |
| $x_{(10)}$ | $x_{(11)}$ | $x_{(12)}$ | $x_{(13)}$ | $x_{(14)}$ | $x_{(15)}$ | $x_{(16)}$ | $x_{(17)}$ | $x_{(18)}$ |
| 1.83       | 1.83       | 1.85       | 1.9        | 1.93       | 1.96       | 1.99       | 2.00       | 2.07       |
| $x_{(19)}$ | $x_{(20)}$ | $x_{(21)}$ | $x_{(22)}$ | $x_{(23)}$ | $x_{(24)}$ | $x_{(25)}$ | $x_{(26)}$ | $x_{(27)}$ |
| 2.11       | 2.18       | 2.18       | 2.31       | 2.34       | 2.37       | 2.45       | 2.59       | 2.77       |

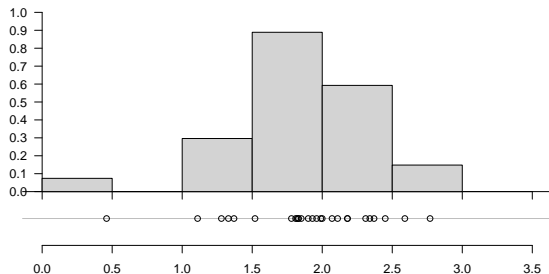
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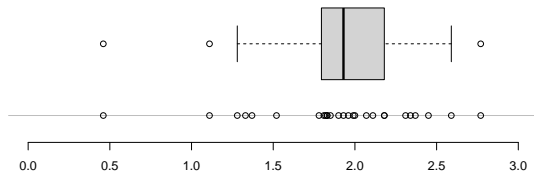


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# Summary statistics and plots for quantative data



Gene expression values of gene “CCND3 Cyclin D3” from 27 patients diagnosed with acute lymphoblastic leukaemia:

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# Two-sample case: independent versus paired samples

Permeability constants of a placental membrane at term (X) and between 12 to 26 weeks gestational age (Y).

|   | 1    | 2    | 3    | 4    | 5    | 6    | 7    | 8    | 9    | 10   |
|---|------|------|------|------|------|------|------|------|------|------|
| X | 0.80 | 0.83 | 1.89 | 1.04 | 1.45 | 1.38 | 1.91 | 1.64 | 0.73 | 1.46 |
| Y | 1.15 | 0.88 | 0.90 | 0.74 | 1.21 |      |      |      |      |      |

Hamilton depression scale factor measurements in 9 patients with mixed anxiety and depression, taken at the first (X) and second (Y) visit after initiation of a therapy (administration of a tranquilizer).

|     | 1     | 2    | 3     | 4     | 5     | 6     | 7     | 8    | 9     |
|-----|-------|------|-------|-------|-------|-------|-------|------|-------|
| X   | 1.83  | 0.50 | 1.62  | 2.48  | 1.68  | 1.88  | 1.55  | 3.06 | 1.30  |
| Y   | 0.88  | 0.65 | 0.60  | 2.05  | 1.06  | 1.29  | 1.06  | 3.14 | 1.29  |
| Y-X | -0.95 | 0.15 | -1.02 | -0.43 | -0.62 | -0.59 | -0.49 | 0.08 | -0.01 |

# Quiz Time

## Sections 1 to 4

On <http://bioinformatics-core-shared-training.github.io/IntroductionToStats/>, select **Online quiz** under **Course Materials**

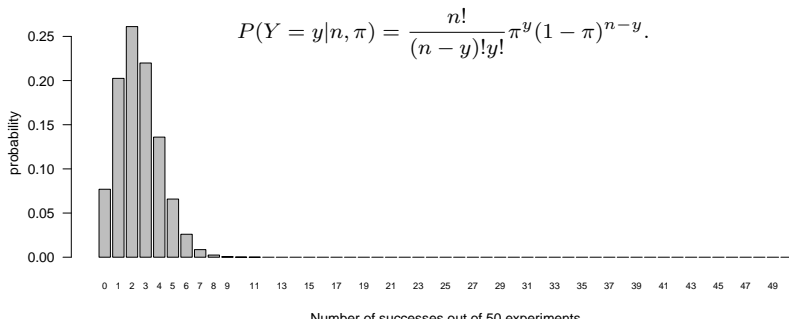
# Statistical distributions

“In probability theory and statistics, a statistical distribution is a **mathematical function** that provides the **probabilities of occurrence of different possible outcomes** in an experiment” [Wikipedia].

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For a given cancer, mutation of the nucleic acid located at position 790 of Exon 20 is assumed to occur with a probability of  $\sim 5\%$ .  
Probability of observing  $y$  patients out of  $n = 50$  cancer patients with this mutation?



