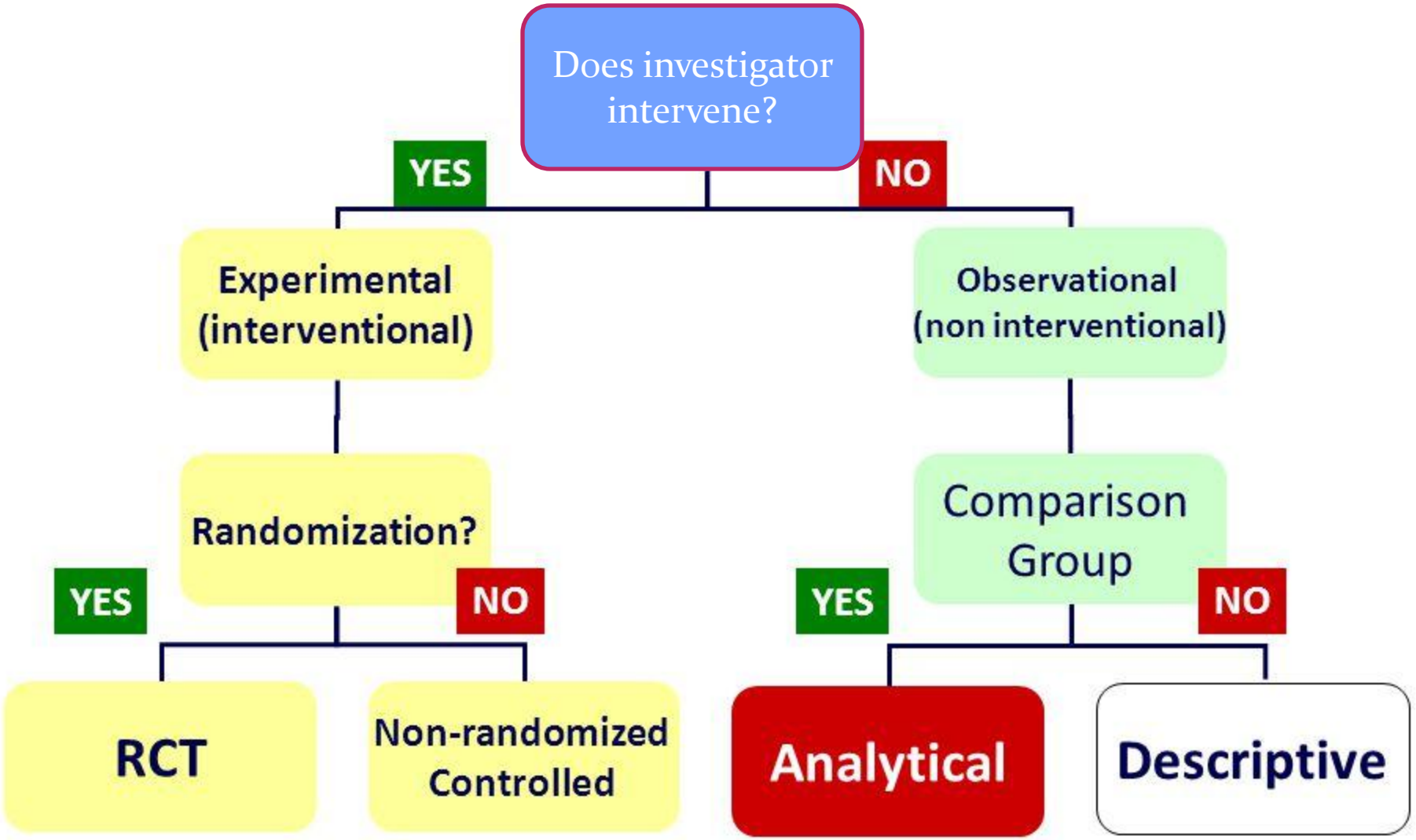
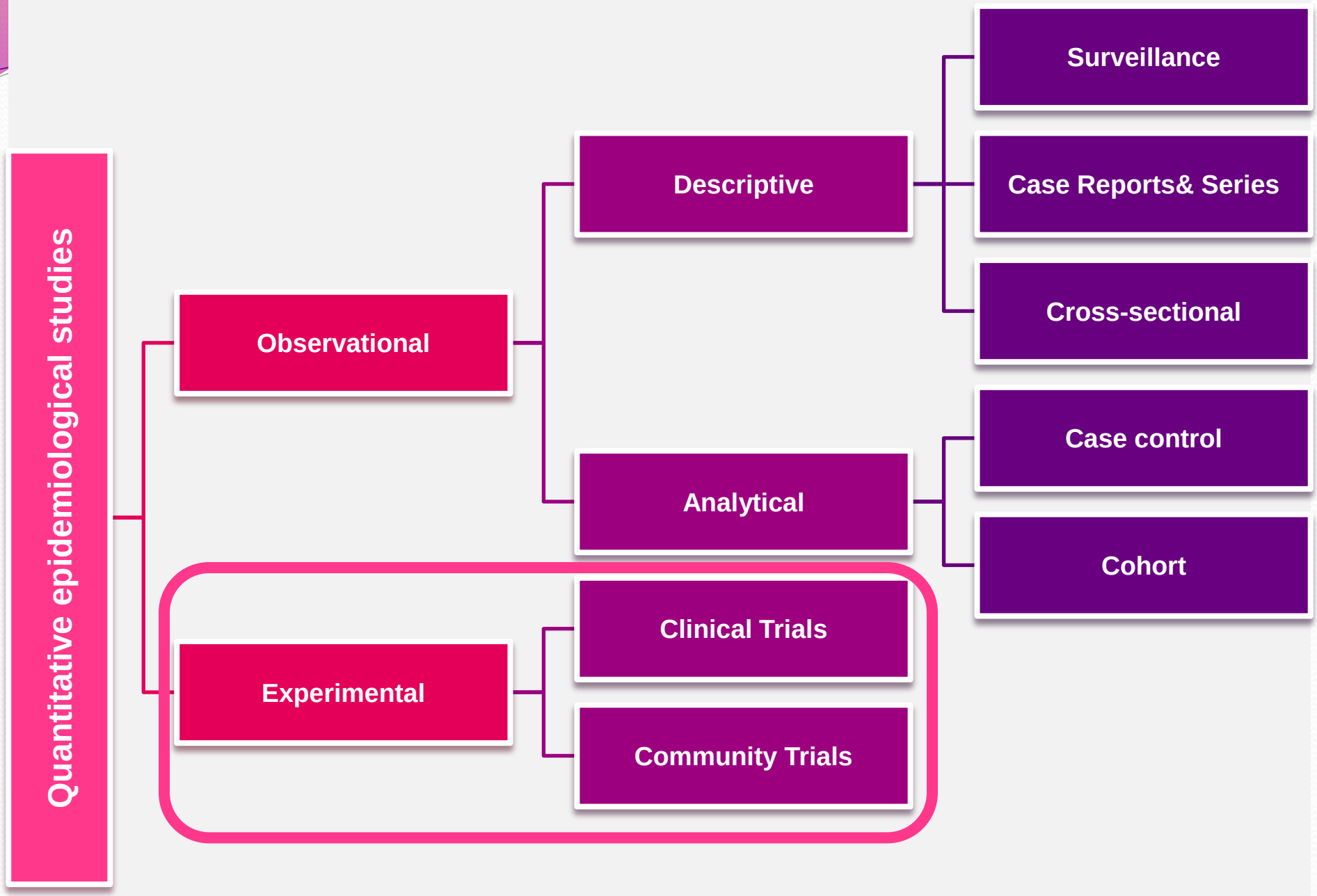
RESEARCH METHODOLOGY


