Experimental Epidemiology

DR. M. SIVA DURGAPRASAD NAYAK, MD, PHD

ASSOCIATE PROFESSOR

Contents

- Introduction
- Randomized Control Trials
  - Steps in RCT
  - Some RCT study designs
- Non Randomized Control Trials

Introduction

“How do we know a drug actually works?”

“Is observing patients enough to prove effectiveness?”

“What is the strongest type of evidence in medical research?”

The answer for all these questions is **Experimental Epidemiology**

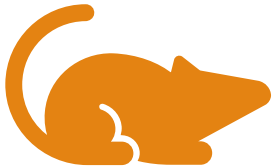
Types of Epidemiological studies

Observational studies

Descriptive studies

Analytical studies

- Case control study
- Cohort study

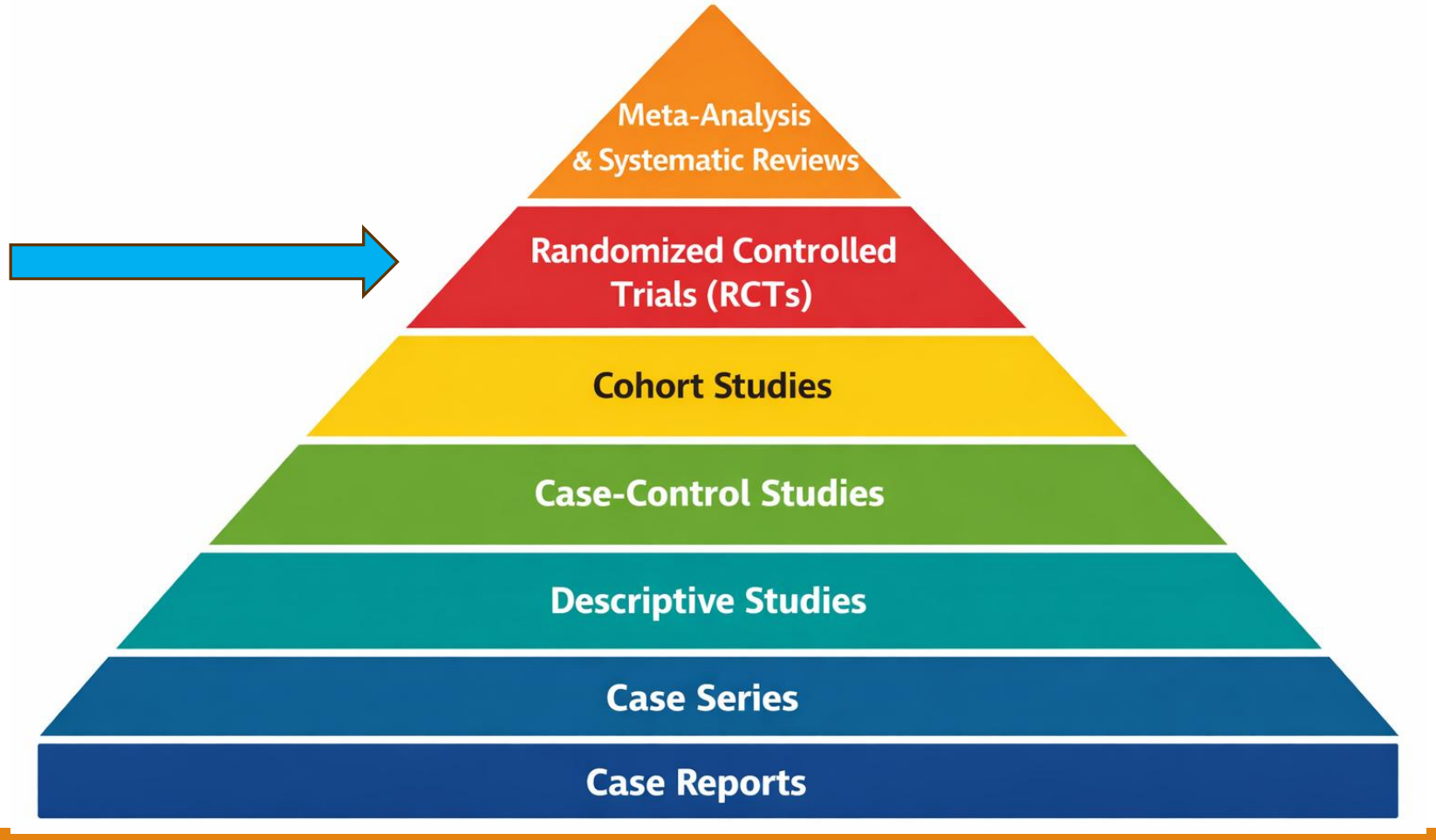


Experimental studies

Randomized Control trial

Non Randomized Control Trial

Different levels of studies



Introduction

Experimental studies involve

- some action, intervention, manipulation such as deliberate application
- or withdrawal of suspected cause
- or changing variable in the causative chain

Aims of Experimental studies

1. To provide scientific proof

2. To provide a method of measuring effectiveness and efficiency of health services for the prevention, control and treatment of disease and improve health of the community.

Animal studies vs Human experiments

Criteria	Animal Studies	Human Experiments
Purpose	To explore disease pathogenesis, toxicology, pharmacology, and safety of interventions before human use.	To evaluate the effectiveness and safety of preventive or therapeutic interventions in human populations.
Ethical Considerations	Ethical guidelines exist but fewer restrictions compared to human studies;	Strict ethical guidelines; requires Institutional Ethics Committee approval, informed consent, and adherence to human research ethics.
Examples	Testing toxicity of a new drug in mice; studying vaccine immune response in rabbits; cancer induction experiments in rats.	Randomized controlled trial of a new antihypertensive drug; field trial of malaria vaccine; community trial of fluoridation of water.

Animal studies vs Human experiments

Criteria	Animal Studies	Human Experiments
Advantages	1. High experimental control. 2. Shorter life cycle allows quicker results. 3. Genetic uniformity reduces variability. 4. Useful for studying disease mechanisms.	1. Results directly applicable to humans. 2. Measures real clinical outcomes. 3. Provides strong evidence for effectiveness of interventions.
Limitations	1. Results may not fully apply to humans due to biological differences. 2. Ethical concerns regarding animal welfare. 3. Some human diseases cannot be reproduced accurately in animals.	1. Ethical constraints limit experimental manipulation. 2. Expensive and time-consuming. 3. Participant non-compliance and loss to follow-up. 4. Risk to human participants must be minimized.

Five classic examples of animal studies

1. Development of Polio Vaccine - Monkeys
2. Discovery of Insulin - Dogs
3. Tuberculosis transmission studies - Guinea pigs
4. Cancer immunotherapy - Mouse models
5. Atherosclerosis research - Rabbits

