Biostatistics

Doctor 2018 | Medicine | JU

Sheet Slides

Done By

Dana Hamo

Contributed in the Scientific Correction

لينا عبد الهادي

Contributed in the Grammatical Correction

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Doctor

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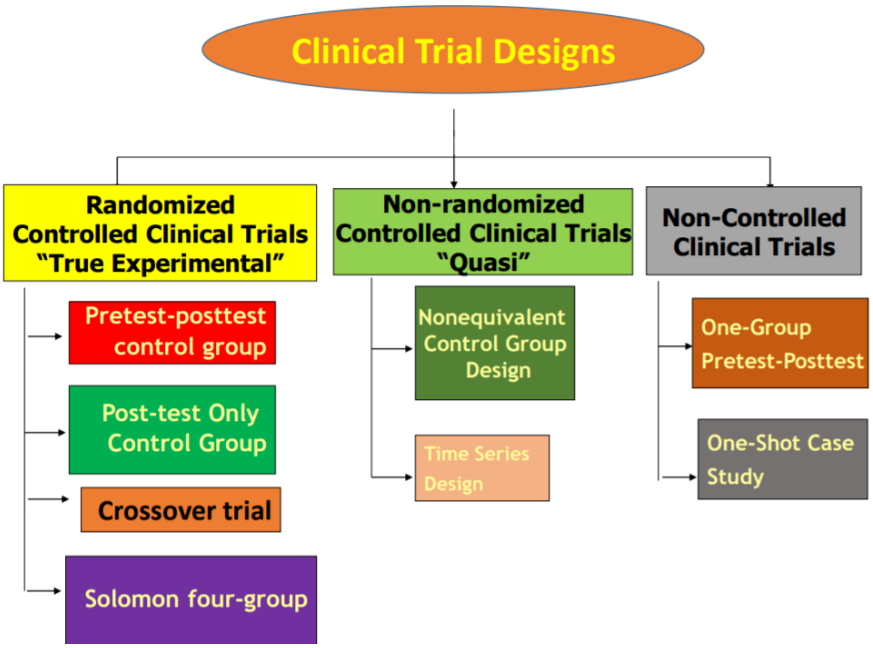
Experimental Epidemiology

At the beginning of this lecture, Dr. Mahmod revised some key points mentioned in the previous lecture:

1. The 3 types of Experimental Designs, and their subtypes.



2. The 4 Criteria of Experimental Design.

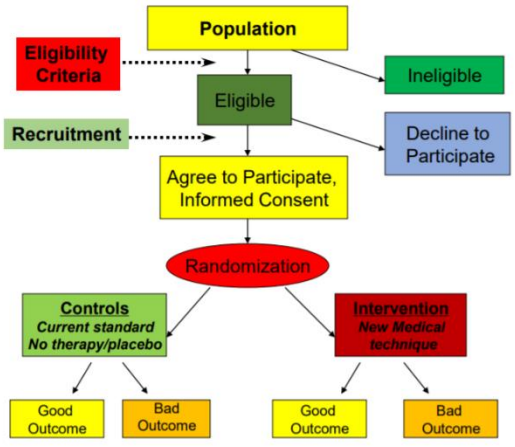
Design Options

1. Controls: Use of a comparison or control group.
2. Randomization: the random (by chance) assignment of participants into exposure groups.
3. **Manipulation: Manipulation of the independent variable**
4. Blinding:

Sponsor's Clinician / Analysis Team	Investigator	Patient		
No	No	No	➡	open/unblinded
No	No	Yes	➡	single blinded
No	Yes	Yes	➡	double blinded
Yes	Yes	Yes	➡	triple blinded

DON'T FORGET! The most common type of blinding technique is DOUBLE BLINDED.

3. The Generic Design of the Randomized, Controlled Clinical Trials "True Experimental"



Before we discuss the types of experimental studies and their characteristics, let's talk about 2 concepts first: (1) The Inferential table and (2) the validity and reliability.