# Some parametric distributions: Binomial distribution

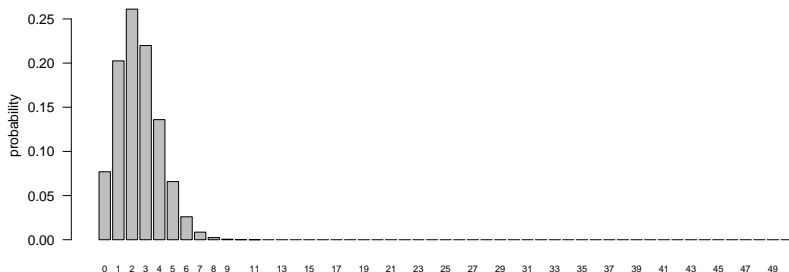
- ▶ the number of successes out of  $n$  trials (experiments),  $Y = \sum_{i=1}^n X_i$ , follows a binomial distribution with parameters  $n$  and  $\pi$ :

$$Y \sim \text{Bin}(n, \pi),$$

$$P(Y = y|n, \pi) = \frac{n!}{(n-y)!y!} \pi^y (1-\pi)^{n-y}.$$

IF

- ▶  $n$  independent experiments,
- ▶ outcome of each experiment is dichotomous (success/failure),
- ▶ the probability of success  $\pi$  is the same for all experiments,



# Some parametric distributions: Poisson distribution

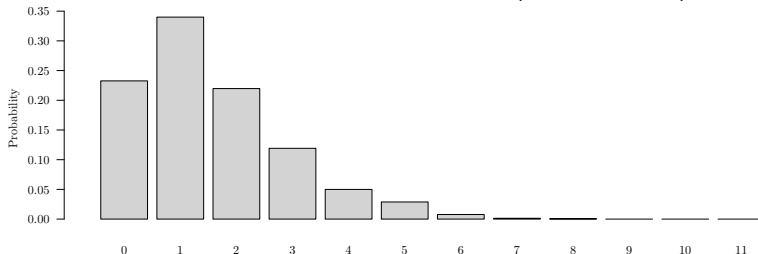
- ▶ the number of events occurring in a fixed time interval or in a given area,  $X$ , may be modelled by means of a Poisson distribution with parameter  $\lambda$ :

$$X \sim \text{Poisson}(\lambda),$$

$$P(X = x|\lambda) = \frac{\lambda^x e^{-\lambda}}{x!}.$$

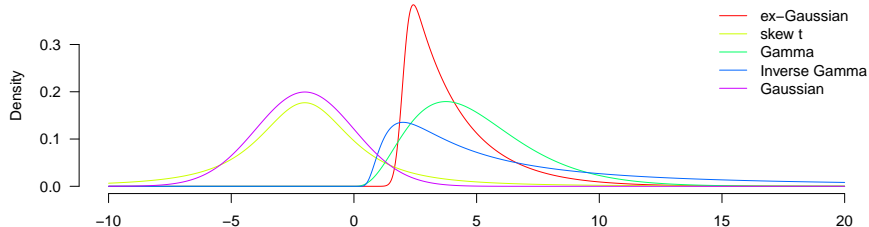
IF, during a time interval or in a given area,

- ▶ events occur independently,
- ▶ at the same rate,
- ▶ and the probability of an event to occur in a small interval (area) is proportional to the length of the interval (size of the area),



Number of chronic conditions per patient (US National Medical Expenditure Survey)

# Some parametric distributions: Continuous distrib.





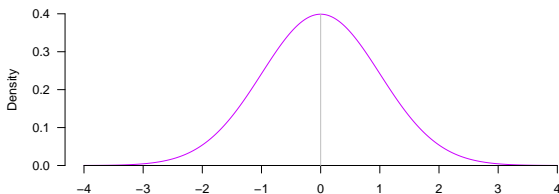
## Some parametric distributions: Normal distribution

$$X \sim N(\mu, \sigma^2), \quad f_X(x) = \frac{1}{\sqrt{2\pi\sigma^2}} e^{-\frac{(x-\mu)^2}{2\sigma^2}}$$

$$\mathbb{E}[X] = \mu, \quad \text{Var}[X] = \sigma^2,$$

$$Z = \frac{X - \mu}{\sigma} \sim N(0, 1), \quad f_Z(z) = \frac{1}{\sqrt{2\pi}} e^{-\frac{z^2}{2}}.$$

Probability density function,  $f_Z(z)$ , of a standard normal:



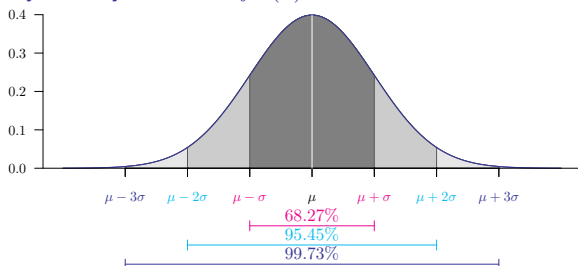
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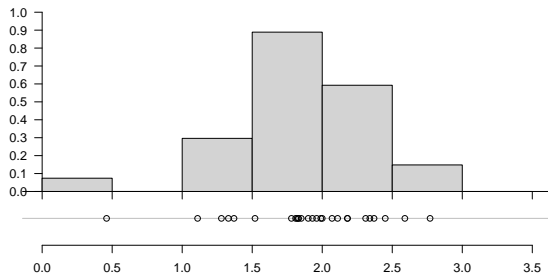
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(i) Suitable modelling for a lot of variables:



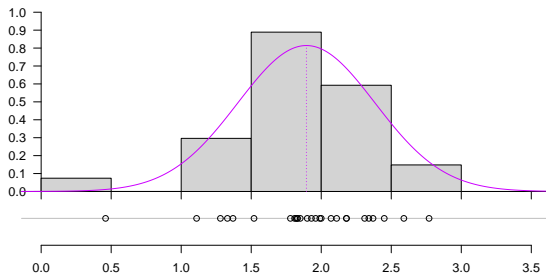
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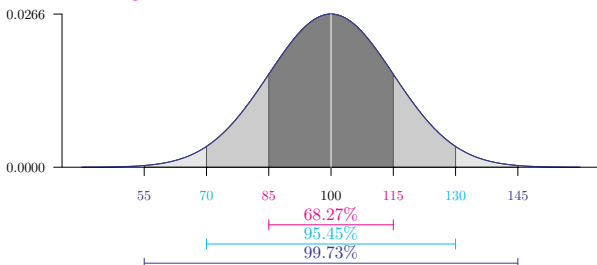
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(i) Suitable modelling for a lot of variables: IQ



# Some parametric distributions: Normal distribution

$$X \sim N(\mu, \sigma^2), \quad f_X(x) = \frac{1}{\sqrt{2\pi\sigma^2}} e^{-\frac{(x-\mu)^2}{2\sigma^2}}$$

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## (ii) Central limit theorem (Lindeberg-Lévy CLT)

- ▶ Let  $(X_1, \dots, X_n)$  be  $n$  independent and identically distributed (iid) random variables drawn from distributions of expected values given by  $\mu$  and finite variances given by  $\sigma^2$ ,
- ▶ then

$$\hat{\mu} = \bar{X} = \frac{\sum_{i=1}^n X_i}{n} \xrightarrow{d} N\left(\mu, \frac{\sigma^2}{n}\right).$$

If  $X_i \sim N(\mu, \sigma^2)$ , this result is true for all sample sizes.

# Central limit theorem shiny app:

## Distribution of the mean

<https://bioinformatics.cruk.cam.ac.uk/apps/stats/central-limit-theorem/>

<https://pauljudge.shinyapps.io/central-limit-theorem-master/>

95% Confidence interval for  $\mu$ , the population mean,  
when  $X_i \sim N(\mu, \sigma^2)$

- ▶ if  $X \sim N(\mu, \sigma^2)$ , then  $\bar{X} \sim N\left(\mu, \frac{\sigma^2}{n}\right)$ ,
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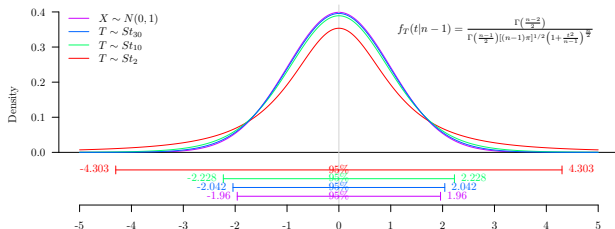
$$P\left( \quad < \quad < \quad \right) = 0.95$$



95% Confidence interval for  $\mu$ , the population mean,  
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- ▶ if  $X \sim N(\mu, \sigma^2)$ , then  $Z = \frac{\bar{X} - \mu}{\frac{\sigma}{\sqrt{n}}} \sim N(0, 1)$ ,
- ▶ if  $\sigma$  unknown, then  $T = \frac{\bar{X} - \mu}{\frac{s}{\sqrt{n}}} \sim St_{n-1}$ .

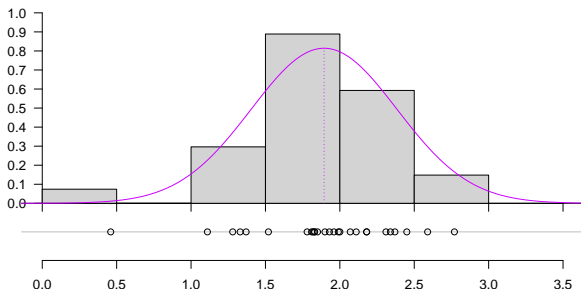
$$P\left( \bar{X} - \frac{s}{\sqrt{n}} \cdot t_{n-1, \alpha/2} < \mu < \bar{X} + \frac{s}{\sqrt{n}} \cdot t_{n-1, \alpha/2} \right) = 0.95$$



95% Confidence interval for  $\mu$ , the population mean,  
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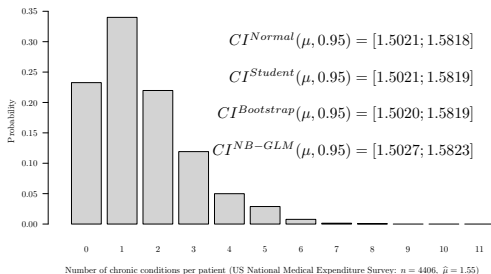
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- ▶ if  $\sigma$  unknown, then  $T = \frac{X - \mu}{s} \sim St_{n-1}$ .

