
بسم الله الرحمن الرحيم
In the name of ALLAH
the most Beneficent and the most merciful

EXPERIMENTAL EPIDEMIOLOGY

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- The experimental studies involve some action, intervention or manipulation such as deliberate application or withdrawal of the suspected cause or
- changing one variable in the causative chain in the experimental group while making no change in the control group, and observing and comparing the outcome of the experiment in both the groups.

EXPERIMENTAL EPIDEMIOLOGY

- The aims of experimental studies may be stated as follows :
- (a) to provide "scientific proof" of aetiological (or risk) factors which may permit the modification or control of those diseases : and

EXPERIMENTAL EPIDEMIOLOGY

- (b) to provide a method of measuring the effectiveness and efficiency of health services for the prevention, control and treatment of disease and improve the health of the community.

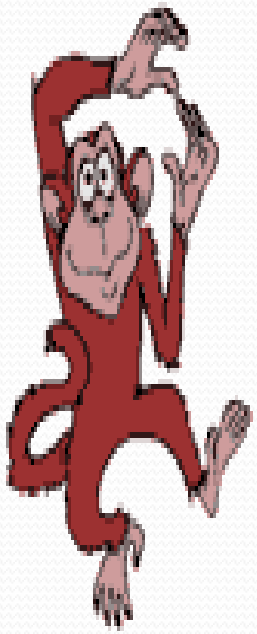
Experimental Studies can be done in :

1) Animals

2) Human Beings

ANIMAL STUDIES

They play an important role in men's quest for knowledge about himself & his environment.



Animal studies

- Experimental reproduction of human disease.
- Testing the efficacy of drugs and vaccines
- Completing the natural history of disease

ADVANTAGES:

- Animals can be bred in labs.
- Animals can be manipulated easily by examiner
- The animals multiply rapidly & help to carry out his experiments
- Cost effective

DISADVANTAGES

- All human diseases cant be produced in animals.
- Findings of experiment cant be applicable to human beings.

HUMAN EXPERIMENTS:

- USEs
- To study occurrence of diseases in human & effectiveness of one method over other method.

HUMAN EXPERIMENTS:

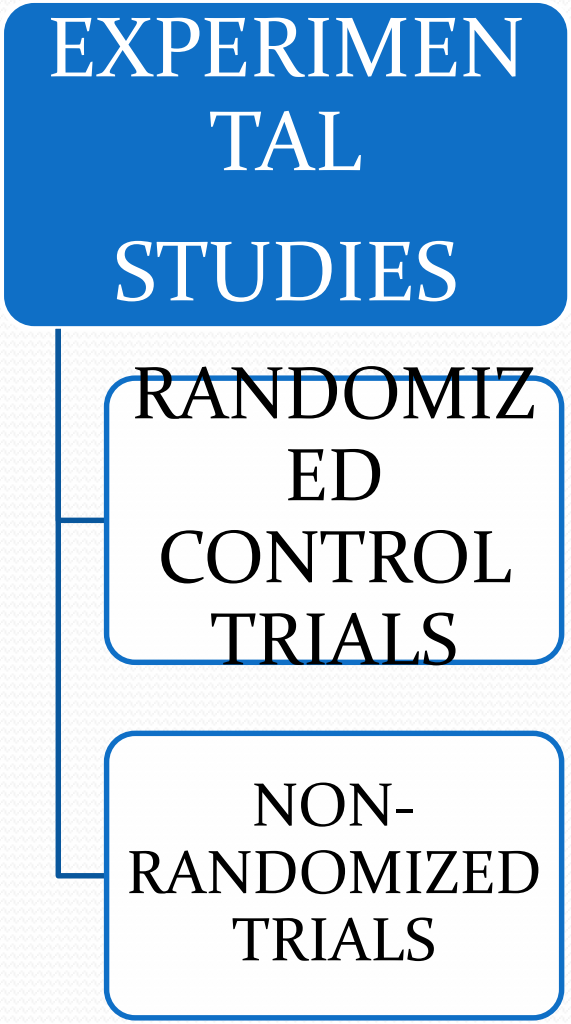
- ADVANTAGES

- Gives precise knowledge of disease in humans.
- Gives correct idea of preventive & therapeutic measures.