1. The Inferential Statistical Analysis table.

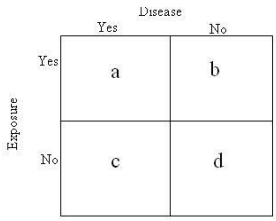
Summary Table of Statistical tests

Level of Measurement	Sample Characteristics					Correlation
	1 Sample	2 Sample		K Sample (i.e., >2)		
		Independent	Dependent	Independent	Dependent	
Categorical or Nominal	X^2 or bi-nominal	X^2	Macnarmar's X^2	X^2	Cochran's Q	
Rank or Ordinal	X^2	Mann Whitney U	Wilcoxin Matched Pairs Signed Ranks	Kruskal Wallis H	Friedman's ANOVA	Spearman's rho
Parametric (Interval & Ratio)	z test or t test	t test between groups	t test within groups	1 way ANOVA between groups	1 way ANOVA (within or repeated measure)	Pearson's r
		Factorial (2 way) ANOVA				

- THIS TABLE IS REQUIRED EXCEPT FACTORIAL (2 WAY) ANOVA.
- We are just required to know about univariant (1 dependent variable) and bivariant (2 dependent variable) statistical tests.
- This table contains statistical approaches we use to analyze that outcome/data from experimental studies.
- Each experimental study has its own design, and each design has its own criteria from which we decide which statistical approach will be used.
- TO DECIDE WHICH STATISTICAL APPROACH, there's two things we should consider in the experimental design: (1) SAMPLE CHARACTERISTICS and (2) LEVEL OF MEASUREMENT
- (1) SAMPLE CHARACTERISTICS:
  - 1 Sample against the standard
  - 1 Sample pre- and posttest (2 sample dependent)
  - 2 different samples (2 sample independent)
  - 3 or more samples of the same group (k sample dependent)
  - 3 or more samples of different groups (k sample independent)

- (2) LEVEL OF MESUREMENT: there are 4 levels of measurement: (1) Nominal (2) Ordinal (3) Interval (4) Ratio

- Both Interval and Ratio, are parametric/quantitative/continuous data that we deal with them as one in the table. We use parametric techniques that work on the **MEAN** (so ordering the data doesn't matter)
- For the data to be continuous, there are 4 assumptions that must be met: (1) the dependent variable is continuous (2) the independent is either dichotomous {2 samples} or categorical {k sample} (3) the groups are homogenous, using Levene's test (4) the data is normally distributed
- Both Nominal and Ordinal are non-parametric/qualitative.
- The Nominal could be dichotomous or categorical. The techniques differ between the dichotomous and categorical, however, it depends on the **PROPORTION**.
- The Ordinal or Rank, their techniques work on the **MEDIAN**. That's why they're called rank as to get the median, you must first rank the data.
- The Chi square is a non-parametric technique. It has 2 types: (1) the independent chi square used when 2 sample/k sample is independent (2) the Goodness-of-fit chi square where one group is compared to the ideal group (1 sample).
- The Chi square measure significance/association but it does NOT measure the strength of the association. To measure the strength of association there are two ways: (1) Phi correlation when there is a 2 by 2 table as in YES/NO table →

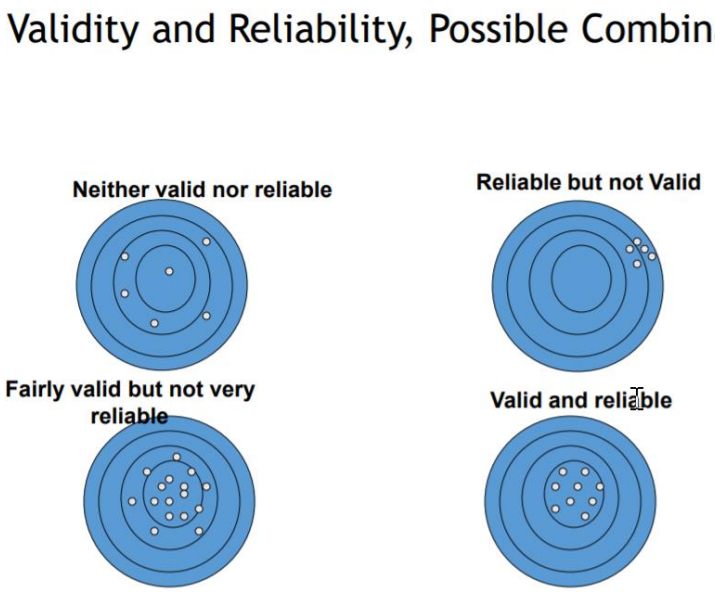


(2) Cramer's V if more than 2 by 2 table.

