BIOSTATISTICS COURSE #1

INTRODUCTION

SEPTEMBER 2025

SUMMARY OF THE COURSE #1

INTRODUCTION

01

INTRODUCTION
TEACHER : FRANÇOIS MACHURON

- Graduated in 2013 from **Polytech'Lille** Engineering School (GIS department)
- Engineer in Statistics and Biostatistics with 12 years of working experience
- Working experience :
  - 2013-2015 : consultant in biostatistics at **NOVARTIS** (Paris)
  - 2015-2016 : consultant in Data Science at **DECATHLON** and **COFIDIS** (Lille)
  - 2016-2019 : **Biostatistician** at CHRU Lille
  - 2020-present : **R&D Statistician** at LESAFFRE INTERNATIONAL
- Expert in Statistics / Biostatistics / Data analysis / Data mining (R & Python)

INTRODUCTION
BIOSTATISTICS COURSE

Course	Date	Content
1) Introduction to the course, R and descriptive statistics	16th September 8:00 – 12:15	History of biostatistics, definition, area of application, R & Rstudio, descriptive statistics
2) Statistical modeling #1	23rd September 8:00 – 12:15	Statistical tests, correlations, linear modeling, ANOVA, multiple regression
3) Statistical modeling #2	30th September 8:00 – 12:15	Generalized linear models, non-linear models

INTRODUCTION
BIOSTATISTICS COURSE

Course	Date	Content
4) Statistical modeling #3	30th September 13:30 – 17:45	PCA, MCA, FCA, clustering, discrimant analysis
5) Biostatistics #1	7th October 8:00 – 12:15	Levels of evidence, clinical trials, scientific publication review, effect size, power and NSN calculation
6) Biostatistics #2	18th November 8:00 – 12:15	Meta-analyzes, survival, longitudinal data analysis
7) Exam	25th November 8:00 – 12:15	Exam : score /20 (with an A4 paper as help)

BIOSTATISTICS

02

BIOSTATISTICS
OVERVIEW

- Application of **statistical methods** to **biological** and **medical** data
- Many tools : **descriptive statistics**, **statistical tests**, **univariate** and **multivariate models**, **survival analysis**, NSN calculation, meta-analyzes, machine-learning…
- Many areas of application : **medicine**, **agriculture**, **biology**, **ecology**…
- More and more data collected through **clinical trials**, **R&D experiments**… => Need to apply and develop more and more biostatistical methods
- **Associated terms** : bio-informatics, data-science, epidemiology, statistics

BIOSTATISTICS
HISTORY

Blaise PASCAL (1623 – 1662) : father of probabilities and applied mathematics to science

Pierre-Simon LAPLACE (1749-1827) : added major contributions to probability theory and statistics

Karl PEARSON (1857–1936) : founder of modern statistics applied to biology and medicine

Ronald FISHER (1890 – 1962) : added major contributions to statistics applied to biology and medicine (ANOVA, maximum likelihood…)

BIOSTATISTICS
EXAMPLES OF ANALYZES

- Study of the effect of an **experimental treatment on a disease** (example : Pfizer-BioNTech COVID-19 vaccine effect on infection, hospitalization and mortality)
- **Comparison** of baseline parameters between groups with statistical tests
- **Meta-analysis** : systematic method that uses statistical techniques for combining results from different studies to obtain a quantitative estimate of the overall effect of a particular intervention or variable on a defined outcome
- **Logistic regression** : construction of a predictive model on smoking status from socio-demographic data of a cohort
- **Survival analysis** : comparison of effect of a treatment on mortality

EXAMPLE OF A CLINICAL TRIAL

03

EXAMPLE OF A CLINICAL TRIAL

PLEASE READ THE ARTICLE (30 MINUTES)

EXAMPLE OF A CLINICAL TRIAL
OVERVIEW

- **Objective** : Prevention of Malaria in HIV-uninfected Pregnant **Women** and **Infants** in **Uganda**
- **Type of study :** Double blinded **randomized** controlled trial (link to the trial : https://clinicaltrials.gov/study/NCT02793622)
- **Intervention :** Monthly **Sulfadoxine-pyrimethamine** (SP) or **Dihydroartemisinin-piperaquine** (DP)
- **Hypothesis :** DP will significantly reduce the **burden of malaria** in pregnancy and infancy compared to SP

EXAMPLE OF A CLINICAL TRIAL
OVERVIEW

- **782 pregnant women** included (391 in each group) (12 to 20 weeks of pregnancy)
- **Two treatments** taken monthly during pregnancy : Sulfadoxine-pyrimethamine (SP) vs Dihydroartemisinin-piperaquine (DP)
- Study conducted between **September 2016 and May 2017.**
- Results published in the **Lancet on 22nd March 2019**

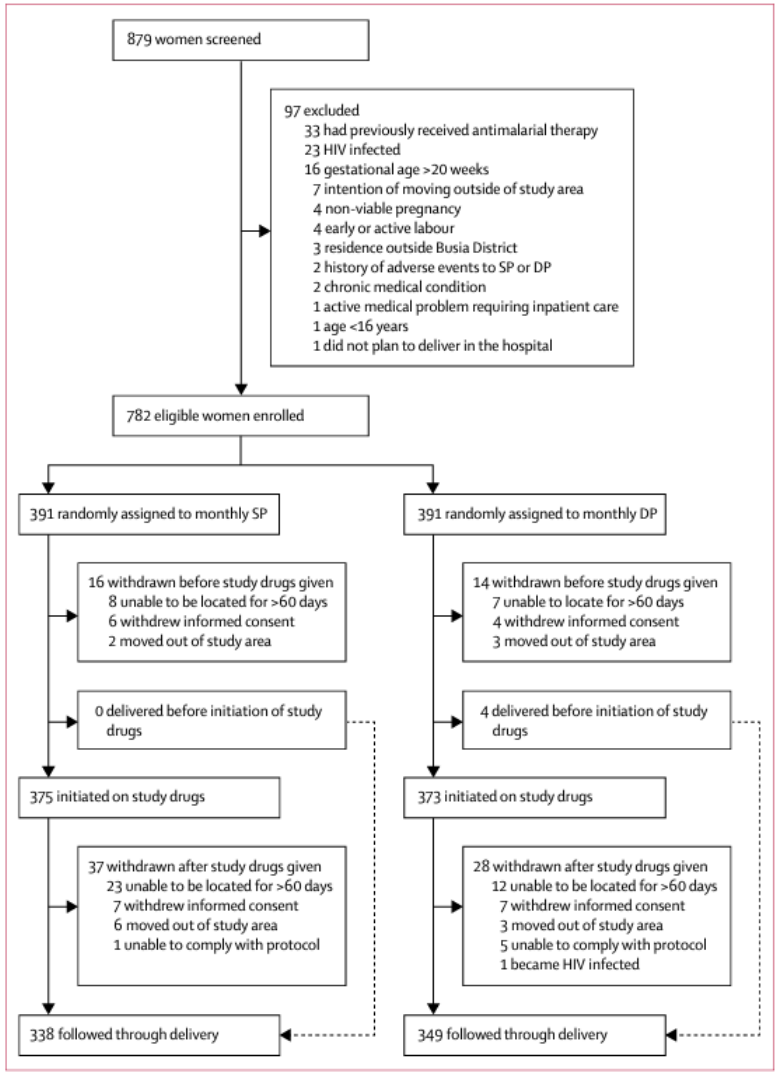
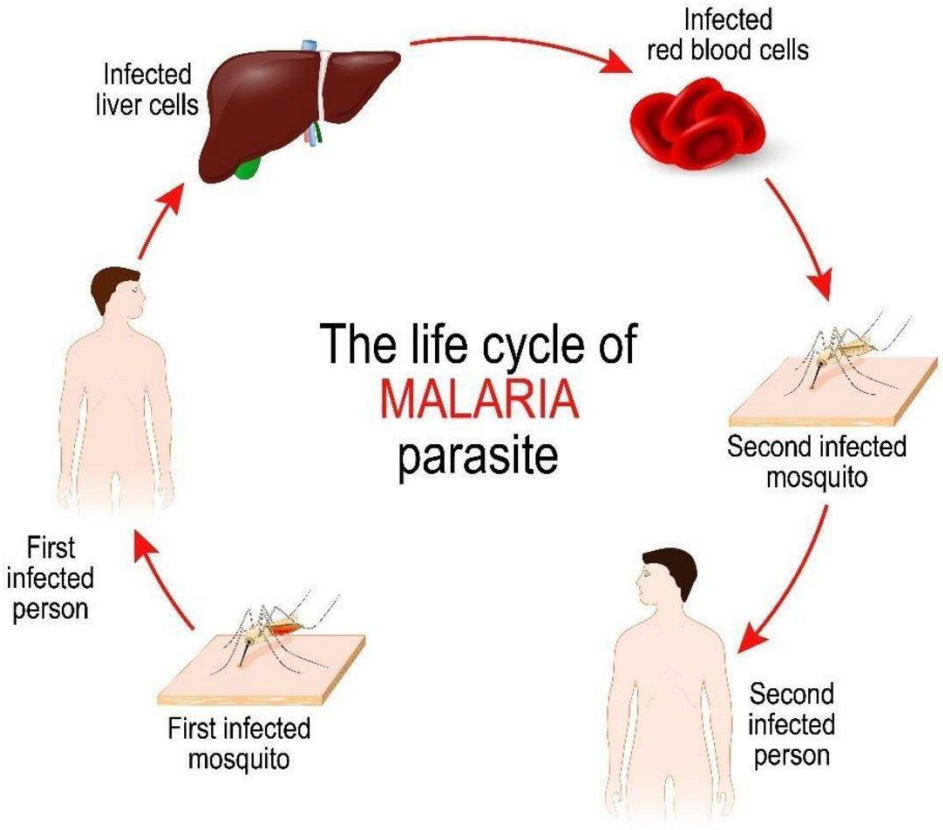


Figure 1: **Trial profile**
DP=dihydroartemisinin-piperaquine. SP=sulfadoxine-pyrimethamine.