Good Morning

EXPERIMENTAL (INTERVENTION) STUDIES

Study Designs




Quantitative epidemiological studies
Observational
Descriptive
Surveillance
Case Reports& Series
Cross-sectional
Analytical
Case control
Cohort
Experimental
Clinical Trials
Community Trials

Experimental (Intervention) studies: (Proving cause-effect relationship)

It involves an active attempt to change a variable in one or more group of people.

They can be considered as a type of prospective cohort study, because participant are identified on the basis of their exposure status & followed to determine whether they develop the outcome or not but the scientists in experimental study controls the exposure not to be left for chance like cohort study.

Experimental (Interventional) Studies

Community trials

Clinical trials

Ethical points must be considered

It should have beneficial effect to patients, not to harm anyone by intervention

Participants should know what the experiment is and have the right to refuse

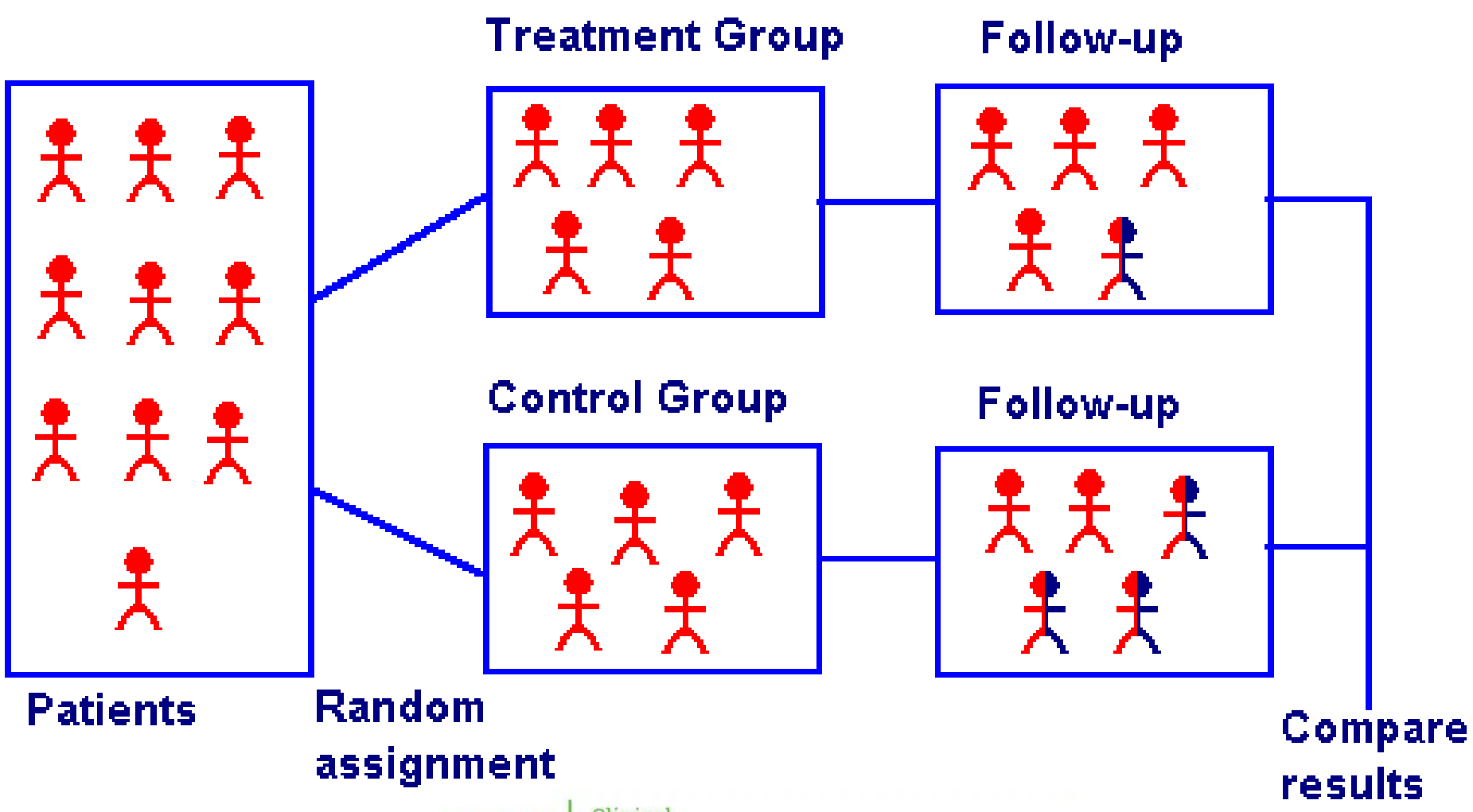
If any unplanned complications occur to any participant he should be excluded from the trial and treated.