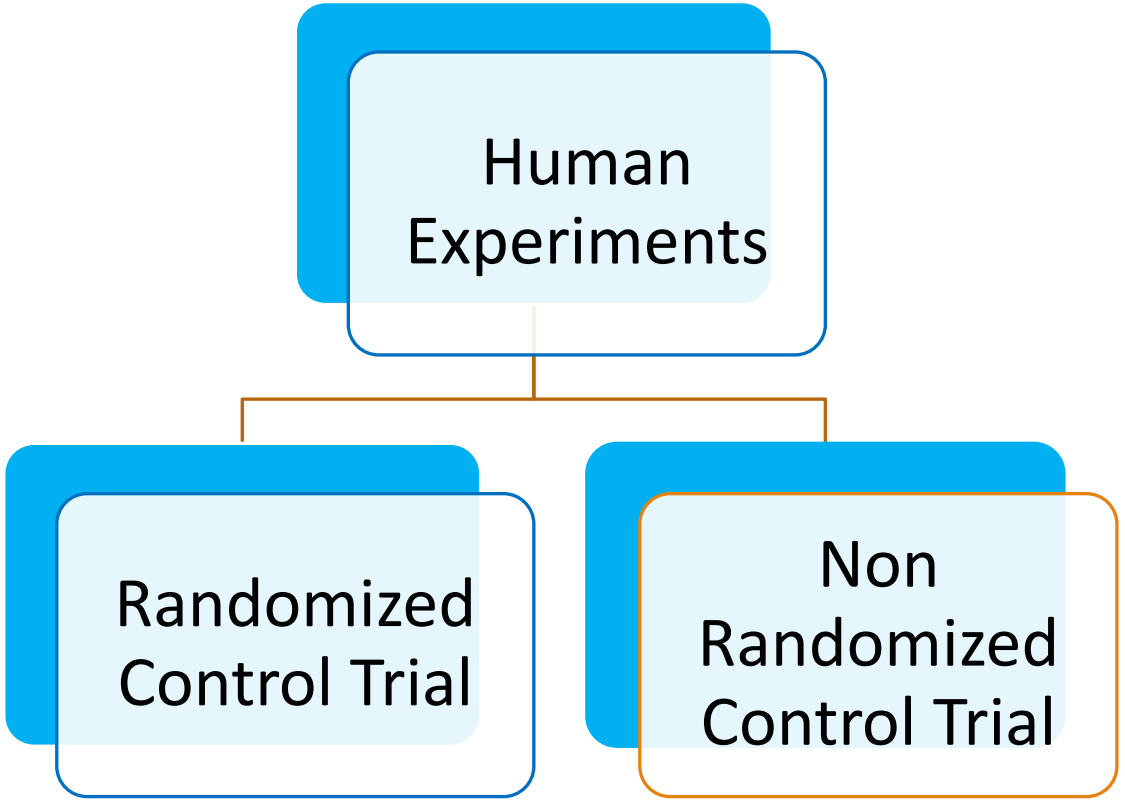
Human Experiments

- Involving Humans to investigate disease aetiology, to evaluate preventive or therapeutic measures
- However involving humans includes ethical problems
- WHO in 1980 laid down a strict code of practice in connection with human trials

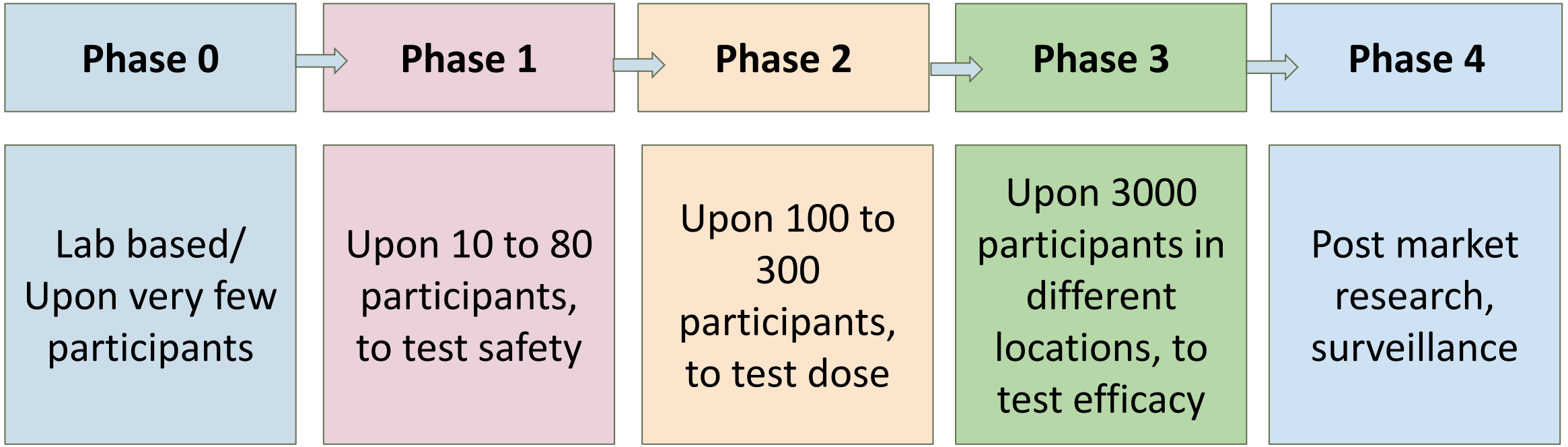
First Human experiment

In the year 1747, James Lind conducted one of the first controlled clinical experiments by giving different treatments to sailors with scurvy and found that those who received citrus fruits (oranges and lemons) recovered rapidly, demonstrating that citrus cures scurvy.