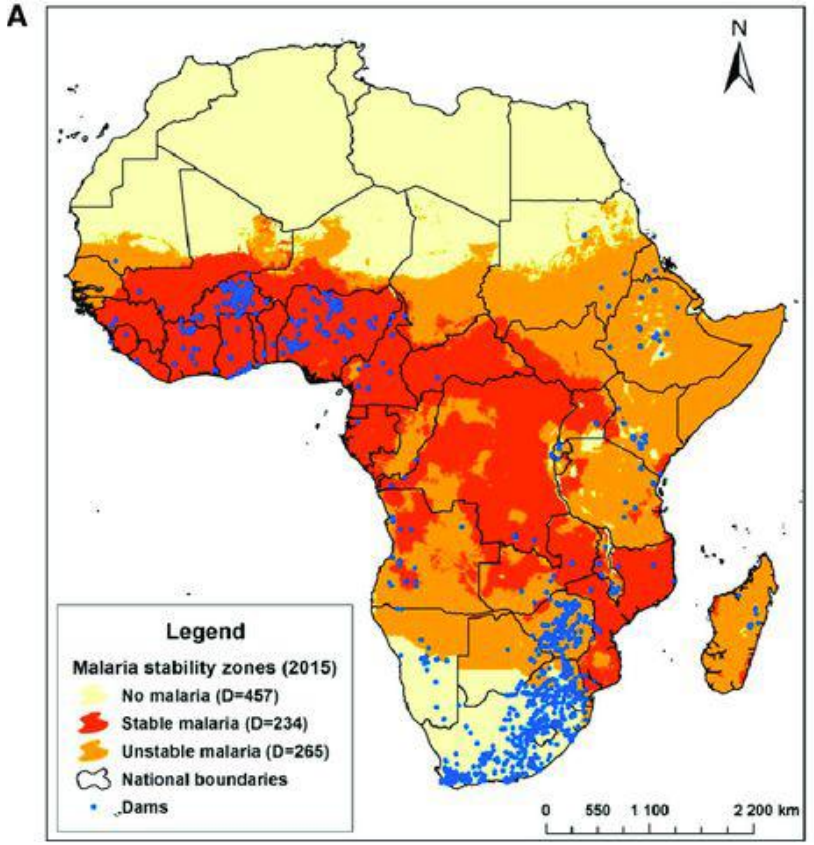
EXAMPLE OF A CLINICAL TRIAL
MALARIA DISEASE

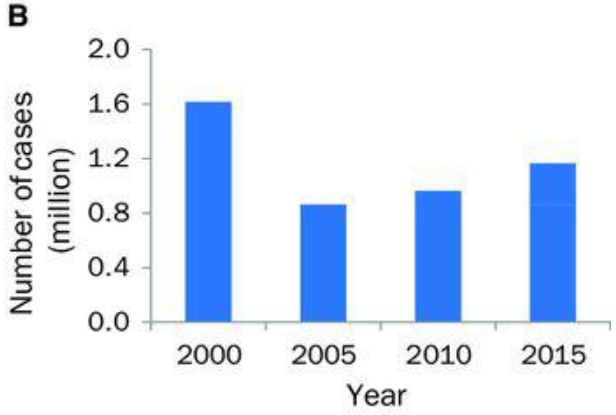
- Caused by single-cell **parasites** that at spread by **mosquitoes**
- Damages especially **liver** and **red blood cells**
- Causes waves of **fevers** every few days, extreme **anemia** and **blood clots**
- May lead to "*complicated malaria*", which is described as **sepsis** which can lead to **death**

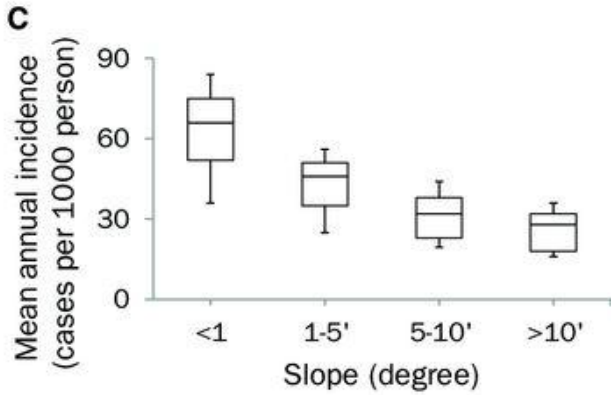


EXAMPLE OF A CLINICAL TRIAL
MALARIA EPIDEMIOLOGY

- Hundreds of millions of cases worldwide, 660,000 deaths each year
- 81% of cases and 91% of deaths are in Africa
- Pregnant women and children under 5 most vulnerable







- Prevention in Africa : Regular or insecticide treated bednets and preventative therapy with Sulfadoxine-pyrimethamine (SP)

EXAMPLE OF A CLINICAL TRIAL
MALARIA DURING PREGNANCY

Maternal outcomes

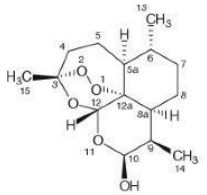
- Maternal anaemia
- Cerebral malaria
- Severe malaria
- Maternal mortality
- Recurrent or new plasmodium infections

Child outcomes

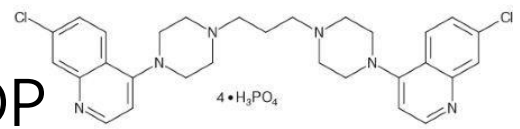
- Abortion
- Stillbirth
- Preterm delivery
- Low birth weight
- Neonatal mortality
- Congenital malaria
- Infant mortality
- Anaemia
- Poor developmental / behavioural outcome

EXAMPLE OF A CLINICAL TRIAL
MOTIVATIONS

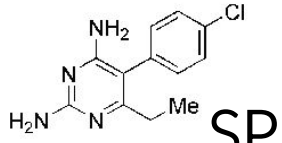
- **Antifolate resistance** of malaria parasite (65% in Eastern Africa) : Sulfadoxine-pyrimethamine (SP) does not work anymore
- **Artemisinin effective** alternative treatment for malaria and is safe for treatment of malaria in pregnant women
- Dihydroartemisinin-piperaquine (DP) together with bednets associated with **a lower incidence of malaria infection during pregnancy and after delivery**
- **Serious adverse events lower** with DP than SP


Dihydroartemisinin

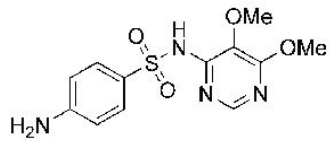
DP


Piperaquine tetraphosphate

versus


pyrimethamine (85)

SP


sulfadoxine (86)

EXAMPLE OF A CLINICAL TRIAL
RESULTS – BASELINE CHARACTERISTICS

	Monthly sulfadoxine–pyrimethamine group (n=391)	Monthly dihydroartemisinin–piperaquine group (n=391)
Age, years	23 (19–27)	23 (19–27)
Gestational age, weeks	15·4 (13·3–17·6)	15·0 (13·4–17·1)
Gestational age category (weeks)		
12–16	234 (60%)	242 (62%)
>16–20	157 (40%)	149 (38%)
Gravidity		
1	102 (26%)	93 (24%)
2	85 (22%)	105 (27%)
≥3	204 (52%)	193 (49%)
ITN coverage		
Ownership of ITN	61 (16%)	50 (13%)
Reported sleeping under an ITN the previous night	48 (12%)	44 (11%)
Haemoglobin concentration (g/dL)	11·5 (1·3)	11·4 (1·2)
Detection of malaria parasites by microscopy	197 (50%)	204 (52%)
Detection of malaria parasites by microscopy or qPCR	326 (83%)	317 (81%)

Data are median (IQR) or n (%). ITN=insecticide-treated net. qPCR=quantitative PCR.

Table 1: **Baseline characteristics**

EXAMPLE OF A CLINICAL TRIAL
RESULTS - OUTCOMES

	Monthly sulfadoxine–pyrimethamine group* (n=338)	Monthly dihydroartemisinin–piperaquine group (n=349)	Protective efficacy† (95% CI)	p value
Outcomes assessed at delivery				
Adverse birth outcomes among livebirths				
Composite (primary efficacy outcome)	60/329 (18%)	54/337 (16%)	12% (−23 to 37)	0·45
Low birthweight	29/329 (9%)	24/337 (7%)	19% (−36 to 52)	0·42
Preterm birth	24/329 (7%)	16/337 (5%)	35% (−20 to 65)	0·17
Small for gestational age	41/329 (13%)	39/337 (12%)	7% (−40 to 38)	0·72
Fetal or neonatal death				
Spontaneous abortion	4/338 (1%)	10/349 (3%)	−142% (−665 to 23)	0·13
Stillbirth	5/334 (2%)	2/339 (1%)	61% (−102 to 92)	0·26
Neonatal death	6/329 (2%)	4/337 (1%)	35% (−129 to 81)	0·50
Composite	15/338 (4%)	16/349 (5%)	−3% (−106 to 48)	0·93
Measures of infection with malaria parasites				
Maternal blood positive for malaria parasites by microscopy	28/336 (8%)	1/342 (<1%)	96% (74 to 99)	0·0010
Placental blood positive for malaria parasites by microscopy	28/320 (9%)	1/333 (<1%)	97% (75 to 99)	0·0009
Placental blood positive for malaria parasites by LAMP	70/312 (22%)	7/328 (2%)	90% (80 to 96)	<0·0001
Placental tissue positive for malaria parasites or pigment	197/322 (61%)	94/331 (28%)	54% (44 to 62)	<0·0001
Incidence measures during pregnancy‡				
Symptomatic malaria	75 (0·52)§	3 (0·02)§	96% (88 to 99)	<0·0001
Prevalence measures during pregnancy‡				
Detection of malaria parasites by microscopy	519/1687 (31%)	9/1757 (1%)	98% (96 to 99)	<0·0001
Detection of malaria parasites by microscopy or qPCR	1105/1676 (66%)	369/1746 (21%)	68% (64 to 71)	<0·0001
Anaemia (haemoglobin <10 g/dL)	171/870 (20%)	89/904 (10%)	50% (32 to 73)	<0·0001

LAMP=loop-mediated isothermal amplification. qPCR=quantitative PCR. *Reference group. †Protective efficacy=1–incidence rate ratio or 1–prevalence ratio. ‡Assessed at the time of routine visits following administration of first dose of study drugs. §Number of events (incidence per person-year at risk).

