Community Medicine
Medical Research
Overview of study designs

Dr's Summary with Student own hand notes.

Written by : Mousa Al-Neimat

Overview of study designs I
Observational descriptive studies

Part 1:

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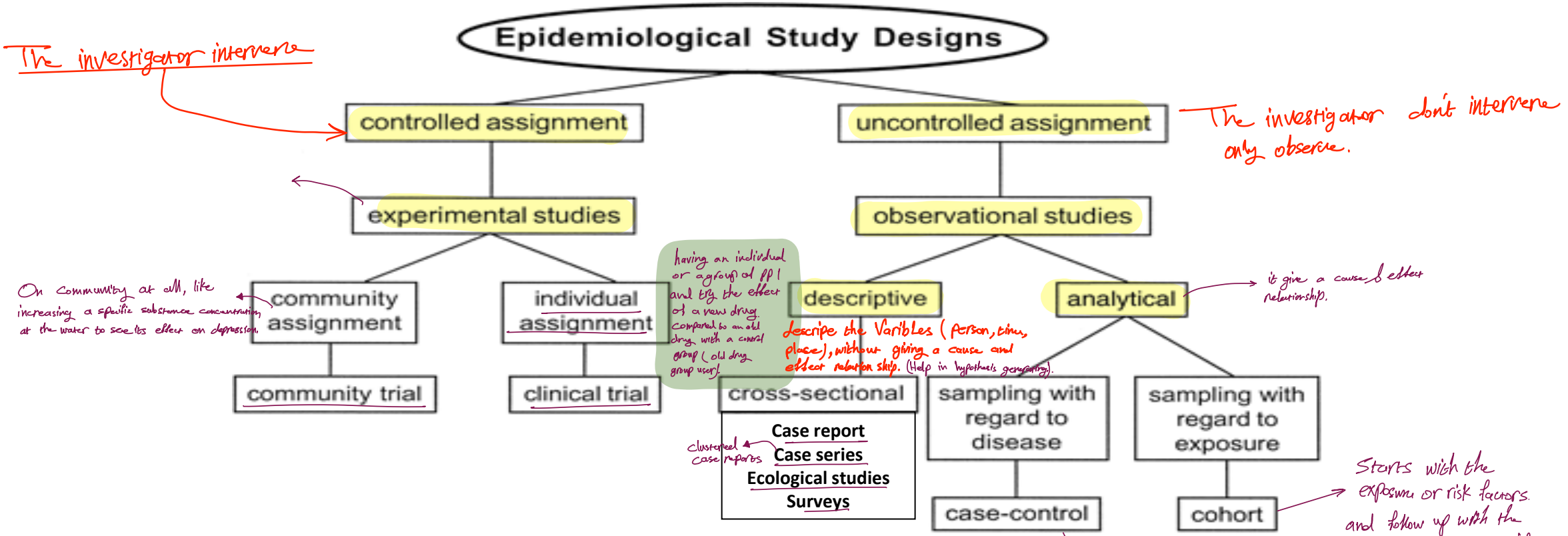
Study design: Definition

A study design is a specific plan or protocol for conducting the study, which allows the investigator to translate the conceptual hypothesis into an operational one.

Epidemiological Study Designs



The investigator intervene

The investigator don't intervene only observe.

On community at all, like increasing a specific substance concentration at the water to see its effect on depression.

having an individual or a group of ppl and try the effect of a new drug compared to an old drug with a control group (old drug group user).

Describe the variables (person, time, place), without giving a cause and effect relationship. (Help in hypothesis generating).

it give a cause & effect relationship.

clustered case reports

Starts with the disease and search in the patient history for possible risk factors, or ask them to remember.

Starts with the exposure or risk factors and follow up with the participants to see if they are going to develop a disease or not.

Source: Waning B, Montagne M: *Pharmacoepidemiology: Principles and Practice*: http://www.accesspharmacy.com

Observational epidemiology

- Provides information about disease patterns or drug use problems by various characteristics of person, place, and time.
- It also is used by epidemiologists to generate hypotheses regarding the causes of disease or drug use problems.

Certain unusual side effect of a specific drug

Who (age gender)

Where (geographical location)

When (time when pattern got discovered. to see if there is a possible risk factor at that time.

What factors causes a specific unusual syptoms. or drug side effects

We can generate a hypothesis that these ppl have a certain medical condition or certain disease is related to that place, time, age.

experimentials

observational

Controlled versus uncontrolled assignment

- Aspirin for prevention of colorectal cancer

- It can be a cohort study: Uncontrolled assignment for patients who are taking Aspirin for different indications

exposure and flow to see if they are less possible to develop colorectal cancer.

- It can be a randomized controlled clinical trial where we allocated patients to take Aspirin or Placebo

دواء مزيف

and we see what group is more possible to develop the disease

if the disease is rare (we should take a very large sample).

Observational epidemiology

a. Descriptive

Case reports and case series

Descriptive analysis (Person place time)

Ecological (correlational)

Surveys

Cross-sectional (snapshots) زي اللي بعلوكنا بالكلية

وصفي

We describe variables that could be factors that can cause the disease (generate a hypothesis). Cause and result relationship.

b. Analytical

Case Control

Cohort

in order to test the hypothesis that has been generated by descreptive studies and generate and cause and result relationship.

Epidemiological studies

- Observational studies are descriptive or analytical in nature.
- Descriptive studies attempt to uncover and portray the occurrence of the condition or problem, whereas analytical studies determine the causes of the condition or problem.
- Investigators in observational studies may plan and identify variables to be measured, but human intervention is not a part of the process.
- Experimental studies, in contrast, involve intervention in ongoing processes to study any resulting change or difference.

Observational epidemiology

- Descriptive studies: provide insight, data, and information about the course or patterns of disease or drug use problems in a population or group.

- Analytical studies are used to test cause–effect relationships, and they usually rely on the generation of new data.

Epidemiological studies

Clinical observation (for example:- A group of patients who are having unusual symptom of a disease)

Variation

Descriptive studies (case series (for example))

Association

Analytical studies (cohort or case-control).

Association

Experimental studies (clinical trial).