Types of Human Experiments



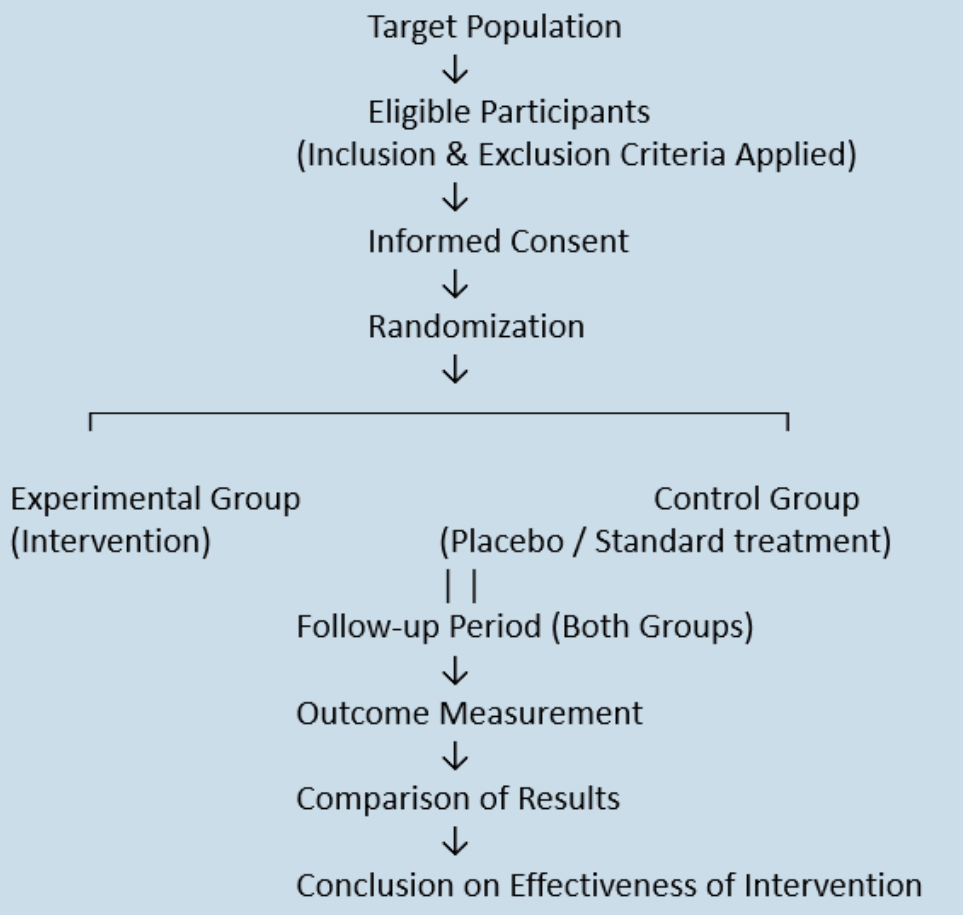
Phases in controlled trials



Randomized Control Trial

Basic steps in conducting Randomized Control Trial are

1. Drawing up a protocol
2. Selecting Reference and Experimental populations
3. Randomization
4. Manipulation or Intervention
5. Follow up
6. Assessment of Outcome



Drawing up a protocol

- Protocol is a plan/ blueprint of study
- It specifies the aims and objectives of the study
- It specifies the methodology of study since from selection of participants, allocation of groups, interventions applied, measuring the outcome, etc..
- Strict adherence to protocol is essential feature of RCT

Registration of RCTs in India

Selecting study participants

- Participants should voluntarily involved in the study
- Study participants will be categorized into two groups
- Reference population → Experimental population → Study & Control groups

Selecting Experimental population

- It is derived from reference population
- It is important to avoid losses to follow up after selecting experimental population
- The participants must fulfill the following criteria
  - must give informed consent
  - should be representative of reference population
  - should be eligible for trial (Hypertensives to test Anti Hypertensive drugs)

Randomization

- Randomization is a statistical procedure to categorize participants into study group or control group
- Randomization is the heart of RCT
- Randomization eliminate bias and allow for comparability
- Investigator has no control over allocation of participants to either study or control group thus eliminating selection bias.