$$P\left( \quad < \quad < \quad \right) = 0.95$$



# 95% Confidence interval for $\mu$ , the population mean, when $X_i \sim iid(\mu, \sigma^2)$

- ▶ CLT:  $\bar{X} \xrightarrow{d} N\left(\mu, \frac{\sigma^2}{n}\right)$ ,
- ▶ if  $X \sim N(\mu, \sigma^2)$ , then  $Z = \frac{X-\mu}{\sigma} \sim N(0, 1)$ ,
- ▶ if  $\sigma$  unknown, then  $T = \frac{X-\mu}{s} \sim St_{n-1}$ .



# 95% Confidence interval for $\mu_Y - \mu_X$ , the difference between population means

If we have

- ▶  $X_i \sim iid(\mu_X, \sigma_X^2), i = 1, \dots, n_X,$
- ▶  $Y_i \sim iid(\mu_Y, \sigma_Y^2), i = 1, \dots, n_Y,$

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then

- ▶ if  $\sigma_X^2 = \sigma_Y^2$  [Student's t-test equation],

$$\triangleright CI(\mu_Y - \mu_X, 0.95) = (\bar{Y} - \bar{X}) \pm t_{1-\frac{\alpha}{2}, n_X+n_Y-2} s_p \sqrt{\frac{1}{n_X} + \frac{1}{n_Y}}$$

$$\text{where } s_p = \frac{(n_X-1)s_X^2 + (n_Y-1)s_Y^2}{n_X+n_Y-2},$$

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- ▶ if  $\sigma_X^2 \neq \sigma_Y^2$  [Welch-Satterthwaite's t-test equation],

$$\triangleright CI(\mu_Y - \mu_X, 0.95) = (\bar{Y} - \bar{X}) \pm t_{1-\frac{\alpha}{2}, df} \sqrt{\frac{s_X^2}{n_X} + \frac{s_Y^2}{n_Y}}, \text{ where}$$

$$df = \frac{\left(\frac{s_X^2}{n_X} + \frac{s_Y^2}{n_Y}\right)^2}{\frac{\left(\frac{s_X^2}{n_X}\right)^2}{n_X-1} + \frac{\left(\frac{s_Y^2}{n_Y}\right)^2}{n_Y-1}}.$$

# Central limit theorem shiny app:

## Coverage of Student's asymptotic confidence intervals

<https://bioinformatics.cruk.cam.ac.uk/apps/stats/central-limit-theorem/>

<https://pauljudge.shinyapps.io/central-limit-theorem-master/>

# Quiz Time

## Practical 1

[https://bioinformatics-core-shared-training.github.io/  
IntroductionToStats/practical.html](https://bioinformatics-core-shared-training.github.io/IntroductionToStats/practical.html)





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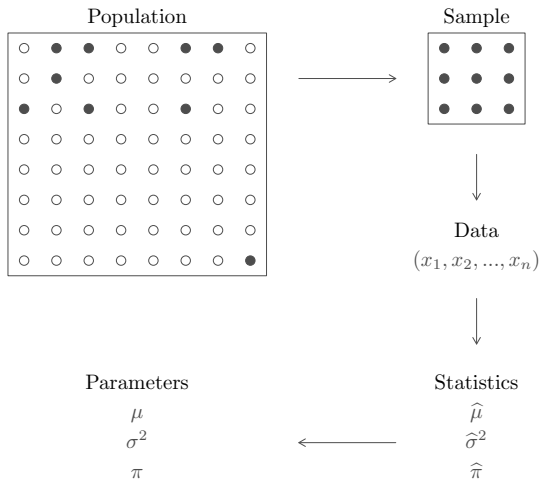
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## PART II: Parametric and non-parametric one-sample location tests

Cancer Research UK – 23<sup>rd</sup> of February 2022

D.-L. Couturier, M. Eldridge & M. Fernandes (Bioinformatics core)

# Grand Picture of Statistics



# Statistical hypothesis testing

A hypothesis test describes a phenomenon by means of two non-overlapping idealised models/descriptions:

- ▶ the null hypothesis **H0**, “generally assumed to be true until evidence indicates otherwise”
- ▶ the alternative hypothesis **H1**.

The aim of the test is to reject the null hypothesis in favour of the alternative hypothesis, and conclude, with a probability  $\alpha$  of being wrong, that the idealised model/description of H1 is true.

Theory 1: Dieters lose more fat than the exercisers

Theory 2: There is no majority for Brexit now

Theory 3: Serum vitamin C is reduced in patients

# Statistical hypothesis testing

Several-step process:

- ▶ Define  $H_0$  and  $H_1$  according to a theory
- ▶ Set  $\alpha$ , the probability of rejecting  $H_0$  when it is true (type I error),
- ▶ Determine the test statistic to be used,
- ▶ Define  $n$ , the sample size, allowing you to reject  $H_0$  when  $H_1$  is true with a probability  $1 - \beta$  (Power),
- ▶ Collect the data,
- ▶ Perform the statistical test, define the  $p$ -value, and reject (or not) the null hypothesis.