1) Clinical Trials

It is usually used to assess the efficacy of a new line of treatment (a new drug for example) or to compare 2 types of treatments (surgical or medical).

The diseased subjects are randomly allocated into 2 groups, "treatment" group (who are given the new drug) & "control group" (who are given the usual treatment or no treatment as placebo).

The results are assessed by comparing the health improvement of the 2 groups at the end.


Treatment Group
Follow-up
Control Group
Follow-up
Patients
Random assignment
Compare results


20 MAY
Clinical Trials Day

Design of a Randomized Clinical Trial

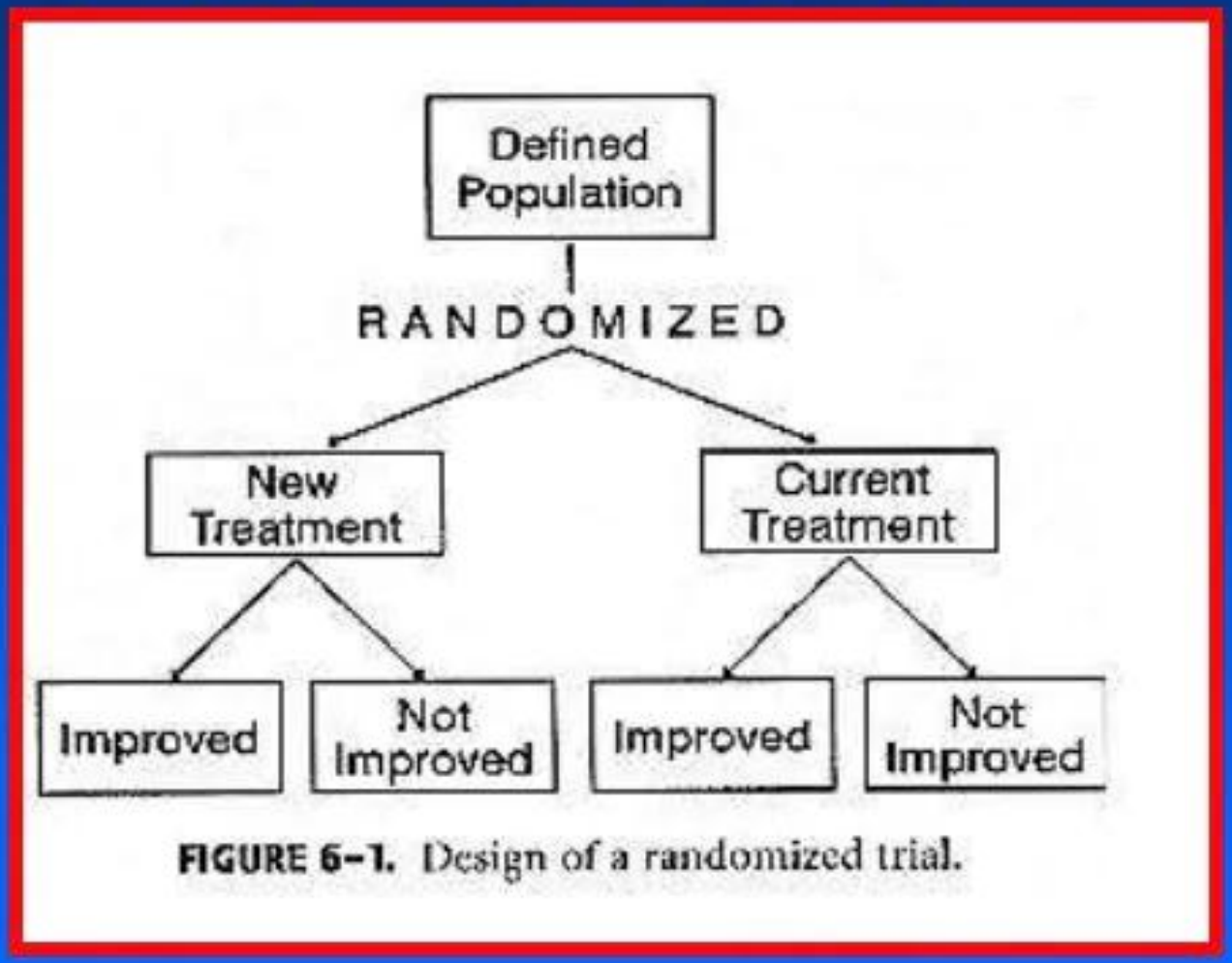
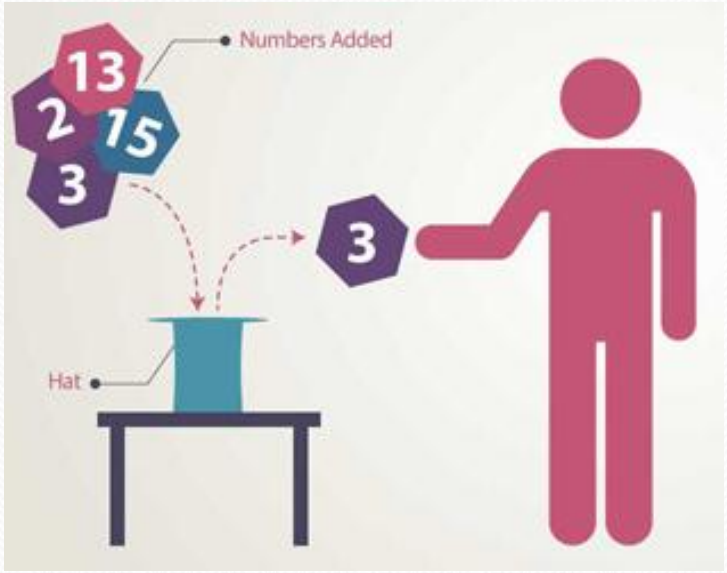


FIGURE 6–1. Design of a randomized trial.

