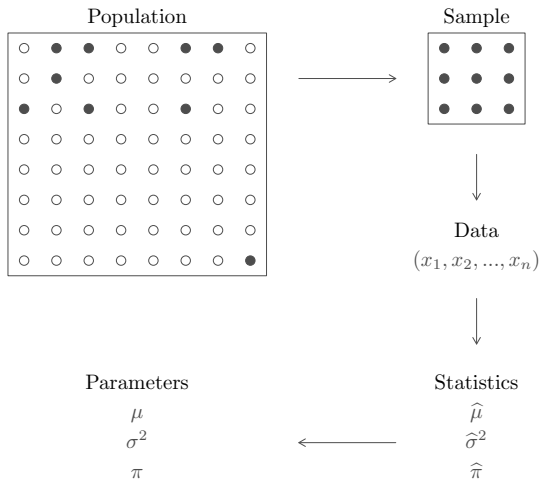# Introduction to Statistical Analysis

Cancer Research UK – 9th of November 2021

D.-L. Couturier / M. Fernandes [Bioinformatics core]

Grand Picture of Statistics

Population

Sample

Data
$(x_1, x_2, ..., x_n)$

Parameters
μ
σ^2
π

Statistics
$\widehat{\mu}$
$\widehat{\sigma}^2$
$\widehat{\pi}$

Data Types

	x_1	x_2	x_3	$\cdots$	x_n
Cancer status	C	C̸	C̸	$\cdots$	C
Nucleic acid sequence	C	T	T	$\cdots$	A
5-level pain score	3	1	5	$\cdots$	4
# of daily admissions at A&E	16	23	12	$\cdots$	17
Gene expression intensity	882.1	379.5	528.3	$\cdots$	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".

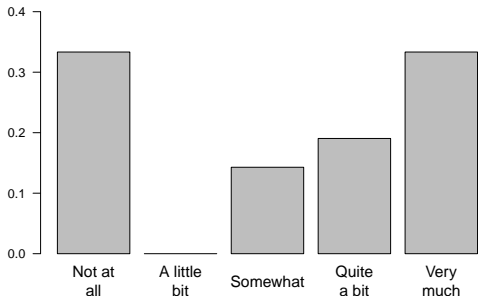# Summary statistics and plots for qualitative data

5-level answers of 21 patients to the question
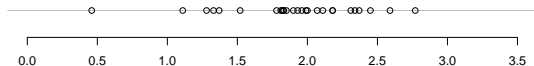"How much did pain due to your ureteric stones interfere with your day to day activities ?":

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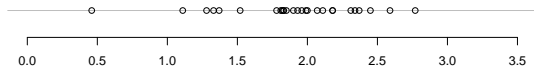- 3 = "Somewhat",
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Summary statistics and plots for quantative data

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

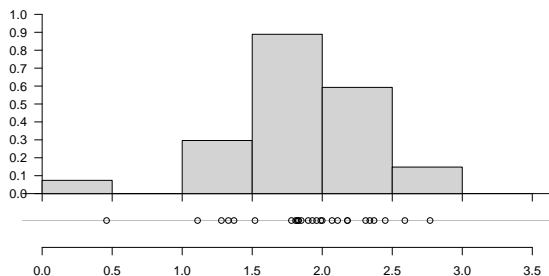| $x_{(1)}$	$x_{(2)}$	$x_{(3)}$	$x_{(4)}$	$x_{(5)}$	$x_{(6)}$	$x_{(7)}$	$x_{(8)}$	$x_{(9)}$
0.46	1.11	1.28	1.33	1.37	1.52	1.78	1.81	1.82
$x_{(10)}$	$x_{(11)}$	$x_{(12)}$	$x_{(13)}$	$x_{(14)}$	$x_{(15)}$	$x_{(16)}$	$x_{(17)}$	$x_{(18)}$
1.83	1.83	1.85	1.9	1.93	1.96	1.99	2.00	2.07
$x_{(19)}$	$x_{(20)}$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

