UE / ENSEIGNANT : Anglais - York

DATE : 17/10/24

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REMARQUES :

Key Concepts

Table des matières

I. Videos watched

A. NEJM Quick Take

NEJM Quick Take : **Rifampin or Isoniazid for Latent Tuberculosis in adults**

An international open-label randomized phase 2-3 clinical trial was conducted in 6859 adults with latent TB infection.

Conclusion: 4 months of rifampicin is non-inferior in efficacy to 9 months of isoniazid.

B. Definitions

Relative risk : 2 groups (placebo and treatment) *calcul le pourcentage de risque de ne pas prendre de traitement*

Odds ratio : compares the odds of an outcome in two differents groups : 1 group of smoker (lung cancer/ non cancer) and 1 group of non smoker (lung cancer/ non cancer)
Smoker/non smoker = *Nombre de fois plus dangereux de fumer que de pas fumer*

Confidence intervals (CI) : A range of values wich likely contains the true value of a given statistic. This actually …

Number needed to treat NNT : The number of people needed to take a treatment for one person to benefit from that treatment

Statistical significance : p-value
How likely it is that the null hypothesis is true. generally a p-value below 0,05 is required to be confident that a true effect have been detected

II. Internal vs external validity

Both affect the reliability of the study results

A. Internal validity

Evaluated based on the design and structure of the study. **Internal validity** measures how well a study is conducted (its structure) and how accurately its results reflect the studied group. *= Ce qui nous intéresse le plus en LCA*

Is affected by :

- bias
- statistical power
- blinding
- randomisation

Biases :

- Attrition and other biases
- Confounding variables
- Interaction between treatment groups
- Naturally occurring changes confused with effect during long study

B. External validity

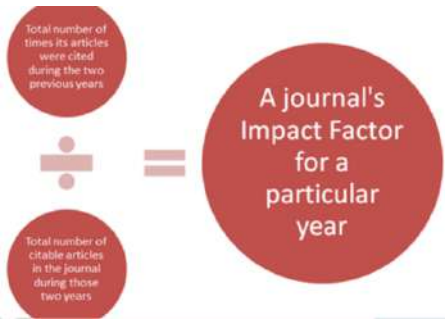
Generalizability of the results to other healthcare settings in real healthcare practice. **External validity** relates to how applicable the findings are in the real world.

Is affected by :

- Applicability of the results of a study to other populations or environments
- sampling (e.g. inclusion/exclusion criteria)
- Replicability

Biases :

- Homogeneous sample
- Recruitment source and process (e.g. social/economic status , health status)
- Treatment repeatability (will most patients likely receive the level of treatment offered in the trial?)



The internal validity influence the external validity.

III. Impact factor

Impact factor (IF) is an index (numerical value) to evaluate the impact of a journal. *It compares the quality of journals in the same field.* Calculated each year based on the citation status of articles from a database. Used to compare the quality journals in the same field.

Example of journals impact factors :

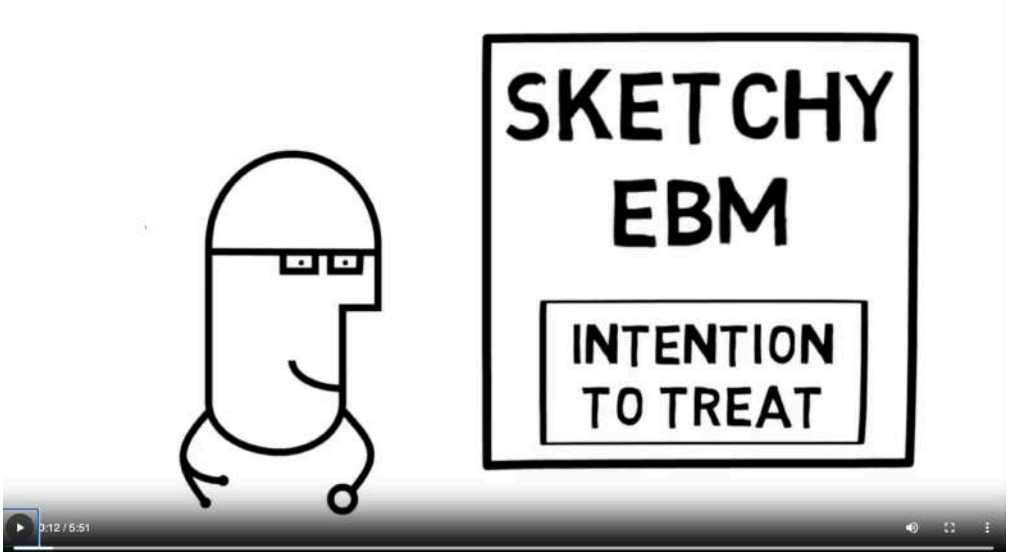
Some limitations to the use of impact factor are :

