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Randomized Control Design (RCT)

- Is the gold standard of all studies
- Is prospective
- Two or more groups assigned by randomization
- Take baseline measure on all groups
- Give different treatments
- Measure outcome
Schemata

- Group 1: O₁ X₁ O₂
- Group 2: O₁ X₂ O₂
- Where O = Observation
- Where X = Treatment
Types of Clinical Trials (1)

- **Treatment trials** test experimental treatments, behavioral therapies, new combinations of drugs, or new approaches to surgery or radiation therapy.

- **Prevention trials** look for better ways to prevent disease in people who have never had the disease, or to prevent a disease from returning.
  - These approaches may include medicines, vitamins, vaccines, minerals, or lifestyle changes.
Types of Clinical Trials (2)

- **Diagnostic trials** are conducted to find better tests or procedures for diagnosing a particular disease or condition.

- **Screening trials** test the best way to detect certain diseases or health conditions.

- **Quality of life trials** (also called supportive care trials) explore ways to improve comfort and the quality of life for individuals with a chronic illness.
• Decide inclusion and exclusion criterion
  o Example of inclusion criterion: “All newly diagnosed head and neck cancer patients with squamous cell carcinoma that smoke”
  o Example of exclusion criterion: “Those who are terminally ill, mentally or cognitively unstable, pregnant, etc.”

• Exclusion criterion control for errors
Randomization (1)

- Assigned to groups by method similar to “flipping a coin”
- If randomization works, groups will be the same/comparable
- The larger the sample, the greater the likelihood of equal groups

- Results should show that the demographic characteristics between groups are similar
- If groups are similar, do not need to control for extraneous variables
Randomization (2)

- Some times cannot randomize people (e.g., cross-contamination or “system” interventions)
- Can randomize hospitals, or units instead
  - For example, testing clinical reminder systems
- Once randomized, always randomized
- Subjects are treated as part of that group, even if they die, are lost to follow up, or withdraw
Fidelity Checks

• Did the investigator make sure the intervention was delivered as it was supposed to be delivered?

• Becomes more of an issue when having multiple sites with multiple providers of the intervention

• Important to provide training and booster sessions and making spot checks
Blinding

- Un-blinded: Everyone knows treatment
- Single Blinded: Researcher or patient does not know treatment
- Double Blinded: Neither researcher or patient knows treatment

- Why blinding?
  - Many people believe they feel better if they are given something
  - This is the placebo effect
Double Blind Example

- **Patient:**
  - Patient agrees that he will be randomized to one of 4 smoking cessation treatments
  - None of these 4 smoking cessation treatments are known to be better than the other

- **Provider:**
  - Providers do not know that patients are assigned to groups
  - Hire different people to run each group and do not tell them about the study
Intervention/Treatment

- Treatment versus placebo
- Treatment versus standard of care

- Treatments should be made to be as same as possible
  - For example, new drug versus sugar pill
## Four Arm Study Example: Factorial Design

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Quit Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cessation counseling and meds</td>
<td>40%</td>
</tr>
<tr>
<td>Cessation counseling only</td>
<td>10%</td>
</tr>
<tr>
<td>Cessation meds only</td>
<td>35%</td>
</tr>
<tr>
<td>Placebo group</td>
<td>6%</td>
</tr>
<tr>
<td>Nothing or Blank patch + Attention Control</td>
<td></td>
</tr>
</tbody>
</table>
The outcome variable should be the same as pretreatment measure

For example,
- Pretreatment: Smoked within the last 24 hours
- Post treatment: Smoked within the last 24 hours at the 7th day and the 30th days

Could have short-term and long term outcomes
- Short-term: Quit rate
- Medium-term: 1-year quality of life
- Long-term: Survival rate
Randomized Cross-Over Design

- 2 groups, each get a different treatment
- Washout period

- Give each group the other treatment
  - O1 X1 O2 washout O3 X2 O4
  - O1 X2 O2 washout O3 X1 O4

- Advantage
  - Can not only compare between groups, but also within groups
  - Subjects serve as their own controls
  - Controls for extraneous variables

- Not a common design
Phases of Clinical Trials (1)

- **Phase I trials** (a pilot study): Researchers test an experimental drug or treatment in a small group of people (5-60 subjects) for the first time to
  - Evaluate its safety
  - Determine a safe dosage range
  - Identify side effects

- **Phase II trials** (a larger pilot study): The experimental study drug or treatment is given to a larger group of people (100 subjects) to see if it is effective and to further evaluate its safety
Phases of Clinical Trials (2)

- **Phase III trials** (RCT): The experimental study drug or treatment is given to large groups of people (200-3,000 subjects) to
  - Confirm its effectiveness
  - Monitor side effects
  - Compare it to commonly used treatments
  - Collect information that will allow the experimental drug or treatment to be used safely