Table 2: **Efficacy outcomes**

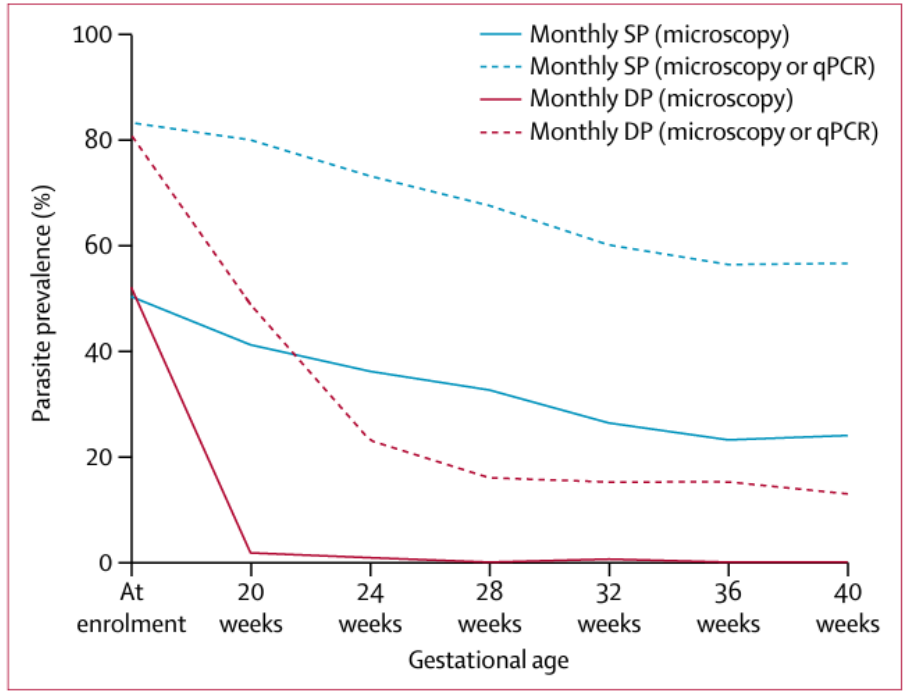


Figure 2: **Parasite prevalence during pregnancy according to week of gestation**
Parasite prevalence was assessed by microscopy and qPCR. Data at 20 weeks gestational age only includes the subset of women who received their first dose of study drugs at 16 weeks gestational age. DP=dihydroartemisinin–piperaquine. qPCR=quantitative PCR. SP=sulfadoxine–pyrimethamine.

R & RSTUDIO

04

R & RSTUDIO
BENCHMARK OF STATISTICAL SOFTWARES

Microsoft Excel
- Spreadsheet software
- Simple mathematical operations
- Graphical UI

Statistical Analysis Software
- “Official” software for clinical trials (FDA…)
- Simple and complex statistics
- Graphical UI & coding language

R
- Collaborative language (lot of libraries available)
- **Particularly suitable in biology and medical statistics**
- Graphical UI (Rstudio) & coding language

IBM SPSS
- Widely used
- Simple statistics and visualization
- Graphical UI

MATLAB
- Complex mathematical processes
- Suitable for engineering studies
- Own coding language

PYTHON
- General-purpose programming language
- Most used for machine-learning and AI
- Own coding language

R & RSTUDIO
MOTIVATIONS TO USE

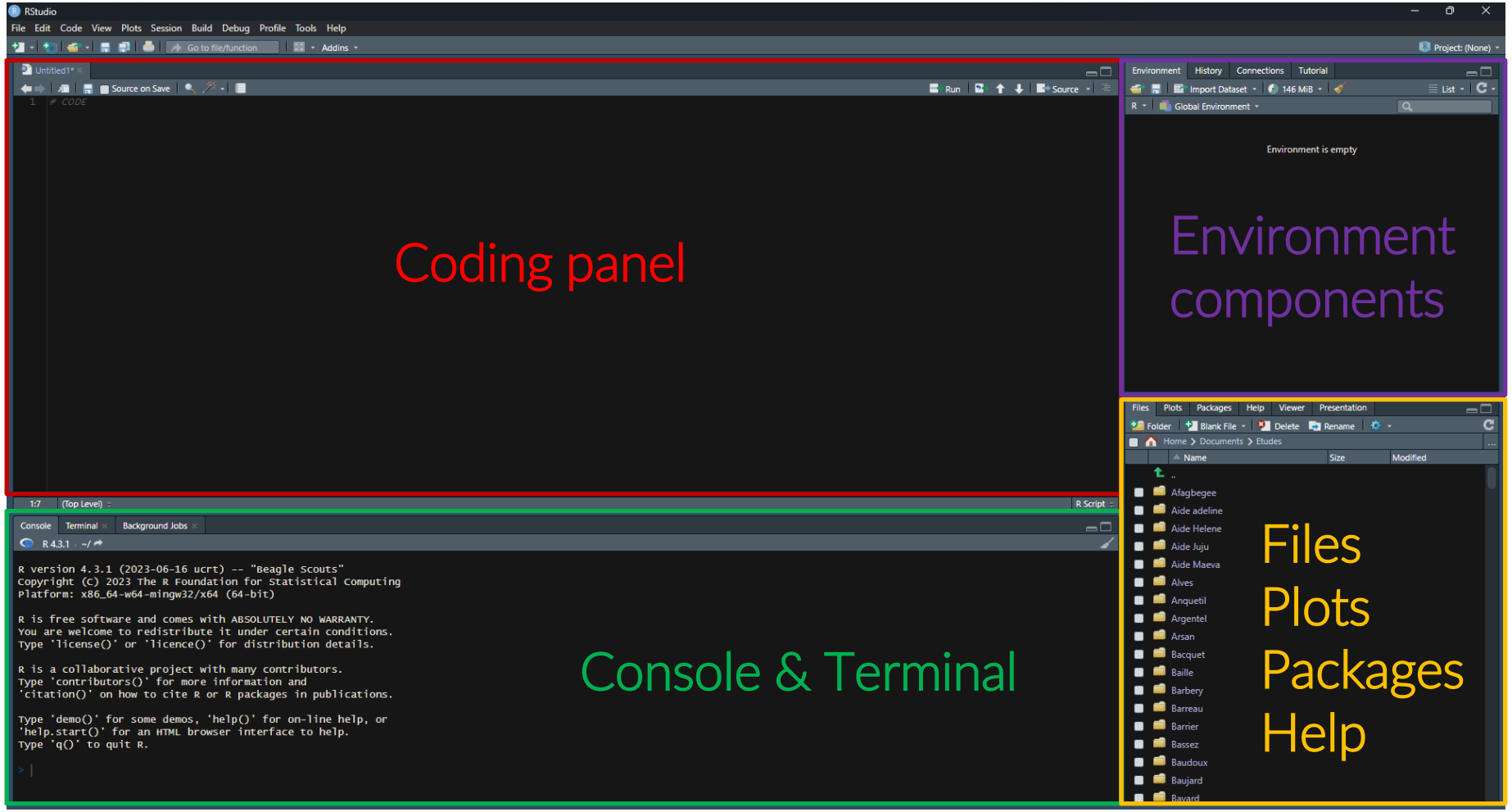
- **Easy-to-learn** and use language (somehow like Python language)
- Strong academical and industrial **community**
- **Thousands of packages** validated, maintained and updated packages specialized in data analysis, machine-learning, AI…particularly for biological and medical data : available on the **CRAN** website (https://cran.rstudio.com/)
- **Well documented** language and packages
- Useful for **data visualization** (ggplot2, plotly, Rmarkdown and Shiny packages)
- Fully integrated by many **LLMs** (Copilot, ChatGPT, Gemini, Claude Code…)

