CRITICAL APPRAISAL_THERAPY (RCT)

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SOURCE

- http://www.cebm.net/critical_appraisal.asp.
- EBM http://www.cebm.utoronto.ca/teach/materials/caworksheets.htm
- The foundation skills program for Egyptian Fellowship Trainees
- Excutive board of the health ministers› council, 2010
- King Fahd national library cataloging-in-publication data

WHAT IS CRITICAL APPRAISAL?

- ***Critical appraisal*** is the way to evaluate any research to be sure that it is telling the truth **(valid),** suitable to your patient , **(relevant)** and the results of the research worth to be used in **clinical practice**.

CRITICAL APPRAISAL - FIVE ELEMENTS

1 - What is the **research question** ?

2 - What is the **design** of the study ?

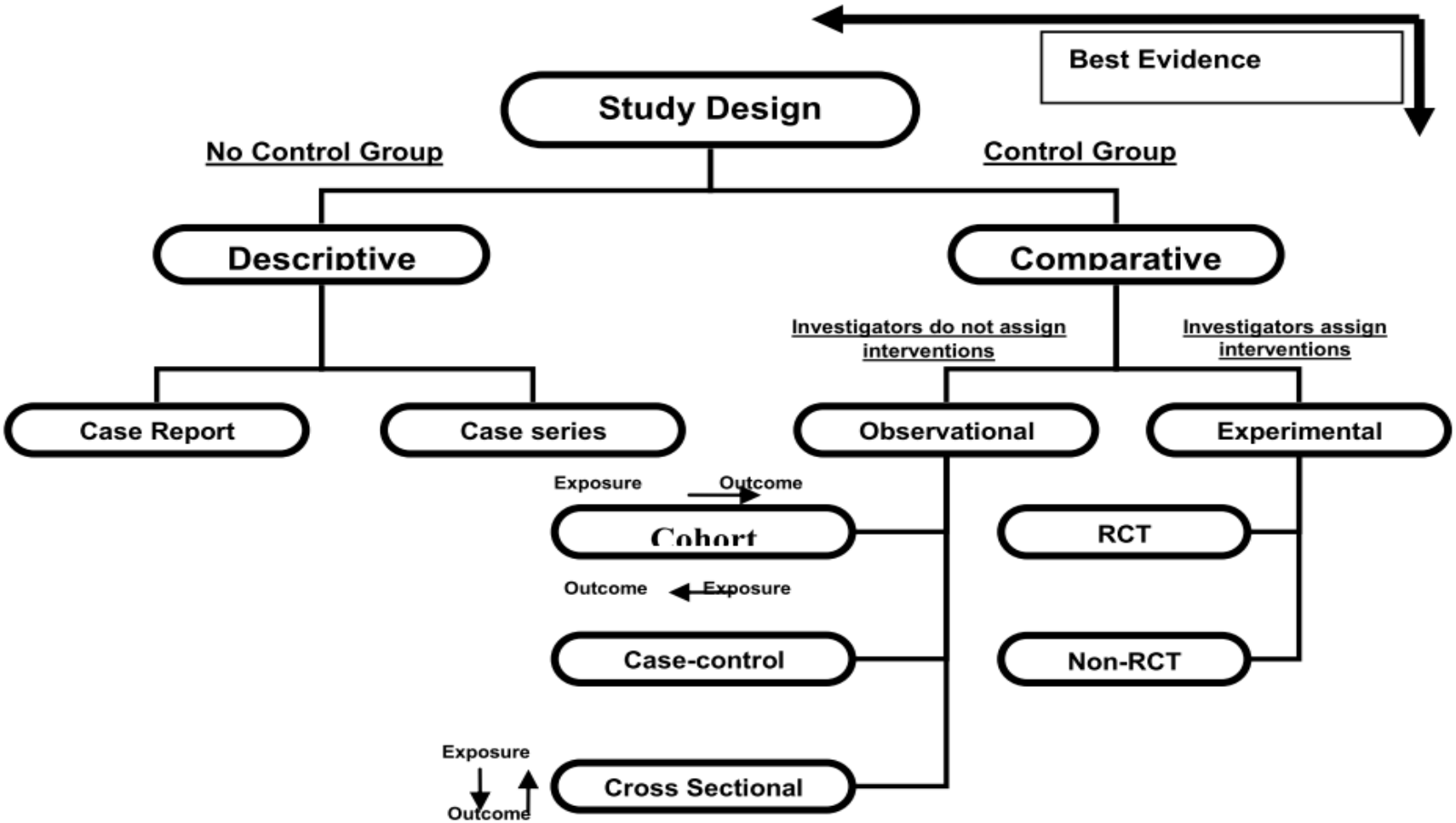
3 - Assess the **study validity** .

