EXPERIMENTAL STUDIES

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INTRODUCTION

- A scientific experiment is an organized and detailed series of steps used to accept or reject the hypothesis.
- It is the preferred way to test the hypothesis.
- Researchers introduce an intervention and study the effects.
- This intervention may be drug, device, method etc.

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There are several steps to follow:

- **Identify the Research Questions:** The first step is to identify the research question or hypothesis that you want to test.
- The research question should be specific and clearly defined.
- **Define the Population and Sample:** It is important to define the population and sample so that the result can be generalised to the population.
- **Select the Independent Variables:** The independent variables is the variable that is manipulated in the study. It should be selected based on its potential to affect the dependent variables.

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- **Select the Dependent Variables:** The dependent variables is the variable that is measured in the study. It should be selected based on its relevance.
- **Determine the Experimental Design:** there are several methods of experimental design such as pre-test/post-test design, randomised controlled etc.
- **Develop a Hypothesis:** A hypothesis is a statement that predicts the relationship between independent and dependent variables.
- **Select the Control Group:** A control group is a group of participants who are not exposed to independent variables.

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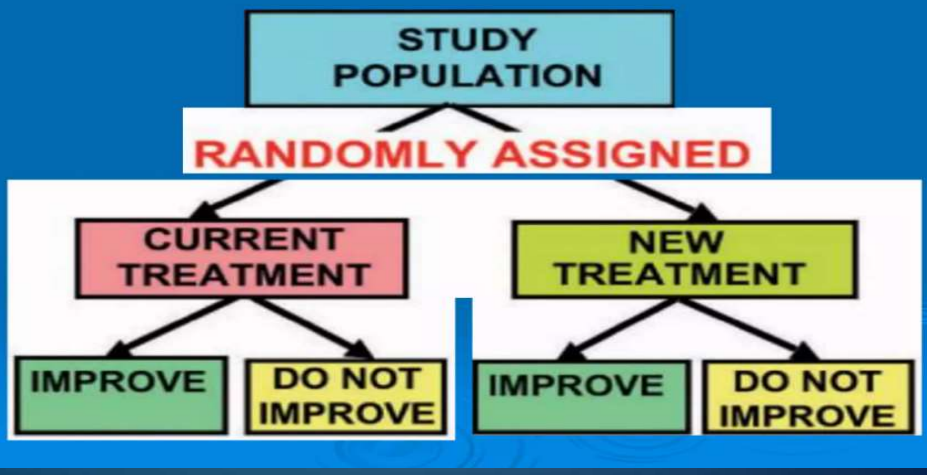
- **Determine the Sample Size:** the sample size is the number of participants in the study. It should be determined on the basis of power analysis.
- **Collect the Data:** Data can be collected using a variety of methods such as surveys, observation and physiological measures.
- **Analyse the Data:** The data can be analysed using statistical method.

Randomized Controlled Trial (RCT) (Synonym: Randomized Clinical Trial)

"An epidemiological experiment in which subjects in a population are randomly allocated into groups, usually called *study* and *control* groups to receive and not receive an experimental preventive or therapetuic procedure, maneuver, or intervention"