R & RSTUDIO
MOTIVATIONS TO USE RStudio

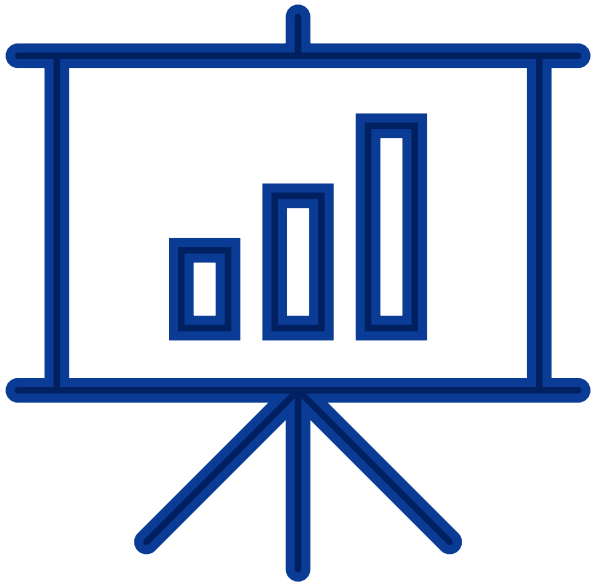
- "*Official*" **R IDE** (Integrated Development Environment)
- **Free and maintained (current version 2024.12.0+467 released on 16th Dec 2024)**
- Clear and customizable interface
- Easy to connect to **databases** and **cloud providers** (AWS, Azure, Google…)
- Able to run **Python code**
- Useful for **web-app development** (Shiny package)
- Download here on the site of POSIT

R & RSTUDIO

INTERFACE OF RStudio

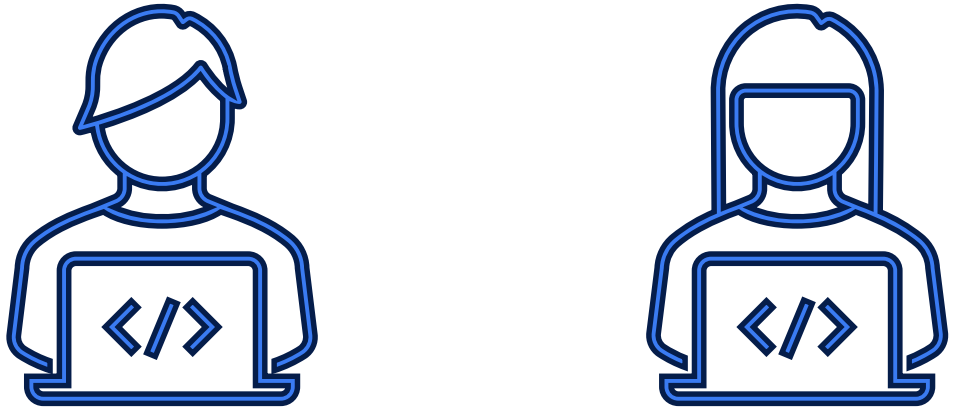


R & RSTUDIO



Live demo

R & RSTUDIO



Time to play !
(15 minutes)

USEFUL PACKAGES

05

USEFUL PACKAGES
PACKAGE DPLYR

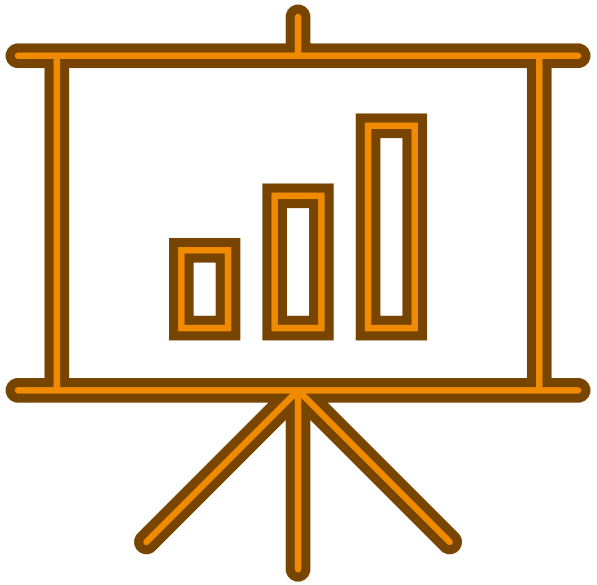
- Powerful package for **data transformation, manipulation & summarization**

- Allow to use **pipes** (%>%) : efficient chain of operations on data

- Main functionalities :
  - Function **mutate** : new variables creation
  - Function **select** : keep or drop variables from a dataset
  - Function **filter** : select specific rows in a dataset
  - Function **arrange** : sort a dataset on one or many variables
  - Function **summarise** : statistics calculation
  - Function **group_by** : group rows (useful before summarise function)

- How to install in R : **install.packages("dplyr")**

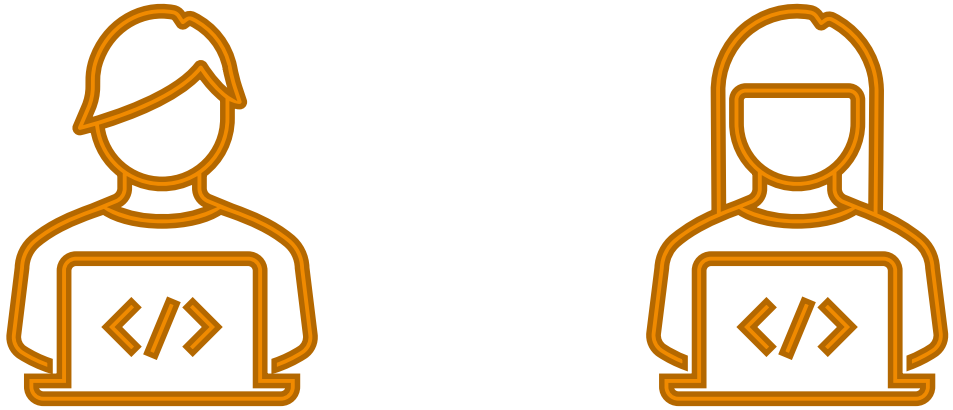
USEFUL PACKAGES
PACKAGE DPLYR



Live demo

dplyr_cheatsheet.pdf

USEFUL PACKAGES
PACKAGE DPLYR



Time to play !
(15 minutes)

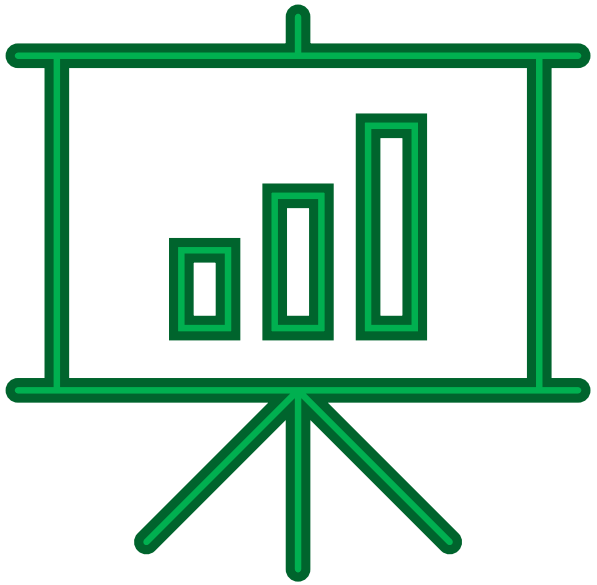
USEFUL PACKAGES
PACKAGE STRINGR

- Powerful package for **string processing**

- Main functionalities :
  - Function **str_detect** : pattern detection in a string (return True or False)
  - Function **str_locate** : locates the first position of a pattern and returns a numeric matrix with columns start and end
  - Function **str_extract** : extracts text corresponding to the first match, returning a character vector
  - Function **str_replace** : replaces the first matched pattern and returns a character vector

- How to install in R : **install.packages("stringr")**
- Regular expressions : regular expressions with stringR

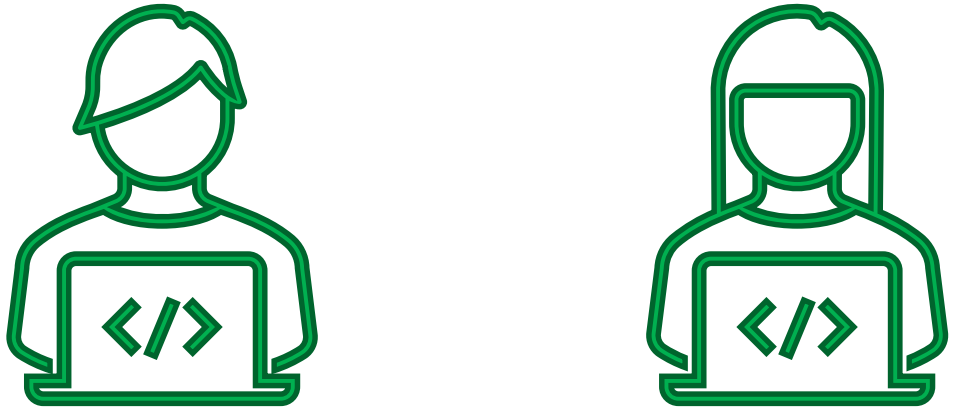
USEFUL PACKAGES
PACKAGE STRINGR



Live demo

stringr_cheatsheet.pdf

USEFUL PACKAGES
PACKAGE STRINGR



Time to play !
(15 minutes)

USEFUL PACKAGES
PACKAGE LUBRIDATE

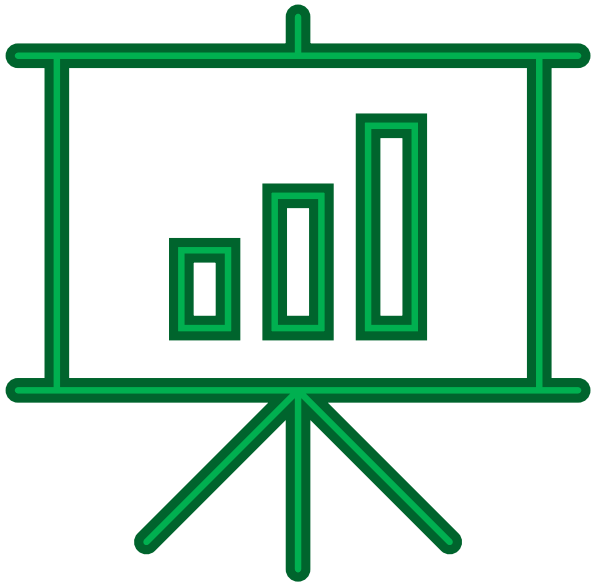
- Powerful package for **dates and times processing**