Prospective vs. retrospective studies

Prospective studies

Starting with exposure

- Watches for outcomes, such as the development of a disease, during the study period and relates this to other factors such as suspected risk or protection factor(s).
- The outcome of interest should be common; otherwise, the number of outcomes observed will be too small to be statistically meaningful (indistinguishable from those that may have arisen by chance).

relation between smoking and lung cancer ✓

relation between smoking and pancreatic cancer. ✗

very rare disease

Selection bias (selecting ppl at one economical level)

- All efforts should be made to avoid sources of bias such as the loss of individuals to follow up during the study.

- Prospective studies usually have fewer potential sources of bias and confounding than retrospective studies.

depend on patients memory and his medical history.

Retrospective studies

Start of the Study

Outcome ⟶ exposure and past experiencies.

exposures that could be suspected or protective risk factors

- A looks backwards and examines exposures to suspected risk or protection factors in relation to an outcome that is established at the start of the study.

- Many valuable case-control studies, such as Lane and Claypon's 1926 investigation of risk factors for breast cancer, were retrospective investigations.

- Confounding factors and bias are more common in retrospective studies than in prospective studies.

⟶ a factor that affect both the disease & risk factor without our knowledge.

Important.

Comparison of Retrospective and Prospective Approaches

Retrospective	Prospective
Inexpensive to conduct	Expensive to conduct
Completed in a shorter time period	Completed over a longer time period
Easier to access a larger number of subjects	More difficult to access subjects and usually requires a larger number of subjects
Allows results to be obtained more quickly	Exposure status and diagnostic methods for disease may change
Useful for studying exposures that no longer occur	Loss of subjects from the study over time may be substantial
Information and data may be less complete and inaccurate	Information and data may be more complete and accurate
Subjects may not remember past information	Direct access to study subjects enhances reliability of data

it dont depend on following up and generation of new information

needing sufficient number of employes to follow up with participants exposing to risk factor

change from segoaring to vaping or from one type of segoraes to another.

may die, or just want to leave the study.

dealing with disease than their possible exposure is a drug that is not used any more.

informational bias.

involved the generation of anew data.

Case Reports and Case Series

Case report is detailed report by one or more clinicians of the profile of a single patient.

Example: 1961; pulmonary embolism 5 weeks after use on oral contraceptive.

Question: Are women who develop pulmonary embolism more likely to have used oral contraceptives than women who did not develop the disease?

Case Series describes the characteristics of a number of patients with a given disease. or under going the same exposure or experinces

Application: Routine surveillance activities (accumulated case reports). Striking clustering of cases may suggest emergence of new diseases or epidemics

Case report and case series

- **Clinician finds unusual features of a disease or effects of a drug, or the patient's medical history, that lead to the formulation of a new research question or hypothesis**

Case Reports Transpl Int
. 2002 Jul;15(7):374-6. doi: 10.1007/s00147-002-0426-9. Epub 2002 Jun 20.

Colchicine myoneuropathy in a renal transplant patient

Peter Dupont 1, Ian Hunt, Lawrence Goldberg, Anthony Warrens
Affiliations expand

PMID: 12122515 DOI: 10.1007/s00147-002-0426-9

Abstract

Colchicine is widely employed for the treatment of gout in renal transplant patients where NSAIDs are contra-indicated and allopurinol prophylaxis is often avoided due to concomitant azathioprine immunosuppression. We report here a case of colchicine-induced myoneuropathy in a renal transplant recipient. Our patient had myalgia, muscle weakness, elevated creatine kinase levels, myopathic changes on electromyography and peripheral neuropathy. Withdrawal of colchicine resulted in recovery within 4 weeks. Renal transplant recipients are likely to be at greater risk of colchicine-induced myoneuropathy due to the unique concurrence of risk factors predisposing to toxicity in such patients. These risk factors include the high incidence of gout in this population, widespread use of colchicine as first-line therapy, impaired renal function and concomitant cyclosporin treatment. The diagnosis should be considered in any renal transplant recipient receiving the drug who develops myopathy. Prompt withdrawal of colchicine therapy should result in rapid clinical and biochemical improvement.

Case reports

- The most common type of study published in the medical literature.
- They note unusual medical occurrences, identify new diseases, and describe adverse effects from drug therapies.

experimental

- Clinical investigators can use challenge–rechallenge data to help establish causality.
- In this approach, administration of a drug (the challenge) might be suspected of producing a specific symptom (side effect or adverse reaction).
- Administration of the drug can be stopped to observe whether the side effect or adverse reaction diminishes.
- If it does, then administration of the drug can be resumed (the rechallenge) to observe whether the effect returns, suggesting a possible relationship between the two events.

if it returns

Case-series:
Clinical case series

- Usually a coherent and consecutive set of cases of a disease (or similar problem) which derive from either the practice of one or more health care professionals or a defined health care setting, e.g. a hospital or family practice.

Clinical Neurology and Neurosurgery
Volume 99, Issue 4, December 1997, Pages 266-270
Clinical Neurology and Neurosurgery
Case report

Acute onset of colchicine myoneuropathy in cardiac transplant recipients: case studies of three patients

Author links open overlay panel Sandeep S Rana a, Michael J Giuliani a, Chester V Oddis b, David Lacomis a c

Abstract

Colchicine causes both muscle and peripheral nerve toxicity of subacute onset in patients with renal insufficiency. We report three cardiac transplant recipients, treated with colchicine for cyclosporin A (CyA)-induced gout, who developed acute weakness due to colchicine myoneuropathy. The onset of disabling weakness occurred over a 1–2 week period. All three patients had concomitant renal insufficiency and an elevated serum creatine kinase and two had elevated CyA levels at the time of presentation. Electromyography revealed features of myopathy and motor axonal neuropathy in all three patients. Two underwent muscle biopsy which confirmed the presence of sarcoplasmic vacuoles characteristic of colchicine-induced myopathy. All patients rapidly improved with either colchicine dose reduction or drug discontinuation. In conclusion, cardiac transplant recipients treated with CyA and colchicine may be at increased risk of developing colchicine-induced myoneuropathy especially in the setting of concurrent renal insufficiency. In patients with post-transplantation gouty arthritis, other treatment modalities are suggested; and if colchicine is administered, the dose should be reduced, CyA levels should be monitored closely and patients should be assessed for signs of neuromuscular toxicity.