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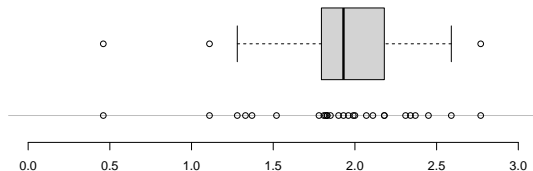| $x_{(1)}$	$x_{(2)}$	$x_{(3)}$	$x_{(4)}$	$x_{(5)}$	$x_{(6)}$	$x_{(7)}$	$x_{(8)}$	$x_{(9)}$
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Two-sample case: independent versus paired samples

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].

Statistical distributions

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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?

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

Number of successes out of 50 experiments
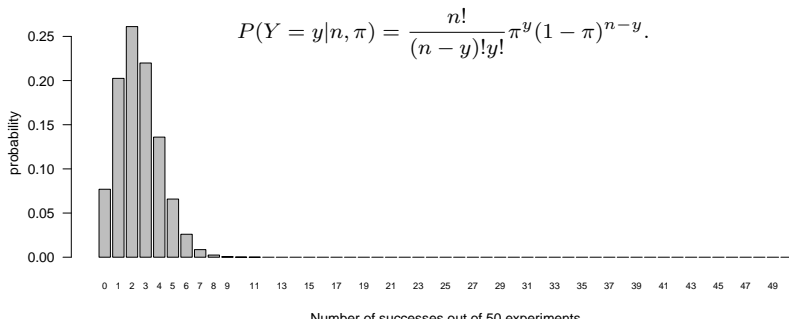
Some parametric distributions: Binomial distribution

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

$$Y \sim Bin(n, \pi),$$

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

IF

▶ n independent experiments,
▶ outcome of each experiment is dichotomous (success/failure),
▶ the probability of success π is the same for all experiments,
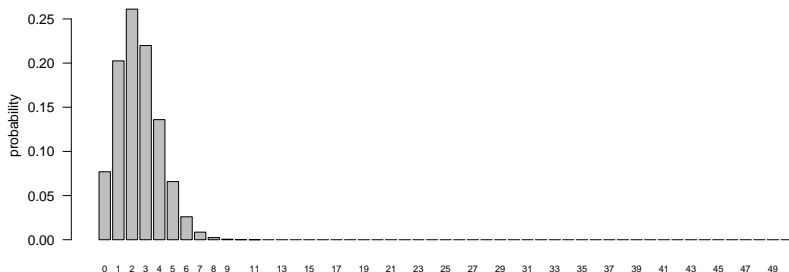
Some parametric distributions: Poisson distribution

▶ 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 λ:

$$X \sim Poisson(\lambda),$$

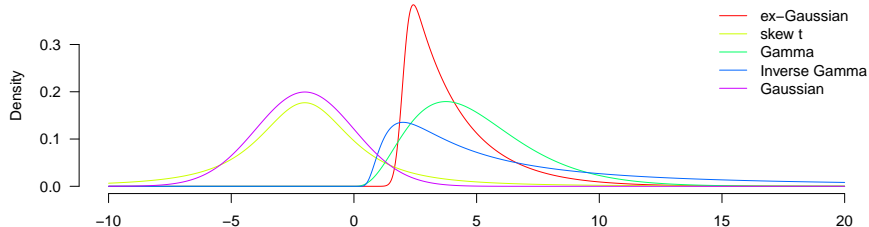$$P(X = x|\lambda) = \frac{\lambda^x e^{-\lambda}}{x!}.$$