- IF cannot be used for comparison between different fields
- IF is not an index for the evaluation of specific papers or researchers
- Be careful when using IF for small-scale academic journals
- IF cannot express properties other than number of citations

IV. Superiority vs non-inferiority

- **Superiority** tests to see if the new treatment is **BETTER** than existing treatment/placebo
- **Non inferiority** tests to see if a treatment is **NOT WORSE** than existing treatment (fewer side effects, shorter treatment time, less invasive, placebo not possible...)

V. ITT (intention to treat) vs PP (per protocol) with a video



Analysis strategy to face the problem of patient who did not followed the treatment completely (deviated from the protocol, were not compliant with the protocol). Should be indicated in the flow chart of the study.

- **ITT** : Analyze the results of each patient as they were originally randomly assigned (no matter what treatment they received). Much closer to real life prescription : take into consideration the actual compliance of the patients
- **PP** : Examine the data only from patients who followed the treatment
- **As treated** : Change the assignment according to the treatment actually received by the patient (rare, complicated to use)

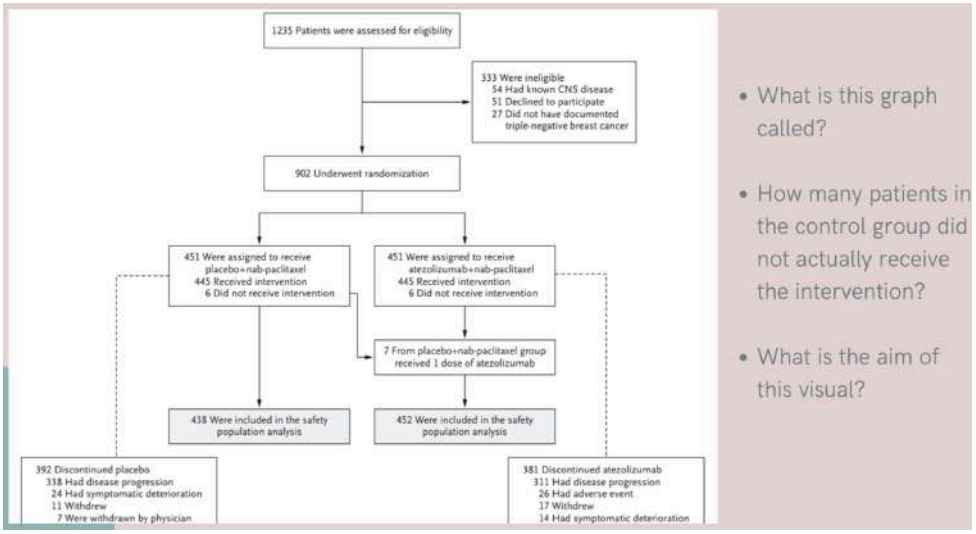
- How many over 41 year-olds were in the control group in the ITT population?
- Which group has the highest median age?
- How many people in the control group were not in the placebo PD-L1 subgroup?