- **Date-time format in R : 2025-01-22 10:30:46 (stored in R in as the number of seconds since 1970-01-01 00:00:00 UTC)**

- Main functionalities :
  - Function **date** : extract the date component of a date-time variable
  - Functions **year, month or day** : extract a specific component of date of a date-time variable
  - Function **hour, minute or second** : extract a specific component of time of a date-time variable

- How to install in R : **install.packages("lubridate")**

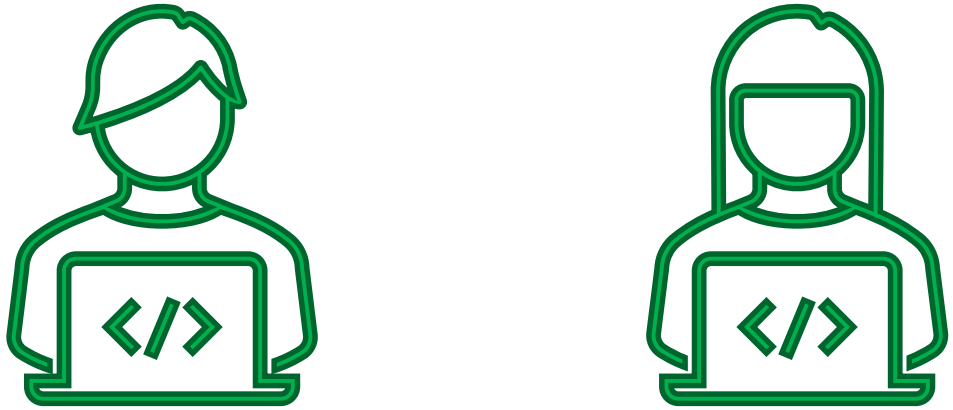
USEFUL PACKAGES
PACKAGE LUBRIDATE



Live demo

lubridate_cheatsheet.pdf

USEFUL PACKAGES
PACKAGE LUBRIDATE



Time to play !
(15 minutes)

USEFUL PACKAGES
PACKAGE GGPLOT2

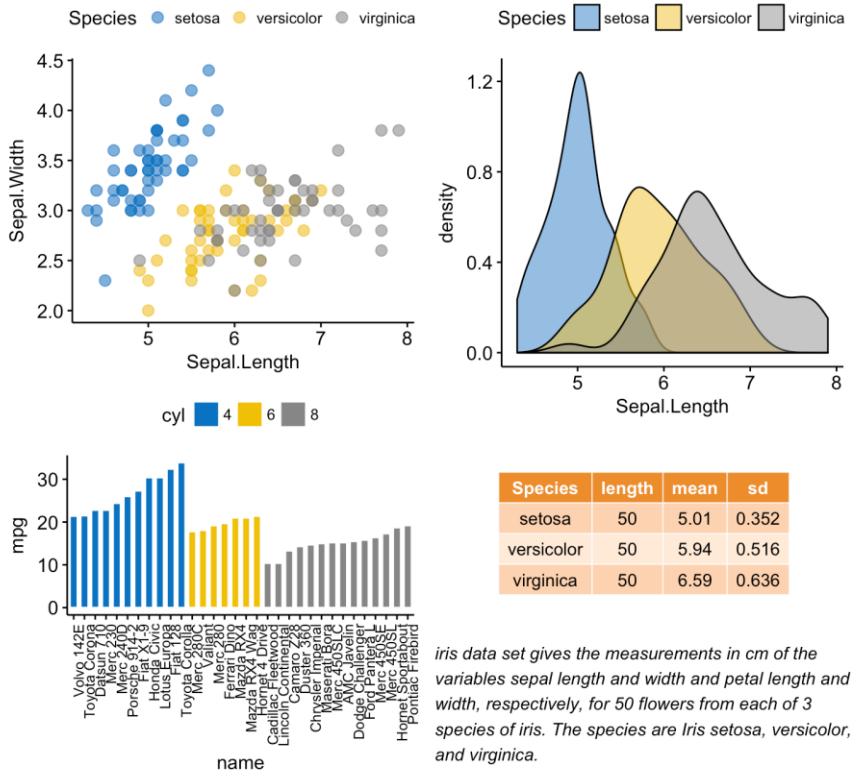
- Powerful package for **data visualization** with highly customizable **static plots**

- Uses a **pipe-wise coding grammar** :

```
ggplot(data=dataset) +
  element_1()+
  element_2()+
  ...
```

- **Elements are added** on the same plot **with layers** (dozen of graphical elements available)

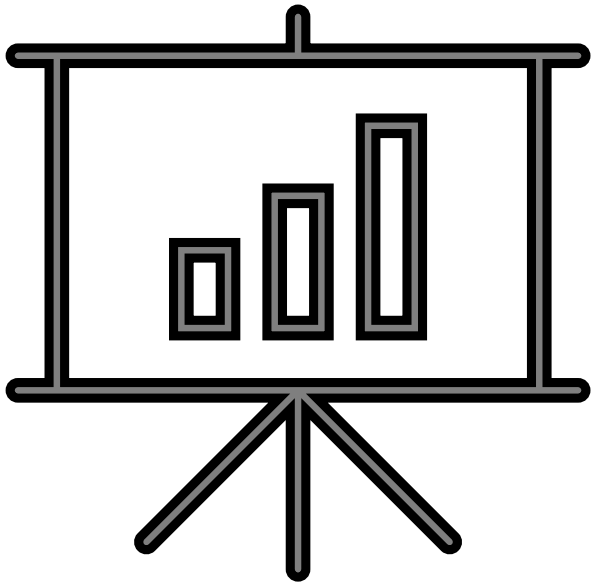
- How to install in R : **install.packages("ggplot2")**



Species	length	mean	sd
setosa	50	5.01	0.352
versicolor	50	5.94	0.516
virginica	50	6.59	0.636

iris data set gives the measurements in cm of the variables sepal length and width and petal length and width, respectively, for 50 flowers from each of 3 species of iris. The species are Iris setosa, versicolor, and virginica.

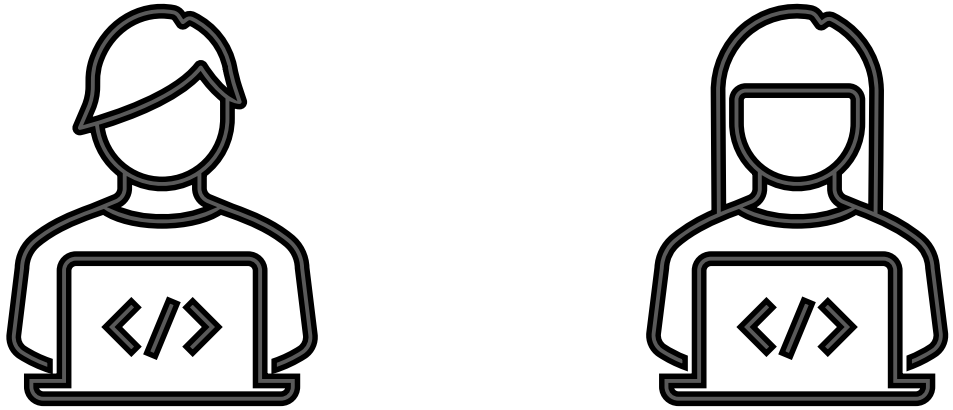
USEFUL PACKAGES
PACKAGE GGPLOT2



Live demo

ggplot2_cheatsheet.pdf

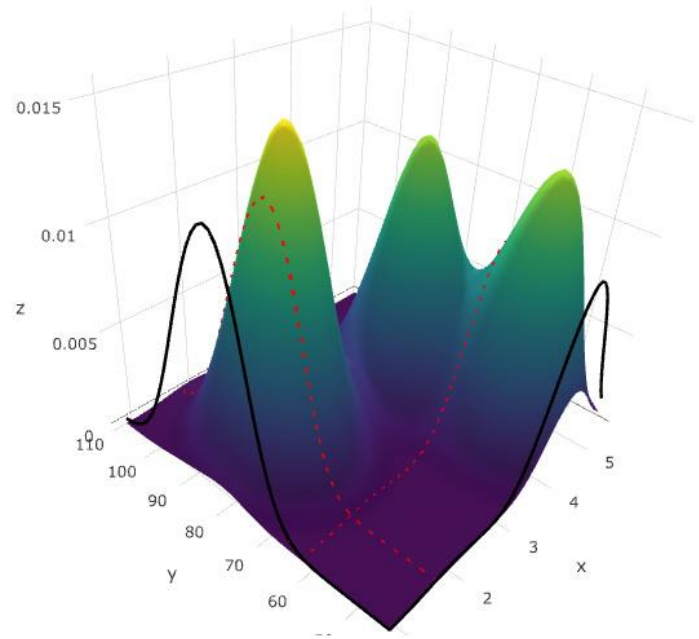
USEFUL PACKAGES
PACKAGE GGPLOT2



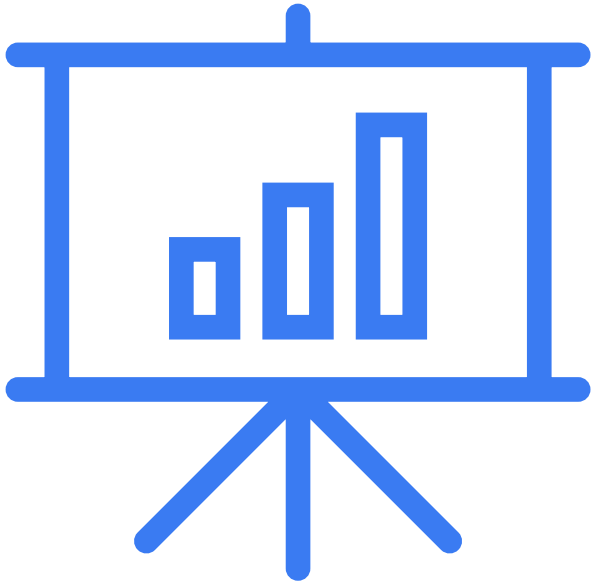
Time to play !
(30 minutes)