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),
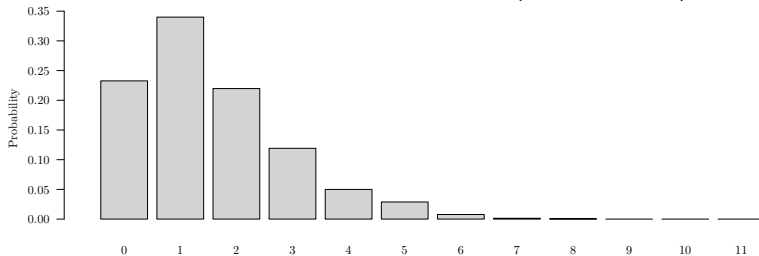
Number of chronic conditions per patient (US National Medical Expenditure Survey)
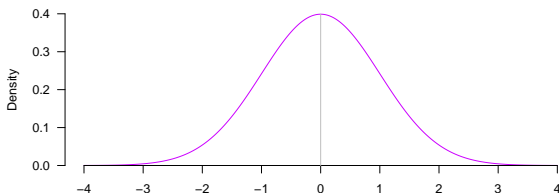
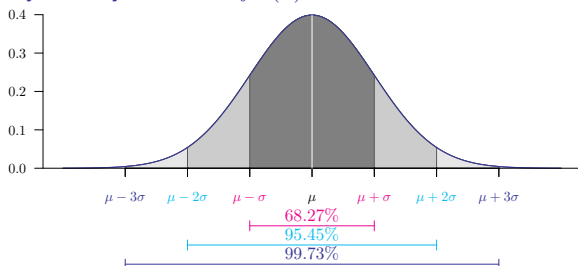# Some parametric distributions: Continuous distrib.

Some parametric distributions: Normal distribution

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

$$\mathsf{E}[X] = \mu, \qquad \mathsf{Var}[X] = \sigma^2,$$

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

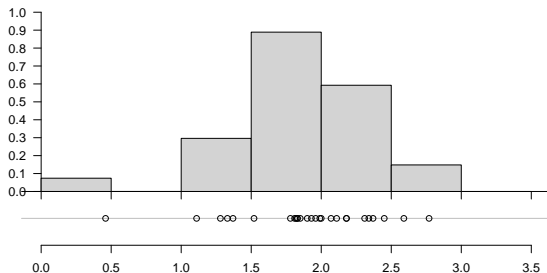Probability density function, $f_Z(z)$, of a standard normal:

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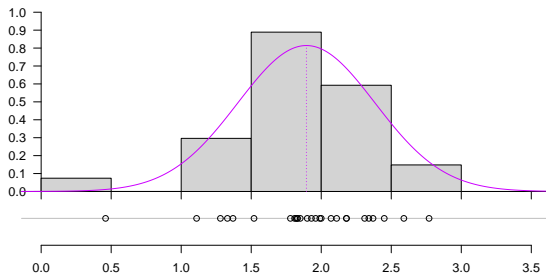(i) Suitable modelling for a lot of variables:

Some parametric distributions: Normal distribution

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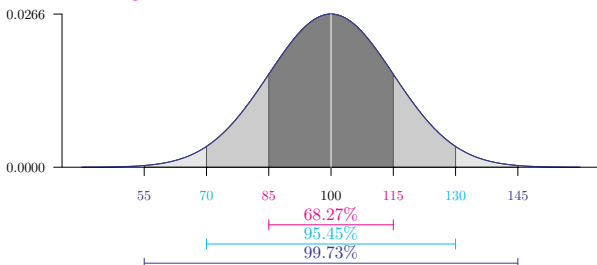(i) Suitable modelling for a lot of variables

Some parametric distributions: Normal distribution

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

Some parametric distributions: Normal distribution

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

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

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

$\triangleright$ Let $(X_1, ..., X_n)$ be n independent and identically distributed (iid) random variables drawn from distributions of expected values given by μ and finite variances given by σ^2,

$\triangleright$ then

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

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/

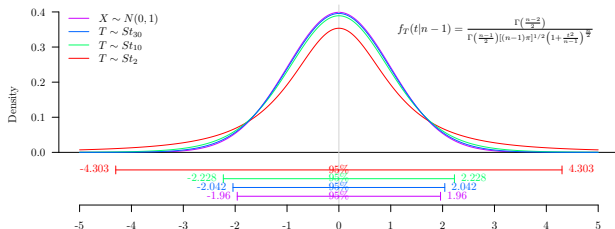# 95% Confidence interval for μ, the population mean, when $X_i \sim N(\mu, \sigma^2)$

