



Introduction to Statistical Analysis

Cancer Research UK -26^{th} of November 2019

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

Timeline

9:30 - Morning

- ~ 45mn Lecture: data type, summary statistics and graphical displays
- ➤ ~ 15mn Quiz

10:30 - 15mn Coffee & Tea break

- ~ 60mn Lecture: some statistical distributions + CLT
- $ightharpoonup \sim 15$ mn Exercises & discussion

12:00 - Lunch break

13:00 - Afternoon

- ▶ ~ 45mn Lecture: One-sample location test
- ightharpoonup \sim 30mn Exercises with shiny app & discussion
- ➤ ~ 45mn Lecture: Two-sample location test

15:15 - 15mn Coffee & Tea break

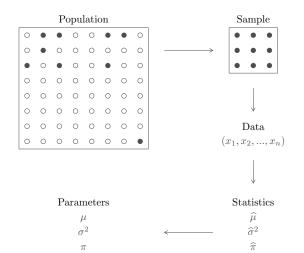
ightharpoonup \sim 30mn Exercises with shiny app & discussion

16:15 - Group based exercises

▶ ~ 60mn



Grand Picture of Statistics





Data Types

	x_1	x_2	x_3	 x_n
Cancer status	С	¢	¢	 С
Nucleic acid sequence	С	Т	Т	 Α
5-level pain score	3	1	5	 4
# of daily admissions at A&E	16	23	12	 17
Gene expression intensity	882.1	379.5	528.3	 120.9



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

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



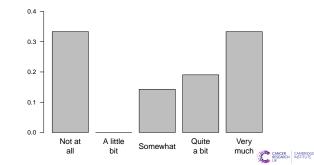
5-level answers of 21 patients to the question

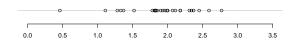
"How much did pain due to your ureteric stones interfere with your day to day activities?":

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

where

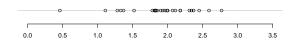
- ightharpoonup 1 = "Not at all",
- ▶ 2 = "A little bit",
- ▶ 3 = "Somewhat".
- ▶ 4 = "Quite a bit",
- 5 = "Very much".





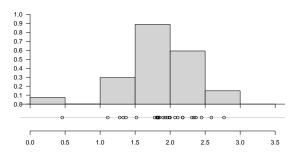
$\frac{x_{(1)}}{0.46}$	$rac{x_{(2)}}{1.11}$	$\frac{x_{(3)}}{1.28}$	$\frac{x_{(4)}}{1.33}$	$\frac{x_{(5)}}{1.37}$	$\frac{x_{(6)}}{1.52}$	$\frac{x_{(7)}}{1.78}$	$\frac{x_{(8)}}{1.81}$	$\frac{x_{(9)}}{1.82}$
$\frac{x_{(10)}}{1.83}$	$\frac{x_{(11)}}{1.83}$	$\frac{x_{(12)}}{1.85}$	$^{x_{(13)}}_{1.9}$	$\frac{x_{(14)}}{1.93}$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





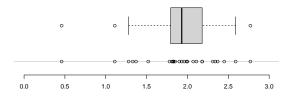
$\frac{x_{(1)}}{0.46}$	$rac{x_{(2)}}{1.11}$	$\frac{x_{(3)}}{1.28}$	$\frac{x_{(4)}}{1.33}$	$\frac{x_{(5)}}{1.37}$	$\frac{x_{(6)}}{1.52}$	$\frac{x_{(7)}}{1.78}$	$\frac{x_{(8)}}{1.81}$	$\frac{x_{(9)}}{1.82}$
$\frac{x_{(10)}}{1.83}$	$\frac{x_{(11)}}{1.83}$	$\frac{x_{(12)}}{1.85}$	$^{x_{(13)}}_{1.9}$	$\frac{x_{(14)}}{1.93}$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





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





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



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).

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
Υ	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

```
https://docs.google.com/forms/d/
1C3RHisRHoWXcnFqX9JhRAk3gy_aJ6FrhouJ6ljsJ-Fc
```



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].

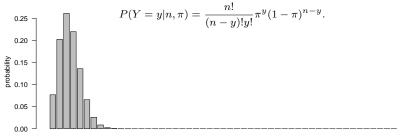


Statistical distributions

"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].

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?





