09

EXPERIMENTAL STUDY DESIGN

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ACKNOWLEDGMENTS

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LECTURE **OBJECTIVES**

By the end of this lecture, I am able to:

- Describe RCT study design
- Explain the advantages and disadvantages of RCT design
- Differentiate between cohort and RCT study designs

Overview

Overview of other study design

• **Difference between retrospective cohort and case control?**
if i have data already documented in a file how can i apply it to a retrospective study or a case control study? (the relationship between smoking and lung cancer)

• **Case control:** people with lung cancer are cases and people without are controlled, and then in i go back to see why they have lung cancer? Smoking family history.. odds ratio

• **Retrospective cohort:** i go back and see at 2000 files of smokers and nonsmokers and then check their files at 2019 to see who developed lung cancer and who didn't develop it risk ratio

• **Cross sectional study:**
take a screenshot at this time point (smoker, nonsmoker, have lung cancer, doesn't have lung cancer) put the data in 2x2 table and you can calculate the prevalence risk ratio or odds ratio

• **Case report** is for something rare, outbreak investigation, unexpected complication, unexpected outcomes
• **Case series** is for more than 1 rare case

Choosing the best study design

• Choosing a study design is based on your research question, some questions can have more than one study design addressed to it (like multivitamins use you can do a cohort study using old files or RCT in this case RCT is the best study design to be address the research question)
• **In observational study cohort** is the best then study control and then cross sectional.
• **Cross sectional** احيانًا احتاجها لو ابي اعرف مدى المشكله

Overview

Experimental Study Design

What is the main difference between observational study and experimental ?

observational study is like the case of lung cancer and smoking (its unethical to do it in an experimental study it will harm the patient)

Experimental study is like the case of giving multivitamins or herbal supplements something that doesn't harm the patient (its unethical to give drugs that has side effects that would harm the patient antihypertensive medications)

Experimental studies interventions doesn't always have to be done with drugs, it can be with programs (diet, exercise, education programs), surgical (open and laparoscopic surgery)

• Experimental study here we don't mean the experimental studies in the lab or animal study, we mean epidemiological study that mean i interfere and assign to the exposure to one group.

We have to types:
• Observational
• Experimental we have 2 or more groups

• **RCT** best type of evidence

Experimental study design

Selection of study design

There is **NO** best type of a study design.

Choosing the study design depends on:

- Research question and objectives
- The knowledge already available about the problem
- Available resources (cost, time, expertise of the researcher)
- Ethics

•**RCT** are expensive i need to sit with patients explain to them, واتعامل مع مصانع الادوية والبلاسيبو
• **Cohort** is considered expensive because it needs long follow ups and for every follow up i need to do sets investigations and sets of questionnaire
• **Case control** and cross sectional are not that expensive
• **Cross sectional** doesn't need much time cohort and RCT need long periods of follow up

Experimental studies can be randomized and non randomized
We're gonna focus on randomized Because it is the best evidence

Think

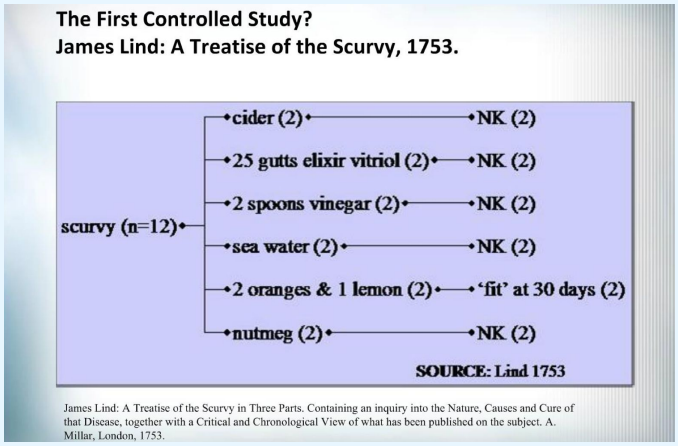
An investigator wants to test the effectiveness of a performance-enhancing herbal supplement on students in his exercise class.

Which study design should the investigator choose?

Randomized control trial

What are experimental studies?

In an experimental study something is given or done to the experimental group but not to the control group.
Any resulting differences in the outcome are compared.



• Experimental studies in general is something given or done (intervention) to the experimental group but not to the control group

• The randomization is why the RCT have highest level of evidence, any results in the experimental group i'll be confident it's from the intervention