Randomization

- Randomization can be done by using random numbers table or Excel software
- Different types of Randomization - Simple randomization, Block randomization, Stratified randomization, Cluster randomization
- Investigators should not involve in Randomization
- Statistician will allocate groups for study participants to eliminate selection bias
- Statistician give covered envelopes with information about study participants group. So that study participant also unaware about the group. It will eliminate hawthorne bias.

Manipulation

- The next step is to intervene the study group
- It may be application or withdrawal or reduction of suspected causal factor
- Example: Drug/ Vaccine/ Dietary component/ Habit
- It creates an independent variable whose effect is constitutes dependent variable
- Anti Hypertensive drug usage → Hypertension controlled/ Not Controlled

Follow up

- It includes examination of study participants at different intervals of time
- Examination should be in a standard manner
- Repeat the examination in the same manner in the same time frame
- Example: Measure Blood pressure of Right hand only with sphygmomanometer
- Measuring instrument should be same every time.
- Once sphygmomanometer and once digital apparatus is not correct
- **Care should be taken to eliminate observer bias/ Instrumental bias**

Assessment

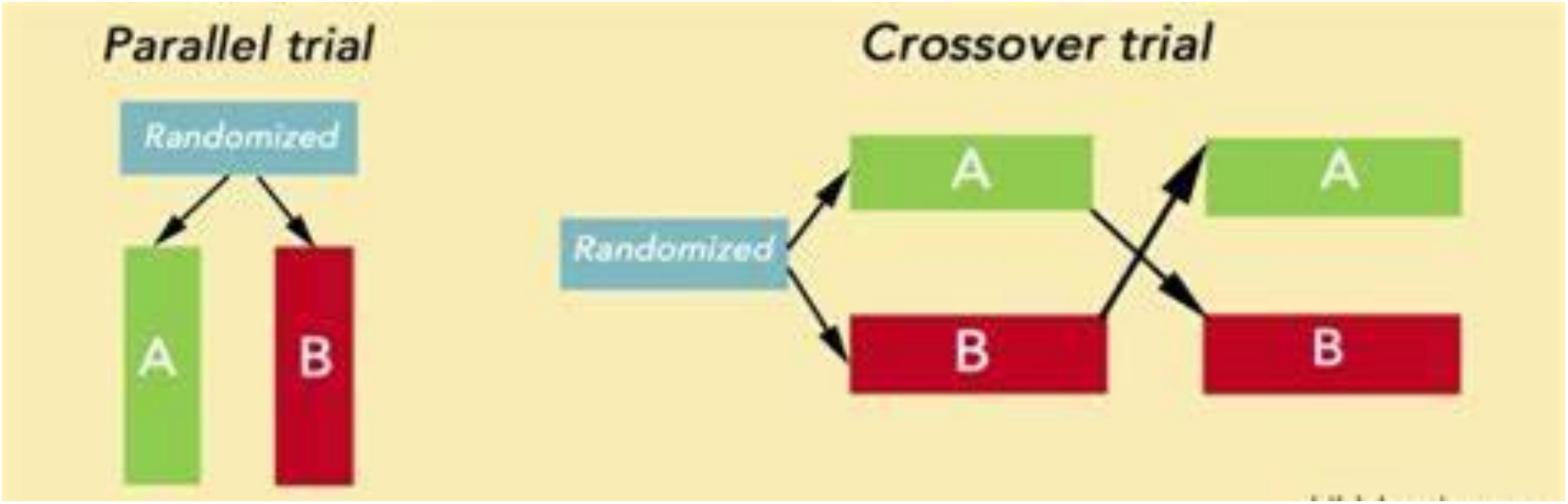
- Assessment of the outcome of trial in terms of
- Positive results (Reduced intensity or severity of disease)
- Negative results (Side effects and complications)
- Both positive and Negative results should be compared in both study and control groups and should be tested for statistical significance of results

Blinding

Type of Blinding	Explanation
Single Blind Trial	Participant not aware about to which group he belongs
Double Blind Trial	Participant and intervening person (Doctor) not aware about group allocation
Triple Blind Trial	Participant, intervening person (Doctor) and person analysing the data not aware about group allocation