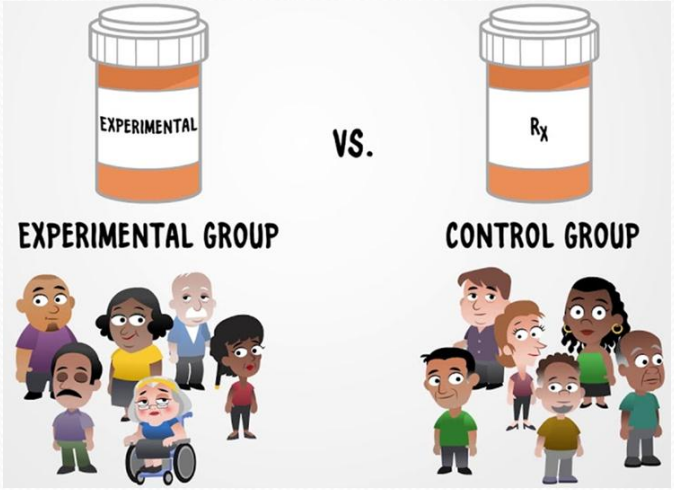
Randomization

- By use of **random table.** It is the most convenient way.
- e.g. odds number assigned to the treatment group & even number to the placebo group.



Random Allocation ?

Yes



No

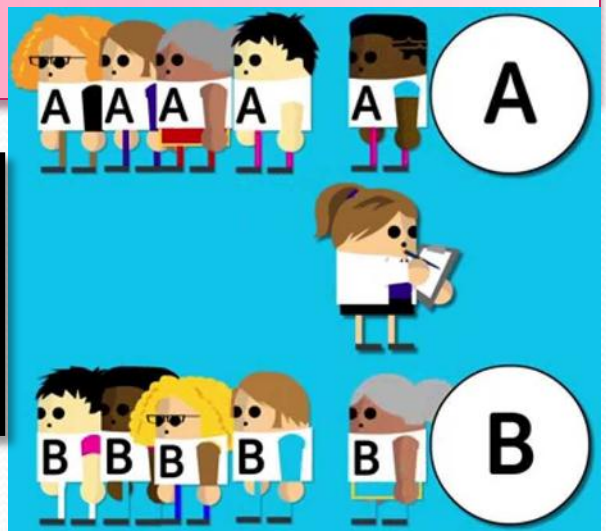
Randomized Controlled trial

(RCT)

Non-Randomized Controlled trial

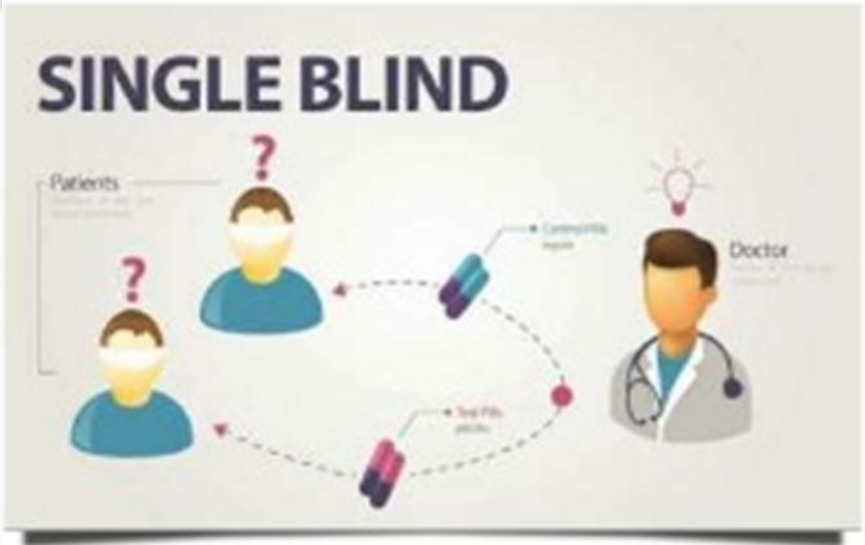
Matching

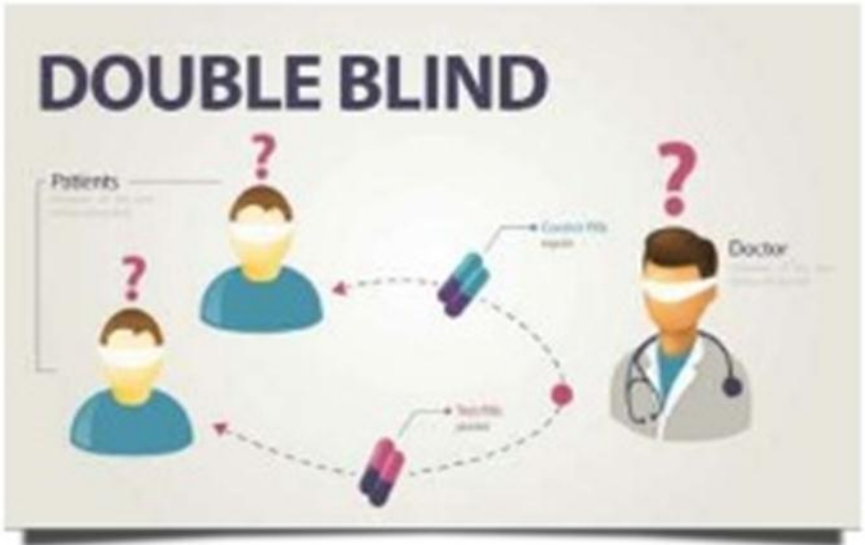
- A matched pair design used to arrange explicitly that the treatment & control groups are similar for the main variables such as age, sex.
- Participants are paired and one from each pair is allocated randomly to either group this matching should be preserved till the level of data analysis.



Single – Double Blind Designs

- A single blind design is when the investigator knows the preparation but not the participants.
- In double blind method, both the investigator & the participants do not know the intervention. A 3rd person (designer) only knows. It assures fair unbiased selection.





Basic types of RCT

1. Preventive trials
2. Intervention trials
3. Therapeutic trials

1.PREVENTIVE TRIALS

- Also known as prophylactic trials
- Focus on individuals without the study disease (i.e, those in the stage of susceptibility).
- Purpose: to determine if a particular intervention reduces the risk of some adverse outcome.
- Ex:

A preventive trial was conducted at the Stanford University school of Medicine to see if reducing the use of television, video tape and video games among a sample of elementary school students reduces obesity. Result showed significant reduction in BMI triceps skin fold thickness, waist circumference and waist to hip ratio among the experimental studies compared to the controls

2.INTERVENTION TRIALS

- These RCT's focus on high risk individuals (i.e, those in the stage of presymptomatic disease)
- Purpose: to test intervention to see if they can forestall disease development.
- Ex:

  A trial to determine the efficacy of treating HTN individuals with ascorbic acid to lower BP might be considered an intervention trail to forestall the development of heart disease and stroke.