- **Phase IV trials** (implementation research):
  - Post marketing studies
  - Delineate additional information, including: the drug's risks, benefits, and optimal use
Non-Randomized Comparison Group

- Next best thing to RCT
- Used when we cannot randomize our subjects
  - For example, due to cross-contamination, or facility- or community-level interventions
- Make sure groups are as similar as possible
Non-Randomized Cross-Over Design

- Same as the previously described randomized cross-over design
- But groups are not randomized

- O₁ X₁ O₂  washout  O₃ X₂ O₄
- O₁ X₂ O₂  washout  O₃ X₁ O₄
Case Control Study

- Quick and dirty, but able to obtain lots of information
- Used in epidemiology to look at exposures
- Retrospective or prospective
- Has a comparison group

- Sometimes, does not control for extraneous variables
- Sometimes, controls for by matching
- Sometimes, nested in a larger study (e.g., nested case control)
## Non-Matched Case Control Example

<table>
<thead>
<tr>
<th></th>
<th>Worked in Coal Mine N=20</th>
<th>Did not work in Coal Mine N=20</th>
</tr>
</thead>
<tbody>
<tr>
<td>Black Lung-Yes</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>Black Lung-No</td>
<td>10</td>
<td>20</td>
</tr>
</tbody>
</table>
Matched Case Control Examples

- **Example 1:** Want to look at the beta carotene blood levels of the head-neck cancer patients, smokers compared to non-smokers
  - Match on age, gender, race, BMI, fruit and vegetable intake, cancer site, cancer stage
  - Please also see next slide

- **Example 2:** Want to look at the effect of Doulas on birth outcomes for pregnant adolescents
  - Match on age, race, BMI, provider type, gestational age, pregnancy complications
<table>
<thead>
<tr>
<th></th>
<th>Smoked N=30</th>
<th>Not Smoke N=30</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beta carotene</td>
<td>50%</td>
<td>50%</td>
</tr>
<tr>
<td>High</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beta carotene</td>
<td>50%</td>
<td>50%</td>
</tr>
<tr>
<td>Low</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Historical Controls (1)

- Not the best design
- Better than no comparison group
- Look at a group before an intervention was implemented compared to after an intervention was implemented
- Comparison not at same time
Example 1:
- Initiation of skin to skin contact following delivery on temperature, breast feeding rates and blood sugar
- Looks at those outcome prior to the intervention and then after this intervention was initiated

Example 2:
- Infections rates in the OR before and after a new protocol implemented
- Compare old rates to new rates
- O1, O2, O3, O4, X, O5, O6, O7
- Where O=Observation of infection rate
- Where X= New operating room procedures
One Group Pre-post Design

- O₁ X O₂

- Used a lot in nursing
- Not a good design because there is no comparison group
- Biggest draw back is it cannot control for historical effect
Cross-Sectional Design

- Takes a measure of a population at a certain point in time (e.g., a survey research)
- Descriptive
- Are easy, fast, and inexpensive
- Can determine prevalence of disease
- Can look at associations between variables
- Cannot determine cause and effect
Cohort Study

- Tim series, longitudinal, repeated measures
- Repeated cross-sectional measures over time
- O₁ O₂ O₃

- Could have a repeated measures design with a comparison group
- Can determine changes in population
- Can determine cause and effect
- Are expensive and take a long time
- Example: Nurses Health Study
Nested Design

- Cohort Study nested within a repeated measures design
- Example: Followed up 600 head-neck cancer patients over time
- Did case-control study (n=60) to see if beta carotene blood levels were different between smokers and nonsmokers
Definitions

- **Causality**
  - Correlation between 2 factors
  - Cause must precede effect
  - Cause is always present when effect occurs

- **Multi-causality** (e.g., smoking, diet, and genes all may cause heart disease)

- **Probability**

- **Bias**- slant from truth

- Reduce bias by blinding or randomization
Summary of Quantitative Designs

- **Experimental**
  - RCT
  - Cross-over RCT

- **Quasi-experimental**
  - Nonrandomized comparison group
  - Nonrandomized cross-over
  - Case control (matched or non-matched)
  - Historical control
  - One group pre-post design
  - Cross-sectional (slice in time)
  - Cohort (repeated measure)
  - Nested (one study nested in another)
Hawthorne Effect

- Example:
  - Implemented an intervention to see if it could increase the workers’ productivity in a factory
  - Watched workers to see if the intervention worked and it did
  - Then, watched workers, who did not have the intervention, and found that their productivity rose too

- Hawthorne effect: Attention alone produces results

- That is why we try to use an equal attention control design
Validity-Truth or Accuracy of Claim

- **Validity**: Are you measuring what you say you are measuring?

- **Reliability**: Does the measure give the same result each time it measures the same thing?
INTERNAL/EXTERNAL VALIDITY AND THE METHODS OF CONTROL

INTERNAL VALIDITY
Are the findings due to the independent variable?