# Statistical hypothesis testing

Many options:

- ▶ One-sided versus two-sided tests,
- ▶ Exact versus asymptotic tests,
- ▶ Parametric versus non-parametric tests.

# Parametric location test

## (One-sided) t-test

We test:

$$H_0: \mu_{IQ} = 100,$$

$$H_1: \mu_{IQ} > 100.$$

We have  $X_i \sim N(\mu, \sigma^2), i = 1, \dots, n,$

We know

$$\bar{X} \sim N\left(\mu, \frac{\sigma^2}{n}\right),$$

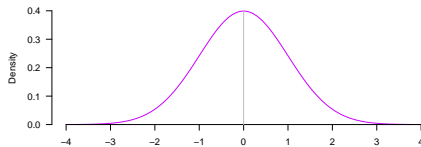
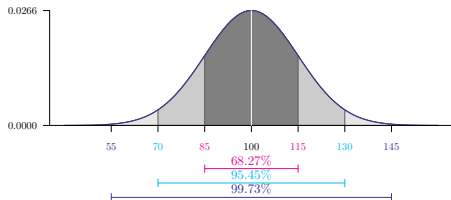
$$Z = \frac{\bar{X} - \mu}{\frac{\sigma}{\sqrt{n}}} \sim N(0, 1),$$

Thus, if  $H_0$  is true, we have:

$$Z = \frac{\bar{X} - \mu_0}{\frac{\sigma}{\sqrt{n}}} \sim N(0, 1).$$

Define the p-value:

$$p\text{-value} = P(T > T_{obs})$$



# Statistical tests

## 4 possible outcomes

Conclude:

- ▶ if  $p\text{-value} > \alpha \rightarrow$  do not reject  $H_0$ .
- ▶ if  $p\text{-value} < \alpha \rightarrow$  reject  $H_0$  in favour of  $H_1$ .

|               |         | Test Outcome      |                  |
|---------------|---------|-------------------|------------------|
|               |         | H0 not rejected   | H1 accepted      |
| Unknown Truth | H0 true | $1 - \alpha$ [TN] | $\alpha$ [FP]    |
|               | H1 true | $\beta$ [FN]      | $1 - \beta$ [TP] |

where

- ▶  $\alpha$  is the type I error, the probability of rejecting  $H_0$  when  $H_0$  is correct,
- ▶  $\beta$  is the type II error, the probability of not rejecting  $H_0$  when  $H_1$  is correct.

Warnings

- ▶ 'absence of evidence is not evidence of absence',
- ▶ design may help minimising FP and FN (ie, maximising TN and TP).

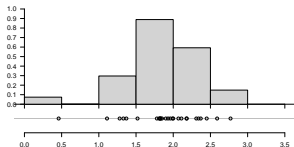
# Parametric location test

## Student's test

A location model is assumed for  $X_i$ ,  $i = 1, \dots, n$ :

$$X_i = \mu + e_i,$$

where  $e_i \sim N(\mu_e = 0, \sigma_e^2)$ , a symmetrical distribution.



Interest for **H0**:  $\mu = \mu_0$  against **H1**:  $\mu < \mu_0$  or  $\mu \neq \mu_0$  or  $\mu > \mu_0$ .

Test statistics :  $T = \frac{\bar{X} - \mu_0}{\frac{s}{\sqrt{n}}}$  ..



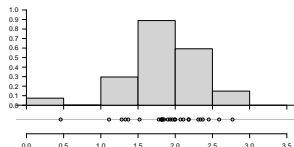
# Parametric location test

## Student's test

A location model is assumed for  $X_i$ ,  $i = 1, \dots, n$ :

$$X_i = \mu + e_i,$$

where  $e_i \sim N(\mu_e = 0, \sigma_e^2)$ , a symmetrical distribution.



Interest for **H0**:  $\mu = \mu_0$  against **H1**:  $\mu < \mu_0$  or  $\mu \neq \mu_0$  or  $\mu > \mu_0$ .

Test statistics :  $T = \frac{\bar{X} - \mu_0}{\frac{s}{\sqrt{n}}}$  ..

Distribution of  $W$  under H0:  $T \sim Student(df = n - 1)$ .

One Sample t-test

```
data: golub[1042, gol.fac == "ALL"]
t = 4.172, df = 26, p-value = 0.0002982
alternative hypothesis: true mean is not equal to 1.5
95 percent confidence interval:
 1.699817 2.087948
sample estimates:
mean of x
 1.893883
```

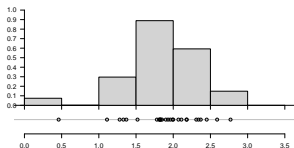
# Non-parametric location test

## Wilcoxon sign-rank test

A location model is assumed for  $X_i$ ,  $i = 1, \dots, n$ :

$$X_i = \theta + e_i,$$

where  $e_i \sim iid(\mu_e = 0, \sigma_e^2)$ , a symmetrical distribution.