USEFUL PACKAGES
PACKAGE PLOTLY

- Powerful package for **data visualization** with highly customizable **interactive plots**
- Available also in Python with a similar syntax
- Easily integrated in websites, web-apps or Rmarkdown HTML documents
- Useful with dplyr pipes (%>%) : elements are added on the same plot **with layers** (dozen of graphical elements available)
- How to install in R : **install.packages("plotly")**



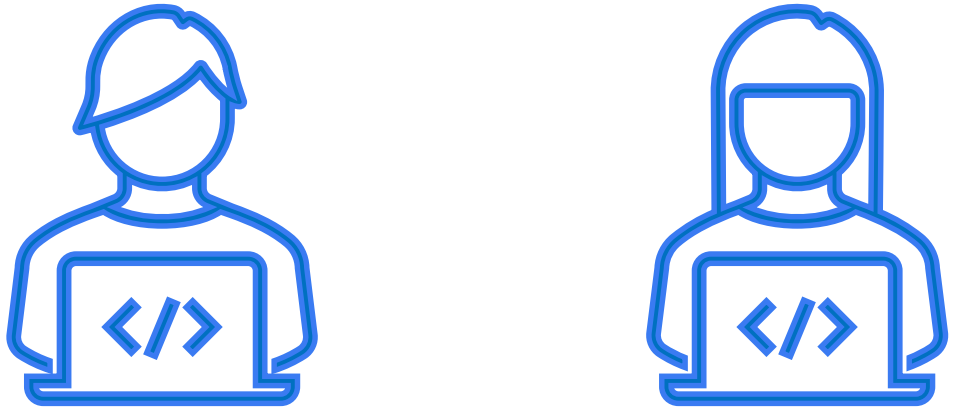
USEFUL PACKAGES
PACKAGE PLOTLY



Live demo

plotly_cheatsheet.pdf

USEFUL PACKAGES
PACKAGE PLOTLY

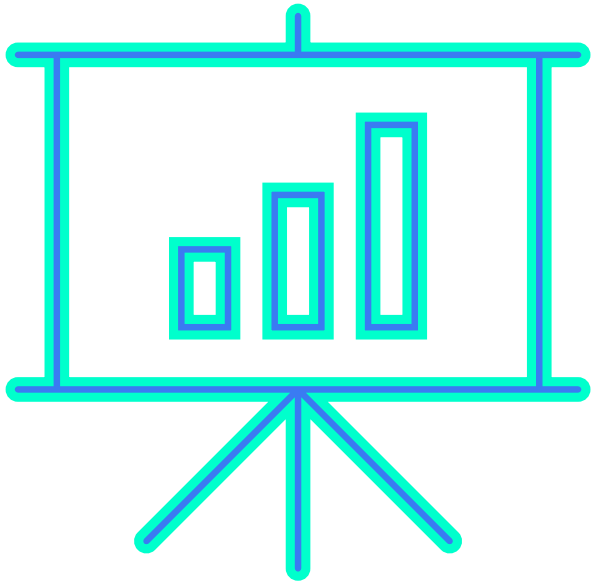


Time to play !
(20 minutes)

USEFUL PACKAGES
PACKAGE RMARKDOWN

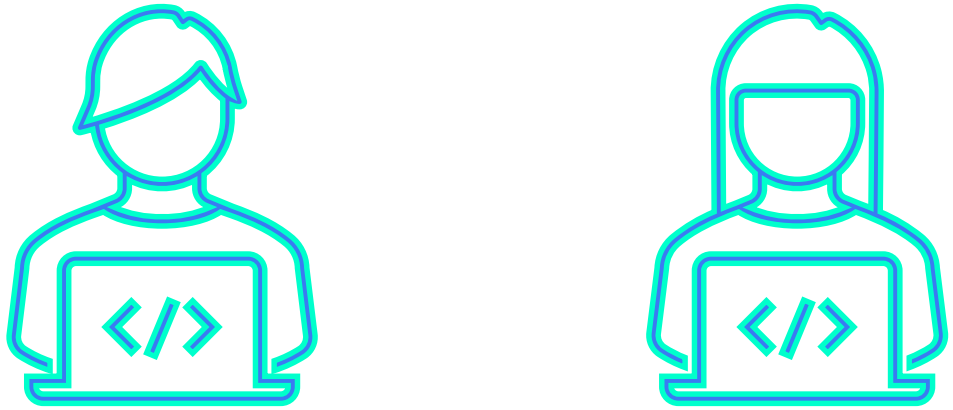
- Powerful package for **highly customizable and interactive documents**
- Can use multiple languages (R, Python, SQL)
- Customizable with HTML, CSS languages
- Can integrate interactive plots (produced with Plotly package)
- Output : Microsoft Word, Powerpoint documents, HTML file, PDF file
- How to install in R : **install.packages("rmarkdown")**

USEFUL PACKAGES
PACKAGE RMARKDOWN



Live demo

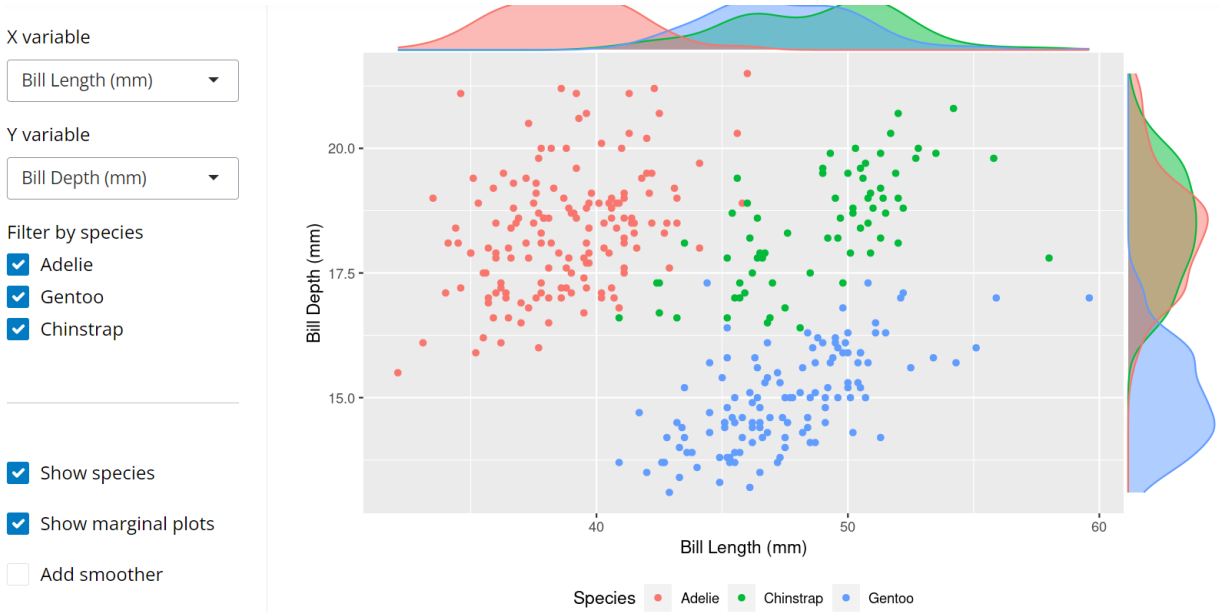
USEFUL PACKAGES
PACKAGE RMARKDOWN



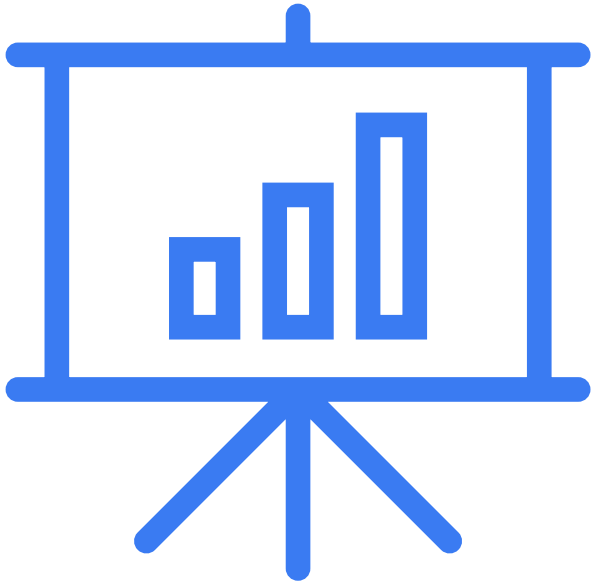
Time to play !
(20 minutes)