4 - Assess the **study results** .

5 - Assess the study **generalizability** or applicability

Type of Question	Suggested Best Type of Study
Therapy	**RCT** > cohort > case control
Diagnosis	Prospective, blind comparison to gold standard
Etiology / Harm	**RCT** > cohort > case control
Prognosis	Cohort study > case control
Prevention	**RCT** > cohort study > case control
Cost	Economic analysis
Questions of therapy, etiology and prevention which can best be answered by RCT can also be answered by a meta-analysis or systematic review.	

STUDY DESIGN :



LEVELS OF THE EVIDENCE :

LEVELS OF EVIDENCE

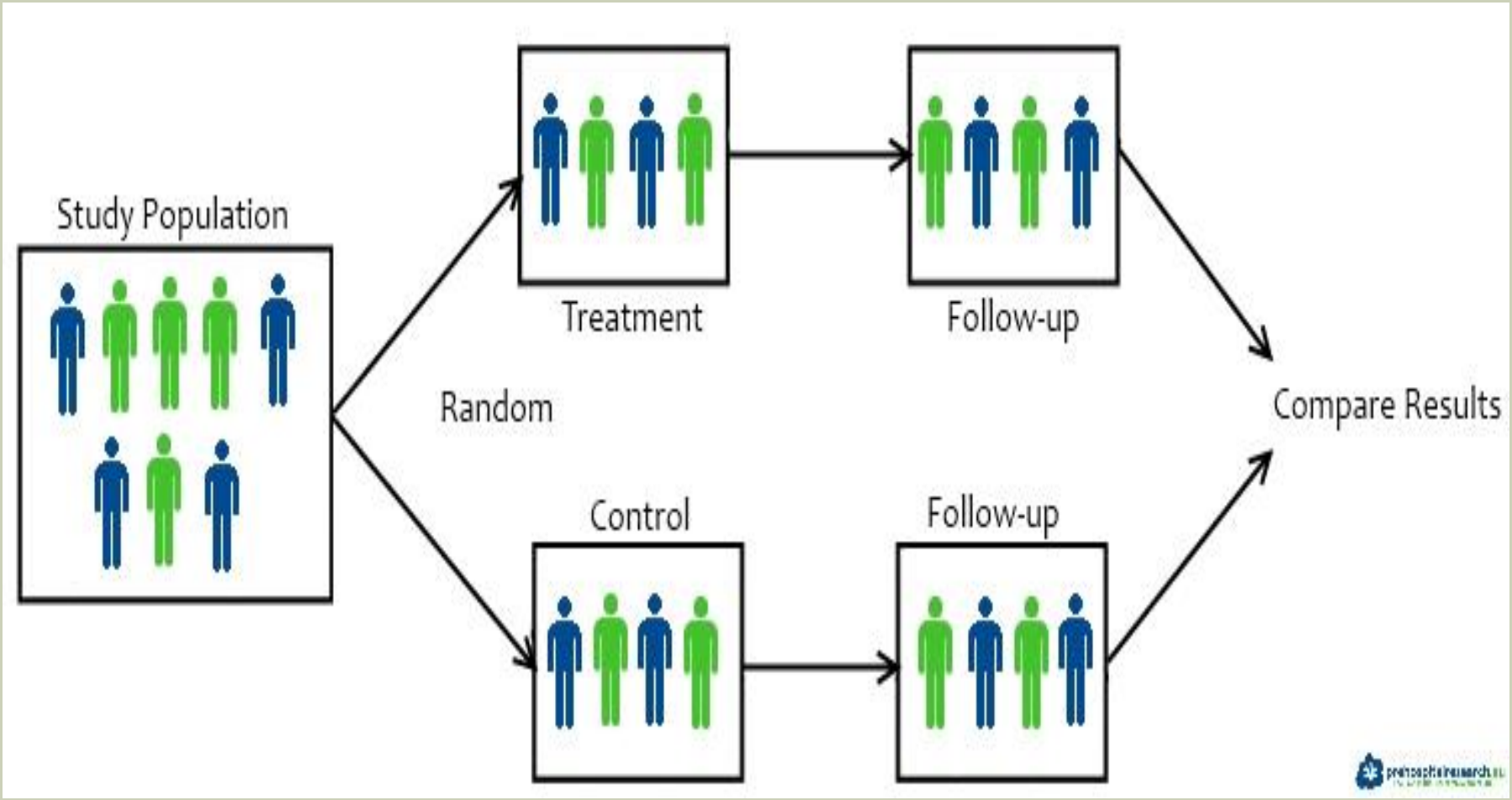
- **Level I**: obtained from at least one properly controlled randomized trial, considered the ***gold standard*** of evidence.
- **Level II**-1:derived from controlled trials without randomization.
- **Level II**-2: well-designed cohort or case-control studies.
- **Level III** evidence is derived from reports of expert committees, because it is often difficult to ascertain the scientific origin of the committee opinion.

