بسم الله الرحمن الرحيم

Interventional studies

This type of study is similar to cohort studies, but the difference is that the investigator themselves will allocate the exposure i.e. Individuals are included on the basis of exposure, but the investigators allocate the exposure.

Two types

- **1-Randomized Controlled Clinical Trial (RCT):** Individuals similar at the beginning are randomly allocated and exposed to a treatment group and a control group. The outcomes of the groups are compared after sufficient follow-up time. Properly executed, the RCT is the strongest evidence of the clinical efficacy of preventive and therapeutic procedures in the clinical setting.
- **2- Community trials :** communities instead of individuals are allocated and exposed to an experiment**.** The experimental group a community exposed to an experimental factor and the control a group a community that is not exposed to the experimental factor. The results are compared.

Randomized Controlled Clinical Trial (RCCT)

Two groups are selected.

The 1st is the experimental group. The subjects are exposed to a factor as an experiment under medical supervision.

The 2nd is the control group. The subjects are not exposed to that factor.

- These two groups are selected on random basis.

Random selection means: every subject in the sample has the an equal chance to be chosen in the experimental group or in the control group.

- The main difference between experimental and analytic cohort studies, is that the investigator in the experimental studies, allocates by himself the study groups into: **experimental group and the control group**. While in the analytic cohort studies the participants are naturally allocated into exposed and non exposed.

Strengths or advantages :-

1. It’s regarded as the gold standard of the epidemiological studies. It is the strongest & the most direct epidemiology evidence to judge the causal association . " like an experiment in the lab where the exposure is under the investigators control , who controls all the factors except the risk factor ".

2. it can detect mild to moderate difference (10-20%) which is difficult in cohort studies .

e.g. conducting a study on which medication should be given after a myocardial infarction MI, should it be B-blockers or Ca++ channel blockers for the prognosis of MI ? Here the difference will be very small (2-5%) but very important to find it out to save patients lives .

3. It can control & manipulate many confounders .
4. It can demonstrate the temporal relationship between the exposure & outcome with the highest degree of confidence .

Limitations or disadvantages :-

1. Expensive & time consuming
2. It doesn't represent the real life situation " because we control all the other factors except the exposure .
3. Ethical problems : for certain factors , there is some doubt about the benefit or harm to the study subject.
4. Feasibility problems: were it is difficult to find the control" non exposed: group.

e.g. a study in a city about Vitamin C supplement & disease , here it was hard to find a control group because the majority of the population used vitamin C supplement .

Types :

1. Therapeutic or secondary prevention trials :-

* the study groups are "Diseased"

it is conducted on patients to evaluate the effect of certain drugs or procedures in minimizing symptoms, complications or death.

e.g. to study the best treatment for coronary heart disease, is it

medical treatment or surgical treatment.

So :

Group 1 : patients with CHD treated by Medication on.

Group 2 : patients with CHD treated Surgically on .

& then we studied CHD mortality rate between both groups .

2. <u>Preventive or primary prevention trials</u> :-

Conducted on healthy people who are at normal risk or high risk to develop an outcome .

e.g. polio vaccine to prevent poliomyelitis ..

Group 1 : took a full vaccination

Group 2 : took a placebo.

Result " vaccination " group 1 was successful

Selection of study groups :-

I- Reference population :

Represents the group on which the results will be applicable

e.g. a study to prevent MI in males at 45 y of age, the reference population Will be males at 45y of age.

II-Experimental population.

Represents the group on whom the study " trials " will be conducted upon .

There should be :-

1. **Sufficient outcome :-**

There must be good no. of people in the study having to outcome . e.g. recovery or death

2. **complete & accurate information :**

Especially information about follow-up

The participants should be informed about :

The aim of the study, possible benefits, side effects & the possibility of having a placebo during the study period .

Causes of exclusion :-

1. Definite history of out come under study.
2. Definite need for the study treatment " like someone has Diabetes Mellitus we must give him a treatment & not placebo.
3. Contraindication to the study treatment. e.g. giving aspirin to someone with peptic ulcer.