EXTERNAL VALIDITY
Can I generalize the results to another group?

Selection Bias

Mortality

Maturation

Instrumentation

Testing

History

Effects of Selection

Effects of Testing

Reactivity

Randomization

Homogenous Samples

Consistency in Data Collection

Manipulation of the independent Variable

Quantitative Research
More About Validity

- Note that the question under the term “internal validity” on the diagram (the previous slide)
- This is the first question for us to consider before we “consume” research and use a study for clinical practice

- How do we know that what the researcher found is really the result of what she did?
Internal Validity (1)

- If internal validity is not strong, it means that something other than the variable we studied may have made the difference.

- As a reader of research, you should always be looking for explanations for the findings, other than the one the researcher is giving you.
Internal Validity (2)

- How will we know that if we find differences in the groups that they are most likely due to the rest period?
  - Selection bias: Low risk due to random assignment, but still there due to small sample size
  - Mortality: Moderate threat, not because clients might die but because they might drop out or not do what is necessary and have to be dropped
  - Maturation: Low threat, no known maturation in this area
  - Instrumentation: Low to moderate threat since different people will be documenting over the period and recording may be inconsistent
  - Testing: Low threat, all patients will have data recorded
    - History: Low threat, should affect both groups equally.
External Validity (1)

- Note the question under “external validity” on your diagram (Slide #34)
- Assessing the threats to external validity helps us to consider how well this study could relate to other groups, not just the one studied

- External versus internal validity:
  - Internal validity deals with the inside of the study
  - External validity deals with outside the study
  - External validity is about the ability to generalize a study’s findings to another group
External Validity (2)

- How well can we apply the results of this study to clients over 60 yrs in other nursing homes?
  - Effects of selection: High since only 1 nursing home will be used, nursing homes could differ easily in factors that might affect the results
  - Effects of Testing: Moderate threat the limitation of 1 site again means that we can’t be too sure any findings aren’t due to other factors
  - Reactivity: Low to moderate threat, clients & staff in this nursing home may react differently than clients/staff in other nursing homes
Methods of Control

- **Methods used**
  - Random Assignment
  - Manipulation of the independent variable: e.g., one group gets the rest period the other doesn’t
  - Data consistency: An operational definition that is easily understood is given for “rest periods”

- **A few other things that could be done depending on resources available**
  - Random sampling from a state wide or national ranking
  - Homogenous grouping with same size nursing homes or limiting types of clients
  - Consistency in data collection with training of staff and developing a set form/procedure for data collection
Randomization (1)

- Randomization
- Two kinds of randomization:
  - Random sampling
    - Every person in a population must have an equal chance of getting into the sample
  - Random assignment
    - Each person in a sample must have an equal chance of getting into the experimental and control group
    - That is, they are randomly placed in one of the groups
Randomization (2)

- Researcher must actually go through some randomization process
  - For example, number each potential subject, and then pull numbers from a box or use a random table to determine assignment to a group

- Randomization is a very strong and positive control method
- Randomization can always strengthen a study
Homogenous Sampling

- Trying to make your sample as much alike is helpful in studies
  - because it can minimize the possibility extraneous variables have affected the results
- However, it also has limitations
  - Because it makes generalization more difficult since the study population is smaller and applies to fewer people
  - It can also make it more difficult to get enough people in the study
- So, homogenous sampling increases internal validity, but decreases external
Consistency in Data Collection

- The researcher needs to make the process the same for everyone in the sample.

- In reality, this can be difficult, because many studies use a number of individuals to collect data and it is easy to have variances.
The Five Elements of Design

- **Setting:**
  - Example: A 110 bed long term care facility in the Midwest, the study will be done from February to April 2009

- **Population:**
  - Example: All the clients over 60 years of age who are in nursing homes

- **Subjects:**
  - Example: 60 clients who are willing to participate in a nursing home where the researcher works. Half will be randomly assigned to an experimental group who will take the rest period, half will be assigned to a control group

- **Instrument used to collect data:**
  - Example: Data collection sheet developed for this study includes demographic data, activity in the afternoon and fall data from medical records
Study Conditions

- **Example:**
  - The RN assigned to the units will establish a protocol to insure that clients in the experimental group get a 1 hour rest period each afternoon between the hours of 1 and 3 pm.
  - The operational definition of a rest period is: A one-hour period where the client remains in bed with no verbal or other mentally stimulating activities.
    - Clients in the comparison group will be encouraged to spend time in the TV area or in the therapy rooms.
    - They will not be allowed to return to bed, but may return to their own room.
Notes

- No study is 100% valid
- Most studies have some aspect of various threats present
- The more control, the less this occurs
- But controlling the threats must be balanced with the resources and realities of the research environment as well as with the skill of the researcher