- Questions of therapy, etiology and prevention which can **best be answered by RCT** can also be answered by a **meta-analysis or systematic review**.

RANDOMIZED CONTROLLED TRIAL (RCT)

- A **randomized controlled trial (RCT)** is a type of scientific experiment most commonly used in testing the safety (information about adverse drug reactions and adverse effects of other treatments) and efficacy or effectiveness of healthcare services or health technologies (such as medical devices or surgery)

TYPICAL DESIGN OF AN RCT



RANDOMIZED CONTROLLED TRIAL (RCT)

- The key distinguishing feature of the usual RCT is that study subjects are randomly allocated to receive one or other of the alternative treatments under study

WHAT IS THE DIFFERENCE BETWEEN RCT AND A RANDOMIZED TRIAL?

- The terms "RCT" and randomized trial are often used synonymously but some authors distinguish between "RCTs" which compare treatment groups with **control** groups not receiving treatment (as in a placebo-controlled study), and "randomized trials" which can compare multiple treatment groups with each other.

EXAMINE RCT FOR THESE ELEMENTS

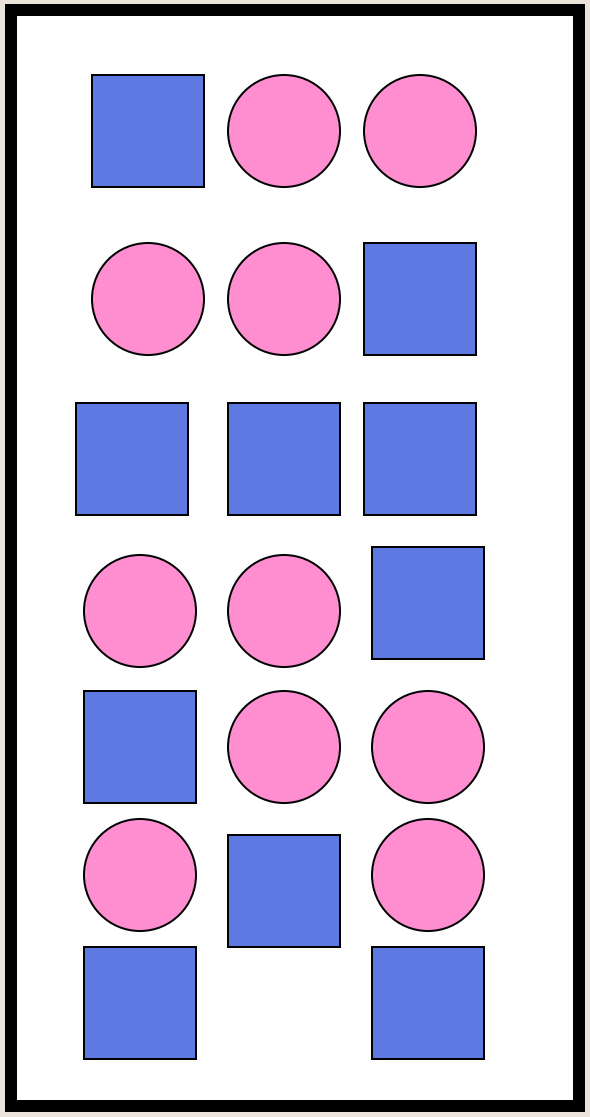
1. Randomization
2. Allocation Concealment
3. Blindness
4. Intention to treat analysis