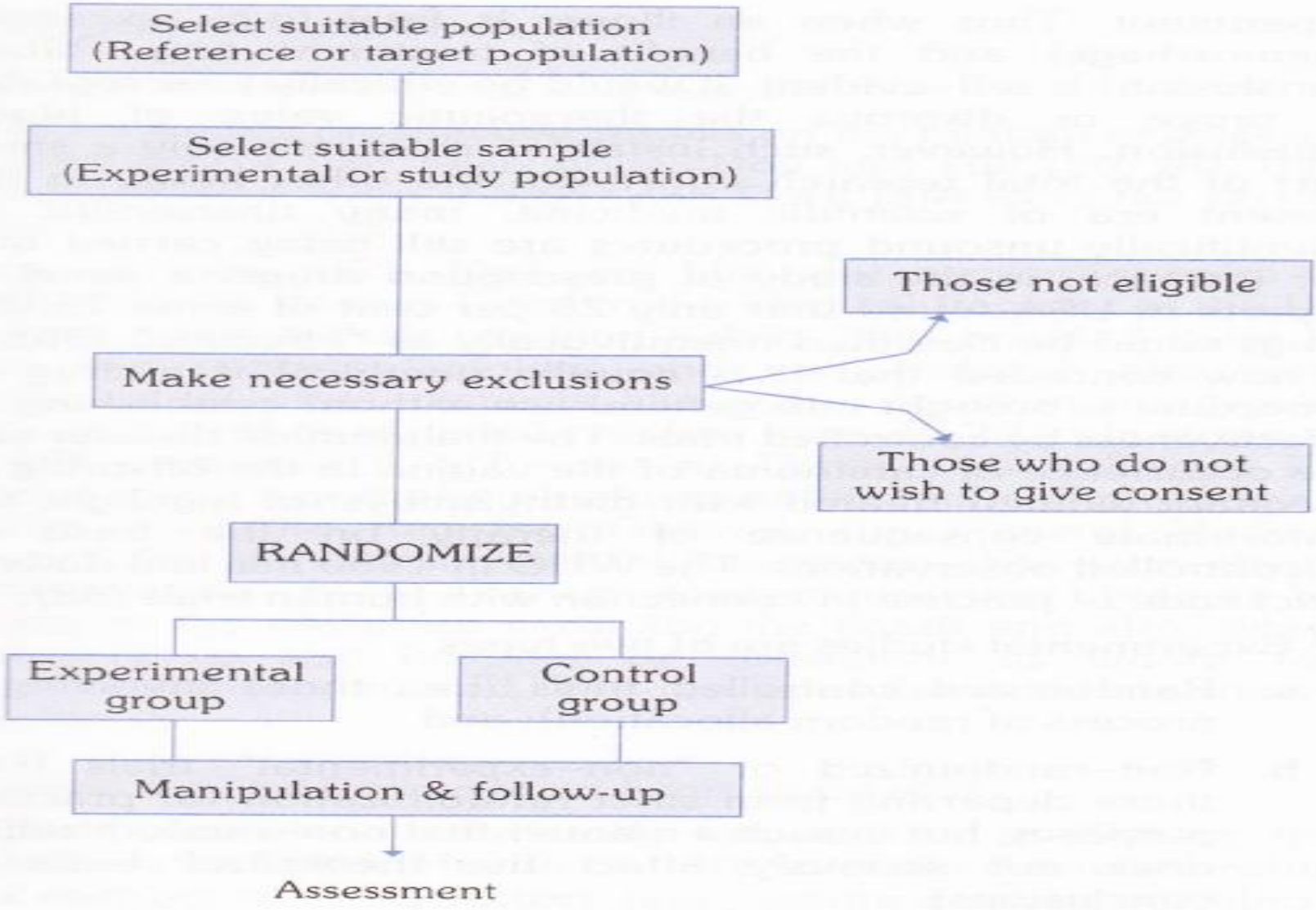
HUMAN EXPERIMENTS:

- DISADVANTAGES
  - Ethical and logistic problems.
  - Unnecessary exposure of humans to the hazards of causative agents

Experimental studies



Flow chart of RCT



EXPERIMENTAL EPIDEMIOLOGY

- 1. Drawing up a protocol.
- 2. Selecting reference and experimental populations.
- 3. Randomization.
- 4. Manipulation or intervention.
- 5. Follow-up.
- 6. Assessment of outcome.

1. The protocol

- One of the essential features of a randomized controlled trial is that the study is conducted under a strict protocol.
- The protocol specifies the aims and objectives of the study, questions to be answered, criteria for the selection of study and control groups, size of the sample, the procedures for allocation of subjects into study and control groups, treatments to be applied when and where and how to what kind of patients, standardization of working procedures and schedules as well as responsibilities of the parties involved in the trial, up to the stage of evaluation of outcome of the study.

2. Selecting reference and experimental populations

- (a) Reference or target population : It is the population to which the findings of the trial, if found successful, are expected to be applicable (e.g., a drug, vaccine or other procedure). A reference population may be as broad as mankind or it may be geographically limited or limited to persons in specific age, sex, occupational or social groups.

2. Selecting reference and experimental populations

- Thus the reference population may comprise the population of a whole city, or a population of school children, industrial workers, obstetric population and so on according to the nature of the study.