- if $X \sim N(\mu, \sigma^2)$, then $\overline{X} \sim N\left(\mu, \frac{\sigma^2}{n}\right)$,
- if $X \sim N(\mu, \sigma^2)$, then $Z = \frac{X-\mu}{\sigma} \sim N(0, 1)$,

$$\mathsf{P}\left(\qquad < \qquad < \qquad \right) = 0.95$$

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

- if $X \sim N(\mu, \sigma^2)$, then $\overline{X} \sim N\left(\mu, \frac{\sigma^2}{n}\right)$,
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- if σ unknown, then $T = \frac{X - \mu}{s} \sim St_{n-1}$.

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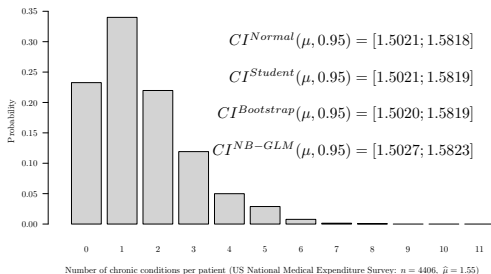# 95% Confidence interval for μ, the population mean, when $X_i \sim N(\mu, \sigma^2)$

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

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

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

$CI^{Normal}(\mu, 0.95) = [1.5021; 1.5818]$

$CI^{Student}(\mu, 0.95) = [1.5021; 1.5819]$

$CI^{Bootstrap}(\mu, 0.95) = [1.5020; 1.5819]$

$CI^{NB-GLM}(\mu, 0.95) = [1.5027; 1.5823]$

Number of chronic conditions per patient (US National Medical Expenditure Survey: $n = 4406$, $\hat{\mu} = 1.55$)

If we have
- $X_i \sim iid(\mu_X, \sigma_X^2)$, $i = 1, ..., n_X$,
- $Y_i \sim iid(\mu_Y, \sigma_Y^2)$, $i = 1, ..., n_Y$,

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

If we have
- $X_i \sim iid(\mu_X, \sigma_X^2)$, $i = 1, ..., n_X$,
- $Y_i \sim iid(\mu_Y, \sigma_Y^2)$, $i = 1, ..., n_Y$,

then
- if $\sigma_X^2 = \sigma_Y^2$ [Student's t-test equation],
  - $CI(\mu_Y - \mu_X, 0.95) = (\overline{Y} - \overline{X}) \pm t_{1-\frac{\alpha}{2}, n_X + n_Y - 2} s_p \sqrt{\frac{1}{n_X} + \frac{1}{n_Y}}$
    where $s_p = \frac{(n_X - 1)s_X^2 + (n_Y - 1)s_Y^2}{n_X + n_Y - 2}$,

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

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    where $s_p = \frac{(n_X - 1)s_X^2 + (n_Y - 1)s_Y^2}{n_X + n_Y - 2}$,
- if $\sigma_X^2 \neq \sigma_Y^2$ [Welch-Satterthwaite's t-test equation],
  - $CI(\mu_Y - \mu_X, 0.95) = (\overline{Y} - \overline{X}) \pm t_{1-\frac{\alpha}{2}, \text{df}} \sqrt{\frac{s_X^2}{n_X} + \frac{s_Y^2}{n_Y}}$, where
    $$\text{df} = \frac{\left(\frac{s_X^2}{n_X} + \frac{s_Y^2}{n_Y} \right)^2}{\frac{\left(\frac{s_X^2}{n_X} \right)^2}{n_X - 1} + \frac{\left(\frac{s_Y^2}{n_Y} \right)^2}{n_Y - 1}}.$$

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

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

D.-L. Couturier / 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 α 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 H0 and H1 according to a theory

- ▶ Set α, the probability of rejecting H0 when it is true (type I error),

- ▶ Determine the test statistic to be used,

- ▶ Define n, the sample size, allowing you to reject H0 when H1 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:
H0: $\mu_{IQ} = 100$,
H1: $\mu_{IQ} > 100$.