RANDOMIZATION

- The advantages of proper randomization in RCTs include:

1. It eliminates bias in treatment assignment selection bias and confounding.

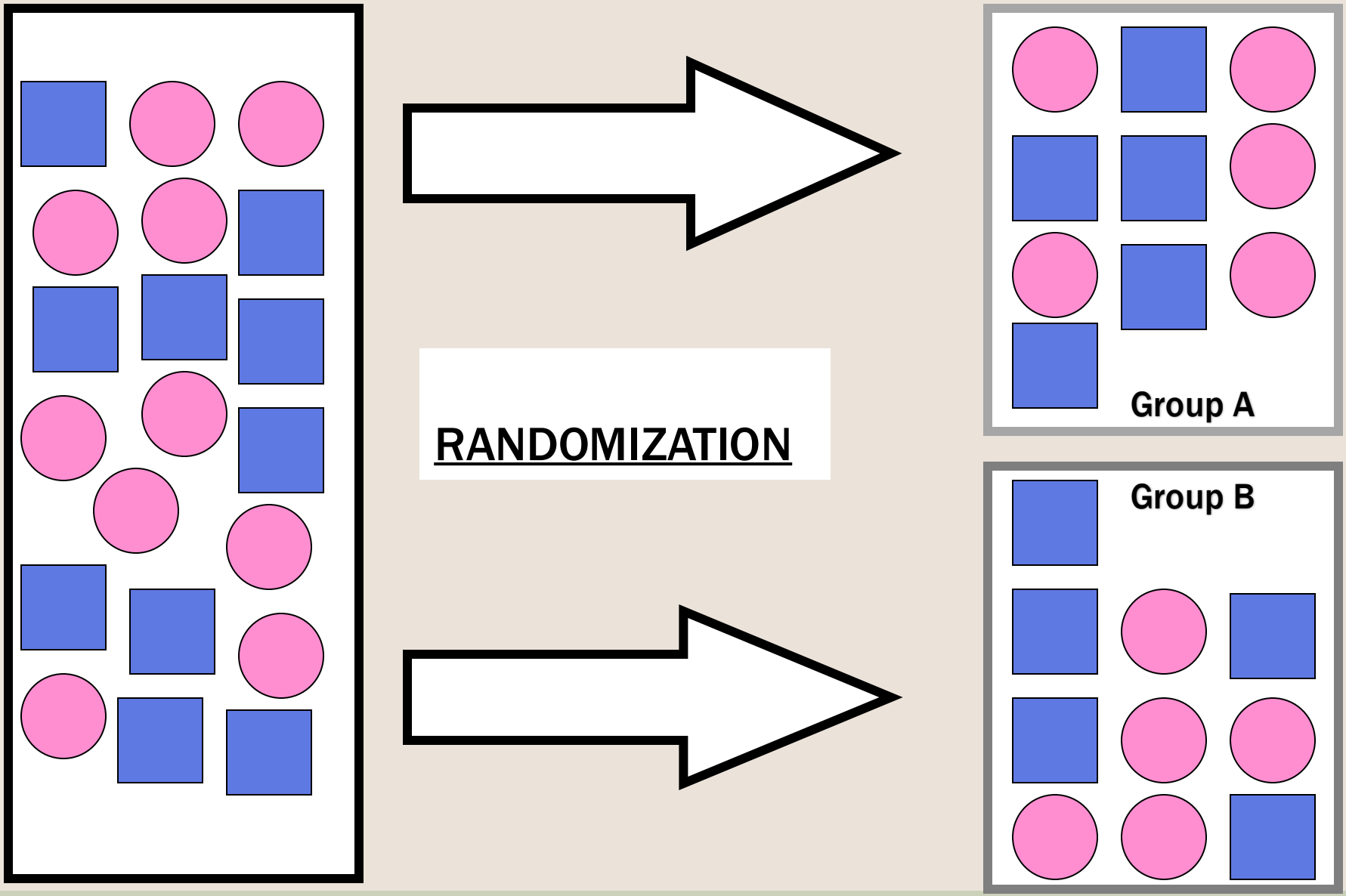
2. It facilitates blinding (masking) of the identity of treatments from investigators, participants, and assessors.