Case-series:
Clinical case series

detailed

- A case-series is, effectively, a register of cases.
- Analyse cases together to learn about the disease. pattern, source and symptoms
- Clinical case-series are of value in epidemiology for:
  - Studying symptoms and signs
  - Creating case definitions
  - Clinical education, audit and research
    the quality of health care provided.
- **can build up a picture of the natural history of a disease**

The natural history of a disease is

> the *course and progression of a disease* in an individual **from its onset (usually from exposure or infection)**, through **the pre-symptomatic and symptomatic stages**, and up to **recovery, chronic disability, or death — in the absence of treatment or intervention**.

from infection, develop of symptoms on different ppl with different characteristics and the recovery and duration of the disease with the absence of treatment.

Case series: Limitations

Usually we cannot estimate the prevalence or incidence rate

- **Breast cancer registry in Jordan: We cannot provide prevalence rates without:**

1. **Population size**
2. **Time- period of data collection**
3. **All cases of breast cancer are registered**

Exception for calculation of the incidence: Jordan National Cancer registry can generate data on the incidence.

All cancer cases in Jordan are reported to the Registry office.

No control group for comparison

Disease registry:
Definition of Registry

- The term *registry* is defined both as the act of recording or registering and as the record or entry itself.

- Therefore, "registries" can refer to both programs that collect and store data and the records that are so created.
- **Special form of case series**

Webster's English Dictionary. [August 12, 2012]. http://www.m-w.com.

Disease Registry

- Patient registries have been defined as:

"an organized system that uses observational study methods to collect uniform data (clinical and other) to evaluate specified outcomes for a population defined by a particular disease, condition, or exposure, and that serves a predetermined scientific, clinical, or policy purpose(s)."

allow the Ministry of Health (example) to have the knowledge that allow it to make human plans.

https://patientregistry.ahrq.gov.

Types of Registries

- Mortality registry (deaths among population).
  - An important thing to know about your patients
- Research Patient Registry (registries of information about patients who are involved in a specific research).
  - Clinical Trials

- Disease or Condition Registries registries of information about patients who have a specific disease or condition
  - Disease or condition registries use the state of a particular disease or condition as the inclusion criterion.
  - One disease or group of diseases: Cancer registry, multiple sclerosis registry, bleeding disorders.

- Service, intervention, device registry (collect data about patients who undergo a specific operation or device or intervention or service quality.

BMT registry, Biosimilars registry

Bone marrow transplant registry

Uses for Patient Registries

- To observe the course of disease
- To understand variations in treatment and outcomes
- To examine factors that influence prognosis and quality of life
- To describe care patterns, including appropriateness of care and disparities in the delivery of care
- To assess effectiveness
- To monitor safety

Components of disease registry

- Personal Domain (name, gender, age)
- Exposure Domain (a specific drug or risk factor or environmental exposure and etc)
- Outcomes Domain disease or medical condition that occurs.

Ecological studies

Are studies in which information on the characteristics and/or exposures of individual members of the population groups are generally not obtained. Existing statistics are used to compare the mortality or morbidity experience of one or more populations with some overall index exposure. care is needed to avoid the 'ecological fallacy' where inappropriate conclusions are made from ecologic data

the effect of confounding factors.

Ecological studies

like adverse effects.

- These studies are used to describe disease or drug use problems in relation to some factor of interest.

whether it was positive correlation or negative correlation

Comparing cigarette consumption with rates of cancer

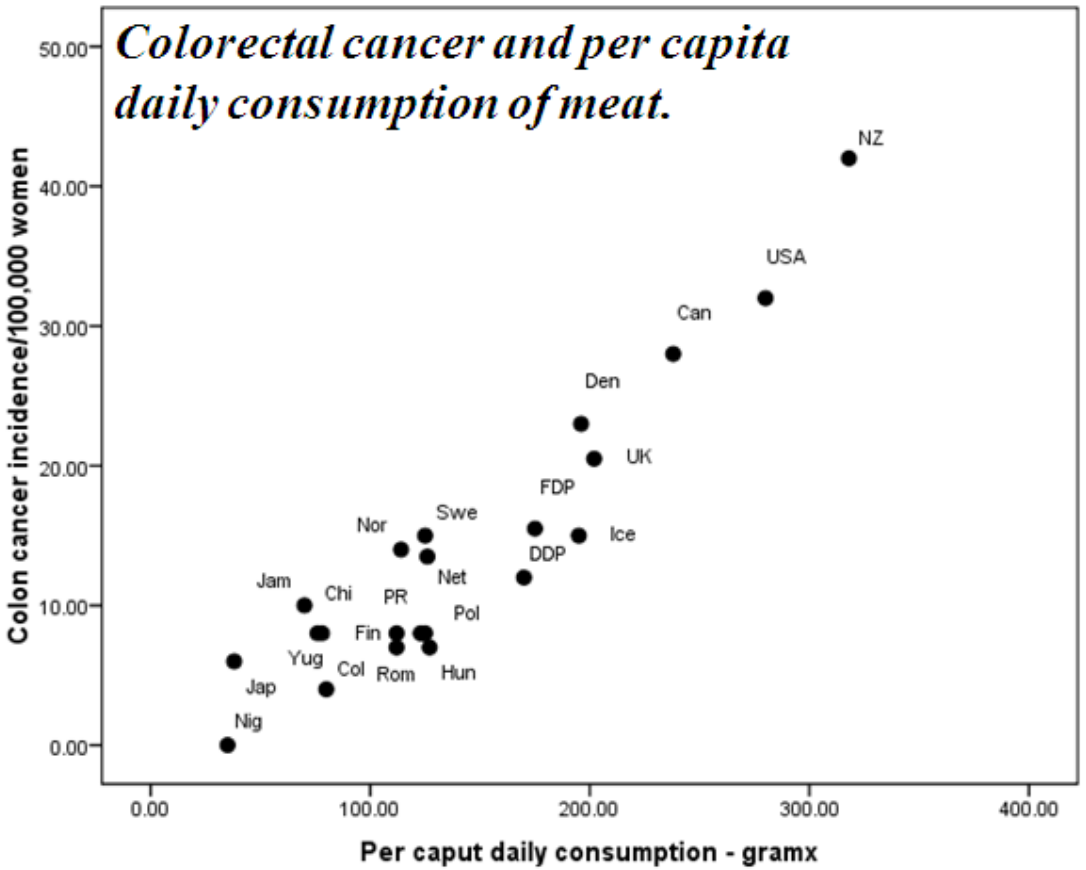
Comparing Alcohol consumption with coronary heart disease mortality

with respect to diffierent aggregate not individual.