• 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),
- \blacktriangleright the probability of success π is the same for all experiments,





Some parametric distributions: Poisson distribution

ightharpoonup 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 :

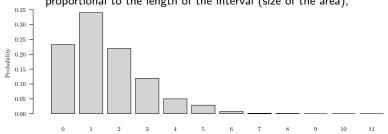
$$X \sim Poisson(\lambda),$$

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

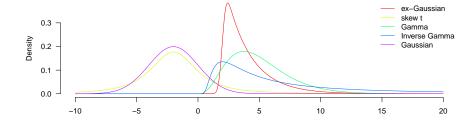
IF, during a time interval or in a given area,

- 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),



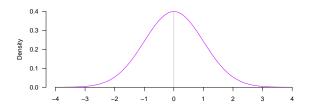
Some parametric distributions: Continuous distrib.





$$\begin{split} X \sim N(\mu, \sigma^2), \qquad f_X(x) &= \frac{1}{\sqrt{2\pi\sigma^2}} \ e^{-\frac{(x-\mu)^2}{2\sigma^2}} \\ \mathrm{E}[X] &= \mu, \qquad \mathrm{Var}[X] = \sigma^2, \\ Z &= \frac{X-\mu}{\sigma} \sim N(0,1), \qquad f_Z(z) = \frac{1}{\sqrt{2\pi}} \ e^{-\frac{z^2}{2}}. \end{split}$$

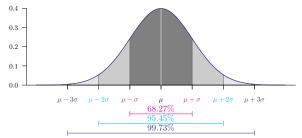
Probability density function, $f_Z(z)$, of a standard normal:





$$\begin{split} X \sim N(\mu, \sigma^2), \qquad f_X(x) &= \frac{1}{\sqrt{2\pi\sigma^2}} \; e^{-\frac{(x-\mu)^2}{2\sigma^2}} \\ \mathrm{E}[X] &= \mu, \qquad \mathrm{Var}[X] = \sigma^2, \\ Z &= \frac{X - \mu}{\sigma} \sim N(0, 1), \qquad f_Z(z) = \frac{1}{\sqrt{2\pi}} \; e^{-\frac{z^2}{2}}. \end{split}$$

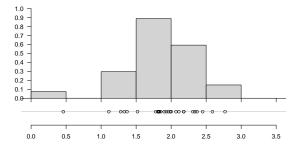
Probability density function, $f_Z(z)$, of a standard normal:





$$\begin{split} X \sim N(\mu, \sigma^2), \qquad f_X(x) &= \frac{1}{\sqrt{2\pi\sigma^2}} \; e^{-\frac{(x-\mu)^2}{2\sigma^2}} \\ \mathrm{E}[X] &= \mu, \qquad \mathrm{Var}[X] = \sigma^2, \\ Z &= \frac{X-\mu}{\sigma} \sim N(0,1), \qquad f_Z(z) = \frac{1}{\sqrt{2\pi}} \; e^{-\frac{z^2}{2}}. \end{split}$$

(i) Suitable modelling for a lot of variables:



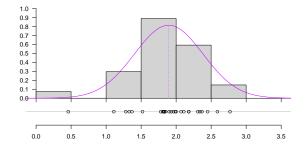


$$X \sim N(\mu, \sigma^2), \qquad f_X(x) = \frac{1}{\sqrt{2\pi\sigma^2}} \, e^{-\frac{(x-\mu)^2}{2\sigma^2}}$$

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

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

(i) Suitable modelling for a lot of variables



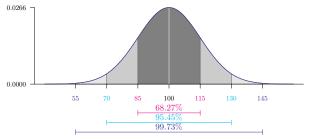


$$X \sim N(\mu, \sigma^2), \qquad f_X(x) = \frac{1}{\sqrt{2\pi\sigma^2}} e^{-\frac{(x-\mu)^2}{2\sigma^2}}$$

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

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

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





$$\begin{split} X \sim N(\mu,\sigma^2), \qquad f_X(x) &= \frac{1}{\sqrt{2\pi\sigma^2}} \; e^{-\frac{(x-\mu)^2}{2\sigma^2}} \\ \mathrm{E}[X] &= \mu, \qquad \mathrm{Var}[X] = \sigma^2, \\ Z &= \frac{X-\mu}{\sigma} \sim N(0,1), \qquad f_Z(z) = \frac{1}{\sqrt{2\pi}} \; e^{-\frac{z^2}{2}}. \end{split}$$

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

- ▶ 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 ,
- ▶ then

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

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

http://bioinformatics.cruk.cam.ac.uk/apps/stats/central-limit-theorem/



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

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

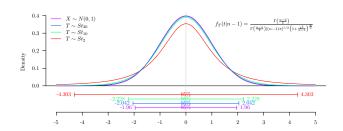
$$P\left(\begin{array}{ccc} < & & \\ \end{array} \right) = 0.95$$



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

- ightharpoonup 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 $Z = \frac{X-\mu}{\sigma} \sim N(0, 1)$,
- ▶ if σ unknown, then $T = \frac{X \mu}{s} \sim St_{n-1}$.