RANDOMIZATION

Examples

- Postal code
- Month of birth
- **Random number**
- Etc.


RANDOMIZATION
Group A
Group B

ALLOCATION CONCEALMENT

- Defined as "the procedure for protecting the randomization process so that the **treatment** to be allocated is **not known** before the patient is entered into the study"

ALLOCATION CONCEALMENT

- Some standard methods of ensuring allocation concealment include sequentially-numbered opaque sealed envelopes (SNOSE); sequentially-numbered containers; pharmacy controlled randomization.

CONCEALED RANDOMIZATION IN PICTURES

73735	45963	78134	63873
02965	58303	90708	20025
98859	23851	27965	62394
33666	62570	64775	78428
81666	26440	20422	05720
15838	47174	76866	14330
89793	34378	08730	56522
78155	22466	81978	57323
16381	66207	11698	99314
75002	80827	53867	37797
99982	27601	62686	44711
84543	87442	50033	14021
77757	54043	46176	42391
80871	32792	87989	72248
30500	28220	12444	71840

Blinding

- An RCT may be Blinded, (also called "masked") by "procedures that prevent study participants, caregivers, or outcome assessors from knowing which intervention was received.

TYPES OF BLINDING

- **Single-blind**
- **Double-blind**
- **Triple-blind**

- RCTs without blinding are referred to as "unblinded", "open", or (if the intervention is a medication) "open-label".

BLINDING

BLINDING

- SINGLE BLINDED:

Pt unaware of what group s/he is in

- DOUBLE BLINDED:

Pt and care giver unaware

- TRIPLE BLINDED:

Pt, care giver and investigator unaware

- OPEN LABEL:

Everyone is aware

THE INTENTION TO TREAT ANALYSIS :

- To apply the intention to treat analysis, two golden rules should be applied for each participant:

1) **Once randomized always analyzed**
2) **Analyzed as randomized.**

THE INTENTION TO TREAT ANALYSIS :

- Each participant outcome should appear in the final analysis and in the same group he was originally randomized to irrespective of change of group or stop of treatment

Advantages of the intention to treat analysis

- Preserves randomization

Disadvantage of the intention to treat analysis

- May lead to **underestimation** of the treatment effect. However, this is safer for the patient.

THE PER- PROTOCOL ANALYSIS :

- Investigators analyze only compliant subjects who took >80% of their assigned study medication.