- Ecological studies are the first identified strong relationships between disease and behavior.

Ecological studies

- In ecological studies the unit of analysis is some aggregate individuals rather than individual persons
- Geographic areas or time period are often used as a basis for defining aggregates
- The analysis centers on determining whether the ecological units with a high frequency of exposure are also unit with a high frequency of disease (+ve correlation) or a low frequency of disease (- ve correlation)



Adapted from: *Int. J. Cancer 15:617, 1973*

Ecological (correlational studies)

- look for associations between exposures and outcomes in populations rather than in individuals.
- They use data that has already been collected.

there should be a different aggregates.

- The measure of association between exposure and outcome is the correlation coefficent *r*.
- This is a measure of how linear the relationship is between the exposure and outcome variables. (Note that correational is a specific form of association and requires two continuous variables)

Ecological (correlational studies)

Advantages of an ecological study

1. An ecological study is quick and cheap to conduct.
2. It can generate new hypotheses. → to analytical studys or clinical trials or both.
3. It can identify new risk factors.

Ecological (Correlational studies)

Disadvantages:

1. It is unable to control for confounding factors. This is often referred to as 'ecological fallacy', where two variables seem to be correlated but their relationship is in fact affected by cofounding factor(s).
2. It cannot link exposure with disease in individuals as those with disease may not be expose. to the exposure.
3. Its use of average exposure levels masks more complicated relationships with disease.
4. Its units of study are populations not individuals. Therefore, the disease rates linked with population characteristics and the association observed at group level does not reflect association at individual level.

Snapshots محاضرات من كلية الطب عنا

CROSS-SECTIONAL STUDY DESIGN

- **Sometimes called *prevalence studies*.**
- **They are studies of total populations or population groups in which information is collected about the present and past characteristics, behaviors, or experiences of individuals.**
- **There are a number of advantages in performing a cross-sectional study.**

- **These studies involve a single data collection and, thus, are less expensive and more expedient to conduct.**

Snapshots

Cross-sectional (or prevalence) studies

Are studies in which a defined population is surveyed and their disease or exposure status determined at one point in time

- The prevalence rates of disease in the whole population as well as in those with and without the exposure under investigation can be determined
- Cross-sectional studies are generally not suitable for a disease which is rare or of short duration as few people will have the disease at any one point in time

CROSS-SECTIONAL STUDY DESIGN

- **Emphasis is on differences between groups at one point in time.**
- **They provide a one-time glimpse at the study population, showing the relative distribution of conditions, diseases, and injuries—and their attributes—in a group or population.**
- **Point prevalence versus Period prevalence**

Cross-sectional studies

- More effective in identifying chronic diseases and problems
- Less effective in identifying communicable diseases of short incubation periods and short durations.

Cross-sectional (or prevalence) studies

- It is often difficult to separate cause and effect as the measurement of exposure and disease at any one point in time

- Because of this limitation, cross-sectional studies are useful when investigating exposures which do not change
e.g genetic characteristics such as ABO blood group and HLA

- Cross-sectional studies are often used as an initial exploration of a hypothesis prior to conducting a case-control or follow-up study

CROSS-SECTIONAL STUDY DESIGN

- They provide information and data useful for the planning of health services and medical programs.
- Assessment of the burden of diseases or healthcare programs leads to setting priorities at the organization, local or national levels.

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- They are based on a sample of the whole population and do not rely on individuals presenting themselves for medical treatment

Cross-sectional studies: advantages

- **Relatively quick**
- **Data on all variables is only collected once.**
- **Sample size depends on the question**
- **Standard measures used** for comparison
- **Prevalence estimated**
- **The prevalence of disease or other health related characteristics are important in public health for assessing the burden of disease in a specified population and in planning and allocating health resources.**
- **Good for descriptive analyses and for generating hypotheses**

Cross-sectional studies

Disadvantages:

- They cannot show cause–effect relationships.

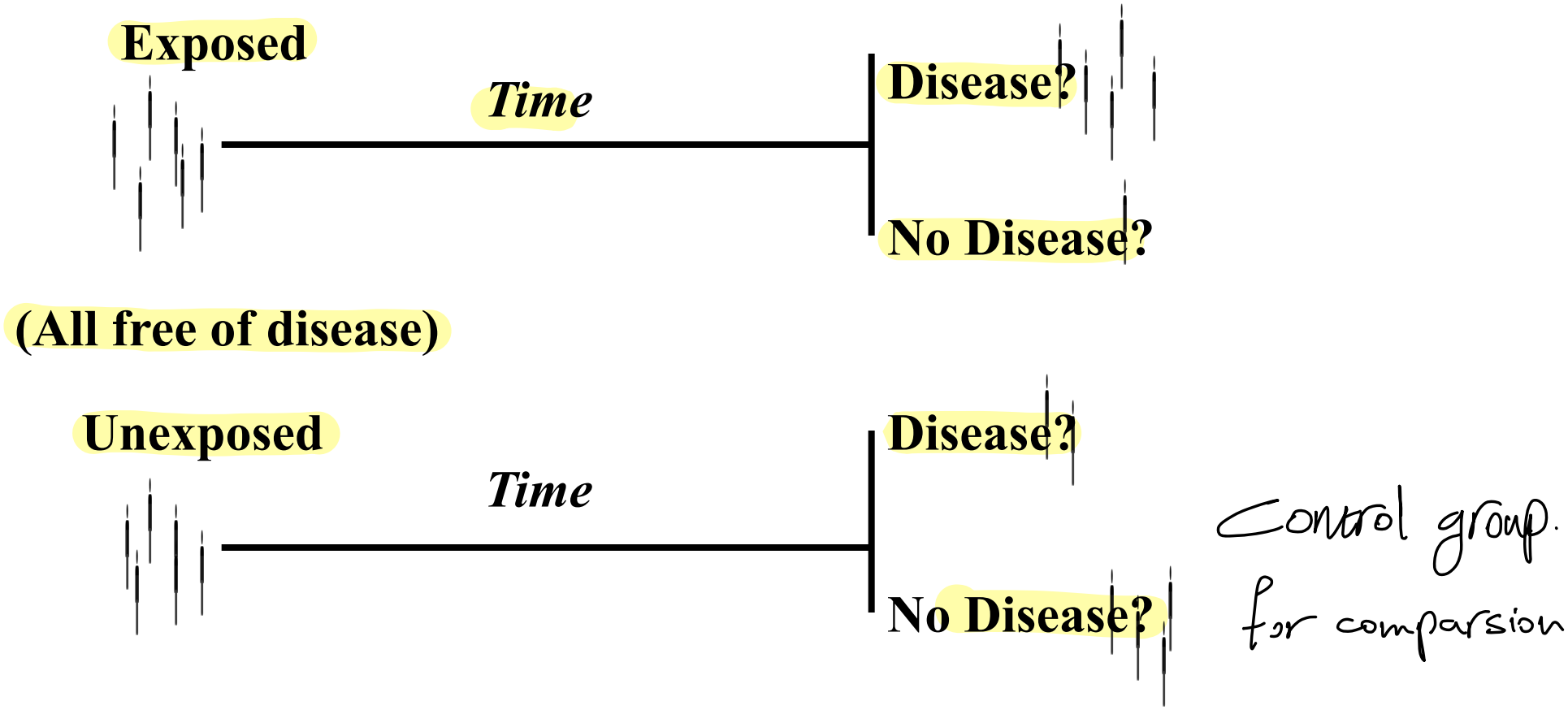
Difficult to determine whether the outcome followed exposure in time or exposure resulted from the outcome.