Table 1. Characteristics of the Patients at Baseline.*

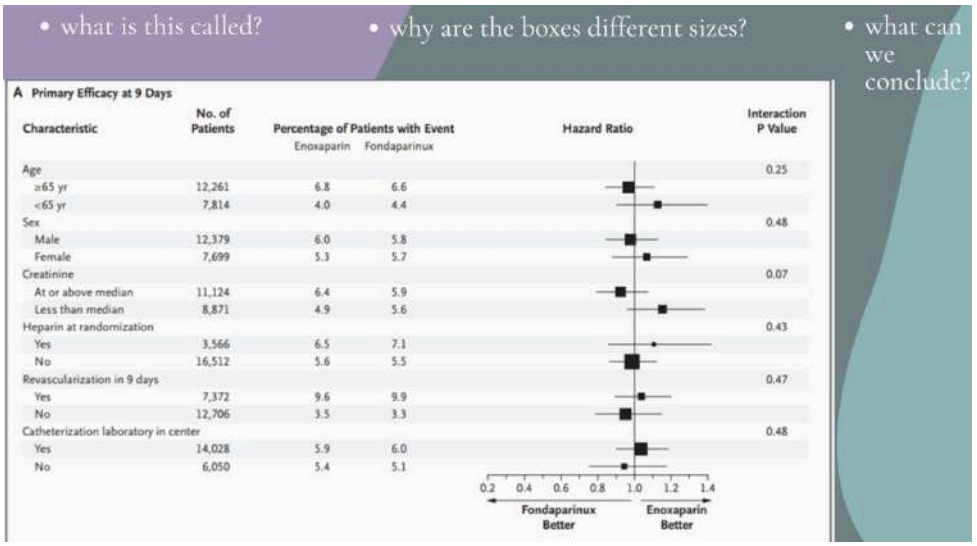
Characteristic	Intention-to-Treat Population		PD-L1–Positive Subgroup	
	Atezolizumab + Nab-Paclitaxel (N = 451)	Placebo + Nab-Paclitaxel (N = 451)	Atezolizumab + Nab-Paclitaxel (N = 185)	Placebo + Nab-Paclitaxel (N = 184)
Age				
Median (range) — yr	55 (20–82)	56 (26–86)	53 (26–82)	53 (28–85)
Distribution — no. (%)				
18–40 yr	63 (14.0)	51 (11.3)	31 (16.8)	24 (13.0)
41–64 yr	284 (63.0)	285 (63.2)	111 (60.0)	117 (63.6)
≥65 yr	104 (23.1)	115 (25.5)	43 (23.2)	43 (23.4)
Female sex — no. (%)	448 (99.3)	450 (99.8)	184 (99.5)	184 (100)
Race or ethnic group — no. (%)†				
White	308 (68.3)	301 (66.7)	125 (67.6)	129 (70.1)
Asian	85 (18.8)	76 (16.9)	38 (20.5)	28 (15.2)
Black	26 (5.8)	33 (7.3)	9 (4.9)	14 (7.6)
Native American	17 (3.8)	23 (5.1)	8 (4.3)	9 (4.9)
Hawaiian or other Pacific Islander	1 (0.2)	0	0	0
Multiple	2 (0.4)	3 (0.7)	0	0
Unknown	12 (2.7)	15 (3.3)	5 (2.7)	4 (2.2)
ECOG performance-status score — no./				

- **How many over 41 years-olds were in the control group in the ITT population ?** 400
- **Which group has the highest median age ?** Control group ITT
- **How many people in the control group were not in the placebo PD-L1 subgroup ?** 267

- This graph is called a **fars plot graph.**

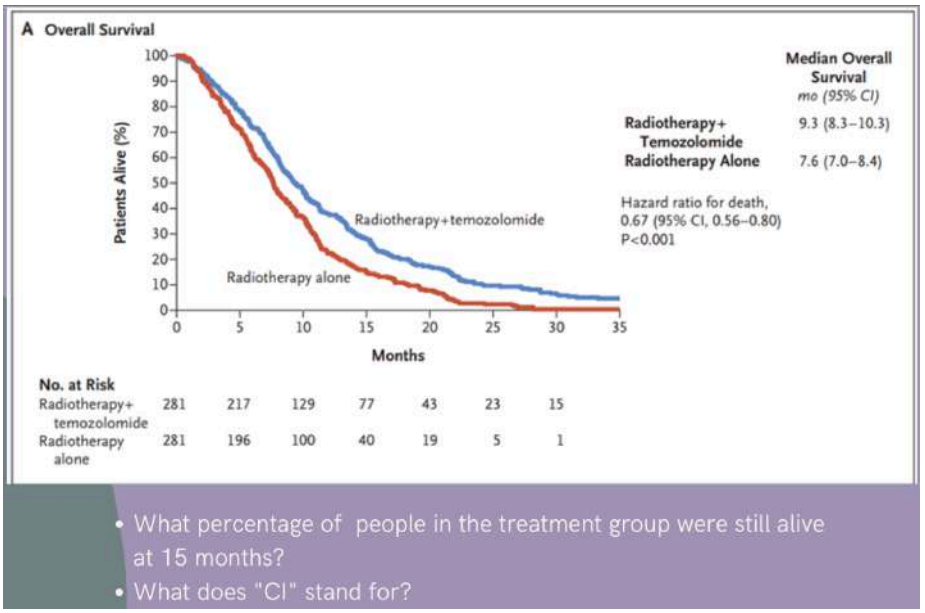


- **What is this graph called ?** Flow chart
- **How many patients in the control group did not actually receive the intervention ?** 6
- **What is the aim of this visual ?** Attrition