THE PER- PROTOCOL ANALYSIS :

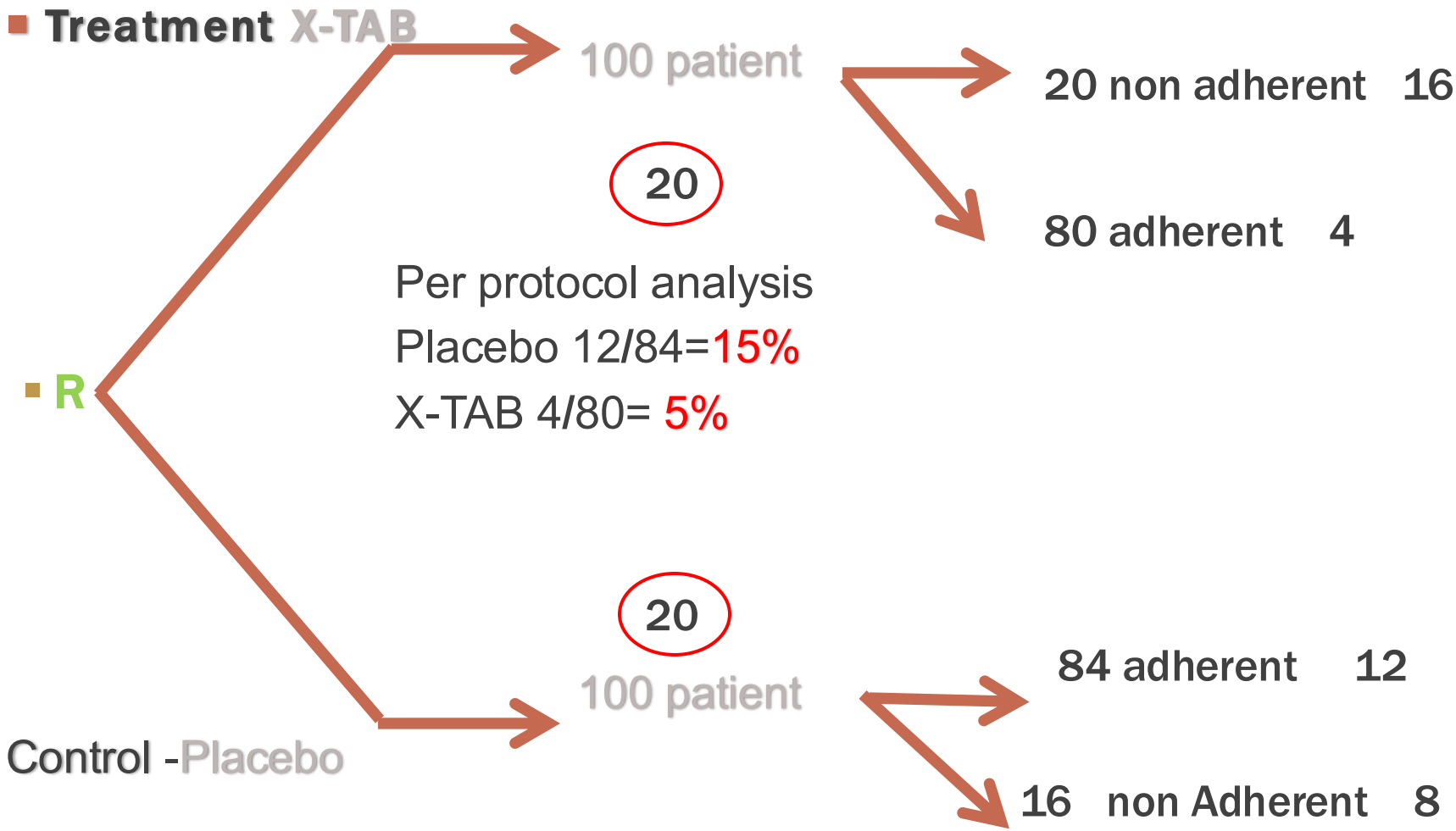
Advantage of the Per-Protocol analysis

- ✓May seem to be more logic !

Disadvantages of the Per-Protocol analysis

- ✓Violates randomization.
- ✓Participants who adhere to a treatment are different from drop outs as related to outcome.
- ✓Missing association with side-effects, which may be the cause of shifting between groups.