- If the sample is not representative, results are representative only of the individuals who participate in the study

Example prevalence of sickle cell anaemia in the Easter region of the KSA does not represent the whd country.

- Not suitable for studying rare diseases or diseases with a short duration.
- Unable to measure incidence
- Associations identified may be difficult to interpret.
- Susceptible to bias due to low response and misclassification

Cohort studies



Cohort (or follow-up) studies

- **Are studies in which people are identified and grouped with respect to whether or not they have been exposed to a specific factor.**

- **The groups are followed up over time to determine whether the incidence of a particular disease is any greater (or less) in the exposed group than in the non-exposed group.**

- **The starting point is the risk factor!**

Cohort study examples:

- Life expectancy of cerebral palsy children
- Fine needle breast biopsy and breast cancer
- Aspirin intake and colorectal cancer

Cohort study:
Primary purposes

- **Descriptive (measures of frequency)**
  - **To describe the incidence rates of an outcome over time, or to describe the natural history of disease**
- **Analytic (measures of association)**
  - **To analyze associations between the rates of the outcomes and risk factors or predictive factors**

COHORT STUDY DESIGN

- This design is the best observational one for establishing cause–effect relationships.
- Prevention and intervention measures can be tested and affirmed or rejected.
- Cohort studies consider seasonal variation, fluctuations, or other changes over a longer period.
- Objective measures of exposure, such as biological markers, are preferred over subjective measures.

COHORT STUDY DESIGN
Strengths

- We can measure incidence of disease in exposed and unexposed groups
- Can get a temporal (time related) sequence between exposure and outcome as all individuals must be free of disease at the beginning of the study.
- Good for looking at effects of rare exposures.
- Allows for examination of multiple effects/diseases of a single exposure.
- Not open to bias as much as other types of study
- Direct calculation of the risk ratio or relative risk is possible.
- Provide information on multiple exposures

COHORT STUDY DESIGN

Limitations:

- Not efficient for rare diseases
- Can be expensive and time-cosuming
- Large sample
- Drop-out biases

  If study goes over many years, can get considerable loss to follow up. This can 'dilute' results or lead to bias, and therefore the validity of result can be seriously affected

- Locating subjects, developing tracking systems, and setting up examination and testing processes can be difficult.
- Changes over time in diagnostic methods, exposures, or study population may lead to biased results.

Cohort study: Example

Hypertension as a risk factor for spontaneous intracerebral hemorrhage

In study risk factors, we start with what is rare!

- Rare disease: we conduct case control study starting with cases
- Rare risk factor: we conduct a cohort study starting with rare risk factors

Calculation of the relative risk

Cohort study

	Disease Present	Disease absent	
Exposure Present	a	b	a+b
Exposure absent	c	d	c+d
Total	a+c	b+d	a+b+c+d

Measuring the association between risk factor and diseases

Relative risk

$$\text{Relative Risk}\,(RR) = \frac{\text{Risk in the exposed}}{\text{Risk in the non exposed}}$$

- **RR=1**
  There is no association between exposure and disease.

- **RR>1**
  Exposure is associated with an *increase* of the frequency of the disease.

- **RR<1**
  Exposure is associated with a *decrease* of the frequency of the disease.

	Disease Present	Disease absent	
Exposure Present	a	b	a+b
Exposure absent	c	d	c+d
Total	a+c	b+d	a+b+c+d

Risk in the exposed=(a)/(a+b)

Risk in the non exposed=(c)/(c+d)

$$Relative\ Risk\ (RR) = \frac{a/(a+b)}{c/(c+d)}$$

ppl who are exposed and has disease / total ppl who are exposed.

ppl who are non exposed and have disease / total ppl who are not exposed

Physical Activity and Incident Cognitive Impairment in Elderly Persons

ARCH INTERN MED/VOL 170 (NO. 2), JAN 25, 2010

Background: Data regarding the relationship between physical activity and cognitive impairment are limited and controversial. We examined whether physical activity is associated with incident cognitive impairment during follow-up.

Methods: As part of a community-based prospective cohort study in southern Bavaria, Germany, 3903 participants older than 55 years were enrolled between 2001 and 2003 and followed up for 2 years. Physical activity (classified as no activity, moderate activity [<3 times/wk], and high activity [≥3 times/wk]), cognitive function (assessed by the 6-Item Cognitive Impairment Test), and potential confounders were evaluated. The main outcome measure was incident cognitive impairment after 2 years of follow-up.

