Experimental Study Design

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### Population vs. Sample

<table>
<thead>
<tr>
<th>Population</th>
<th>All possible subjects that share a characteristic</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Disease</td>
</tr>
<tr>
<td></td>
<td>• Geographical area</td>
</tr>
</tbody>
</table>

| Sample     | Subset of the population                           |
Why is sampling important?

- It’s generally impossible (too expensive or not feasible) to collect information from the entire population

- External validity (ability to generalize your results) depends on having a representative sample

- Account for other patient characteristics (e.g., gender, race)

- Larger sample, higher power
  - The IRB asks you for a power analysis
  - Want to make sure the sample is large enough to detect a difference and not waste time/resources
  - Unethical to conduct trial if no power to find a clinically meaningful difference
What does a representative sample look like?

If this is your population...

... which of these would be a representative sample?
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Components of a Research Question

A good research question answers these questions:

1. Who are the subjects?

2. Are the subjects organized into groups? If so, how?

3. What are the measurements to be taken on the subjects?

4. What is the research goal?
   - Estimation
   - Change
   - Comparison/relationship
Research Question vs. Study Design

- The important components of study design and a good research question are almost identical

- Having a clear, complete study design will help formulate a good research question

- You cannot achieve your research goal without a valid study design

- A statistician should be able to assign the statistical method based on your research question and study design alone
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Goals of Study Design

- Specify the research goal
  - Estimation
  - Change
  - Comparison/relationship

- Define how the outcome will be measured
  - Number or category
  - Time to event

- Decide the number of groups needed

- Determine the timing of measurements
  - Pre/Post
  - All subjects measured at same time points
  - Subjects measured at different time points
Goals of Study Design Cont.

- Ultimately, the research goal is to show causality
- To show causality you need:
  - Treatment before the outcome
  - Groups equal
  - A difference exists
  - The difference is not attributable to anything else
Prospective vs. Retrospective

**Prospective study**

Researcher wants to see if the outcome occurs within the sample
- You control the measurements in a prospective study

**Retrospective study**

The outcome has occurred and the researcher is looking back to search for possible risk or protective factors
- Beware of comparison in retrospective studies

Some study designs are inherently prospective, some are inherently retrospective, some can be both
Popular Study Designs

Cross-sectional Study

- All measurements made at once
- Measures prevalence of disease or condition (estimation)
- Also can measure a relationship
- Subjects must be representative of the population
- This study design is never causal
Popular Study Designs

Cross-sectional Study

Q: What is the rate of unanticipated adverse events one week after sedation in pediatric patients sedated by a physician alone, a nurse alone, or a physician and nurse team for a non-invasive radiology procedure?
Popular Study Designs

**Cohort Study**

- Follow a group of patients over time
- Interested in estimation or change over time
- *Prospective cohort* enrolls patients and follows them until the end of the study period
- *Retrospective cohort* samples patients based on inclusion/exclusion criteria and looks back in their medical history for the outcome of interest
  - Chart review
Popular Study Designs

Cohort Study

Q: Do patients undergoing a non-invasive radiology procedure who received sedation from a single provider versus a team of providers have the same odds of an unanticipated adverse event?
Popular Study Designs

Case-Control Study

- Cases: subjects with the disease or condition
- Controls: subjects without the disease or condition
- Match cases and controls on demographics or other patient characteristics
  - Takes confounding into account in the study design itself
- Good for rare diseases
  - You start with those who have the condition
  - Easier to start with cases than to wait for them to occur when the disease is rare in your population
- Measure a relationship
Popular Study Designs

Case-Control Study

Q: Controlling for the type of care team providing sedation (physician alone, nurse alone, or physician and nurse team), is there a difference in the rate of adverse events for patients receiving a non-invasive versus an invasive radiology procedure?
Clinical trials and randomized controlled trials (RCTs)

- Prospective, time consuming, expensive
- Approval of new drugs
- RCTs
  - Baseline vs. Follow-up
  - At least two groups (e.g., placebo and treatment)
  - Patients are randomized
  - This study design is the most causal
  - Consult a biostatistician!
Popular Study Designs

Clinical trials and randomized controlled trials (RCTs)

- Consent
  - yes → Randomize
  - no → Exclude

Randomize

- Treatment 1
- Treatment 2
Popular Study Designs

Clinical trials and randomized controlled trials (RCTs)

Phases of a Clinical Trial:

- Phase I: Dose-finding (estimation)
- Phase II: Efficacy (estimation, change, relationship)
- Phase III: Confirmatory (RCT) (estimation, relationship)
- Phase IV: Effectiveness (estimation, change, relationship)
Popular Study Designs

Clinical trials and randomized controlled trials (RCTs)

Q: Do pediatric patients receiving a non-invasive radiology procedure have less incidence of adverse events when sedation is delivered by a nurse and physician team compared to those whose sedation is delivered by a nurse or physician alone?
Randomization

- Random doesn’t always mean random!

- Types of randomization:
  - Randomized sample
  - Stratified sampling
  - Blocked randomization
Randomization

- Random doesn’t always mean random!

- Types of randomization:
  - **Randomized sample**
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Randomization

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- Types of randomization:
  - Randomized sample
  - **Stratified sampling**
  - Blocked randomization
Randomization

- Random doesn’t always mean random!

- Types of randomization:
  - Randomized sample
  - Stratified sampling
  - **Blocked randomization**

![Diagram of Randomization](image-url)
Randomization

- Random doesn’t always mean random!

- Types of randomization:
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- Beware of the convenience sample
  - Why might taking a sample only in the winter be a bad idea?
  - What might be an issue with sampling patients only at VCU?

- Ask a biostatistician
Collecting Measurements

Consider the following questions:

- What outcome do you want to measure?

- How will you measure your outcome? Can it be measured directly?

- How well does your measurement capture your outcome?

- Is your measurement continuous or categorical?
  - Avoid cutoffs when possible
  - Is the difference between a BMI of 30 and a BMI of 29.9 meaningful?
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Study Design Activity

**Article:** "Nebulized Hypertonic Saline for Bronchiolitis" (Wu et al.)

**Directions:**

1. Read the introduction and methods up to "Outcome Measures"

2. In pairs, answer the questions on the handout

3. We will come back together to discuss
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Why is this important?

• These details are necessary in order to determine the appropriate statistical methodology to analyze your data

• Garbage in, garbage out

• Keep your biostatistician happy
Thank you for listening and participating!

Parting advice

If you are designing a study, get a biostatistician involved as early as possible, preferably before you start data collection.

Contact the Biostatistical Consulting Laboratory:
http://www.biostatistics.vcu.edu/bcl/

These slides will be available at the link above.

Thanks to Dr. Sima and Dr. Sabo for their guidance!