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

We know
- $\overline{X} \quad \sim \quad N\left(\mu, \frac{\sigma^2}{n}\right)$,
- $Z = \frac{\overline{X} - \mu}{\frac{\sigma}{\sqrt{n}}} \sim N(0, 1)$,

Thus, if H0 is true, we have:
- $Z = \frac{\overline{X} - \mu_0}{\frac{\sigma}{\sqrt{n}}} \sim N(0, 1)$.

Define the p-value:
- $p - \text{value} = P(T > T_{obs})$
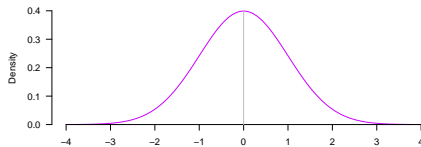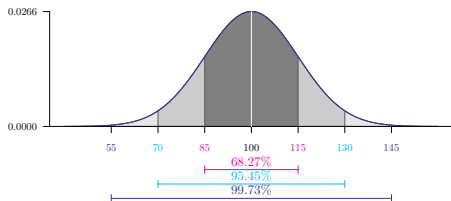
Statistical tests
4 possible outcomes

Conclude:
- if p-value $> \alpha$ $\rightarrow$ do not reject H0.
- if p-value $< \alpha$ $\rightarrow$ reject H0 in favour of H1.

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

where
- α is the type I error, the probability of rejecting H0 when H0 is correct,
- β is the type II error, the probability of not rejecting H0 when H1 is correct.

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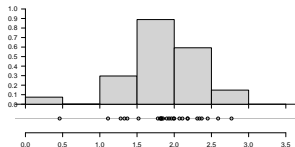- design may help minimising FP and FN (ie, maximising TN and TP).

Parametric location test
Student's test

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

$$X_i = \mu + e_i,$$

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 $\mu > \mu_0$.

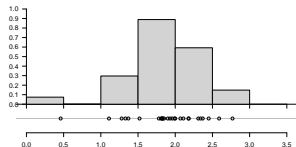Test statistics : $T = \dfrac{\overline{X} - \mu_0}{\frac{s}{\sqrt{n}}}$..

Parametric location test
Student's test

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

$$X_i = \mu + e_i,$$

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 : $T = \dfrac{\overline{X} - \mu_0}{\frac{s}{\sqrt{n}}}$..

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
```
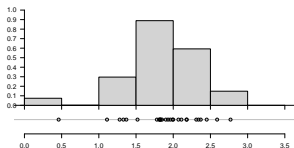
Non-parametric location test
Wilcoxon sign-rank test

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

$$X_i = \theta + e_i,$$

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 $X_i,\ i = 1, ..., n$:

$$X_i = \theta + e_i,$$

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 $\theta > \theta_0$.

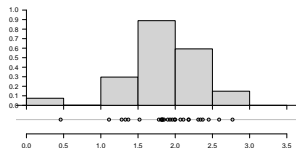Test statistics : $W^+ = \sum_{i=1}^n \iota(X_i - \theta_0 > 0)\ \text{Rank}(|X_i - \theta_0|)$.

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 ?

T-test		Outcome(s) normally distributed		
		Yes	Mildly	No
	Small			
Sample size	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

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

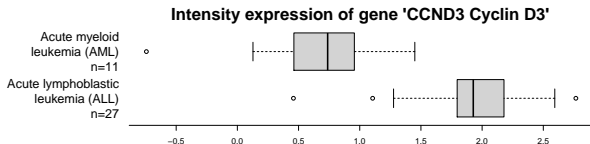D.-L. Couturier / M. Fernandes [Bioinformatics core]

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

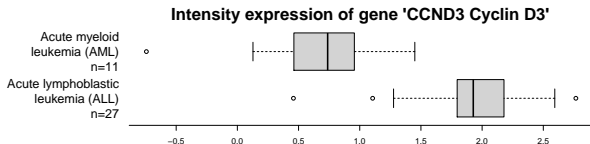**Intensity expression of gene 'CCND3 Cyclin D3'**

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

We know:

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

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

Parametric two-sample location test
Two-sample two-sided Student-s & Welch's t-tests

Intensity expression of gene 'CCND3 Cyclin D3'

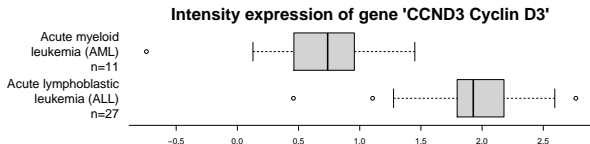We test **H0**: $\mu_Y - \mu_X = 0$ against **H1**: $\mu_Y - \mu_X \neq 0$.

We know:

► Student's t-test [assume $\sigma_X^2 = \sigma_Y^2$]: $\dfrac{(\overline{Y} - \overline{X}) - (\mu_Y - \mu_X)}{s_p \sqrt{\frac{1}{n_X} + \frac{1}{n_Y}}} \sim t_{1 - \frac{\alpha}{2}, n_X + n_Y - 2}$

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

