

Experimental designs  
Sources of Bias  
Participation question  
Ethics

# L09: Study Designs

February 10, 2020

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# Learning objectives for today

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- ▶ Understanding different types of experimental designs
- ▶ Thinking about sources of bias
- ▶ bias from the design or conduct of sampling
- ▶ bias from lack of adherence to protocol
- ▶ bias in assessment
- ▶ bias in analysis
- ▶ Ethics in randomization

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## Experimental designs

## Level of randomization

When we are assigning an exposure/treatment we can do this for different levels (think about our units of analysis).

These could be:

- ▶ Individuals
- ▶ Households
- ▶ Groups
- ▶ clinics

If we think about our resulting data, each of these might be a row in our data frame.

What are some examples of exposures we might randomize at these different levels?

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# Control group

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Usually in a trial, we recruit our participants and randomize them to either an intervention or a “control” condition.

What are some of the reasons we might want to include a control group?

# Blinding



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When we talk about blinding we are talking about keeping the treatment assignment hidden. There are multiple groups we might want to consider keeping this knowledge from.

# Blinding

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- ▶ In a single blind trial it is usually the participants who are blinded
- ▶ In a double blind trial we are generally talking about blinding of the participants and the people doing the assessment of outcomes
- ▶ Triple blinding is often referring to blinding the participants, study staff, and also the investigators and statistical analysts.

Why do you think blinding is important?

Why might we have a trial where we do not blind?

# Placebo



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A placebo is a non-active substitute for treatment. In a drug trial, the placebo is usually a pill made to look identical to the medication being tested, but that does not have the active ingredient.

# What is the placebo effect?

- ▶ from New York Times Magazine, November 2018:



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## Sources of Bias

# Sampling bias

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If our sampling frame does not cover our target population, this is a bias in the sampling process.

Your book refers to this as under-coverage bias.

Lack of representation of homeless individuals is one example we talked about, what might be another example of this?

## Small size

As we saw previously in our example of online reviews, small samples often give unpredictable results. The smaller an effect is, or the more rare the conditions you are studying, the larger the sample needs to be in order to draw conclusions.

We will talk much more about sample size later in the course.

Often trials are designed to find a **statistically significant** difference between treatment and control. This means an observed effect so large that it would rarely occur by chance.

As we move into the next sections we will talk more about probability and assessing the role of chance. In part III of the course we will talk more about statistical significance in assessing differences between groups.

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# Participation

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Once sampled an individual may not agree to participate.

This is referred to as [response bias](#) or [non-response](#). If there is enough information about who did and did not respond, the data may be adjusted to try and compensate for this type of bias. This kind of adjustment is common in survey samples.

Participants may also start the study and then drop out or become [lost to follow up](#). If one of your study groups is more likely to be lost this can create bias.

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When either the study participants randomized to control receive the medication or exposure that was intended to be given only to treatment arm participants.

Examples:

- ▶ MRFIT trial
- ▶ SHAZ!

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Once a participant is randomized to a given treatment, they do not always **adhere** to that treatment.

Often we do two types of analyses with trial data when there are issues of adherence.

**Intention to treat** and **Per protocol**

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Errors associated with imperfect measurement including:

- ▶ imprecise measurement equipment
- ▶ poorly designed or worded questions
- ▶ responses of the individual to the measurement process
  - ▶ white coat hypertension
  - ▶ sleep studies in lab environments

Important to distinguish errors that are systematic

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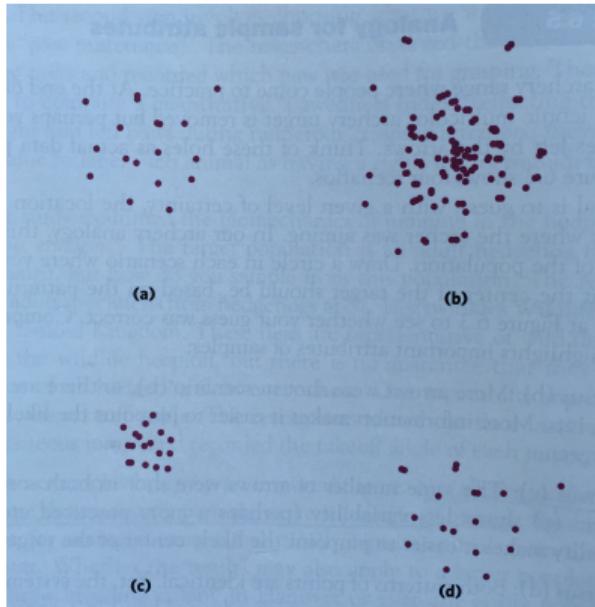
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The process of drawing conclusions about a population based on a sample