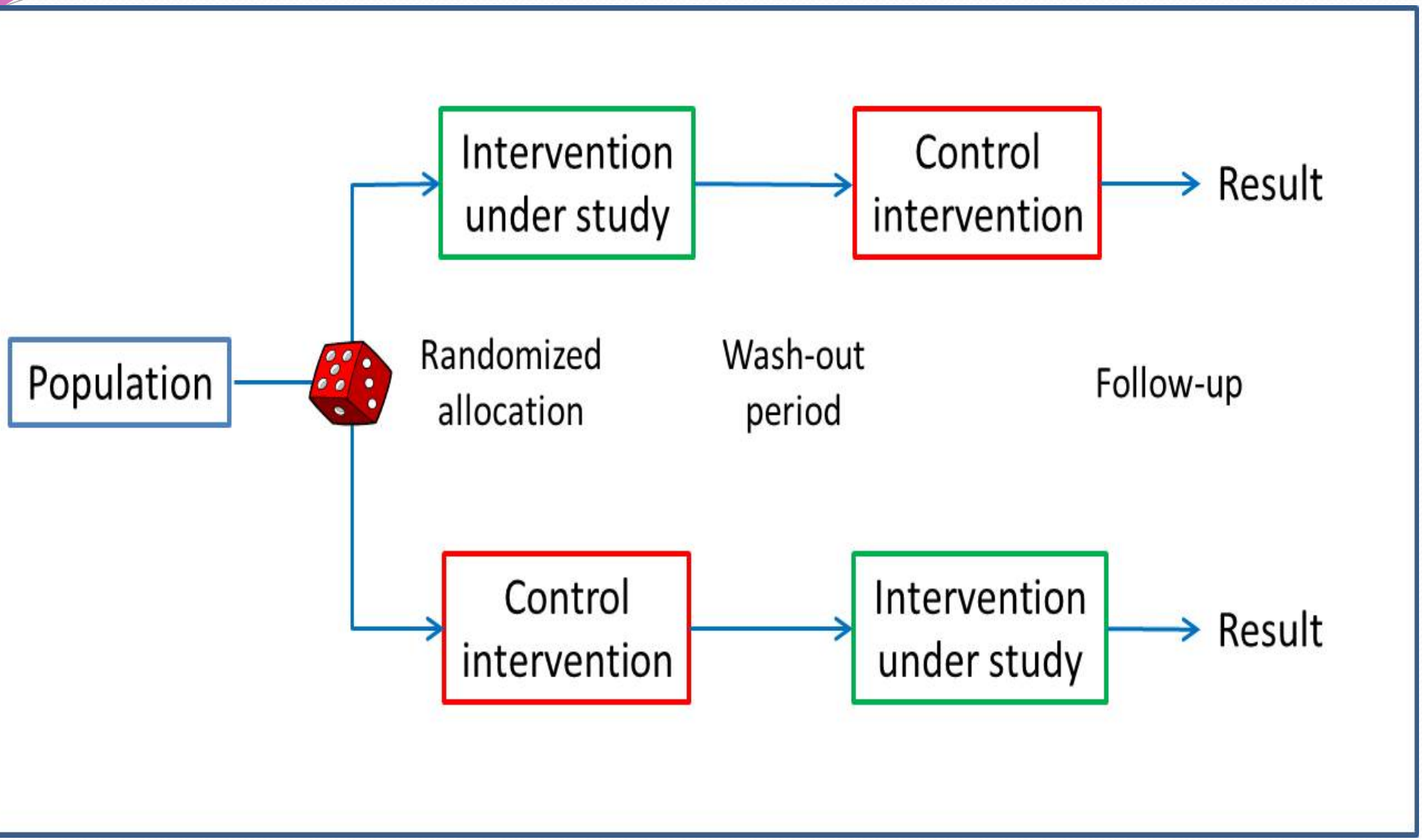
3.THERAPEUTIC TRIALS

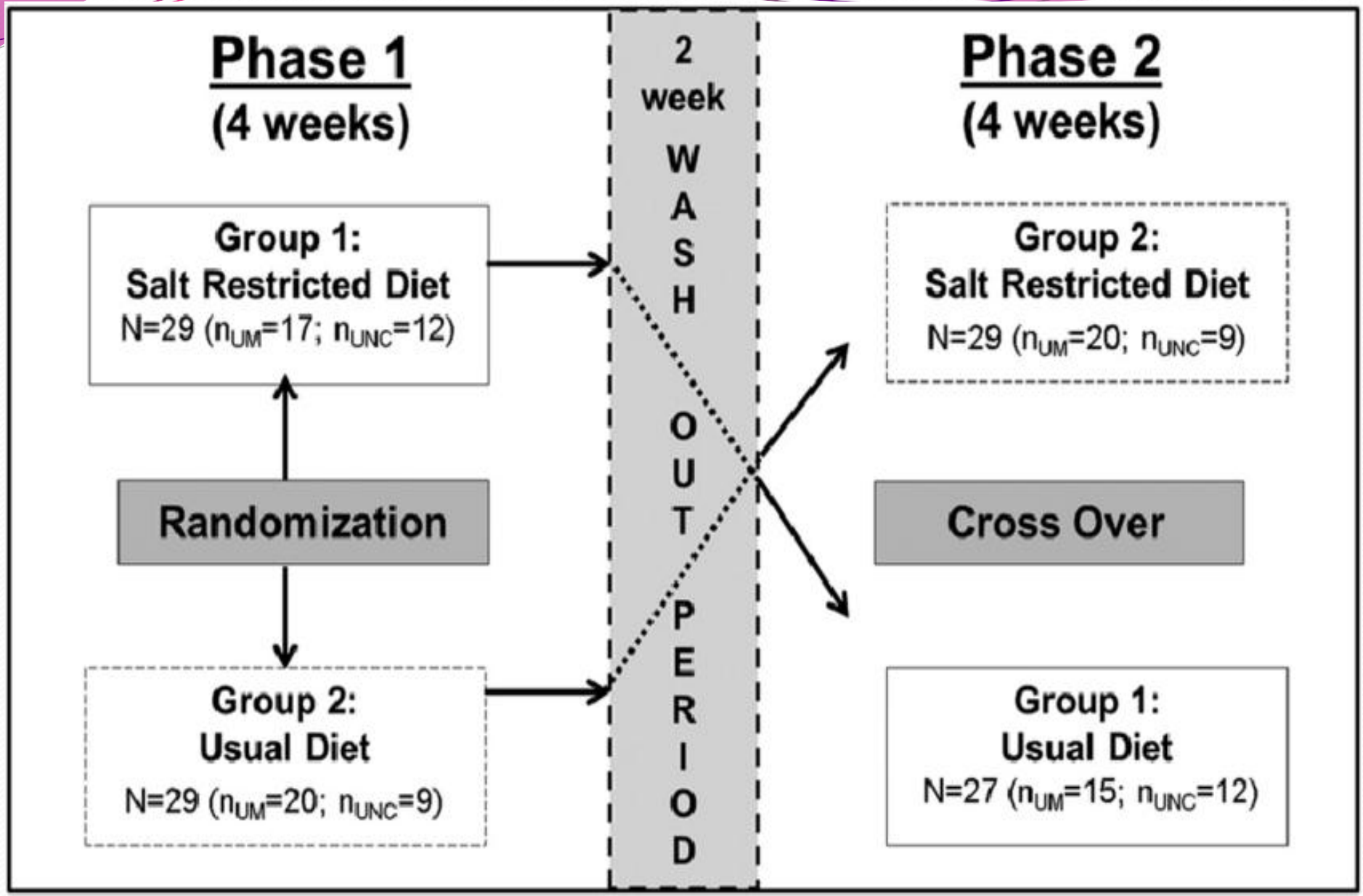
- Focus on patients with existing disease or disability (i.e, those in the stages of clinical disease are diminished capacity)
- Purpose: to test interventions that might cure disease or improve a patients quality of life.
- Commonly used in testing the new drugs and medical procedures.
- Ex:

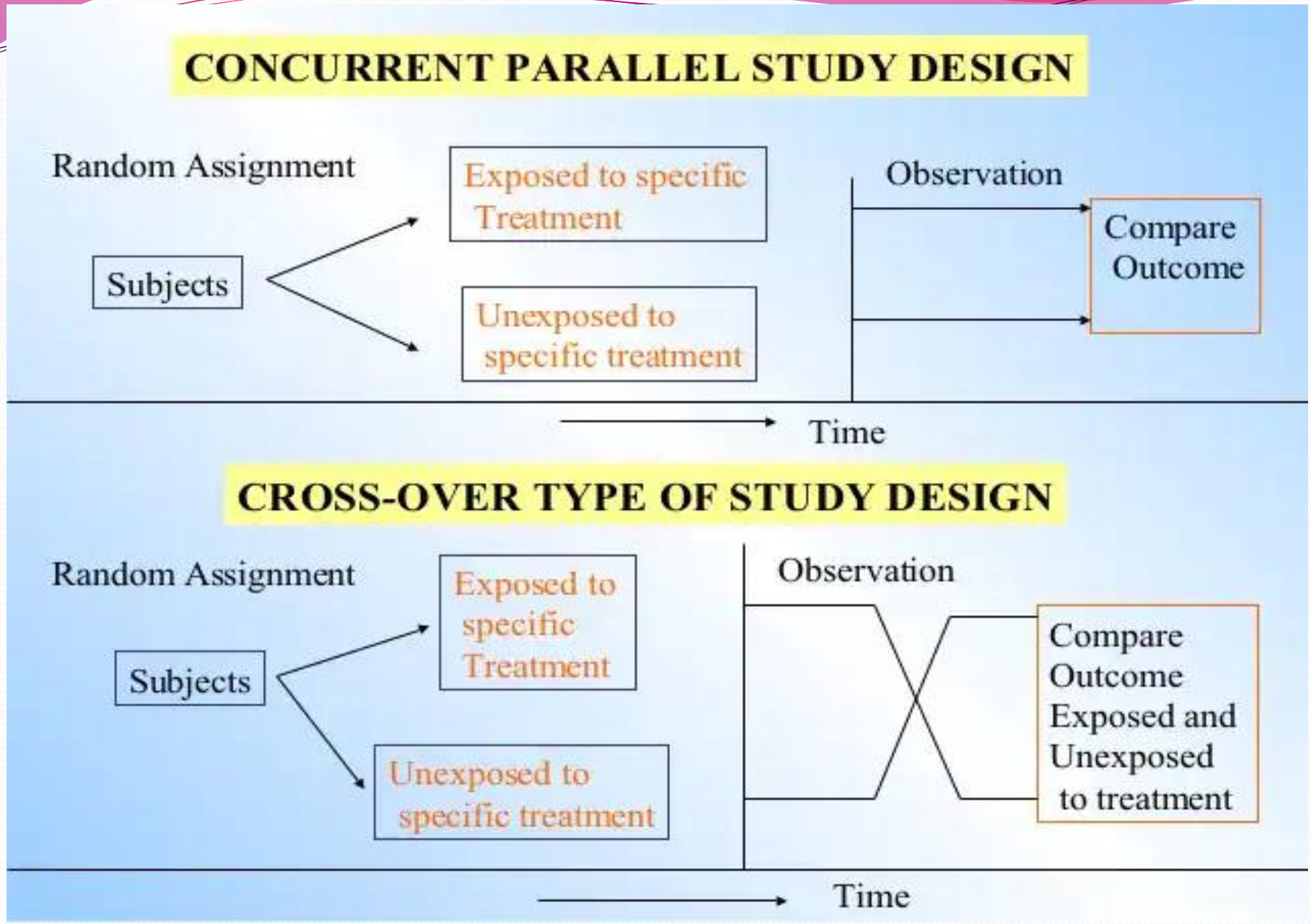
Effectiveness of manual physical therapy and exercise in osteo- arthritis of the knee

Cross–over design:

- In a clinical trial of short term benefits it may be appropriate to use participants as their self-controls.
- For example: the same participant shares in the first drug experiment then shares in the second drug experiment.
- This method will match the difference between participants.


