Study Design Overview
Mary Lipscomb Hamrick Research Course
Pre-Workshop

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Resources


https://www.nice.org.uk

https://hsl.lib.umn.edu/biomed/help/understanding-research-study-designs

http://www.cebm.net/study-designs/
Agenda

Key Steps Prior to Determining Study Design
  o PICO
  o Key Measurements

Categories of Research

Defining Characteristics of the Study Designs

General Overview of Study Designs
  o Degree of Scientific Rigor
  o Resource Cost

Study Design Selection & Descriptions

Helpful Algorithm
Key Steps Prior to Determining the Study Design
Determine the Aim

What is the **aim** of the study?

- To describe a population (PO) = **descriptive**
- To quantify the relationship between factors (PICO) = **analytic**
Define PICO

- Patient, population or problem
- Intervention, Prognostic factor, or Exposure
- Comparison or Intervention (as appropriate)
- Key Outcomes – measurements
Key Measurements

INDEPENDENT VARIABLE: predictor variable
  o the parameter that varies between the groups, e.g. the intervention, exposure or predictor factors

DEPENDENT VARIABLE: outcome variable
  o Response or effect presumed to vary depending on the independent variable; the outcome of interest

CONFOUNDING VARIABLE:
  o outside factors that may influence the results of another variable
Categories of Research

**Experimental**
- Randomized Controlled Trial (RCT)
- Single-subject designs
- Quasi-experimental studies

**Exploratory**
- Cohort study
- Case-control studies
- Predictive Research

**Descriptive**
- Case study
- Case series
- Developmental research
- Normative research
- Qualitative research
- Descriptive surveys
Experimental vs. Observational

How was the intervention assigned?

- Yes = experimental
- No = observational
Observational Study

What was the **timing** of the measurement of outcome?

- After the exposure or intervention = cohort (prospective)

- At the same time as the exposure or intervention = cross-sectional or survey

- Before the exposure was determined = case-control (retrospective)
  - Based on recall of the exposure
Defining Characteristics of Study Designs

**Intervention/Exposure**
- Clinical trial

**Observational**
- Cohort studies – group of subjects over time
- Cross-sectional studies – single occasion
- Case-control studies

**Time Frame of Data Collection**
- Prospective
- Retrospective
Overview of Study Designs
Common Study Designs

Randomized Controlled Trial (RCT)
Cross-over
Cross-sectional
Cohort
Case-control
Before-and-after
Surveys
Less Common Study Designs

Factorial
Single group cohort (inception)
Retrospective cohort
Ambispective cohort
Nested case-control
Historical controls
Study Design Selection
Study Design Selection

What is the “job” or clinical question?
What tools can address the job?
What tools are available to complete the job?
How many resources are available?
What is the time frame to completion?
What is the “job” or clinical question?

Establish the value of a therapeutic intervention.

Establish a “cause-effect” relationship.

Demonstrate associations.

Examine risk factors, predictors.

Calculate prevalence rates.

Calculate incidence rates.

Establish the accuracy of a diagnostic test.
Degree of Scientific Rigor

How much does the study resemble a lab experiment?

- Presence of randomization – controls for confounders at the beginning of the study
- Manipulation of the independent variable
- Control over other study parameters – controls for confounders during the study
Resource Cost of Study Designs

Randomized Clinical Trial

Cohort Study
  - Prospective > Retrospective

Cross Sectional

Case Control
  - Nested > Other

Retrospective Case Series
Rules for Study Design Selection

**Rule 1:** don’t use an expensive “sharp shooters rifle” when the target is broad and a shotgun will do

- Know the difference between a preliminary (pilot) study or hypothesis generating study and a hypothesis answering study

**Rule 2:** when the target is highly specific and the goal is an exact answer, use the most precise tool available

- To argue a true “cause-effect” relationship, use an experimental design with the highest degree of scientific rigor feasible
Common Study Design Descriptions
Randomized Clinical Trials

- Should be preceded by highly supportive data
  - less scientific human studies
  - pre-clinical animal studies
- Used as the **definitive answer** to a research question
- Must be able to **randomize**
- Is the most **resource expensive** design
Cross-over Studies

Essentially an RCT variation
Each subject gets two different treatments, in random order
Since each subject is their own control, extraneous variables are absolutely balanced between the groups
Must insure an adequate “wash-out” period between the different study treatments
True-experimental designs: Problems

- Resource expensive
- Not always ethical, or possible to randomize
- Require patient consent, which is not always possible
- Impractical for uncommon clinical conditions
Group Sequential Design

Similar to a factorial or a cross-over design in that each subject receives both independent variables.

Difference is that they each get them in a set order;

No individual randomization.