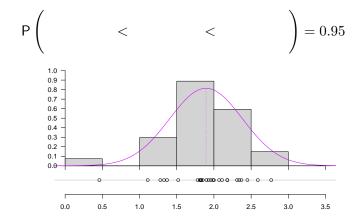
$$P\left(\begin{array}{ccc} & & \\ & & \\ \end{array} \right) = 0.95$$





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

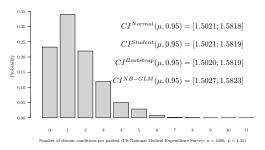
- if $X \sim N(\mu, \sigma^2)$, then $\overline{X} \sim N\left(\mu, \frac{\sigma^2}{n}\right)$,
- if $X \sim N(\mu, \sigma^2)$, then $Z = \frac{X \mu}{\sigma} \sim N(0, 1)$,
- ▶ if σ unknown, then $T = \frac{X \mu}{s} \sim St_{n-1}$.





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

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





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

If we have

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



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

If we have

- $X_i \sim iid(\mu_X, \sigma_X^2), i = 1, ..., n_X,$
- $Y_i \sim iid(\mu_V, \sigma_V^2), i = 1, ..., n_V,$

then

• if
$$\sigma_V^2 = \sigma_V^2$$
 [Student's t-test equation],

$$\begin{array}{c} \Gamma \\ \rhd CI\left(\mu_{Y}-\mu_{X},0.95\right) = (\overline{Y}-\overline{X}) \pm t_{1-\frac{\alpha}{2},n_{X}+n_{Y}-2}s_{p}\sqrt{\frac{1}{n_{X}}+\frac{1}{n_{Y}}} \\ \text{where } s_{p} = \frac{(n_{X}-1)s_{X}^{2}+(n_{Y}-1)s_{Y}^{2}}{n_{X}+n_{Y}-2}, \end{array}$$



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

$$lackbox{ if } \sigma_X^2 = \sigma_Y^2 \ [{
m Student's t-test equation}],$$

$$\hspace{-0.5cm} \begin{array}{l} \triangleright \ CI\left(\mu_Y-\mu_X,0.95\right) = (\overline{Y}-\overline{X}) \pm t_{1-\frac{\alpha}{2},n_X+n_Y-2} s_p \sqrt{\frac{1}{n_X}+\frac{1}{n_Y}} \\ \text{where } s_p = \frac{(n_X-1)s_X^2+(n_Y-1)s_Y^2}{n_X+n_Y-2}, \end{array}$$

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

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

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



Central limit theorem shiny app:

Coverage of Student's asymptotic confidence intervals

http://bioinformatics.cruk.cam.ac.uk/apps/stats/central-limit-theorem/



Quiz Time Practical 1

http://bioinformatics-core-shared-training.github.io/ IntroductionToStats/practical.html

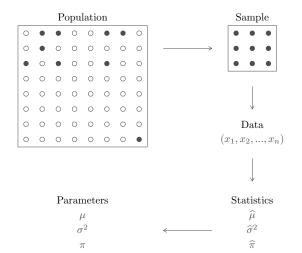


PART II:

Parametric and non-parametric one-sample location tests

Cancer Research UK – 12^{th} of February 2019 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),
- ▶ Define n, the sample size, allowing you to reject H0 when H1 is true with a probability 1β (Power),
- ▶ Determine the test statistic to be used,
- ► Collect the data,
- ▶ Perform the statistical test, define the *p*-value, and reject (or not) the null hypothesis.



Statistical hypothesis testing

Many options:

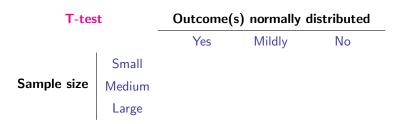
One-sided versus two-sided tests,

Exact versus asymptotic tests,

▶ Parametric versus non-parametric tests.



Parametric or non-parametric?



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.



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

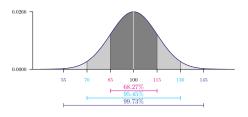
$$ightharpoonup \overline{X} \sim N\left(\mu, \frac{\sigma^2}{n}\right),$$

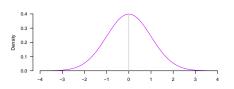
Thus, if Ho is true, we have:

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

Define the p-value:

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





Statistical hypothesis testing 4 possible outcomes

Conclude:

- $\begin{array}{cccc} \blacktriangleright & \text{if p-value} > \alpha & \rightarrow & \text{do not reject H0.} \\ \blacktriangleright & \text{if p-value} < \alpha & \rightarrow & \text{reject H0 in favour of H1.} \\ \end{array}$

		Test Outcome		
		H0 not rejected	H1 accepted	
Unknown Truth	H0 true	$1-\alpha$	α	
	H1 true	β	$1 - \beta$	

where

- \triangleright α is the type I error,
- \triangleright β is the type II error.