- One last thing to talk about is the correlation. There are 4 types:
  - Pearson's r: it ranges between 0 and 1. The 1 could be negative or positive as an indication of the direction of association. Weak correlation if less than 0.4. Moderate correlation if between 0.4 and 0.8. Strong correlation if greater than 0.8. NEVER 1 unless with the variable itself (never 2 variables that are identical).
  - Spearman's rho
  - Point-by-serial
  - The chi square followed by phi correlation if 2 by 2 table or by Cramer's v if more than 2 by 2 table.

2. Validity and Reliability.

- Validity means the findings and conclusions are TRUE.
- Validity = Accuracy
- Reliability means that someone else using the same method in the same circumstances should be able to obtain the SAME FINDINGS.
- Reliability = Consistency and Stability

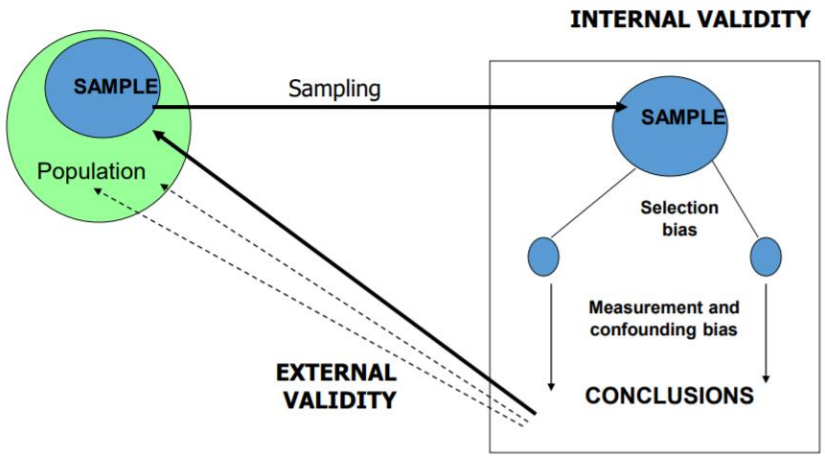


Validity means TRUE FINDINGS, in other words, hitting the target. In this example, the target is the innermost circle.

Reliability means SAME FINDINGS. It doesn't matter if the findings are correct or not, what matters is that all the results are close to one another.

- Validity has two types – Internal and External. To understand the difference, let's consider the following example:

❖ We have a population; access which is the one we take the sample from and reference population which we generalize the conclusion on.



❖ A sample is taken (from access population) and is divided into an experimental group (administered the drug) and control group (comparison). However, there will be some selection bias where the groups could have some degree of heterogeneity (not 100% identical) and leads to threatening the internal validity.

❖ What is the internal validity? in any study, the cause should be the one (the only one) that leads to the outcome (y is due to x) EX: relief of low back pain is ONLY due to the administration of treatment. However, there are some factors that threat the relationship between the cause and the effect. It's usually measured by power

(100%), the closer it is to 100, the higher the internal validity (The effect is 100% due to the cause).

- ❖ At the end of an experimental study, we end up with a conclusion (assuming it is internally valid) and we must generalize it on the reference population. In this case, we have external validity.
- ❖ What is external validity? it is the Generalizability, the extent to which findings from a study can be applied to a larger population or different circumstance.

Summary of what we said:

Conclusion Validity

Refers to the extent of researcher's ability to draw accurate conclusions from the research. That is, the degree of a study's:

a) Internal Validity—correctness of conclusions regarding the relationships among variables examined
   - Whether the research findings accurately reflect how the research variables are really connected to each other.

b) External Validity -Generalizability of the findings to the intended/appropriate population/setting
   - Whether appropriate subjects were selected for conducting the study

Validity

- ❑ **Internal validity** is the degree to which the results of a study are correct for the sample of participants being studied
  - Determined by how well the design, data collection and analyses are carried out
  - Threatened by all of the biases
- ❑ **External validity** is the degree to which the results of an observation hold true in other settings i.e. **Generalisability**

Internal Validity

- **The degree to which changes in the dependent variable (effect) can be attributed to the independent variable (cause).**
- **Threats to internal validity are factors other than the independent variable that influence the dependent variable. These factors constitute rival explanations or competing hypotheses that might explain the study results.**

External Validity

- External validity: is the degree to which study results can be generalized to other people or other settings.
  - Questions to be asked in external validity are:
    - With what degree of confidence can the study findings be transferred from the sample to the entire population?
    - Will these study findings hold true with other groups in other times and places?