Intervention under study
Control intervention
Result
Population
Randomized allocation
Wash-out period
Follow-up
Control intervention
Intervention under study
Result


Phase 1
(4 weeks)
2 week WASHOUT PERIOD
Phase 2
(4 weeks)
Group 1:
Salt Restricted Diet
N=29 (n_{UM}=17; n_{UNC}=12)
Randomization
Group 2:
Usual Diet
N=29 (n_{UM}=20; n_{UNC}=9)
Group 2:
Salt Restricted Diet
N=29 (n_{UM}=20; n_{UNC}=9)
Cross Over
Group 1:
Usual Diet
N=27 (n_{UM}=15; n_{UNC}=12)


CONCURRENT PARALLEL STUDY DESIGN
Random Assignment
Subjects
Exposed to specific Treatment
Unexposed to specific treatment
Observation
Compare Outcome
Time
CROSS-OVER TYPE OF STUDY DESIGN
Random Assignment
Subjects
Exposed to specific Treatment
Unexposed to specific treatment
Observation
Compare Outcome Exposed and Unexposed to treatment
Time

STRENGTHS	WEAKNESS
• They can demonstrate causal relationships with a high level of confidence due to tightly controlled conditions not possible in observational studies. • They allow investigators to control the exposure levels as needed.	• They have limited applicability due to ethical considerations, It may be difficult to achieve adequate sample size requirements due to reliance on volunteers and strict eligibility criteria. • They are usually costly and time consuming to implement. • An ecological fallacy can occur if inferences based on the group data are made about individuals in the communities.

2) Community trials:

They involve people who are not diseased (but presumed likely to be at risk) & the sample is drawn from the community.

Data collection takes place in the field.

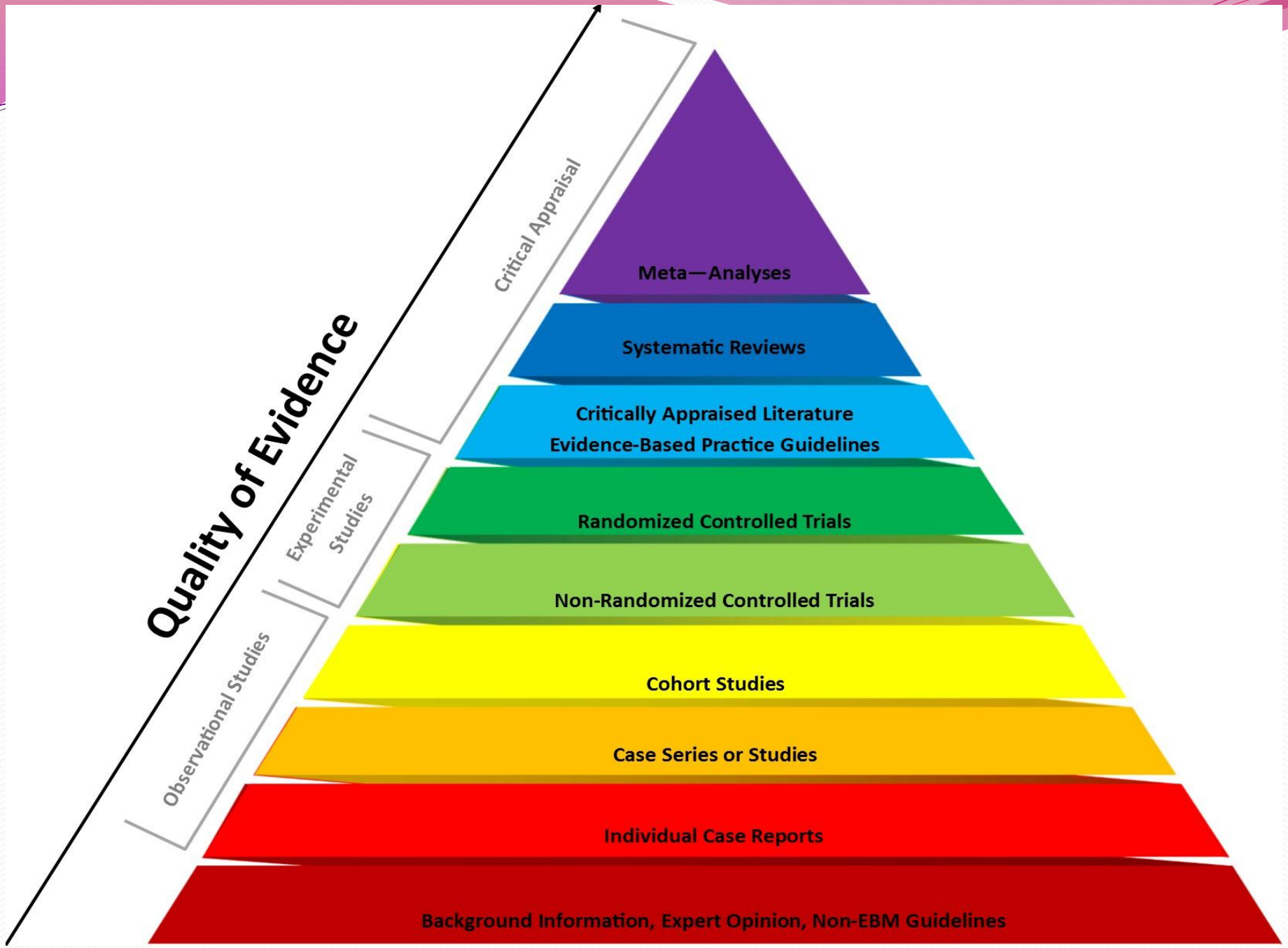
For example: in studies carried out to assess the efficacy of new vaccines.

The participants are divided into 2 groups: 1st who is the experimental group (will take the new vaccine) and the 2nd is the control group (will not take the vaccine).

The participant will be followed to compare the level of occurrence of the disease in both groups. Therefore, these groups should be alike as much as possible in all aspects other than the treatment /intervention received.

CONCLUSION

- One important advantage of experiments over observational studies is that well designed experiments can provide good evidence for causation.