Cohort study

Physical activity	Cognitive impairment		Total
	Yes	No	
Moderate	10	990	1000
None	100	900	1000
Total	110	1880	2000

Risk of outcome in exposed (not active) = 100/1000 = 10%

Risk of outcome in non-exposed (active)=10/1000 =1%

Relative risk 10%/1%=10 =

Case-control studies

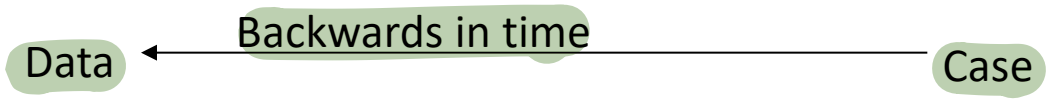
Are studies in which a group of people with a particular disease (the cases) are compared with a group of people without the disease (the controls). The purpose of the comparison is to determine whether, in the past, the cases have been exposed more (or less) often to a specific factor than the controls

- This type of study is done to identify factors that could be responsible for the development of a disease or drug use problem.

CASE-CONTROL STUDIES

- The direction of time

- Cases identified now
- Data on past events collected



CASE-CONTROL STUDY DESIGN

- Designed to assess association between disease occurrence and exposures (e.g., causative agents, risk factors) suspected of causing or preventing the disease.

Case-control studies

- A group of people with a disease are compared to a group without the disease from the same population.
- Compare exposure to risk factors in both groups
- Able to look at many different possible risk factors
- Able to study diseases with a long latency period
- Most common analytic study design seen in the medical literature today

take many time for symptoms to appear.

Case-control studies

- In general, the cases included in a case-control study include people with one specific disease only
- But, a case-control study can provide information on a wide range of possible exposures that could be associated with that particular disease
- Useful for the study of rare diseases
- Not suitable for the study of rare exposure
- Relatively small and inexpensive
- Takes a relatively short time to complete
- Can test current hypotheses
- Cannot measure disease incidence

CASE-CONTROL STUDIES

- Cases have the disease of interest

Eg. Cerebral palsy

- Controls do not have the disease

Eg. Healthy babies born at the same time

Design of case control studies

- **Comparability:Two groups must be as similar to each other as possible so selection of controls is very important. Controls must be as similar as possible to cases – except that they do not have the outcome (disease).**

- **Outcome (disease) must be very clearly defined. (Diagnostic criteria must be clear)**

data that are registered rather than patient memory

- **Use objective data about exposure status wherever possible, to reduce the risk of bias**

like patient history his work career (to see if he was exposed to a certain exposure).

CASE-CONTROL STUDIES

Strengths

- Suited to study disease with long latency periods, but can be used in outbreaks investigations
- Optimal for rare diseases
- Efficient in terms of time and costs: relatively quick and inexpensive
- Allows for evaluation of a wide range of possible causative factors that might relate to the disease being studied
- Odds ratio estimated

CASE-CONTROL STUDIES

Limitations

- Very susceptible to bias (especially selection and recall bias) as both the disease and the exposure have already occurred when participants enter the study. Cases and controls might not be representative of the whole population
- We cannot calculate incidence or prevalence rate of disease
- We cannot be certain that exposure came before disease
- Choice of controls difficult
- Controls do not usually represent non-exposed population
- Past records incomplete
- No absolute risk estimates

especially in long latency period disease

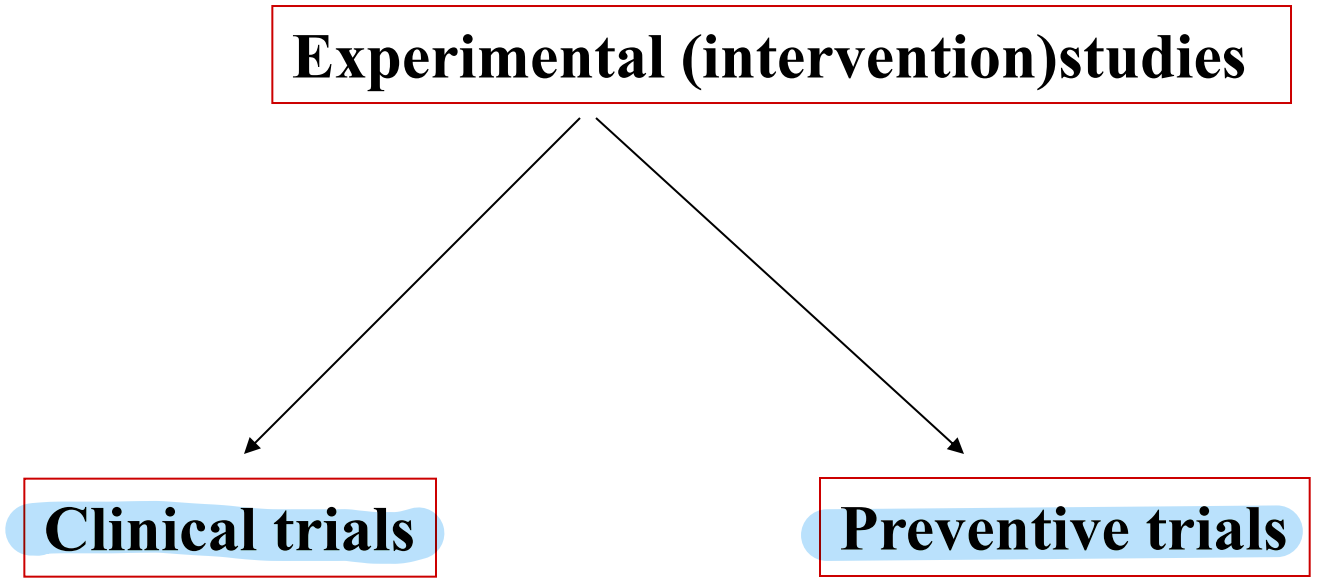
Experimental Study Design

A study in which a population is selected for a planned trial of a regimen, whose effects are measured by comparing the outcome of the regimen in the experimental group versus the outcome of another regimen in the control group.

specific intervinsion

a specific intervension

Experimental studies (Intervention)



Experimental Study Design

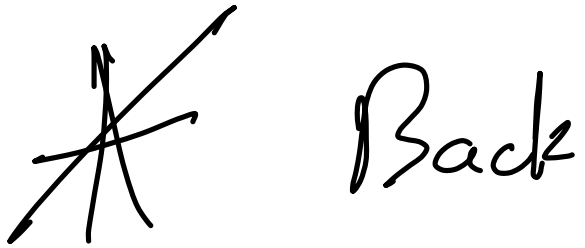
Different from observational designs by the fact that there is manipulation of the study factor (exposure), and randomization (random allocation) of subjects to treatment (exposure) groups.

intervension (controlling).

subjects and classified randomly to experimental and controlled group.