# Where is the target?

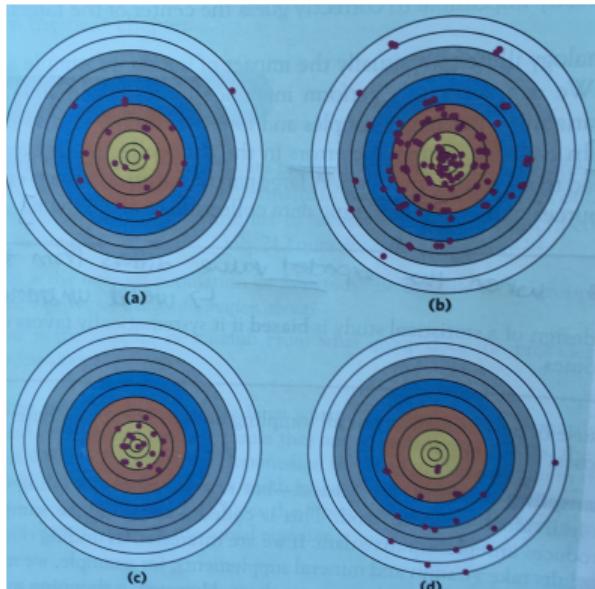
- ▶ Four samples are shown. Imagine guessing the location of the center of the population from the center of the sample distribution



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# Where is the target?

- ▶ The samples are now superimposed on archery targets representing the target population. Sample (d) in this analogy is a biased sample



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# Where is the target?

Key takeaways from the previous figures:

1. A vs. B: More arrows make it easier to pinpoint the center of the target (assuming the archer has good aim)
2. A vs. C: Less variability makes it easier to pinpoint the center of the target
3. A vs. D: Systematic downward misses in scenario D bias our best guess of where the target is.

In real life we do not know where the target actually is, so we can't be sure whether our guesses are biased or not. But we can discuss the possibility of bias, and quantify how much bias would be required to negate a conclusion

Which of these is precise and which is accurate?

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# Issues with self report

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In addition to the biases that may come with the design of questions you ask a participant in surveys, there can be biases associated with willingness or ability to report information:

- ▶ social desirability biases
- ▶ poor recall
- ▶ biased recall
- ▶ diary compliance

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## Participation question

# Internal vs external validity

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- ▶ Are individuals/clinicians aware of the treatment being received? How can this affect results?
- ▶ Can the findings be replicated in another experiment? Are the findings valid in other populations?
- ▶ If they aren't valid in another population, this means the results are not **externally valid**.
- ▶ Studies can be **internally valid** (meaning they can estimate causal effects for the population included in the study) but not externally valid.

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## Ethics

# Equipoise

## Equipoise in the context of trials

Unethical not to give a treatment or exposure condition that is known to be better.

Famous example of an unethical trial is the Tuskegee syphilis study which started in 1932. There were many ethical issues in this trial, one of which was a lack of equipoise. Penicillin became available in 1947.

- ▶ timeline of the study is here [CDC](#)

# Informed consent

- ▶ from [Statnews.com](#), February 2019:

FIRST OPINION

## ‘Three Identical Strangers’: It’s not too late to address the ethical violations

By KAREN GLANZ and HOLLY FERNANDEZ LYNCH / FEBRUARY 7, 2019



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If the incentives to join a study are too strong, participants may be willing to consent (even with informed consent) to conditions they would not otherwise accept.

- ▶ Large payments
- ▶ Access to treatment not otherwise available
- ▶ Fear of losing medical care

# Who benefits from the study, who is included

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There is also a larger issue of ethics related to who benefits from the trial.

- ▶ Is there a direct benefit to participants?
- ▶ Is there a potential benefit to individuals who are similar to the study participants?
- ▶ Is there a group that is excluded from participation unfairly?

# Parting humor



**"Miss Peterson, may I go home? I can't assimilate  
any more data today."**

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