Quality of Evidence
Critical Appraisal
Experimental Studies
Observational Studies
Meta—Analyses
Systematic Reviews
Critically Appraised Literature
Evidence-Based Practice Guidelines
Randomized Controlled Trials
Non-Randomized Controlled Trials
Cohort Studies
Case Series or Studies
Individual Case Reports
Background Information, Expert Opinion, Non-EBM Guidelines

RISK ASSESSMENT

Aim of risk assessment

- To measure the degree of **association** between certain risk factor and the occurrence of a disease
- To **quantify** this risk in order to provide preventive measures.

In cohort study

A group of individuals, some are **exposed** to certain risk factor and others are **not exposed**, are followed over time and the rate of occurrence of the disease among the two groups are compared.

Therefore, we can calculate the **incidence** of occurrence of the disease among both groups.

The ratio between the two incidences is called the **Relative Risk (RR).**

1- The relative risk (RR):

- Ratio of the incidence of the disease among exposed to the incidence of disease among non exposed.
- Measure of the strength of association between the suspected cause & the effects.

$$\mathbf{RR = \frac{Incidence\ among\ exposed}{Incidence\ among\ none\text{-}exposed} = \frac{(I_e)}{(I_0)} = \frac{10}{1} = 10}$$

Interpretation of RR

< 1

- Risk in exposed less than non-exposed "-ve association; possible protective"

1

- Risk in exposed equal to non-exposed "no association"

> 1

- Risk in exposed greater than non-exposed "+ve association; possible casual"

2- Attributable Risk (AR)

- AR is the portion of disease incidence in the exposed that is due to the exposure "the **excess risk** due to specific factor".

- Therefore = the incidence of a disease in the exposed that would be eliminated if the exposure were eliminated.

- **AR = risk(incidence) in exposed – risk(incidence) in non-exposed** which provides the risk difference

$$AR = I_e - I_0$$

Example: to study the association between smoking & cancer lung, a cohort of 200 workers was followed for one year and the following was found:

Cigarette smoking	+ve lung cancer	-ve lung cancer	Total
Yes	35	65	100
No	5	95	100

The incidence of cancer among smokers=**35/100**

The incidence of cancer among non-smokers=**5/100**

RR=0.35/0.05=7

meaning that smokers are at risk of cancer lung **7** times more than non-smokers.

AR=0.35-0.05=0.3

meaning that smoking increase risk of cancer lung by **0.3** (**30%**).

Case-control study

The sampling is carried according to **disease** rather than exposure status. A group of individuals are identified as having the disease (the **cases**) is compared with a group of individuals not having the disease (the **control**) and their status of prior exposure to a certain factor is assessed. Information about incidence among exposure and non-exposure cannot be calculated.

$$OR = \frac{\text{No. of diseased among exposed/ No. of not diseased and exposed}}{\text{No. of diseased among non-exposed/ No. of not diseased and non–exposed}}$$

Exposure	Disease	
	Cases	Control
Exposed	a	b
Not Exposed	c	d
Total	a+c	b+d

How to calculate the odds ratio?

What is the odds that a case is being exposed?

$$\frac{a}{a+c} \div \frac{c}{a+c} = \frac{a}{c}$$

What is the odds that a control is being exposed?

$$\frac{b}{b+d} \div \frac{d}{b+d} = \frac{b}{d}$$

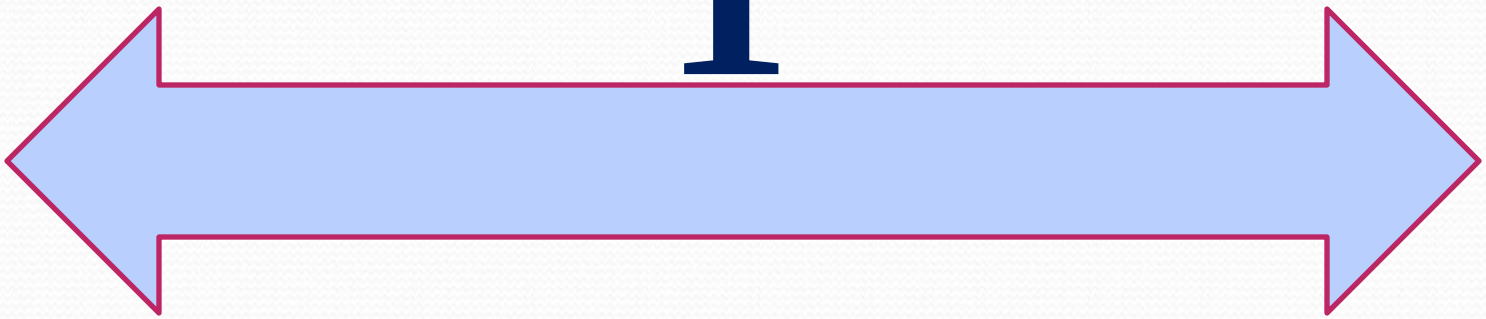
$$OR = \frac{ad}{bc}$$

What is the estimated risk (**odds ratio**)?

$$\frac{a}{c} \div \frac{b}{d} = \frac{ad}{bc}$$

An odds ratio of

1.0 or (≈ 1.0)	• **Means that the odds of exposure among cases is the same as the odds of exposure among controls**	• The exposure is not associated with the disease.
> 1.0	• Means that the odds of exposure among cases is greater than the odds of exposure among controls.	• The exposure may be a risk factor for the disease
< 1.0	• Means that the odds of exposure among cases is lower than the odds of exposure among controls	• The exposure may be protective against the disease.



Protective

No relation between exposure & disease

Risk

Example: to study the association between smoking & cancer lung, a cohort of 200 workers was followed for one year and the following was found:

Cigarette smoking	+ve lung cancer	-ve lung cancer	Total
Yes	35	65	100
No	5	95	100

OR= 35/65 ÷ 5/95 = 10.23

which is different from the **relative risk**.

Therefore **OR** should be used cautiously


THANK YOU
THANK YOU VERY MUCH
MERCI
OBRIGADO
ASANTE
GRAZIE
SPASIBO
MULTUMESC
VINAKA
ZIKOMO
SUWUN
MATONDO
EIO
MAAKE
どうも
СПАСИБО
БАЯРЛАЛАА
MOCHCHAKKERAM
SAAGHA XALDA HWA
RAIBH MAITH AGAT
NIRRINGRAZZJAK
MATUR NUWUN
MOCHCHAKKERAM
WELALIN
CHOKRANE
KHUBLEI
MATONDO
MAAKE