Why experimental study design?

- Limitations of theory
- Previous disasters



Clofibrate:

Successfully lowers cholesterol

Treated group: reduced CHD incidence, but higher all causes mortality

- Spontaneous improvements
- Importance of small effects

Clinical trials

- Individuals with particular disease are randomly allocated into experimental or control groups. randomization is used to ensure that both groups are comparable with respect to all other factors except for the one under investigation.

- The experimental group is given the agent being tested and the control group is given either an agent in current use or a placebo(if not available approved treatment)

Pseudodrug

- Ideally both patients and the observers should be 'blind' to the treatment being given. This in order to reduce bias.

Clinical trials

- Are studies of the effect of a specific treatment on patients who already have a particular disease

- They are used to evaluate the efficacy of a preventive or therapeutic agent in the treatment or prevention of a disease

What trials assess

- Drugs
- Surgery
- Type of management
- New services

Randomized Clinical Trial

RCT Disadvantages

- Large trials (may affect statistical power) → Sometime require long trials which are so expensive
- Long term follow-up (possible losses)
- Compliance الإلتزام بالعلاج
- Expensive
- Public health perspective ? results may not be applicable to all people.
- Possible ethical questions
- As above, may take a long time.
- Must be ethically and laboriously conducted.
- Requires treatment on basis (in part) of scientific rather than medical factors. Patients may make some sacrifice

سلبيات RCTs بشكل مبسط

1. **كلفة عالية**
   - التجارب تحتاج مال كثير لإجراءها ومتابعة المشاركين.
2. **تستغرق وقت طويل**
   - أحيانًا تحتاج متابعة طويلة، وقد يترك بعض المشاركين الدراسة قبل نهايتها.
3. **صعوبة الالتزام بالعلاج**
   - بعض المرضى لا يلتزمون بالعلاج أو التدخل المطلوب، وهذا يؤثر على النتائج.
4. **قد تكون غير مناسبة للجميع**
   - النتائج قد لا تنطبق بسهولة على كل الناس أو على المجتمع بشكل عام.
5. **مسائل أخلاقية**
   - أحيانًا يتم إعطاء بعض المرضى علاج وهمي (placebo) أو حرمانهم من علاج فعّال، وهذا يحتاج مراقبة صارمة لضمان الأخلاق.
6. **تضحيات المشاركين**
   - المرضى قد يضطرون لتجربة أشياء علمية قد لا تكون مفيدة لهم مباشرة، بهدف البحث العلمي.

Defining the patients

- Diagnostic features
- Eligibility criteria (inclusion and exclusion)

Assessing the outcome

- Clinically relevant
- Easily measured
- Accurately measured

Types of outcomes

- Death
- Clinical measurement
- Symptoms
- Quality of life
- Psychological wellbeing

Definitions

- **Single Blind Study**: A clinical trial where the participant does not know the identity of the treatment received
- **Double Blind Study**: A clinical trial in which neither the patient nor the treating investigators know the identity of the treatment being administered.
- **Triple Blind study: Biostatisticians is also blinded**

To Reduce the bias.

Summary of trial design

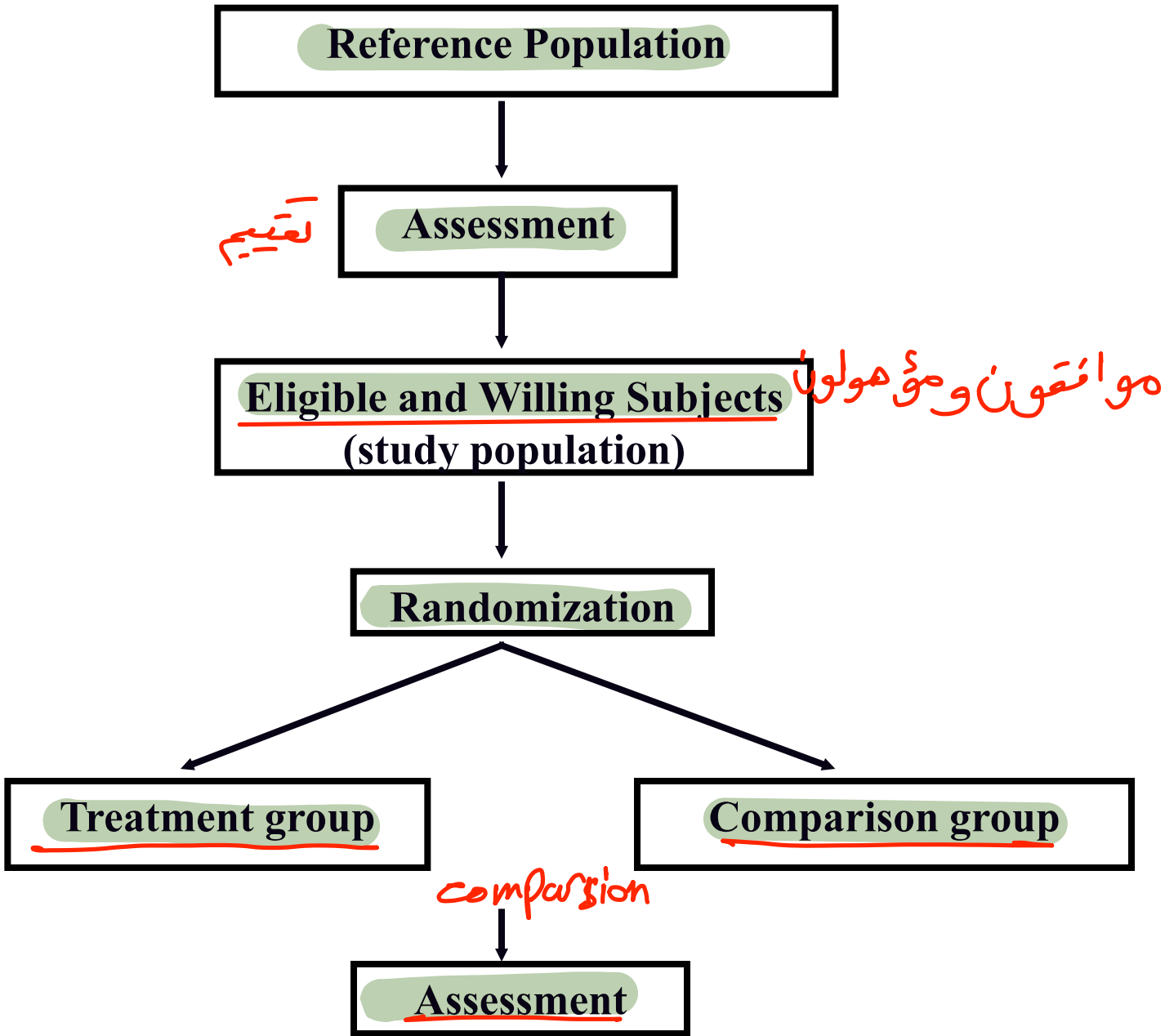
- Specify the treatment
- Define study group
- Random allocation
- Blinded outcome assessment
- Fair interpretation