Some study designs

1. Concurrent parallel study design
2. Cross over study design



Types of RCTs

Type of Trial	Purpose	Public Health Example
1. Clinical Trial	To evaluate efficacy/safety of a therapeutic intervention	Testing a new oral rehydration formulation for acute diarrhoea in children in India
2. Preventive Trial	To prevent occurrence of disease in healthy individuals	HPV vaccination trial to prevent cervical cancer among adolescent girls

Types of RCTs

Type of Trial	Purpose	Public Health Example
3. Risk Factor Trial	To study the effect of modifying a risk factor	Salt-reduction intervention to measure effect on population blood pressure levels Stanford three community study, Oslo study, Multiple Risk factor Intervention trial (MRFIT)
4. Cessation Experiment	To test interventions that help individuals stop harmful behaviours	Nicotine-replacement therapy (NRT) trial to promote smoking cessation in adult smokers

Types of RCTs

Type of Trial	Purpose	Public Health Example
5. Trial of Aetiological Agents	To test a suspected causal factor by altering exposure	Trial reducing indoor air pollution exposure (clean cookstoves) to assess impact on childhood pneumonia
6. Evaluation of Health Services	To measure the effectiveness, efficiency, or quality of health services	Comparing home-based vs facility-based postnatal care services for reducing neonatal mortality
7. Evaluation of Screening Tests	To determine accuracy, feasibility, or impact of a screening method	Comparing VIA (visual inspection with acetic acid) vs Pap smear for early detection of cervical cancer in low-resource settings