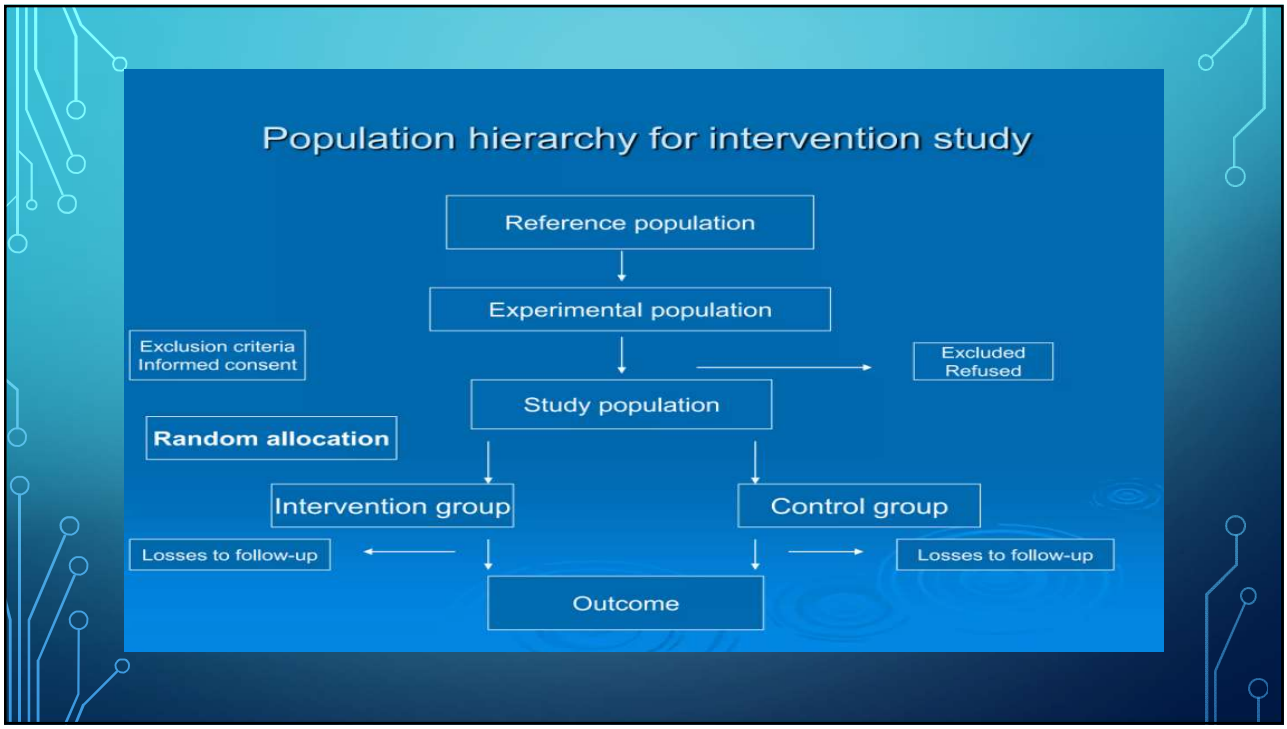
John M.Last, 2001

Design of a randomized trial



Basic steps of RCT

1. The protocol
2. Selecting reference and experimental populations
3. Randomization
4. Intervention
5. Follow up
6. Assessment



1. The protocol

- Rationale
- Aims and objectives, Research questions
- Design of the study: selection of study and control groups
- Ethics: patient consent, adverse events
- Documentation
- Procedure

2. Selecting Reference and Experimental Populations

a. Reference or target population - population to which the findings of the trial, if found successful, are expected to be applicable (eg. drugs, vaccines, etc.)

b. Experimental or study population - actual population that participates in the experimental study

Participants must fulfill the following criteria:

- Must give informed consent
- Should be representative of the population
- Should be qualified or eligible for the trial

3. Randomization

- Heart of the control trial
- Procedure: Participants are allocated into study and control groups
- Eliminates bias and allows comparability
- Both groups should be alike with regards to certain variables that might affect the outcome of the experiment
- Best done by using table of random numbers

Both groups should be alike with regards to certain variables that might affect the outcome of the experiment

4. Manipulation / Intervention

- Deliberate application or withdrawal or reduction of a suspected causal factor
- It creates an independent variable

5. Follow Up

- Implies examination of the experimental and control group subjects
  - at defined intervals of time,
  - in a standard manner, with equal intensity, under the same given circumstances
- Attrition: Inevitable losses to follow up

6. Assessment

- Positive results
- Negative results

- Biases: Subject variation, Observer bias, Evaluation bias

- Can be corrected by blinding

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

COMMUNITY TRAILS

- Assign intervention to entire community or other grouping of people (Eg. School)
- If one community receives the intervention, other one serves as the control.
- Four steps:
  1. Selection of participating communities
  2. Collection of baseline data on the study outcome
  3. Assignment and application of the community intervention
  4. Follow up, outcome assessment and evaluation

Non-Randomized Trials

- Also known as Quasi-Experimental Designs.
- It is a type of research in which the investigator manipulates the study factor but does not assign individual subjects randomly to the exposed & non- exposed groups.
- These are designed as:
  - It is always not possible for ethical, administrative and other reasons to resort to a RCT.
  - Some preventive measures apply only to groups or community-wide basis.
  - When disease RCT require follow-up of thousands of people for a decade or more.
- As here randomization is not done. So, low comparability than RCT and chances of spurious results are high than RCT.

Non-Randomized Trials

- These studies may be of following types:
  - Uncontrolled Trials
  - Natural Experiments
  - Before and after comparison studies
    - With control
    - Without control

Uncontrolled Trials

- There is no comparison group.
- Initially may be helpful in :
  - Evaluating whether a specific therapy appears to have any value in a particular disease.
  - To determine an appropriate dose.
  - To investigate adverse reactions etc.
- Use of implied "**historical controls**" i.e., the experience of earlier untreated patients affected by the same disease.

Historical controls

- **Advantage:**
  - When the disease is uniformly fatal and a new drug becomes available a decline in case fatality that parallels the use of the drug would suggest that the drug is having effect.
- **Disadvantages:**
  - Data Records :
    - We are comparing very meticulous system for data collection to the medical records for the historical controls. So, whether a true difference in outcome was there or not in doubted.
  - Many things change over time (ancillary supportive therapy, living conditions, nutrition and lifestyles).
  - Less likely to have clearly defined patient criteria.

Natural Experiments

- When experimental studies are not possible in humans, **Natural circumstances** that "mimic" an experiment are identified.
- **Example:** Group of smokers and non-smokers (naturally separated).
- **Other** population groups involved include: migrants, religious or social groups etc.
- **John Snow's** discovery that **cholera** is a water borne disease was an outcome of a **natural experiment.**

Before and after comparison studies without control

- Experiment serve as its own control.
- Incidence of disease before and after introduction of intervention is measured here.
- Standard for comparison: events which took place prior to use of new treatment or intervention.
- All group differences are virtually eliminated.
- Examples:
  - Prevention of scurvy among sailors by James Lind (1750).
  - Studies on transmission of cholera by John Snow (1854).
  - Prevention of polio by Salk and Sabin.

Before and after comparison studies with control

- In absence of control group, results of comparison may be misleading.
- Alternative is to utilize a "**Natural control group**" i.e., the one provided by nature or natural circumstances.
- Example:
  - Effect of seat belt legislation in one district on RTA related mortality, compared with the another district with no seat belt legislation.