THREATS TO INTERNAL VALIDITY.

- **Selection bias: subject differences to begin with rather than the manipulation of the independent variable. (selection of a group who is different 'in motivation' more than in the control group to change**
- **History: When some event other than the experimental treatment occurs during the course of the study (Introducing a teaching program and a newspaper article is published in the same topic area of the independent variable)**
- **Maturation: Changes that occur within the subjects during the experimental study influence the study results. (people may become older, taller, or sleepier from the time of pretest to the posttest. (studies of growth among children with the introduction of an independent variable as the cause and at the same time changes may occur in these children during the course of the study)**
- **Testing:**
  - **It refers to the influence of the pretest or knowledge of baseline data on the posttest**
  - **Subjects may remember the answers they put on the pretest and put the same on the posttest e.g., in a study of weight reduction program, knowledge of your pretest result (weight) may make you more effort in reducing weight regardless whether you take the program or not**

1. **SELECTION BIAS:** Degree of heterogeneity
2. **HISTORY**: let's say you have designed a weight loss program and the participants in your sample start to lose weight ☺ but the real reason for their weight loss is due to another weight loss program on TV. Some events occurring beside your program/experiment. (extraneous variables)

3. **MATURATION**: changes occur among patients during the experiment.

Children → adults

Women → pregnant

Adult → elderly

4. **TESTING**: the answer of the participants in the posttest is not due to the treatment, but due to the answer they have used in the pretest. EXTRA: it refers to the effect of taking a pretest of subject's performance posttest. The effect of taking a pretest may sensitize an individual and improve the score of the posttest. For example, individuals generally score higher when they take the test a second time regardless of the treatment (because they remember the correct answer).

- **Instrumentation change:**
  - When mechanical instruments or judges (in observational studies) are used in the pretest and posttest phases of the study.
  - A change of the instrument itself or the difference in the ratings of the judges as they became more tired or make less or more observations
- **Mortality:**
  - Subject dropout: dropouts are of a particular characteristics different from those who remained in the study
  - The longer the study lasts the more subjects drop out will occur
  - Subjects mortality is another factor.

5. **INSTRUMENTATION CHANGE**: the group of doctors present in the pretest is different than the those in the posttest (different judges). It also could be a change in the device/instrument used.

6. **MORTALITY**: is the study last for 4 to 5 years, then we might lose some participants (maybe because they don't want to participate anymore). We could start with 1000 participants and end up with only 100 participants.

7. **HAWTHORNE EFFECT** (explained down below)

THREATS TO EXTERNAL VALIDITY.

- Hawthorne effect: when the study participants respond in a certain manner because they are aware that they are being observed (also a threat to internal validity)

- **Experimental effect: A threat that occurs when the researcher characteristics or behaviors influence the subjects behaviors (e.g., facial expressions, age, gender etc.).**
  - **Used in experimental design research**
  - **Rosenthal effect: the influence of the interviewer on respondents answers, e.g.., the way the researcher dresses might influence the study participants**

1. HAWTHORNE EFFECT: referred to as the observer effect. Individuals modify or improve an aspect of their behavior in response to their awareness of being observed (also a threat to internal validity).
2. ROSENTHAL EFFECT: conscious or unconscious actions of the researchers affect the participants' performance and response. EXAMPLE: if you send a man in suit to interview drug users, the drug user won't give him his/her data as they're afraid that he might be undercover ☹ However, if you send a man covered in tattoos, the drug user will give his/her data to him.

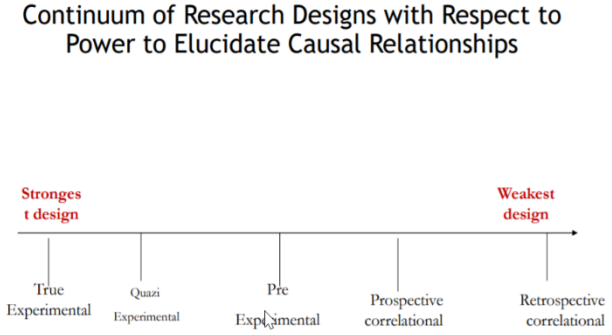
- **Reactive effects of the pretest:**
  - **Also called measurement effect: the subjects are sensitized to the treatment through taking the pretest**

3. REACTIVE EFFECT: EXTRA: a researcher wants to conduct a study to assess the effect of a health education program. In this instance, the researcher conducts a pretest to collect baseline data before health education. This pretest may sensitize the subjects to learn about health issues irrespective if the health program is provided or not.