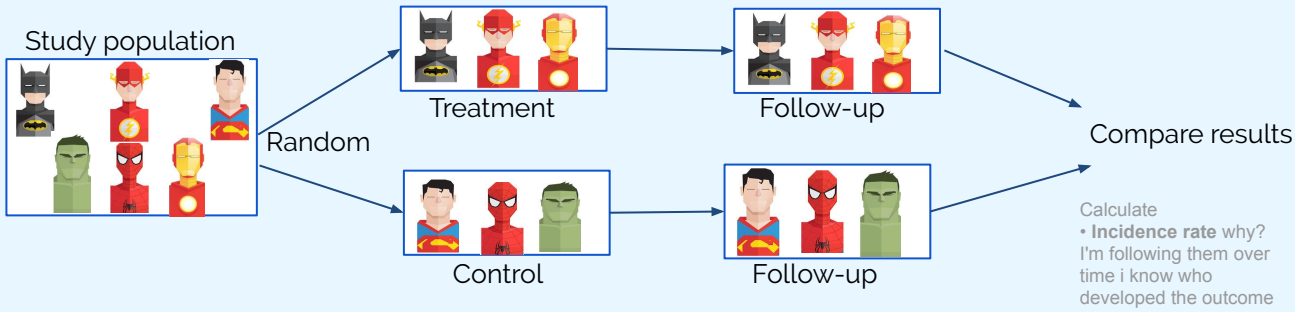
• In RCT the randomization gives any individual in the study a 50% chance to be in the experimental (interventions) group or the controlled group

• كل ما كان randomized كل ما كان more likely انها تكون accurate results and this is the strength of RCT

***This is only to show that it is not a new science**

Randomized Control Trial

Randomized control trial (RCT)



*Follow up both groups to see if there is a difference in when the outcome happened for both experimental and controlled group

Calculate
• **Incidence rate** why? I'm following them over time i know who developed the outcome
• **Risk ratio** to compare the experimental (interventions) group and the control group

Simplest definition:
Individuals are allocated at random to receive one of several interventions (at least two total).

RCT's are experimental —the intervention is controlled by the investigator

Random allocation 1

What?[2]

Random allocation means that all participants have a defined probability of assignment to a particular intervention

- Allocation is NOT determined by the investigator, clinicians, or participants
- Allocation is NOT predictable based on a pattern

Why?

What purpose is served by random allocation?

-Covariates[3] are distributed equally across the groups at baseline

-Affects both measured and, more importantly, unmeasured variables

1-This is an important step لصحة الدراسة
2-The more it's randomized the more it will be accurate why?
It will guarantee that all the factors distributed equally between the two groups, and that will guarantee that any changes in the experimental group will be from the intervention.
3-The main limitation in observational study is confounders, but here i'm 90% sure that the confounders are distributed equally between two groups سواء كانت (known or unknown factors) this is one of the main strength in RCT

If i did a random selection the male to female ratio will be almost the same in both groups, but if one group by change had more males and the other group had more females i can control this in statistical analysis

Randomized Control Trial

Random allocation

Which?

Methods of Randomization

All the methods are correct

- Date of birth (odd to group 1; even to group 2)
- Hospital record number (last digit; odd to group
- 1, even to group 2)
- Day of enrollment (Monday=Rx, Tues=Placebo, etc)
- Alternating (first person=Rx, second person=placebo, etc)

It can be a simple randomization coin toss ويحدد اي قروب

Most commonly used

What elements of a trial can be randomized?

Most common unit is individual patient

Sometimes groups are randomized = cluster randomization

Examples: families, schools, towns, hospitals, communities

Worry about contamination in cluster randomization

Contamination: الاختلافات الشخصية من شخص لشخص in the cluster.

The randomization can be done to groups not only individuals, i can say that all patients attended the clinic in Tuesday are in the intensive group and all patients attended the clinic on Thursday are in the controlled group

I can go to schools and take all students in those schools as sample, selection of the schools are cluster randomization احدد المدارس randomly

Special statistical techniques needed to cope with the loss of independence of the individual units

How?

لو الباحث عرف التوزيع ممكن لو عنده مريض حالته حرجة يحس انه يحتاج دعم اكثر و يغير ل experimental group وكذا ندخل في selection bias وتصير نتائج الدراسة غير صحيحة وغير دقيقة

Allocation concealment means: **Patient X** in interventions group, **Patient Y** in controlled group

You **don't** tell the patient or physician or researcher which patient in which group UNTIL the beginning of the study

يعني من الفتره الي ابدا اسوي راندوميزايشن الين ابدا الدراسة ايش فكرته؟ عشان امنع ال selection bias

Two steps involved:

Generation of allocation sequence

★ **Simple randomization**:
Analogous to a repeated fair coin tossing

★ **Restricted randomization** (Blocking): :
Done to ensure equal balance of arms throughout all portions of the study. For example, blocks of six would have 3 active/3 control. Block size itself can/should vary.

★ **Stratified randomization Individuals:**
Are identified based on important covariates (sex, age, etc.) and then randomization occurs within the strata.

Concealment of allocation

★ Concealing the allocation sequence from those assigning participants to the intervention groups, until the moment of assignment.

★ It prevents researchers from (unconsciously or otherwise) influencing which participants are assigned to the intervention or control group.

★ If those making the decision about patient eligibility are aware of the arm of the study to which the patient will be allocated (if randomization is unconcealed) they may systematically enroll sicker or less sick patients to either treatment or control groups.

★ This will defeat the purpose of randomization and the study will yield a biased result..