Interest for **H0**:  $\theta = \theta_0$  against **H1**:  $\theta < \theta_0$  or  $\theta \neq \theta_0$  or  $\theta > \theta_0$ .

Test statistics :  $W^+ = \sum_{i=1}^n \iota(X_i - \theta_0 > 0) \text{ Rank}(|X_i - \theta_0|)$ .

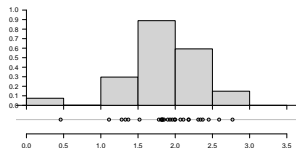
# Non-parametric location test

## Wilcoxon sign-rank test

A location model is assumed for  $X_i$ ,  $i = 1, \dots, n$ :

$$X_i = \theta + e_i,$$

where  $e_i \sim iid(\mu_e = 0, \sigma_e^2)$ , a symmetrical distribution.



Interest for **H0**:  $\theta = \theta_0$  against **H1**:  $\theta < \theta_0$  or  $\theta \neq \theta_0$  or  $\theta > \theta_0$ .

Test statistics :  $W^+ = \sum_{i=1}^n \iota(X_i - \theta_0 > 0) \text{Rank}(|X_i - \theta_0|)$ .

Distribution of  $W$  under H0:  $W^+$  has no closed-form distribution.

Wilcoxon signed rank exact test

```
data: golub[1042, gol.fac == "ALL"]  
V = 333, p-value = 0.0002363  
alternative hypothesis: true location is not equal to 1.5  
95 percent confidence interval:  
 1.73868 2.09106  
sample estimates:  
(pseudo)median  
 1.926475
```

# Parametric or non-parametric ?

|             |        | Outcome(s) normally distributed |        |    |
|-------------|--------|---------------------------------|--------|----|
|             |        | Yes                             | Mildly | No |
| Sample size | Small  |                                 |        |    |
|             | Medium |                                 |        |    |
|             | Large  |                                 |        |    |

Situations which may suggest the use of non-parametric statistics:

- ▶ When there is a small sample size or **very unequal groups**,
- ▶ When the data has **notable outliers**,
- ▶ When one outcome has a **distribution other than normal**,
- ▶ When the data are **ordered** with many ties or are rank ordered.

**Non-parametric does not mean assumption free**

# Introduction to Shiny Apps and Exercises



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## PART III: Parametric and non-parametric two-sample location tests

Cancer Research UK – 23<sup>rd</sup> of February 2022

D.-L. Couturier, M. Eldridge & M. Fernandes (Bioinformatics core)

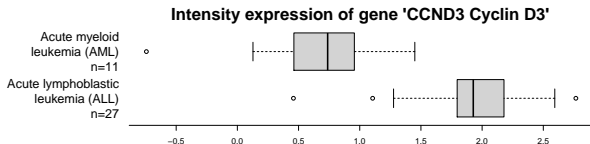
# Two-sample case

Many options:

- ▶ One-sided versus two-sided tests,
- ▶ Exact versus asymptotic tests,
- ▶ Parametric versus non-parametric tests,
- ▶ Tests for paired versus independent data.

# Parametric two-sample location test

## Two-sample two-sided Student-s & Welch's t-tests



We test **H0**:  $\mu_Y - \mu_X = 0$  against **H1**:  $\mu_Y - \mu_X \neq 0$ .

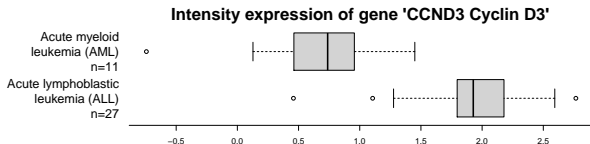
We know:

- ▶ Student's t-test [assume  $\sigma_X^2 = \sigma_Y^2$ ]:  $\frac{(\bar{Y} - \bar{X}) - (\mu_Y - \mu_X)}{s_p \sqrt{\frac{1}{n_X} + \frac{1}{n_Y}}} \sim t_{1 - \frac{\alpha}{2}, n_X + n_Y - 2}$
- ▶ Welch's t-test [assume  $\sigma_X^2 \neq \sigma_Y^2$ ]:  $\frac{(\bar{Y} - \bar{X}) - (\mu_Y - \mu_X)}{\sqrt{\frac{s_X^2}{n_X} + \frac{s_Y^2}{n_Y}}} \sim t_{1 - \frac{\alpha}{2}, df}$



# Parametric two-sample location test

## Two-sample two-sided Student-s & Welch's t-tests



We test **H0**:  $\mu_Y - \mu_X = 0$  against **H1**:  $\mu_Y - \mu_X \neq 0$ .