```
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

Intensity expression of gene 'CCND3 Cyclin D3'

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

We know:

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

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

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

Intensity expression of gene 'CCND3 Cyclin D3'
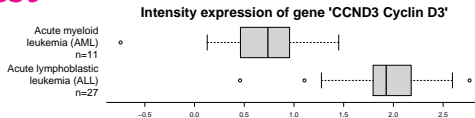
Interest for **H0**: $\delta = \delta_0$ against **H1**: $\delta < \delta_0$ or $\delta \neq \delta_0$ or $\delta > \delta_0$.

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 $(X_1, ..., X_{n_X}, Y_1, ..., Y_{n_Y})$.

Non-parametric two-sample location test
Mann-Whitney-Wilcoxon test

Let

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

Intensity expression of gene 'CCND3 Cyclin D3'

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

Standardised test statistic: $z = \frac{\sum_{i=1}^{n_Y} R(Y_i) - [n_Y(n_X + n_Y + 1)/2]}{\sqrt{n_X n_Y (n_X + n_Y + 1)/12}}$,
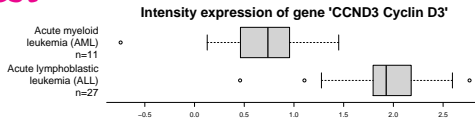
where $R(Y_i)$ denotes the rank of Y_i amongst the combined samples, i.e., amongst $(X_1, ..., X_{n_X}, Y_1, ..., Y_{n_Y})$.

Distribution of Z under H0: $Z \sim N(0, 1)$.


```
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
```
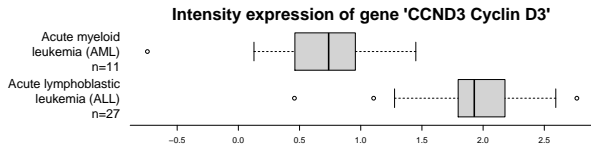
F-test of equality of variances

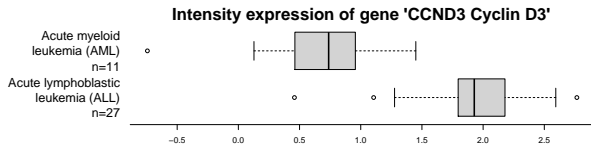**Intensity expression of gene 'CCND3 Cyclin D3'**

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

Intensity expression of gene 'CCND3 Cyclin D3'

We test $\quad$ **H0**: $\sigma_Y^2 = \sigma_X^2$ $\quad$ against $\quad$ **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 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 H0 (and accept H1) when H0 is true equals α.

For k tests, the probability of rejecting H0 (and accept H1) at least 1 time when H0 is true, α_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
- $X_i \sim Uniform(1.5, 2.5), \ i = 1, ..., n_X,$
- $Y_i \sim Uniform(0, 4), \ i = 1, ..., n_Y,$

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

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

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.

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

Exercises