Clinical trial

Common problems

- Too few patients not many people accept.
- Failed randomization
- Patients lost to follow-up (drop out the study).
- Flawed analysis-interpretation تفسير خاطئ
- Power of study: not big enough when it is very small trial

Parallel Design



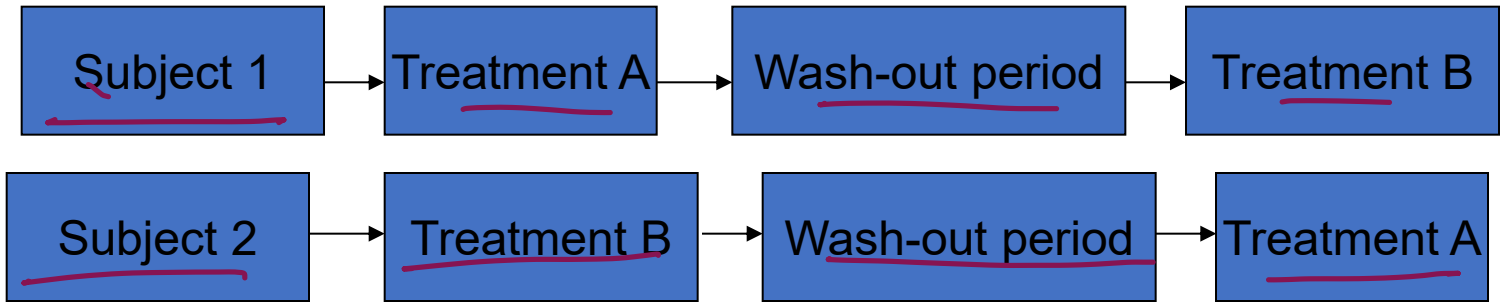
Cross-over clinical trial

Each patient gets both treatments

Half get A then B

Half get B then A

Wash-out period in between to remove the effect of the first drug



Cross-over clinical trial

- Cross-over design
- Patient as own control The are both experimental and controlled group.

-Reduce variations The control group and experimental group aren't different since they are the same

-Much smaller sample size

Requirements: Carry over period(s)

wash out periods.

Preventive trials

Are studies of the effect of a possible preventive measure on people who do not yet have a particular disease.

Another type of preventive trial is a study of the effect of a possible preventive measure on whole community

Preventive trials

- The risk of developing any particular disease among the people who are free from disease is small. Because of this, preventive trials usually require a greater number of subjects than clinical trials, and are therefore more expensive

- This expense limits their use to the study of preventatives of extremely common or extremely severe diseases
  e.g. vaccination to prevent whooping cough
  vaccination to prevent poliomyelitis

- When a disease occurs rarely, it is more efficient to study those people thought to be at high risk of disease , e.g. vaccine to prevent Hepatitis B

Preventive trials

- As in clinical trials, the preventatives should be given so that the individuals who do and do not receive the preventative are as comparable as possible. This is often difficult.

they should be as similar as possible

- In some types of trials the preventative have to be administered to communities rather than individuals, e.g. water fluoridation to prevent dental caries

Community Trials

- A community participates in a behavioral intervention, nutritional intervention, a screening intervention, etc
- Intervention: Any program or other planned effort designed to produce changes in a target population.
- *Community* refers to a defined unit, e.g., a county, state, or school district.
- Communities are randomized and followed over time.
- Determine the potential benefit of new policies and programs.

not always a chemical substance and see it's effect.

Examples:

- A community-level intervention for tobacco control might combine a school curriculum for youth to prevent initiation of smoking
- A media campaign aimed at reducing smoking rate

Examples

الإقلاع عن التدخين

- Smoking cessation interventions for secondary schools
- Medical Research participation interventions: one for JU and another intervention for JUST

- Increasing fluoride level within acceptable limits in all drinking water sources in Aqaba and comparing with Irbid, keeping this as they are.

Primary outcome: dental cases incidence for children younger than the age of 5.

🩺 1. Smoking cessation interventions for secondary schools

- Targets school students as a community.
- Goal: reduce smoking rates through awareness or counseling.
- Compare smoking rates before and after the intervention.

  ✅ **Type:** Behavioral community trial.

🧬 2. Medical research participation interventions (JU vs. JUST)

- Two university communities (JU and JUST) receive different interventions to boost research participation.
- Compare participation rates between both universities.

  ✅ **Type:** Educational community trial.

💧 3. Increasing fluoride levels in drinking water (Aqaba vs. Irbid)

- Fluoride level adjusted in Aqaba water, Irbid kept as control.
- Measure dental caries in children under 5.

  ✅ **Type:** Environmental community trial.

إدعوا لنا بظهر الغيب...