Clinical Study Design
Lecturer: Dr. Bryant England

Purpose: Give an introduction to clinical study designs to improve ability to critically appraise literature and to encourage/make reading methods easier!

Theory

- **Hill's criteria for causation** (strength, consistency, specificity, temporality, biological gradient, biological plausibility, coherence, experimental evidence, and analogy)
- **What makes a good study?** Ask important questions and obtain valid results

Bias:
- **Chance** (random error – statistics problem) vs **Bias** (systematic error = design problem)
- **Bias in studies makes me SIC** – Selection, Information, Confounding
  - **Selection Bias** – How are we selecting people for our study or selecting who stayed in our study
    - “Relationship between exposure and disease is different for those who participate” – Selection into a study & surveillance/selection out of study (retention)
  - **Confounding Bias** – Is there another variable that explains our association?
    - Risk factor for the disease
    - Associated with the exposure
    - Must not be affected by exposure (not an intermediate)
  - **Information Bias** – How are we measuring things?
    - “Bias in estimating an effect caused by measurement errors”
    - Special type of Information Bias – **Misclassification** – Measurement error of discrete variables (categorical data)

Take Home: There are a lot of ways to screw up in research – we need to be on the lookout for them

Application

- **Randomized Controlled Trial** – we are testing whether randomization leads to better outcomes.
  - Define what is the population you want to study in
  - Randomize – Experimental therapy vs Control therapy
  - Study endpoint: Outcome assessment (study follow-up)
  - **Randomization** – chance determines intervention or control so that balances known and unknown confounders
    - Eliminates selection & confounding bias
    - Main Types: Simple, Block, Stratified
  - **Outcomes** – we want the appropriate study outcomes
    - Before you start the study, decide what is the most clinically relevant and validated outcome in the study (primary outcome)
    - All other relevant measures (secondary outcome)
    - **Clinical Trial Statistics**
      - Typical stats: incidence rates, relative risk, absolute risk difference, hazard ratio, p values
      - Effect size = magnitude of difference in outcomes between groups
      - P value = hypothesis test (Smaller P value does NOT equal stronger effect)
      - Power calculations – most important to critique when study findings are null
  - **Pearl**: First sentence of the method has a lot of information on RCT description

- **Other study designs when a RCT is not possible**: Cohort, Case-Control, Case Study, Ecological, Systematic Review & Meta-Analysis, Basic Science designs

Pearl: Design (and critique) the study like a RCT even if it is not a RCT

Q&A Pearls:
In general, you do not want to change the primary outcome of the study after designing and beginning the study. However, if by the time a study has been initiated a more clinically relevant outcome with better psychometric properties has been developed/validation, it may make sense to change. Changing the primary outcome should never be because you don’t like what your data is showing!