HOW TO DEAL WITH THREATS TO VALIDITY

- Careful design and pretesting
- Knowledge of environmental events
- Control group
- Random assignment of subjects
- Well defined diagnostic criteria
- Well trained research assistants
- Appropriate data collection methods
- Ensuring adequate follow up

Note: Dr. Mahmod didn't explain the slide below ☺

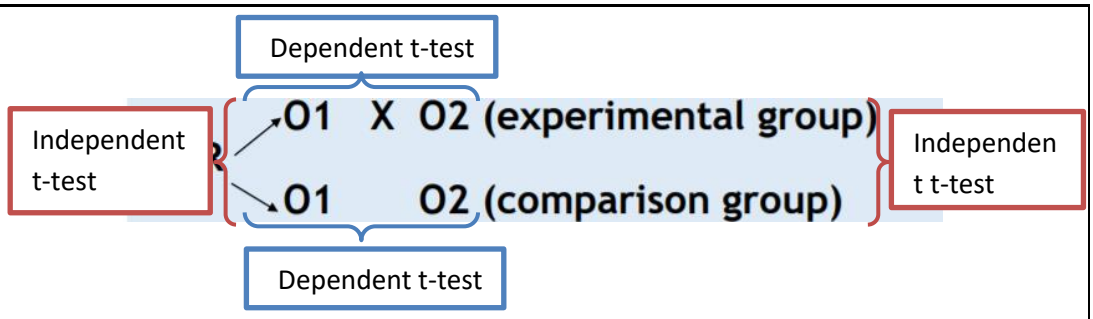


Now, let's discuss experimental studies and their subtypes. ☺

Randomized Controlled Clinical Trials "True Experimental" Designs:

- Randomization ☺
- Control Group ☺
- Manipulation ☺

1.Pretest-posttest control group	• Pretest-posttest control group R → O1 X O2 (experimental group) R → O1 O2 (comparison group)
METHODOLOGY	○ We have 2 groups; experimental and comparison. First, we observe the 2 groups before administering any treatment (pretest), in other words, we collect baseline data (This step is important as we can use Levene's test to test for Homogeneity). ○ Then, the experimental group is given the new treatment while the comparison is given the current/standard treatment. ○ After that, we observe the 2 groups again (posttest) ○ Time-consuming (3-6 months up to 1 year)
ANALYSIS	○ If it's **Homogenous** (according to Levene's test) and **normally distributed**, then we use parametric techniques: ○ First parametric technique is using dependent and independent T-test ○ Dependent t-test: within the same group → between the pretest 01 and the posttest 02 of the experimental and comparison group. ○ Independent t-test: 2 different groups → between the pretest 01 of both groups and the posttest 02 of both groups.

<table>
<tr><td></td><td>


However, we will be committing <u>Type 1 Error</u> → the alpha will be more than 20% as each time the alpha will increase by 5% so <u>we cannot use t-test</u>. ☹
We use the second parametric technique (which has an alpha of 0.05) which is the <u>ANCOVA</u>.
Let’s take an example:

<table>
<tr><td>Marks of Students in the Final (Mean)</td><td>Pretest</td><td>Posttest</td></tr>
<tr><td>Group 1 (experimental)</td><td>30</td><td>60</td></tr>
<tr><td>Group 2 (comparison)</td><td>20</td><td>55</td></tr>
</table>

If we used the independent t-test between the posttest outcome of group 1 and group 2 → 60-55= 5 → then, there’s a difference in the means <u>BUT THIS IS NOT A REAL VALUE</u> → so we will commit Type 1 error by rejecting the Null Hypothesis while it’s true.
In the ANCOVA, 60-30= <u>30</u> and 55-25=<u>35</u> →yes, there is a real difference between the comparison and experimental (where the comparison is higher) so we reject the Null Hypothesis.
Remember! The Null hypothesis is the hypothesis that there is no significant difference between specified population.
EXTRA: if the data is Heterogenous, use Mann-Whitney.

</td></tr>
<tr><td>ADVANTAGES</td><td>

Most frequently used experimental design
Controls for all threats to internal validity

</td></tr>
<tr><td>DISADVANTAGES</td><td>

The external threat of the reactive effects of the pretest. Results can be generalized only to situations with pretest administration before treatment.