Parametric location test (One-sided) binomial exact test

We test: H0: $\pi = 5\%$, H1: $\pi > 5\%$.

We have $X_i \sim Bernoulli(\pi), i = 1, ..., n$,

We know

$$Y = \sum_{i=1}^{n} X_i \sim Binomial(\pi, n),$$

Thus, if H0 is true, we have:

$$Y = \sum_{i=1}^{n} X_i \sim Binomial (5\%, n),$$

Parametric location test (One-sided) binomial exact test

We test:

H0: $\pi = 5\%$, H1: $\pi > 5\%$.

We have $X_i \sim Bernoulli(\pi), i = 1, ..., n$,

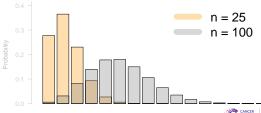
We know

$$Y = \sum_{i=1}^{n} X_i \quad \sim \quad Binomial(\pi, n),$$

Thus, if H0 is true, we have:

$$Y = \sum_{i=1}^{n} X_i \sim Binomial (5\%, n),$$

Define the p-value:

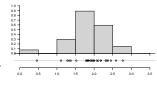


Non-parametric location test Wilcoxon sign-rank test

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



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.

00 05 19 15 20 25 30 35

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

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

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

Wilcoxon signed rank test

```
data: golub[1042, gol.fac == "ALL"]
V = 268, p-value = 0.05847
alternative hypothesis: true location is not equal to 1.75
95 percent confidence interval:
1.73868 2.09106
sample estimates:
(pseudo)median
1.926475
```



Introduction to Shiny Apps and Exercises



PART III:

Parametric and non-parametric two-sample location tests

Cancer Research UK -12^{th} of February 2019 D.-L. Couturier / M. Eldridge / M. Fernandes [Bioinformatics core]

Two-sample case

Many options:

One-sided versus two-sided tests,

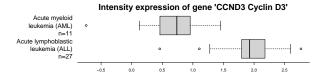
Exact versus asymptotic tests,

▶ 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



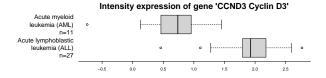
We test **H0**: $\mu_Y - \mu_X = 0$ against **H1**: $\mu_Y - \mu_X \neq 0$.

We know:

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



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:

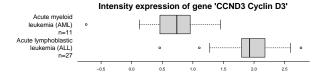
- $\qquad \text{Welch's t-test [assume } \sigma_X^2 \neq \sigma_Y^2] \text{: } \frac{(\overline{Y} \overline{X}) (\mu_Y \mu_X)}{\sqrt{\frac{s_X^2}{n_X} + \frac{s_Y^2}{n_Y}}} \sim t_{1 \frac{\alpha}{2}, df}$

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:

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

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

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

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

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

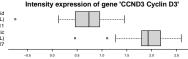
where $R(Y_i)$ denotes the rank of Y_i amongst the combined samples, i.e., amongst $(X_1, ..., X_{n_N}, Y_1, ..., Y_{n_N})$.



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

Let

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



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

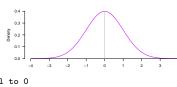
alternative hypothesis: true location shift is not equal to 0 95 percent confidence interval:

0.89647 1.57023

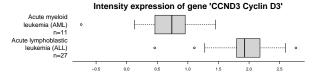
34

sample estimates:

difference in location 1.21951



F-test of equality of variances



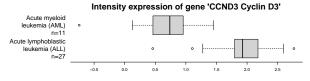
$$\mbox{We test} \quad \mbox{\bf H0:} \ \sigma_Y^2 = \sigma_X^2 \quad \mbox{ against } \quad \mbox{\bf H1:} \ \sigma_Y^2 \neq \sigma_X^2.$$

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



 $\text{We test} \quad \textbf{H0} : \ \sigma_Y^2 = \sigma_X^2 \quad \text{ against} \quad \textbf{H1} : \ \sigma_Y^2 \neq \sigma_X^2.$

We know:

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

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 $\alpha.$

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 $\alpha = 0.05$,

- \blacktriangleright if k = 1, $\alpha_1 = 1 (1 \alpha)^1 = 0.05$,
- if k = 2, $\alpha_2 = 1 (1 \alpha)^2 = 0.0975$,
- \blacktriangleright 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{lpha}		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