2. Selecting reference and experimental populations

- (b) Experimental or study population : The study population is derived from the reference population. It is the actual population that participates in the experimental study. Ideally, it should be randomly chosen from the reference population, so that it has the same characteristics as the reference population. If the study population differs from the reference population, it may not be possible to generalize the findings of the study to the reference population

3. Randomization

- Randomization is a statistical procedure by which the participants are allocated into groups usually called "study" and "control" groups, to receive or not to receive an experimental preventive or therapeutic procedure, manoeuvre or intervention. Randomization is an attempt to eliminate "bias" and allow for comparability.

3. Randomization

- Randomization is the "heart" of a control trial. It will give the greatest confidence that the groups are comparable so that "like can be compared with like". It ensures that the investigator has no control over allocation of participants to either study or control group, thus eliminating what is known as "selection bias". In other words, by random allocation, every individual gets an equal chance of being allocated into either group or any of the trial groups.

4. Manipulation

- To intervene or manipulate the study (experimental) group by the deliberate application or withdrawal or reduction of the suspected causal factor (e.g., this may be a drug, vaccine, dietary component, a habit, etc) as laid down in the protocol

5. Follow-up

- This implies examination of the experimental and control group subjects at defined intervals of time, in a standard manner. The duration of the trial is usually based on the expectation that a significant difference (e.g., mortality) will be demonstrable at a given point in time after the start of the trial.
- Thus the follow-up may be short or may require many years depending upon the study undertaken

6. Assessment

- The final step is assessment of the outcome of the trial in terms of :
- (a) Positive results : that is, benefits of the experimental measure such as reduced incidence or severity of the disease, cost to the health service or other appropriate outcome in the study and control groups.

6. Assessment

- (b) Negative results : that is, severity and frequency of side-effects and complications, if any, including death. Adverse effects may be missed if they are not sought.

6. Assessment

- Bias may arise from errors of assessment of the outcome due to human element. These may be from three sources :
- First, there may be bias on the part of the participants, who may subjectively feel better or report improvement if they knew they were receiving a new form of treatment. This is known as "subject variation".

6. Assessment

- Secondly there may be observer bias, that is the investigator measuring the outcome of a therapeutic trial may be influenced if he knows beforehand the particular procedure or therapy to which the patient has been subjected. This is known as "observer bias."

6. Assessment

- Thirdly, there may be bias in evaluation that is, the investigator may subconsciously give a favourable report of the outcome of the trial. Randomization cannot guard against these sorts of bias, nor the size of the sample. In order to reduce these problems, a technique known as "blinding" is adopted, which will ensure that the outcome is assessed objectively

Blinding

- Blinding can be done in three ways
- (a) SINGLE BLIND TRIAL : The trial is so planned that the participant is not aware whether he belongs to the study group or control group.
- (B) DOUBLE BLIND TRIAL : The trial is so planned that neither the doctor nor the participant is aware of the group allocation and the treatment received.

Blinding

- (C) TRIPLE BLIND TRIAL : This goes one step further. The participant, the investigator and the person analyzing the data are all "blind". Ideally, of course, triple blinding should be used; but the double blinding is the most frequently used method when a blind trial is conducted. When an outcome such as death is being measured, blinding is not so essential.

SOME STUDY DESIGNS

1. Concurrent parallel study designs.

- In this situation, comparisons are made between two randomly assigned groups, one group exposed to specific treatment, and the other group not exposed. Patients remain in the study group or the control group for the duration of the investigation

SOME STUDY DESIGNS

2. Cross-over type of study designs

- With this type of study design, each patient serves as his own control. As before, the patients are randomly assigned to a study group and control group. The study group receives the treatment under consideration. The control group receives some alternate form of active treatment or placebo.

SOME STUDY DESIGNS

- The two groups are observed over time. Then the patients in each group are taken off their medication or placebo to allow for the elimination of the medication from the body and for the possibility of any "carry over" effects. After this period of medication the two groups are switched. Those who received the treatment under study are changed to the control group therapy or placebo, and vice versa.