We know:

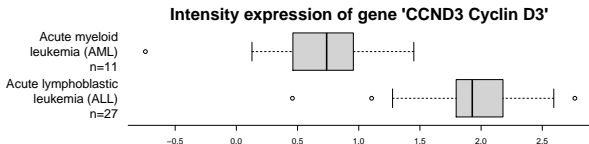
- ▶ Student's t-test [assume  $\sigma_X^2 = \sigma_Y^2$ ]: 
$$\frac{(\bar{Y} - \bar{X}) - (\mu_Y - \mu_X)}{s_p \sqrt{\frac{1}{n_X} + \frac{1}{n_Y}}} \sim t_{1 - \frac{\alpha}{2}, n_X + n_Y - 2}$$
- ▶ Welch's t-test [assume  $\sigma_X^2 \neq \sigma_Y^2$ ]: 
$$\frac{(\bar{Y} - \bar{X}) - (\mu_Y - \mu_X)}{\sqrt{\frac{s_X^2}{n_X} + \frac{s_Y^2}{n_Y}}} \sim t_{1 - \frac{\alpha}{2}, df}$$

Two Sample t-test

```
data: golub[1042, gol.fac == "ALL"] and golub[1042, gol.fac == "AML"]
t = 6.7983, df = 36, p-value = 6.046e-08
alternative hypothesis: true difference in means is not equal to 0
95 percent confidence interval:
 0.8829143 1.6336690
sample estimates:
mean of x mean of y
1.8938826 0.6355909
```

# Parametric two-sample location test

## Two-sample two-sided Student-s & Welch's t-tests



We test **H0**:  $\mu_Y - \mu_X = 0$  against **H1**:  $\mu_Y - \mu_X \neq 0$ .

We know:

- ▶ Student's t-test [assume  $\sigma_X^2 = \sigma_Y^2$ ]: 
$$\frac{(\bar{Y} - \bar{X}) - (\mu_Y - \mu_X)}{s_p \sqrt{\frac{1}{n_X} + \frac{1}{n_Y}}} \sim t_{1 - \frac{\alpha}{2}, n_X + n_Y - 2}$$
- ▶ Welch's t-test [assume  $\sigma_X^2 \neq \sigma_Y^2$ ]: 
$$\frac{(\bar{Y} - \bar{X}) - (\mu_Y - \mu_X)}{\sqrt{\frac{s_X^2}{n_X} + \frac{s_Y^2}{n_Y}}} \sim t_{1 - \frac{\alpha}{2}, df}$$

Welch Two Sample t-test

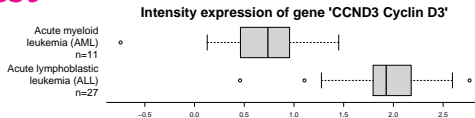
```
data: golub[1042, gol.fac == "ALL"] and golub[1042, gol.fac == "AML"]
t = 6.3186, df = 16.118, p-value = 9.871e-06
alternative hypothesis: true difference in means is not equal to 0
95 percent confidence interval:
 0.8363826 1.6802008
sample estimates:
mean of x mean of y
1.8938826 0.6355909
```

# Non-parametric two-sample location test

## Mann-Whitney-Wilcoxon test

Let

- ▶  $X_i \sim iid(\mu_X, \sigma^2), i = 1, \dots, n_X,$
- ▶  $Y_i \sim iid(\mu_X + \delta, \sigma^2), i = 1, \dots, n_Y.$



Interest for **H0**:  $\delta = \delta_0$  against **H1**:  $\delta < \delta_0$  or  $\delta \neq \delta_0$  or  $\delta > \delta_0$ .

Standardised test statistic:  $z = \frac{\sum_{i=1}^{n_Y} R(Y_i) - [n_Y(n_X + n_Y + 1)/2]}{\sqrt{n_X n_Y (n_X + n_Y + 1)/12}},$

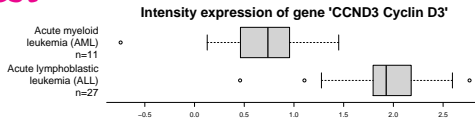
where  $R(Y_i)$  denotes the rank of  $Y_i$  amongst the combined samples, i.e., amongst  $(X_1, \dots, X_{n_X}, Y_1, \dots, Y_{n_Y})$ .

# Non-parametric two-sample location test

## Mann-Whitney-Wilcoxon test

Let

- ▶  $X_i \sim iid(\mu_X, \sigma^2), i = 1, \dots, n_X,$
- ▶  $Y_i \sim iid(\mu_X + \delta, \sigma^2), i = 1, \dots, n_Y.$



Interest for **H0**:  $\delta = \delta_0$  against **H1**:  $\delta < \delta_0$  or  $\delta \neq \delta_0$  or  $\delta > \delta_0$ .

Standardised test statistic:  $z = \frac{\sum_{i=1}^{n_Y} R(Y_i) - [n_Y(n_X + n_Y + 1)/2]}{\sqrt{n_X n_Y (n_X + n_Y + 1)/12}},$

where  $R(Y_i)$  denotes the rank of  $Y_i$  amongst the combined samples, i.e., amongst  $(X_1, \dots, X_{n_X}, Y_1, \dots, Y_{n_Y})$ .