Randomized Control Trial

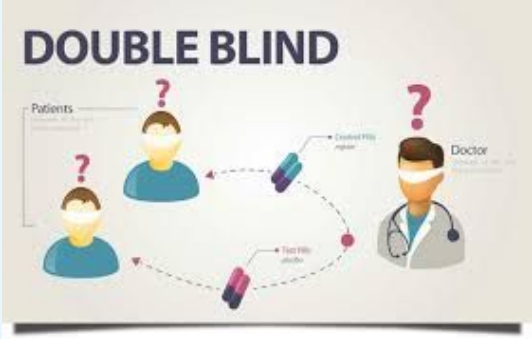
Blinding (Masking):

★ Process that attempts to keep the group (e.g. active drug or placebo) to which the study subjects are assigned not known or easily ascertained by those who are "masked."

★ Relevant groups who may/may not have knowledge of treatment assignments

1. Participants
2. Investigators/clinicians administering intervention
3. Investigators assessing outcomes
4. Data analyst(s)

*All interventions can be concealed
Not all interventions can be blind (surgical, program) but in case of medication you can blind the interventions



Concealment من التوزيع الى بداية الدراسه
blinding بعد بداية الدراسه صار اسمه
Blinding types:
Open label
Single blind: patient doesn't know which group he is, but the physician and researchers know
Double blind: both patient and physician doesn't know, the researcher know
Triple blind

Concealment of Allocation vs. Blinding

Concealment of allocation:	Blinding:
Procedure to protect the randomization process before the subject enters the trial	Masking of the treatments after randomization (once trial begins)
Concealment of allocation is ALWAYS feasible	Blinding is not always feasible
If not done, results in selection bias (randomization benefits are lost, and treatment assignment is no longer truly random)	If not done, can result in patients biasing their responses because of their knowledge of treatment; can also lead to biased outcome assessment because investigators have knowledge of treatment

Randomized Control Trial

Strengths and Limitations

Strengths

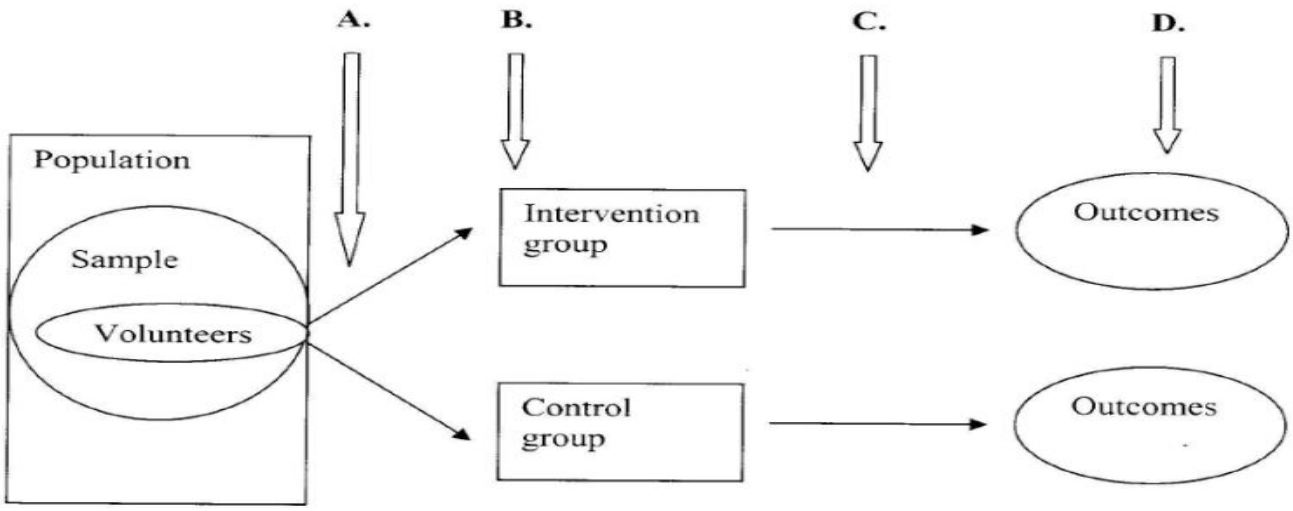
High level evidence in RCT

- ★ One treatment is directly compared to another to establish superiority.
- ★ This study design can make causal inferences, i.e. it is the strongest empirical evidence of a treatment efficacy.
- ★ Minimum bias.

Limitations

- ★ Time consuming, expensive.
- ★ Results may not mimic real life application.
- ★ Ethical implications: denying treatment to one group, ability to provide informed consent.

General Design of a Randomized Controlled Trial



A. Randomization and allocation concealment
B. Actual assignment that can be followed by masking subjects as to their assigned group
C. Prospective evaluation period during which health care providers, investigators, and/or external monitoring committees (eg, data safety monitoring board) can be masked as to the subjects' assigned group
D. Outcome evaluation or adjudication during which outcome asessors can be masked as to the subjects' assigned group