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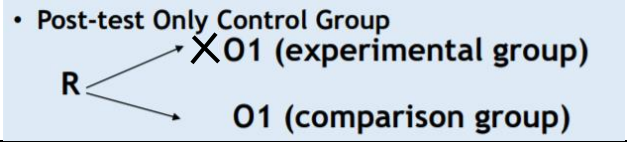
<tr><td>2.Post-test Only Control Group</td><td>


</td></tr>
<tr><td>METHODOLOGY</td><td>

NO pretest groups EX: car accidents
Administer treatment to experimental group, then observe.
The same thing to control but no manipulation (no treatment)

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<tr><td>ANALYSIS</td><td>

2 outcomes (means), 2 independent groups → Independent t-test

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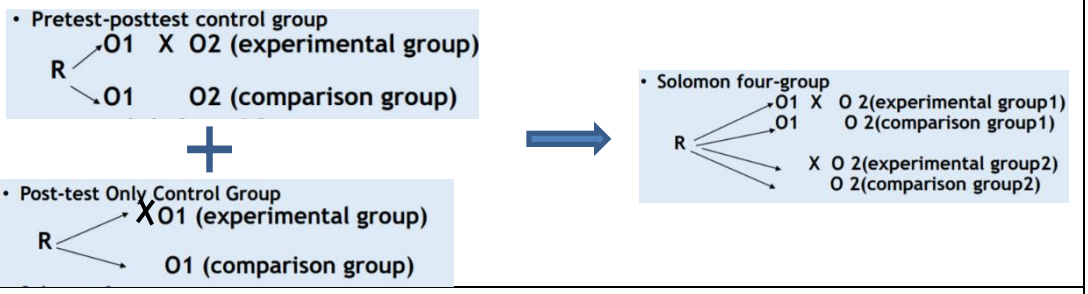
</table>

ADVANTAGES	○ not time-consuming ○ Easier and superior to pretest-posttest design ○ Random assignment of subjects into groups in the posttest-only group ensures equality
DISADVANTAGES	○ NO pretest→ NO baseline data → NO levene's test→ NO indication if homogenous or heterogenous

3. Crossover trial (Dr. Mahmod explained this design in the previous lecture)

2 groups → Experimental (new treatment)→observe
2 groups → Control (current treatment)→observe

THEN, switch between the groups (crossover) → the participant in the control group becomes in the experimental group and vice versa.

4.Solomon four-group	
METHODOLOGY	○ Subjects are randomly assigned to one of four groups: two experimental and two comparison groups. ○ 2 designs together 
ANALYSIS	○ K sample (as more than 2), independent → one-way anova ○ The anova test shows a significance between the 4 groups but doesn't tell which group the highest difference has (doesn't discriminate between the groups) ○ Solution? Using **Post-hoc analysis**. This test has more than 20 types, in the Solomon four-group design, we use **Scheffe test** to tell the difference between the 4 groups. It works by comparing each 2 groups together (group1 with group2, group1 with group 3, group 2 with group 4, group3 with group2 and so on)
ADVANTAGES	○ **Most powerful experimental design** because it minimizes threats to internal and external validity ○ It controls for all threats to internal validity and for reactive effects of the pretest. Any differences between the experimental and the comparison groups can be more confidently associated with experimental treatment.
DISADVANTAGES	○ Time-consuming, huge budget, **requires large sample size** so huge outcome and **complicated analysis**

Experimental Studies
Advantages

- Randomisation distributes confounders equally between the groups to be compared for the outcome. Hence any difference can be confidently attributed to intervention.
- Provides evidence for cause and effect.
- Allows standardisation of eligibility criteria, treatment and outcome assessment.
- Allows use of statistical tests with few in built assumptions.