Concurrent and Cross over study

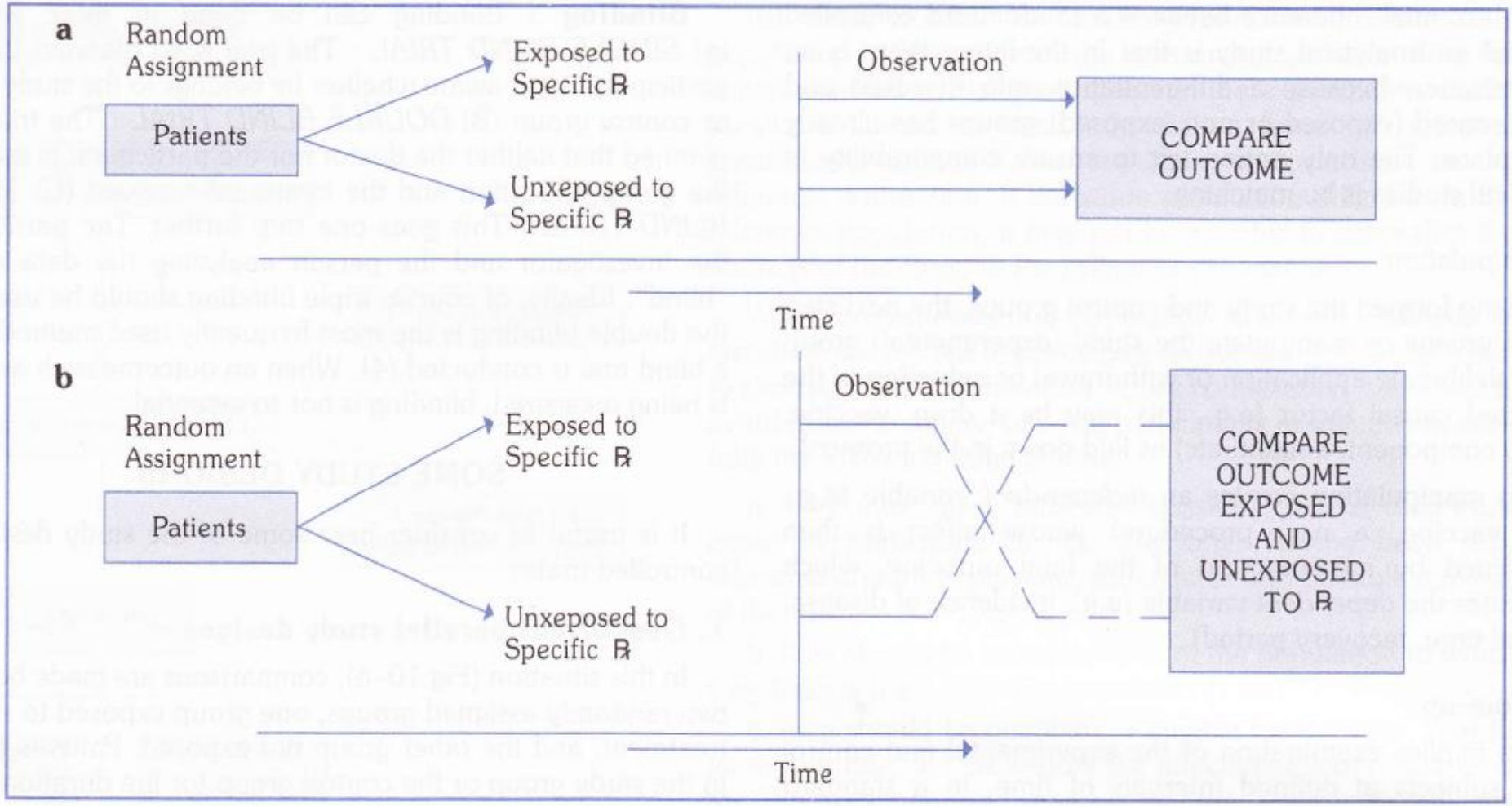


FIG. 10

Schematic diagram of the design of concurrent parallel and cross-over controlled therapeutic trials (69)

TYPES OF RANDOMIZED CONTROLLED TRIALS

- 1. Clinical trials
- 2. Preventive trials
- 3. Risk factor trials
- 4. Cessation experiments
- 5. Trial of aetiological agents
- 6. Evaluation of health services

NON-RANDOMIZED TRIALS

- Although the experimental method is almost always to be preferred, it is not always possible for ethical, administrative and other reasons to resort to a randomized controlled trial in human beings. For example, smoking and lung cancer and induction of cancer by viruses have not lent themselves to direct experimentation in human beings.

NON-RANDOMIZED TRIALS

- Secondly, some preventive measures can be applied only to groups or on a community-wide basis (e.g., community trials of water fluoridation). Thirdly, when disease frequency is low and the natural history long (e.g., cancer cervix) randomized controlled trials require follow-up of thousands of people for a decade or more.

NON-RANDOMIZED TRIALS

- The cost and logistics are often prohibitive. These trials are rare. In such situations, we must depend upon other study designs these are referred to as non-randomized (or non-experimental) trials.

NON-RANDOMIZED TRIALS

- A few examples of· non-randomized trials are
- 1. Uncontrolled trials
- 2. Natural experiments
- 3. Before and after comparison studies


Thanks