Distribution of  $Z$  under  $H_0$ :  $Z \sim N(0, 1)$ .

Implementation 1:

statistic = -4.361334 , p-value = 1.292716e-05

Implementation 2:

W = 284, p-value = 6.15e-07

alternative hypothesis: true location shift is not equal to 0

95 percent confidence interval:

0.89647 1.57023

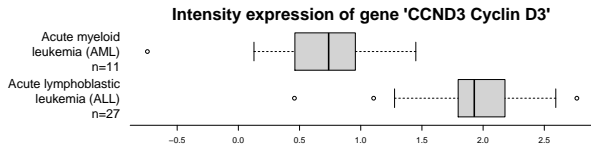
sample estimates:

difference in location

1.21951



# F-test of equality of variances

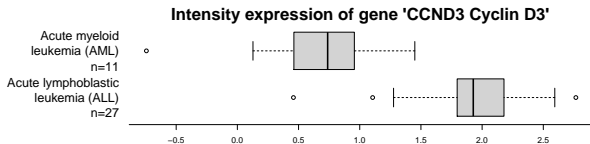


We test **H0:**  $\sigma_Y^2 = \sigma_X^2$  against **H1:**  $\sigma_Y^2 \neq \sigma_X^2$ .

We know:

► F-test [assume  $X_i \sim N(\mu_X, \sigma_X)$  and  $Y_i \sim N(\mu_Y, \sigma_Y)$ ]:  $\frac{s_Y^2}{s_X^2} \sim F_{n_Y-1, n_X-1}$

# F-test of equality of variances



We test  $H_0: \sigma_Y^2 = \sigma_X^2$  against  $H_1: \sigma_Y^2 \neq \sigma_X^2$ .

We know:

► F-test [assume  $X_i \sim N(\mu_X, \sigma_X)$  and  $Y_i \sim N(\mu_Y, \sigma_Y)$ ]:  $\frac{s_Y^2}{s_X^2} \sim F_{n_Y-1, n_X-1}$

F test to compare two variances

```
data: golub[1042, gol.fac == "ALL"] and golub[1042, gol.fac == "AML"]
F = 0.71164, num df = 26, denom df = 10, p-value = 0.4652
alternative hypothesis: true ratio of variances is not equal to 1
95 percent confidence interval:
 0.2127735 1.8428387
sample estimates:
ratio of variances
 0.7116441
```

# Warning

## Multiplicity correction

For each test, the probability of rejecting  $H_0$  (and accept  $H_1$ ) when  $H_0$  is true equals  $\alpha$ .

For  $k$  tests, the probability of rejecting  $H_0$  (and accept  $H_1$ ) at least 1 time when  $H_0$  is true,  $\alpha_k$ , is given by

$$\alpha_k = 1 - (1 - \alpha)^k.$$

Thus, for  $\alpha = 0.05$ ,

- ▶ if  $k = 1$ ,  $\alpha_1 = 1 - (1 - \alpha)^1 = 0.05$ ,
- ▶ if  $k = 2$ ,  $\alpha_2 = 1 - (1 - \alpha)^2 = 0.0975$ ,
- ▶ if  $k = 10$ ,  $\alpha_{10} = 1 - (1 - \alpha)^{10} = 0.4013$ .

Idea: change the level of each test so that  $\alpha_k = 0.05$ :

- ▶ Bonferroni correction :  $\alpha = \frac{\alpha_k}{k}$ ,
- ▶ Dunn-Sidak correction:  $\alpha = 1 - (1 - \alpha_k)^{1/k}$ .

# Warning

## Non-parametric is not assumption free: Type I error

Simulate 2500 samples with

- ▶  $X_i \sim \text{Uniform}(1.5, 2.5)$ ,  $i = 1, \dots, n_X$ ,
- ▶  $Y_i \sim \text{Uniform}(0, 4)$ ,  $i = 1, \dots, n_Y$ ,

so that  $E[X_i] = E[Y_i] = 2$  (i.e., same mean, same median).

Assume

- ▶  $X_i \sim \text{iid}(\mu_X, \sigma^2)$ ,  $i = 1, \dots, n_X$ ,
- ▶  $Y_i \sim \text{iid}(\mu_X + \delta, \sigma^2)$ ,  $i = 1, \dots, n_Y$ .

Test **H0**:  $\delta = \delta_0$  against **H1**:  $\delta \neq \delta_0$ , at the 5% level, by means of

- ▶ Mann-Whitney-Wilcoxon test (MWW),
- ▶ T-test,
- ▶ Welch-test.

|             |                       | $\hat{\alpha}$ |                  |              |
|-------------|-----------------------|----------------|------------------|--------------|
|             |                       | Tests          |                  |              |
| Sample size | $n_X = 200, n_Y = 70$ | MWW            | Student's t-test | Welch's test |
|             | $n_X = 20, n_Y = 7$   | 0.145          | 0.202            | 0.055        |
|             |                       | 0.148          | 0.240            | 0.062        |



# Exercises