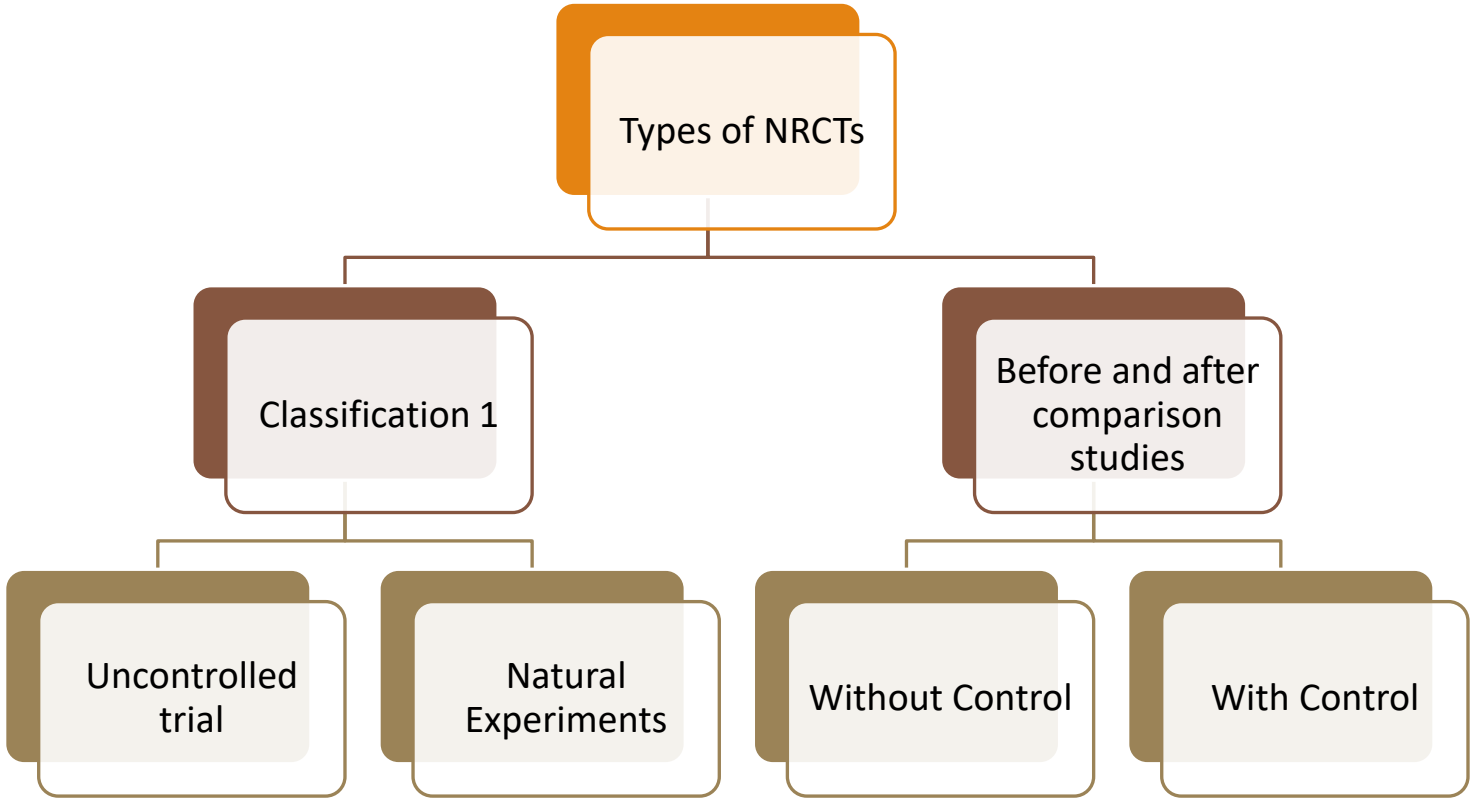
Non Randomized Trials

- **Non-Randomized Trials (Quasi-Experimental Studies)** are intervention studies where the investigator **introduces an intervention but does not allocate participants randomly** to groups.
- These are commonly used in **public health, community medicine, and health education research** when randomization is not feasible or ethical.

Criteria for conducting Non Randomized trial

1. **When randomization is not ethically acceptable**
   Ex: Evaluating the effect of oral rehydration therapy (ORT) education in mothers when it is already known to reduce child mortality.
2. **When administrative or logistic reasons prevent randomization**
   Ex: Introducing a school health education program for all students in one school and comparing with another school.
3. **When intervention is applied to an entire population or community**
   Ex: Implementation of mass vaccination campaign or sanitation program in a village and comparing disease rates before and after the program.

Types of NRCTs



Uncontrolled trial

- Trials with no comparison group
- The effect of the intervention is assessed by **comparing outcomes before and after the intervention in the same group**.

Examples of Uncontrolled Trials

  - Lifestyle modification program for hypertension
  - Health education program on diabetes awareness
  - Cervical cancer screening for reducing mortality from this disease

Natural Experiments

Natural Experiments are studies in which the exposure or intervention occurs naturally due to social, environmental, or policy changes, and the researcher observes its effect without controlling the intervention.

The investigator does not introduce the exposure. The investigator only compares populations that were naturally exposed and unexposed.

Examples of Natural Experiments

- Smoking Ban and Respiratory Illness prevalence
- Fluoridation of Drinking Water and Dental caries prevalence