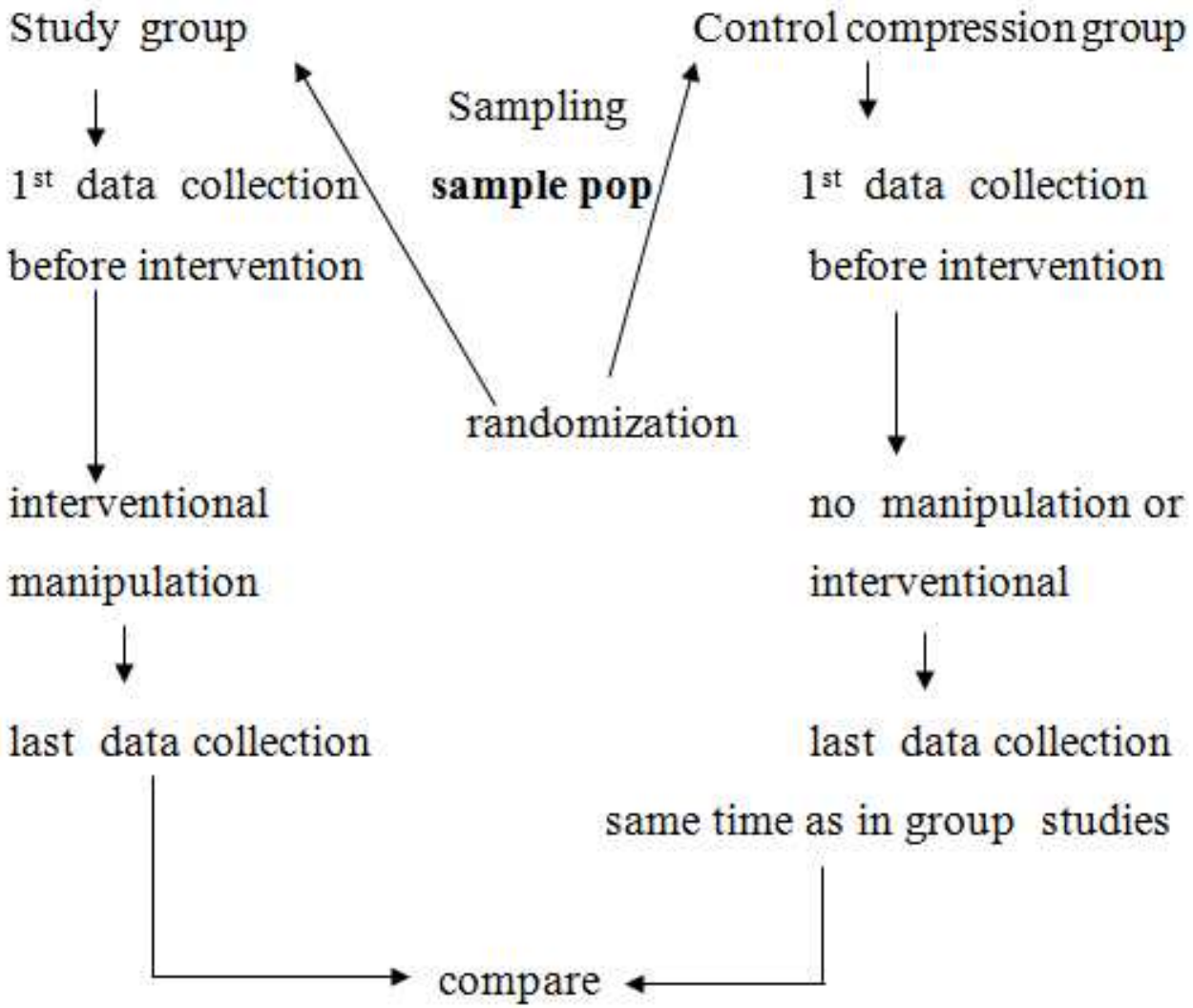
***Volunteer Bias:-**

The volunteers do not represent the true community population on which we will generalize the study result " because not everyone will accept to participate in the study".

***Randomization**

Allocation of the individuals to be included in the exposure status is random, that is to say every individuals is given an equal chance to be allocated in the exposure or non-exposure groups .

Study population



NOTE : The measure of association between disease & exposure is the relative risk attributable risk and attributable risk % as in cohort study .

Maintenance of Assessment of compliance :

Compliance : the commitment of the study participants by the treatment التزام المشارك.

The **non- compliance** is the major problem in the intervention. it's related to the complexity & the length of the follow-up .

Causes of non -compliance :

(non –compliance decrease as the statistical power of the study)

1. Development of side effects .
2. Forgetting to take the treatment.
3. Withdrawal from trials.
4. Choosing the alternative method.
5. The intervention becomes contraindicated .

Enhancement of compliance is by :

1. Inclusion of interested & reliable group
2. Frequent contact with participants
3. Use of calendar pack of study treatment as in contraceptive pills each pill has a date on it .
4. Provision of in centuries " حوافز " either financial or medical insurance "

How do check compliance:-

1. Self report
2. Pill count of non used medication
3. Used of biochemical markers: e.g. we give a drug that is secreted in urine & check the presence of the drug in urine .

Placebo: A placebo is the non treatment material used in a control group in place of the actual treatment. If a drug is being evaluated, the inactive vehicle or carrier is used alone so it is as similar as possible in appearance and in administration to the active drug. Placebos are used to blind observers and, for human trials, the patients to which group the patient is allocated.

Limitation of placebo :

1. There is a tendency of the patient to report a good result of any treatment.
2. Tendency to report side effects with the Rx or placebo

Stopping rules :

These are criteria for early termination or modification of the trial when the appearance of extreme benefit or harm from early results .