PER-PROTOCOL AND INTENTION TO TREAT COMPARISON



ADVANTAGES OF RCT

RCT design minimizes probability of

1. Selection bias by (Randomization and Allocation Concealment).
2. Ascertainment bias by investigators and participants bias by (Double blinding) .
3. Drop out bias by (Intention to treat analysis)

Check for elements of a sound RCT by using the ACRONYM RADI

CRITICAL APPRAISAL OF RESEARCH PAPER ABOUT (THERAPY)

Critical appraisal is done using specific appraisal sheets that contain certain questions that address the three important criteria of a study namely:

- **Is the study valid?**
- What are the results?
- Is the study relevant/ applicable?

Q1. IS THE STUDY VALID?

a) Was the assignment of patients to treatments **randomized?**

b) Was the randomization list **concealed?**

c) Were patients and clinicians kept **"blind"** to treatment ?

d) Were the groups **treated equally**, apart from the experimental treatment?

e) Was **follow-up** of patients sufficiently **long** and **complete**?

g) Were all patients **analyzed** in the groups to which **they were randomized?**

Q2. WHAT ARE THE RESULTS?

1. How significant and precise were the results?
2. What is the real clinical value of the treatment?

"It is a golden statistical rule that statistical significance does not mean clinical importance"

RESULTS

The importance of the new treatment is done by calculating the **absolute risk reduction** (**ARR**) and the **number needed to treat** (**NNT**) for the new treatment in comparison to the alternative one.

SCENARIO:

"You are appraising a RCT trial that test the effect of new antihypertensive drug in comparison to an old drug which is used in practice since many years. The trial enrolled 200 patients, one hundred in each treatment arm. The outcome was the occurrence of stroke? You have already answered the Q1 about the validity of the study and you wish to calculate the NNT?

SCENARIO

- From the **one hundred** patients taking the new antihypertensive drug, **five** patients developed stroke.
- **From the one hundred patients taking the old antihypertensive drug, ten patients developed stroke.**

How could you interpret the results in a meaningful way?

STEPS

First, calculate the risk of the event in the control group (patients taking the old antihypertensive drug). It is also called the Control Event Rate (CER)

CER = number of events/total number of group = 10/100 = 0.1 (or 10%)

Second, calculate the risk of the event in the treatment group (patients taking the new antihypertensive drug). It is also called the Experimental Event Rate (EER)

EER = number of events/total number of group = 5/100 = 0.0 5 (or 5%)

STEPS

Third, calculate the absolute reduction in the risk of stroke because of the new treatment. It is also called the **Absolute Risk Reduction (ARR).**

ARR= CER-EER. ARR in the risk of stroke=10%-5%=5%

i.e. there is a five percent absolute reduction in the risk of stroke because of the new treatment.

Fourth, calculate the number needed to treat .

THE NUMBER NEEDED TO TREAT (NNT)

- It is the number of subjects needed to be treated by a treatment modality to get **"one more benefit"** compared to the other treatment .
- It is calculated by **dividing 1/ARR**

THE NUMBER NEEDED TO TREAT (NNT)

- To calculate NNT in our example:
- 1/ARR= 1/0.05 = 100/5= 20. i.e (NNT is 20)

❖ The number needed to treat is 20, which mean that out of each 20 patients treated with the new antihypertensive drug, we will get one more benefit over the old one.

❖ In other words if we gave the new antihypertensive drug to 20 patients, only one of them will suffer from stroke. While if we gave the old antihypertensive instead to the same twenty patients, two of them will suffer from stroke. Thus, we prevented one stroke by using the new treatment .

Q3. IS THE STUDY RELEVANT??

1. Is your patient so different from those in the study that its results cannot apply?
2. Is the treatment feasible in your setting?
3. What are your patient's potential benefits and harms from the therapy?
4. Are your patient's values and preferences satisfied by the regimen and its consequences?

THANKS