- Industrial Air Pollution Exposure and Respiratory Illness prevalence

Before and after comparison studies

1. Before and after comparison studies without control
2. Before and after comparison studies with control

Before and after comparison studies without control

Definition: A study in which the same group of participants is observed before and after an intervention, and the outcomes are compared. There is no separate control group.

Limitation: Changes observed may be influenced by external factors (history, maturation, seasonal changes) since there is no comparison group.

Examples

- Hypertension lifestyle intervention
- Diabetes awareness program for a period of 2 weeks
- Hand hygiene training for nurses

Before and after comparison studies with control

Definition: A study in which **two groups are observed**: **Intervention group** (receives intervention), **Control group** (does not receive intervention). Both groups are measured **before and after the intervention**, and results are compared.

Examples

- School nutrition education program in one school and not in another school
- Community physical activity program in one village and not in another village

Summary

- Experimental epidemiology studies disease causation and evaluates preventive or therapeutic interventions by deliberately introducing or modifying an exposure.
- The main types of experimental studies are Randomized Controlled Trials (RCTs) and Non-Randomized Controlled Trials (quasi-experimental studies).
- RCTs involve random allocation of participants into study and control groups, followed by intervention, follow-up, and outcome assessment to obtain strong scientific evidence.
- Non-randomized trials are used when randomization is not feasible due to ethical, administrative, or community-level interventions.
- Common non-randomized designs include uncontrolled trials, natural experiments, and before–after comparison studies (with or without control groups).

Thank you