USEFUL PACKAGES
PACKAGE SHINY

- Powerful package for **web-app development**
- Available also in Python with a similar syntax
- Many input elements (buttons, sliders, selectors, panels…)
- Customizable with HTML, Javascript languages
- How to install in R : **install.packages("shiny")**



USEFUL PACKAGES
PACKAGE SHINY



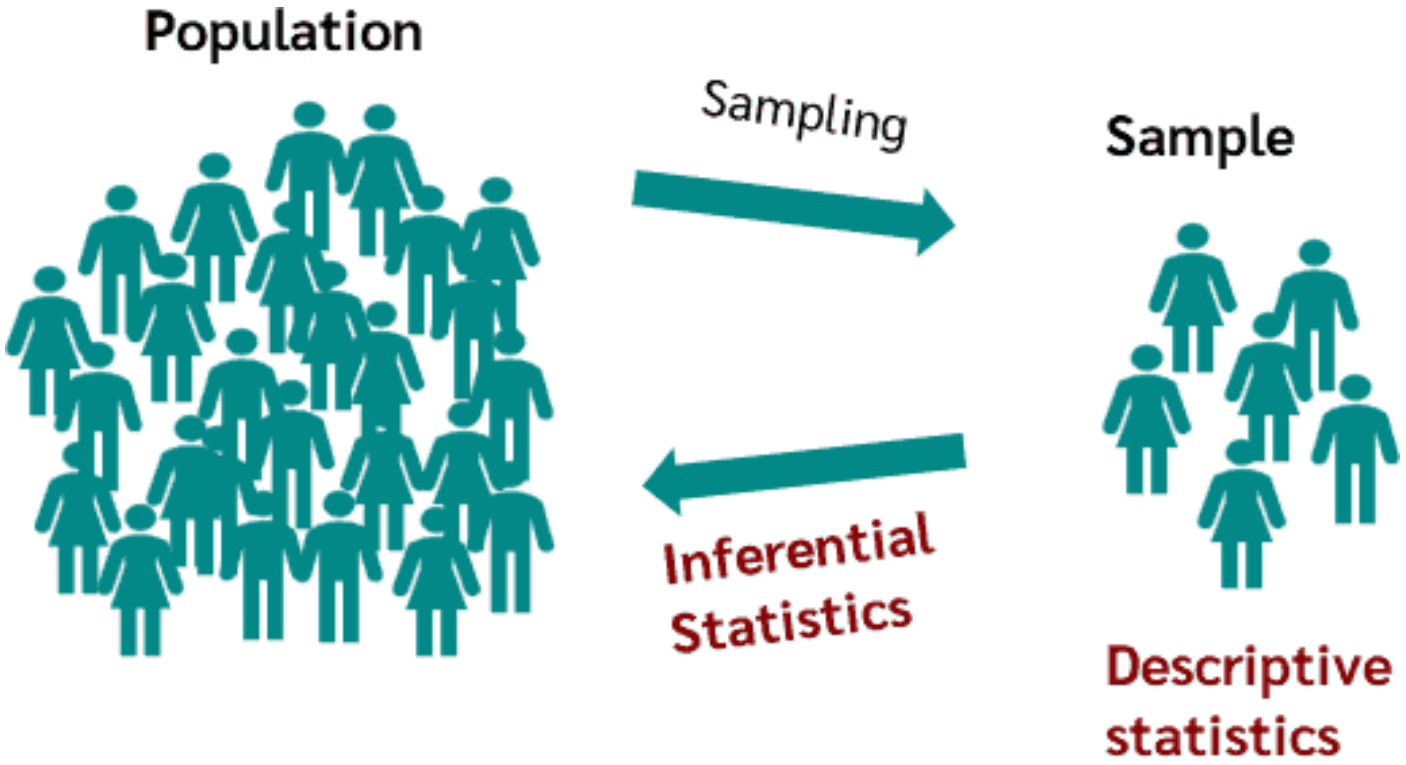
Live demo

DESCRIPTIVE STATISTICS

06

DESCRIPTIVE STATISTICS

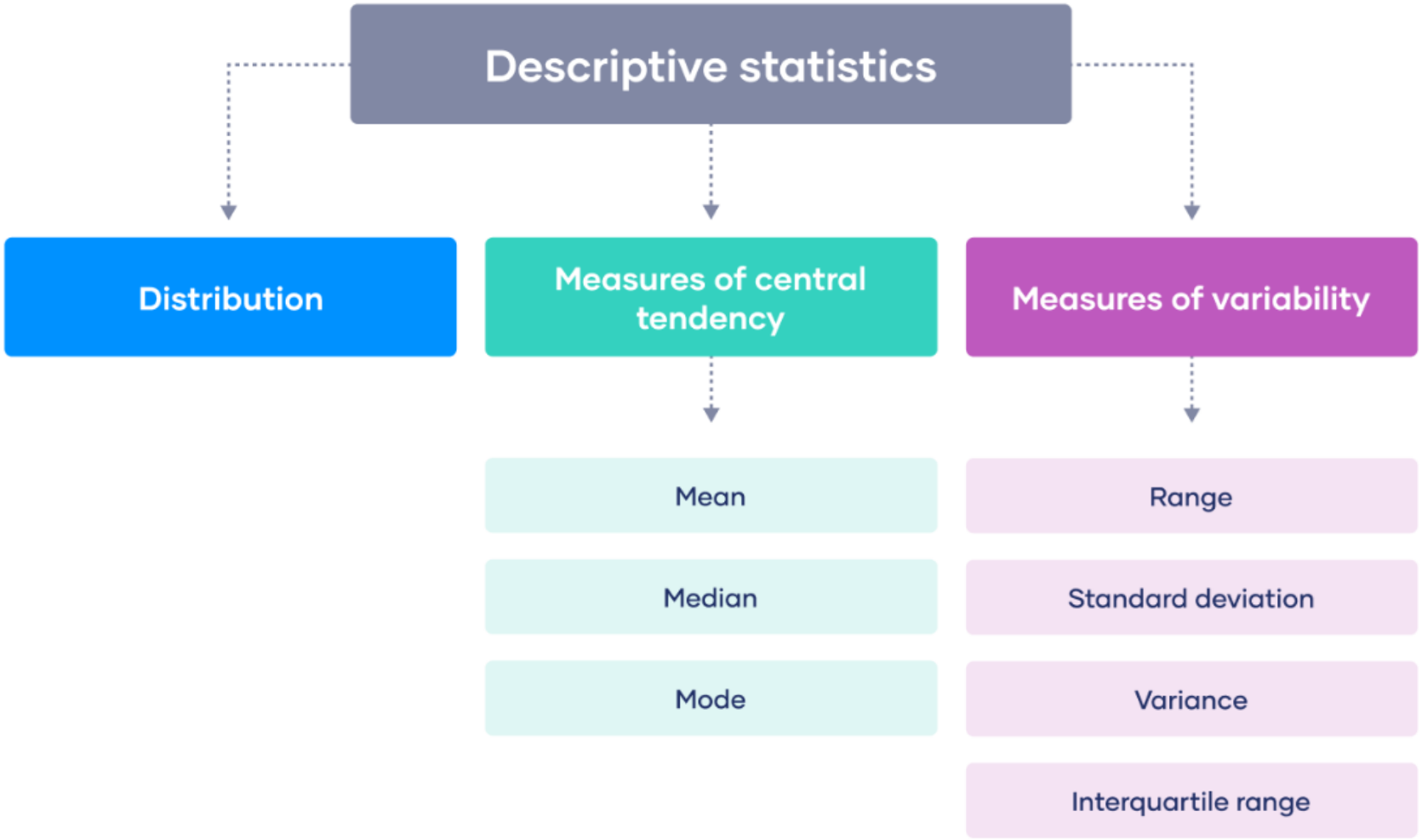
DESCRIPTIVE VS INFERENTIAL STATISTICS



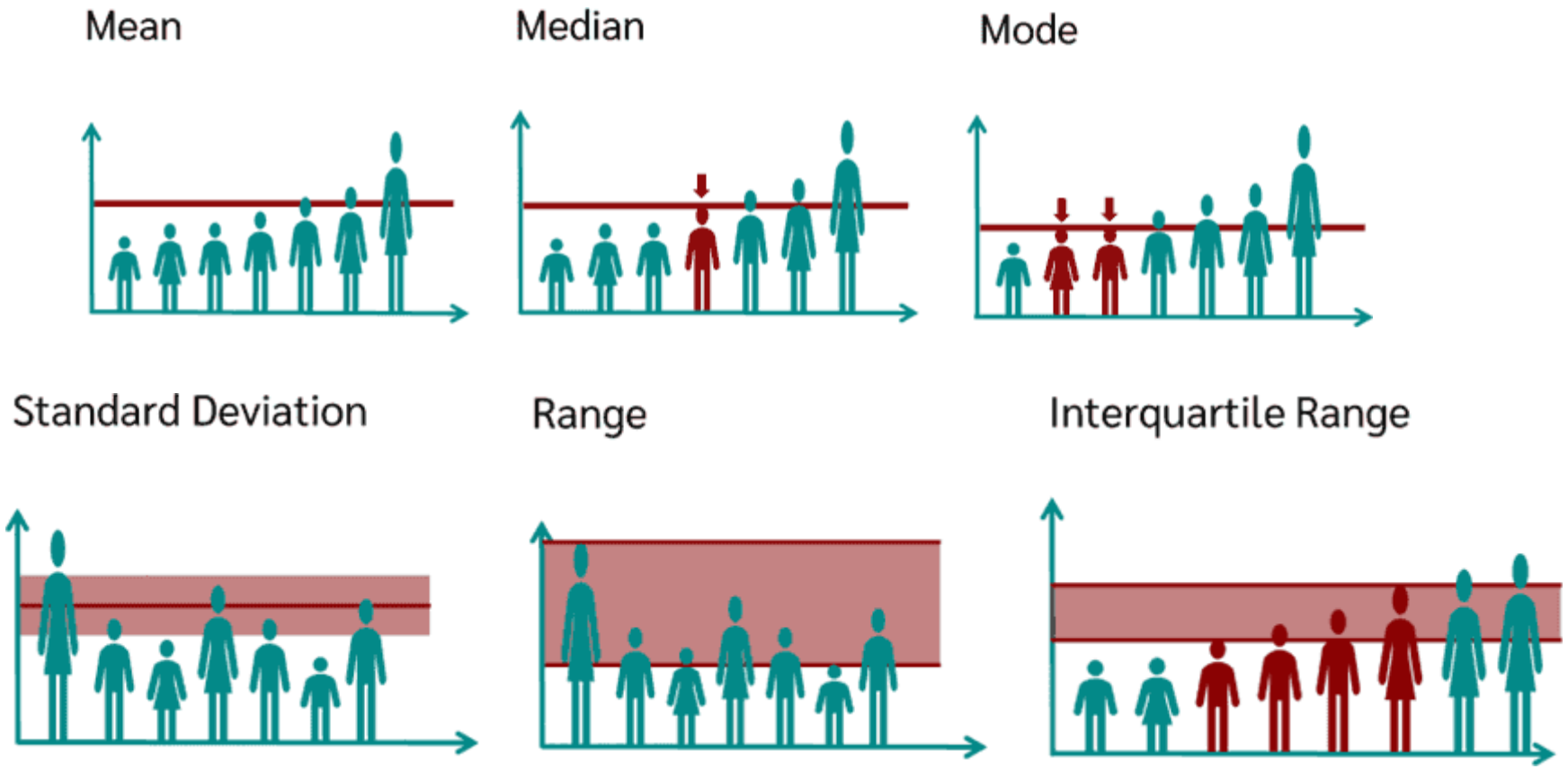
DESCRIPTIVE STATISTICS
DESCRIPTIVE VS INFERENTIAL STATISTICS

DESCRIPTIVE	INFERENTIAL
It is the analysis of data that helps to describe, show and summarize data under study	It is the analysis of random sample of data taken from a population to describe and make inference about the population
Organize, analyze and present data in a meaningful way	Compares, test and predicts data
It is used to describe a situation	It is used to explain the chance of occurrence of an event
It explain already known data and limited to a sample or population having small size	It attempts to reach the conclusion about the population
Types: Measure of central tendency & Measure of variability	Types: Estimation of parameters & Testing of hypothesis
Results are shown with help of charts, graphs, tables etc.	Results are shown with help of probability scores

DESCRIPTIVE STATISTICS
OVERVIEW



DESCRIPTIVE STATISTICS
OVERVIEW



DESCRIPTIVE STATISTICS

FUNCTIONS FOR CONTINUOUS VARIABLES

The functions to use in R are included in the ***stats*** package :

- Arithmetic mean $\hat{x}$: *mean* function

  $$\hat{x} = \frac{1}{N} \times \sum_{i=1}^{N} x_i$$

  Parameters : *x* = list of continuous values
  na.rm (boolean : true or false) = remove NA values ?

- Standard-deviation σ : *sd* function

  $$\sigma = \sqrt{\frac{1}{N} \times \sum_{i=1}^{N} (x_i - \hat{x})^2}$$

  Parameters : *x* = list of continuous values
  na.rm (boolean : true or false) = remove NA values ?

- Median : *median* function

  Parameters : *x* = list of continuous values
  na.rm (boolean : true or false) = remove NA values ?

DESCRIPTIVE STATISTICS

FUNCTIONS FOR CONTINUOUS VARIABLES

- Mode (available in package *DescTools*) : *mode* function (most frequent value)
  Parameters : *x* = list of continuous or categorical values
  na.rm (boolean : true or false) = remove NA values ?

- Minimum / Maximum : *min* and *max* functions (**range = max – min**)
  Parameters : *x* = list of continuous values
  na.rm (boolean : true or false) = remove NA values ?