- **What is this called ?** Forest plot
- **Why are the boxes different sizes ?** The group size
- **What can we conclude ?** Neither enoxaparin and fondaparinux are good drugs because the line touches the vertical line *(si ça touche la ligne verticale c'est pas bon…)*

-> This graph is called a **Kaplan Meier graph** or survival curve. It presents the survival of patients who were treated with a specific treatment.

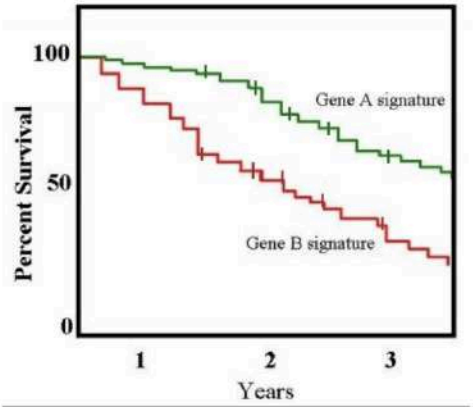


What percentage of people in the treatment group were still alive at 15 months ? 30 %

What does "CI" stand for ? Confidence Interval

VI. Socratives

1/10 :



What type of graph is this?

This graph is called a **kaplan-meier graph** or a survival curve.

2/10 :

Biases are only found in RCTs because they are interventional types of studies.

T True F False

False *because biases have to do with human design so it can happen in any type of studies at any stage*.

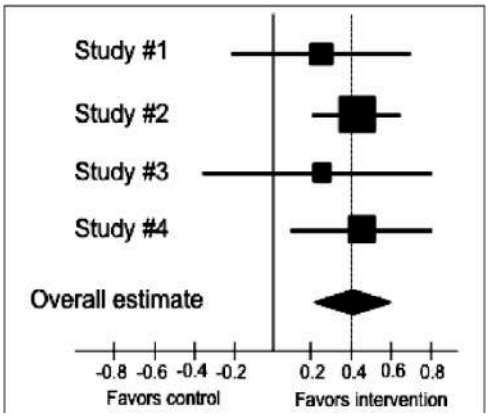
3/10 :

ITT always provides reliable results.

T True F False

Fasle*, it depends on the loss of follow-up.*
NEJM has guidelines for referring to RCTs and it says that the best, of course, is ITT and PP because the intention to treat shows you a certain picture but the per protocol also shows you the efficacy so if you have a combination of both you can really interpret the efficacy of the intervention.

4/10 :



What type of graph is this?

It is a Forest blot.

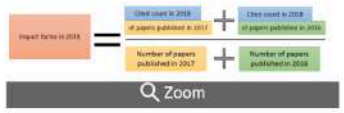
5/10 :

Drug X is used to treat a certain condition; it is currently administered intravenously but can be administered orally, which is more convenient. Which trial should you conduct to decide of means of adminstration?

Non inferiority RCT *you are testing the syndrome but you are going to see if the treatment 1. could be <u>less costly</u>, and 2. could bring <u>more benefits for the patient</u>*

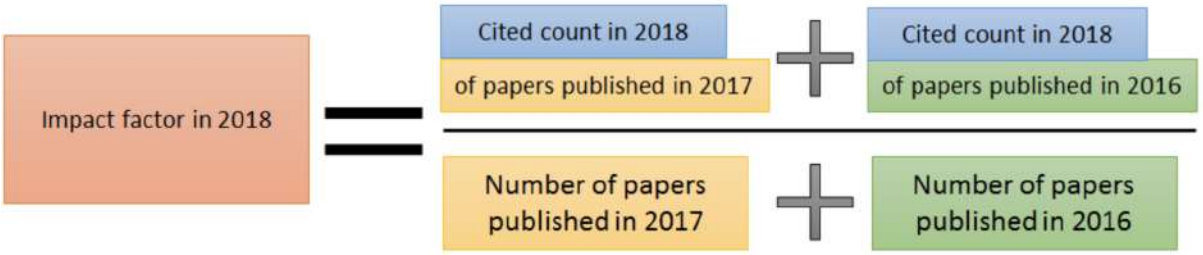
It can never be a case control, it is about analyzing risk factors.