This stopping should be :-

1. Done by an external investigation
2. Based on experience of adequate no .of subjects
3. The statistical difference should be high .

The power of clinical trials to detect mild to moderate differences depend on :-

- Sample size
- Total no. can be increase by
- selection of high risk group
- increasing the length of follow up .

Sampling

A sample is a group of individuals that is a subset of a population and has been selected from the population in some fashion (random or haphazard).

Types :

1.Simple Random Sampling / Allocation:

Require a complete list of identified individuals making up the population (the list frame) before the sampling can be done. Choose haphazardly the size of participants is small. e.g. 10 of 30 no.

2. **Systematic Sampling:** From a random start in first n^{th} individuals, sampling every n^{th} animal as they are presented at the sampling site (clinic, chute, ...). Systematic sampling will not produce a random sample if a cyclical pattern is present in the important characteristics of the individuals as they are presented.

3. **Stratified Random Sampling:** The group from which the sample is to be taken is first stratified on the basis of a important characteristic related to the problem at hand (e.g., age, parity, weight) into subgroups such that each individual in a subgroup has the same probability of being included in the sample but the probabilities are different between the subgroups or strata.

4. **Cluster Sampling:** Staged sampling in which a random sample of natural groupings of individuals (houses, households) are selected and then sampling all the individuals within the cluster.

WAYS OF EXPRESSING THE RESULTS OF RANDOMIZED TRIALS

1. The results of randomized trials can be expressed in a number of ways. The risks of death or of developing a disease or complication in each group can be calculated, and the *reduction in risk* (efficacy) can then be calculated.

$$\text{Efficacy} = \frac{\left(\begin{array}{c}\text{Rate in those who}\\ \text{received the placebo}\end{array}\right) - \left(\begin{array}{c}\text{Rate in those who}\\ \text{received the vaccine}\end{array}\right)}{\text{Rate in those who received the placebo}}$$

2. Another approach to reporting results from randomized trials is to calculate the *ratio of the risks* in the two treatment groups (the relative risk).
3. In addition, often we compare the survival curves for each of the groups and determine whether they differ.

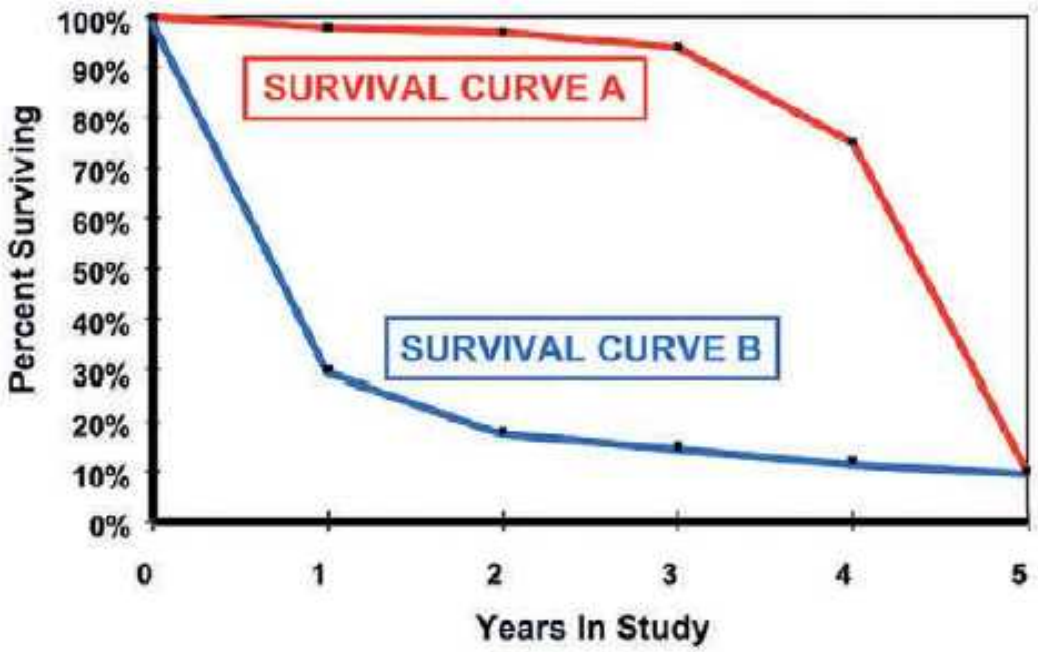


Figure 6-10. Five-year survival curves in two hypothetical populations.

4. Another approach, therefore, for expressing the results of randomized trials is to estimate the number of patients who would need to be treated (NNT) to prevent one adverse outcome such as one death. This can be calculated by:

$$\text{NNT} = \frac{1}{\left(\begin{array}{c}\text{Rate in}\\ \text{untreated group}\end{array}\right) - \left(\begin{array}{c}\text{Rate in}\\ \text{treated group}\end{array}\right)}$$