- Quartiles (Q1, Q2 (median), Q3 and more) : *quantiles* function
  (**interquartile range also called IQR = Q3 – Q1**)
  Parameters : *x* = list of continuous values
  probs = list of probabilities (Q1 : 0.25, Q2 : 0.5 and Q3 : 0.75)
  na.rm (Boolean : true or false) = remove NA values ?

DESCRIPTIVE STATISTICS

FUNCTIONS FOR CONTINUOUS VARIABLES

- Correlation between two variables (available in package ***stats***) : ***cor*** function

  Parameters : ***x*** = list of continuous values
  y = list of continuous values
  method (*pearson*, *spearman*) = in case of non-normality of data : use spearman method.

Values : from -1 (perfect negative correlation) to +1 (perfect positive correlation)

- Covariance between two variables (available in package ***stats***) : ***cov*** function

  Parameters : ***x*** = list of continuous values
  y = list of continuous values
  method (*pearson*, *spearman*) = in case of non-normality of data : use spearman method.

DESCRIPTIVE STATISTICS
FUNCTIONS FOR CATEGORICAL VARIABLES

- Mode (available in package *DescTools*) : *mode* function (most frequent value)
  Parameters : *x* = list of continuous or categorical values
  na.rm (boolean : true or false) = remove NA values ?

- Contingency table : use *table* function :
  Parameters : *x* = dataset (two categorical variables)
  useNA ("*no*", "*ifany*" or "*always*") = remove NA values ?

- Percentages : use a **contingency table** to calculate % with *sum* function
  percentages within groups : use *group_by* function

DESCRIPTIVE STATISTICS
DESCRIPTIVE TABLE IN SCIENTIFIC PAPERS

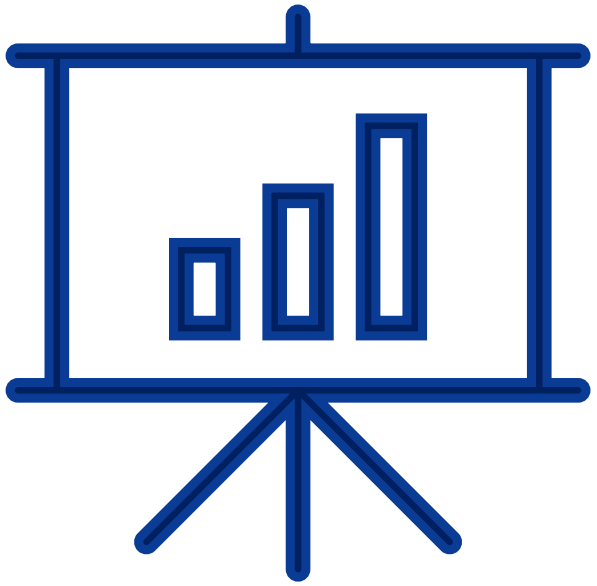
- Descriptive table is **mandatory** in research papers
- Goal : give to reviewers **an overview** of the data used
- Content of table :
  - **Normally** distributed parameter : **mean ± standard-deviation**
  - **Not-normally** distributed parameter : **median (quartile 1 ; quartile 3)**
  - **Categorical** parameter : **count (%)** for each modality

Table 1. Demographics

	Not diabetic (N=9,850)	Diabetic (N=499)
Age (years)	46.92 (17.19)	60.69 (11.47)
Weight (kg)	71.66 (15.22)	76.67 (17.18)
Systolic blood pressure	130.09 (22.76)	146.65 (28.39)
Sex		
Male	4,698 (47.7%)	217 (43.5%)
Female	5,152 (52.3%)	282 (56.5%)
Race		
White	8,659 (87.9%)	404 (81.0%)
Black	1,000 (10.2%)	86 (17.2%)
Other	191 (1.9%)	9 (1.8%)

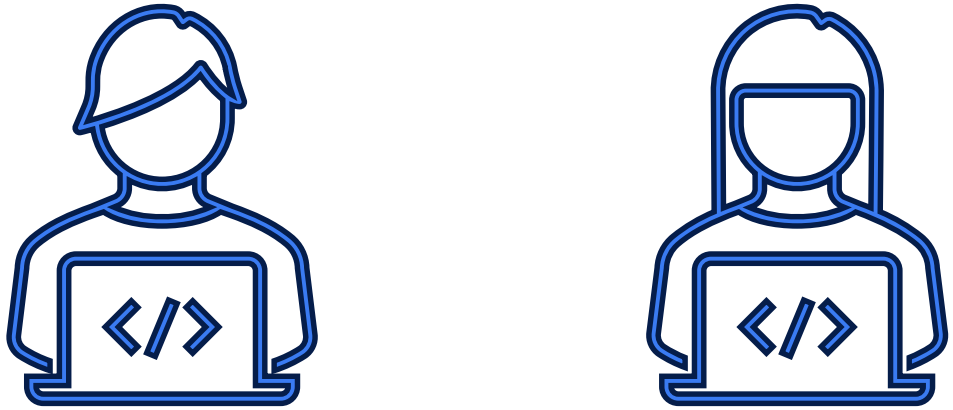
Total sample: N = 10,349

DESCRIPTIVE STATISTICS



Live demo

DESCRIPTIVE STATISTICS



Time to play !
(30 minutes)

QUESTIONS

07

THANK YOU FOR YOUR ATTENTION

SEPTEMBER 2025