Often used for diagnostic studies, but can be used for therapeutic studies.
Cross-sectional Studies

Almost always prospectively performed
Are purely observational
Take a single “snap-shot” in time
Do not look backwards at predictors
Do not look forward at outcomes
Fast, easy, inexpensive.
Provides great deal of information quickly.
Best for:
  o Prevalence rates
  o Simple descriptive summaries
  o Possible associations
  o Preliminary data to guide future studies
Cross-Sectional Study Example

Research Question:
What is the prevalence of helmet use in adolescents involved in bicycle accidents?

- More accurate than a simple chart review
- Allows collection of additional data that may identify risk factors for non-helmet use
Cross-sectional Design
Comments

Observations can be done
  o at one single time for the entire study (i.e., all at once) OR
  o at an equivalent time per enrolled study subject

Advantage for prevalence calculations is that the denominator is directly measured at the same time as the numerator
Cohort Studies

Latin: cohors

- An enclosed company or yard of soldiers
- All of the same type
- In Roman armies, 300-600 soldiers
- Fought together as a unit

Concept: a group of individuals that all share a common characteristic and move forward together (in time)
Cohort Confusion

Probably the most confusing term in research
Has one core definition
Has multiple study applications and variations
Generally thought of as prospective studies
Often called “longitudinal” studies, because after selection, subjects are followed over time for development of the outcome of interest
Main Cohort Types

Individuals selected for a common trait

**Birth cohort**: all born in a set period, usually in a set area

**Inception cohort**: group selected at point in time based on residence, work location, etc

**Exposure cohort**: group selected based on a common exposure
Cohort Purposes

Descriptive (measures of frequency)
- Usually single group (inception)
- Calculate incidence rates
- Describe the natural history of conditions

Analytic (measures of association)
- Requires two groups (with, without exposure)
- Analyzes possible associations between predictor variables and outcomes
Cohort Studies Applications

Single Group Longitudinal
- e.g. Framingham Study
- great for establishing incidence rates, RRs

Prospective analytic (2 groups)
- when want a RCT, but can’t randomize

Retrospective Comparative (2 groups)
- best for relatively rare conditions
- want to compare therapies or exposures
Retrospective Cohort Design

Study groups still selected and sorted by exposure, and followed to measured outcomes.

However, data is all retrospective, i.e., the outcomes have occurred before the research question was determined.

Most valid when applied to existing complete database, e.g., from a prior trial (called “nested”).

Done properly, is only slightly less scientific than a prospective cohort study.
Cohort Design Comments

After controlled clinical trials, one of the most compelling design types to establish associations. However, more prone to bias, so not as strong to prove a true "cause-and-effect" relationship. Overall strength is highly dependent upon the group selection process and the quality of the comparison control group.
Case-Control Studies

Starts with the patient outcome and looks "backward" at prior events.

Generally looks for associations/predictors and generates "Odds Ratios".

Must have very compelling results to argue for a "cause-effect" relationship.
Case-Control Studies

generally used for two reasons:
- Examine aspects of rare outcomes that cannot be studied prospectively.
  - Looks for predictors, associated exposures
- To quickly study predictors of selected outcomes.
  - These usually are hypothesis generating studies that lead into prospective hypothesis testing studies
Case-control Study Limitations

Only one outcome can be studied

Information is limited – retrospective
  - Can not calculate incidence rates or prevalence rates

Susceptible to bias
  - Separate sampling of the case and controls
  - Retrospective measurement of predictor variables
Case Series

- Purely descriptive, observational studies
- Much more powerful than a case report
- Useful for describing new or uncommon disorders or treatment techniques
- No comparison group, so no statistical comparisons
- For rare situations, can provide the most useful information available

Algorithm for Classification

Appendix E Algorithm for classifying quantitative (experimental and observational) study designs

1. Does the study compare outcomes between 2 groups (e.g. intervention/exposure vs comparison)?
   - Yes: Did investigator assign intervention or exposure?
     - Yes: Experimental study
     - No: Observational study
2. Did investigator assign intervention or exposure?
   - Yes: Before and after study or interrupted time series
     - Before and after study or interrupted time series
   - No: Concurrent control group included in study?
     - Yes: Interventions/controls randomly allocated?
     - No: Concurrent control group included in study?
     - Yes: Representative (random) samples of the population?
     - No: Concurrent control group included in study?
8. Exposure and outcome assessed at the same point in time?
   - Yes: Case control study
   - No: Sample group is population level or individual level?
   - Yes: Groups followed forward in time?
   - No: Groups followed forward in time?
   - Yes: Cluster controlled trial
   - No: Individual controlled trial
   - Yes: Individuals or groups (clusters) randomised?
Please feel free to send questions or feedback to MAJ Sharon Rosser at sharon.l.rosser.mil@mail.mil