Experimental Studies
Disadvantages

- Expensive in terms of time, personnel and resources.
- Ethical issues for certain interventions or circumstances.
- May be unsuitable because of problems of likely co-operation or rarity of outcome.
- Tend to induce artificial situation because of
  - Volunteerism
  - Strict eligibility criteria
  - Highly standardised interventions that may be different from occurs in common practice (difference between efficacy and effectiveness)

Quasi-Experimental studies Designs:

- In a quasi-experimental study, one characteristic of a true experiment is **missing**, either **randomization** or the use of separate **control group**.
- **Always** includes the **manipulation** of an independent variable which serves as the intervention

A. Non-equivalent Control Group

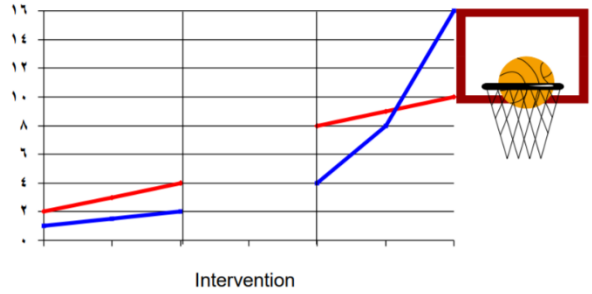
1. It is similar to pretest-posttest control group design but with no random assignment of subjects to experimental and comparison groups
   O1 X O2 (experimental group)
   O1 O2 (comparison group)
2. Problems of this design:
   1. Threats to internal validity are history, testing, maturation, and instrumentation change.
   2. Biggest threat is selection bias (no one can tell if the two groups were similar to start with)

B. Time-Series Design

1. The researcher periodically observes or measures the subjects
   O1 O2 O3 X O4 O5 O6
2. Assessing pain level of a group of people with low back ache over three weeks then give a specific exercise to reduce the pain. Pain level is measured again to determine if low backache still persists
3. Problems with this design: Threats to validity are history and testing

- Time consuming
- Analysis? repeated measures anova

Interrupted Time Series



Sometimes, the treatment may last for 6 months, thus, creating a gap in the time series.

Pre-experimental Designs

- NO randomization ☹
- NO control group ☹
- YES manipulation ☺

- Types:
  - One-Group Pretest-Posttest Design
    - O1 X O2
    - Threats to internal validity: history, maturation, testing, and instrumentation change.
  - One-Shot Case Study:
    - X O
    - exposure of one group to an experimental treatment and observed after the treatment.
      - No comparisons made
      - No one can tell whether they had the knowledge before the intervention
      - Threats to internal validity are history, maturation and selection bias

Analysis? dependent t-test

Analysis? 1 sample t-test

GOOD LUCK ☺☺

QUESTIONS

Which is used to find efficacy (past paper)

A. Cross section
B. Cohort
C. Case control
D. Clinical
E. B&D

Ans: D

Explain experimental studies

A. This is the difference between the rate of disease in the nonexposed segment of the population and the overall rate in the population.
B. These are a form of intervention studies, two types are randomized controlled trials and quasi experiments
C. is designed to test preventive measures
Ans: B

What are randomized control trials

A. evaluates new treatment methods
B. are an experiment in which subjects in a population are randomly allocated into groups, usually called study and
control groups.
C. involves the administration of a test regimen to humans to evaluate its efficacy and safety.
Ans: B

What are quasi experimental designs

A. When sensitivity tests correctly identify all potential cases as either negative or positive
B. Describes when a definitive diagnosis that has been determined by biopsy, surgery, autopsy or other method and has been accepted as the standard.
C. Where the investigator manipulates the study factor but does not assign individual subjects randomly to the exposed and non-exposed groups.
Ans: C

What is external validity

A. This is the generalizing of the study to the population
B. Was the conclusion true? It is the extent to which you can believe your results
C. It is the third variable that relates to the exposure and the outcome
Ans: A

What is internal validity

A. Was the conclusion true? It is the extent to which you can believe your results
B. This is the generalizing of the study to the population
C. It is the third variable that relates to the exposure and the outcome
Ans: A

Fill in the blanks with Experimental or Observational

1. A strength of the ??? study is the investigator's control in the assignment of individuals to treatment groups.

2. A potential advantage of an ??? study is that they are often carried out in more natural settings, so that the study population is more representative of the target population.

3. The major limitation of ??? studies are that they afford the investigator the least control over the study situation; therefore, results are generally more susceptible to distorting influences.

4. A weakness of an ??? study is that randomization to treatment groups may not be ethical if an arbitrary group of subjects must be denied a treatment that is regarded as beneficial.

5. One community in a state was selected by injury epidemiologists for a media campaign and bicycle helmet discount with any bicycle purchase. A similar community about 50 miles away was identified as a comparison community. The epidemiologists compared the incidence of bicycle-related injuries through emergency room surveillance and telephone survey. This is an example of an ??? study.

1. Experimental

2. Observational

3. Observational

4. Experimental

5. Experimental

6. Observational