6/10 :



The maximum value for IF is 100.

T True F False



False *because it is a ratio*
It means that you cannot predict the impact factor, the number of times a paper will be cited, that is not possible. => the IF has no maximum value, it is a ratio.
Because if we take the example of the NEJM (its IF has become higher and higher in the past few years) : this journal is taken as the best journal, basically everybody reads this paper : the idea is if we do a research project we will need to cite another paper already published for our background informations and also for our discussion, so we will probably more choose a paper that is already famous, that everybody has read, that everybody trust because it was published in a famous journal. So we are likely, in 2023, to choose as a citation a paper from the NEJM. Therefore → the NEJM gets more and more citations.
You can cite as many times as you want, so the figures from the top line are probably keep going up, whereas the figures in the line below are not changing because the NEJM remains the NEJM (= every week it publishes the same amount of articles, it has a limited number of paper).

*<u>= en-dessous de la ligne ça ne change pas, au-dessus de la ligne ça ne fait qu'augmenter → so there is no limit for the impact factor in terms of value **because it is a ratio** "remember that"</u>*

7/10 :

What are the differences between phase 3 and phase 4 trial?

A	They are both obligatory	B	Phase 3 tests safety whereas phase 4 does not
C	Phase 3 cannot be funded by a sponsor whereas phase 4 can	D	Phase 4 tests drugs that are publicly available
E	None of the above		

D

Phase 4 is going to test drugs that are already on the market whereas phase 3 is going to test the efficacy of a drug before it is allowed on the market.

All the phases of a study focus on safety, and ***the phase 4 focuses on long term safety****.*

8/10 :

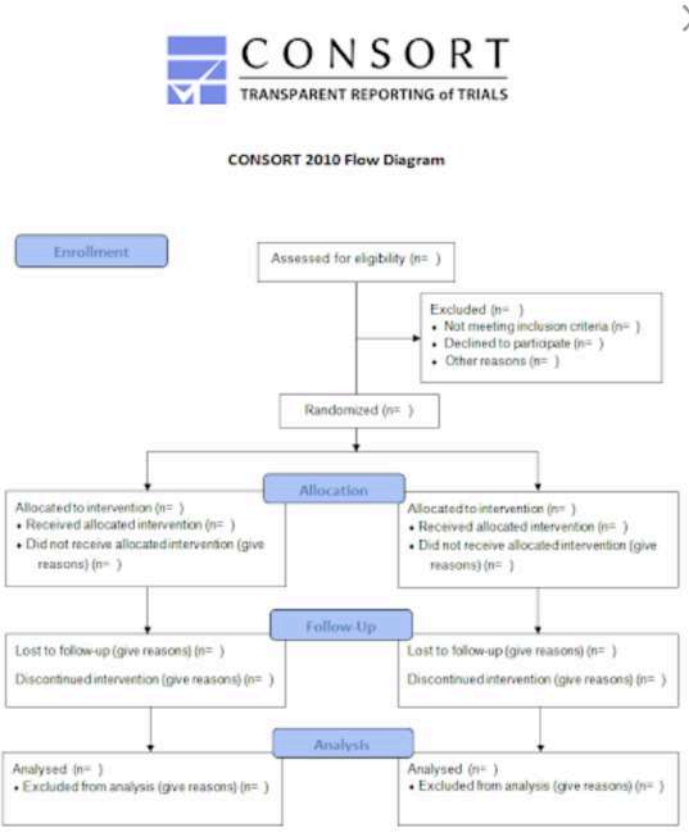
You are conducting a study; 2500 participants enrol in the study. By the end of the study you have 2 015 participants. What type of statistical issue do you need to consider?

Attrition bias

9/10 :

What graph can tell you about loss of follow up?

(participants lost to follow up/ withdrawal)



It is called a **Flowchart**.

10/10 :

You have conducted a study but have not come up with any statistically significant results. The NEJM will not publish your study.

T True F False

False

What is important is that well conducted studies are or should be published regardless of results to avoid publication bias. It is true, though, that in reality journals are more interested in study with robust findings (= statistically significant results), but it should not impact the publishability of the paper.

So the answer is false, the NEJM can refuse a paper but it has no rights to refuse it just because the results are not statistically significant.