Study Design
Objectives

- Distinguish between primary and secondary studies.
- Discuss ways to assess methodological quality.
- Review limitations of all studies.
Key Terms

- Evidence based medicine
- Primary studies
- Secondary Studies
- Sampling
- Bias
- Confounding
- Power, beta error
Evidence Based Medicine

- Enhancement of a clinician’s traditional skills in diagnosis, treatment, prevention, and related areas.
  - Systematic framing of relevant and answerable questions.
  - Use of mathematical estimates of probability and risk.

Evidence Based Medicine

- Steps:
  1. Convert your information needs into answerable questions.
  2. Find the best evidence (literature).
  3. Critically appraise the evidence.
  4. Implement changes based on your appraisal.
  5. Evaluate the results.
Primary vs. Secondary Studies

- **Primary:**
  - Descriptive/Observational
  - Analytic
  - Experimental/Interventional

- **Secondary:**
  - Meta-analysis, Systematic reviews
Primary Studies: Descriptive

- Describe occurrence or distribution of disease.
- Do not attempt to explain a causal relation or test a hypothesis.
- Can be used to generate hypotheses about the cause of disease, its diagnosis, or treatment.
- Cannot be used to establish cause, diagnosis or treatment of the disease in question with any validity.
Primary Studies: Descriptive

- **Examples**
  - **Case report**: Careful, detailed description of a single patient or a series of patients (case series) with a specific disease or characteristic. No comparison group. Generally used to report a new disease, new manifestation of a known disease, adverse drug response, or new possible treatment.
  
  - **Prevalence Survey**: Data collected at a single time point yielding a "snapshot" of what is happening in the population at that time. Most useful for estimating the frequency of disease in a population (prevalence). Also used to study the utility of diagnostic tests.
Primary Studies: Analytic

- Analytic
  - Observe groups of individuals; various characteristics are recorded for analysis. No controlled intervention (experiment), but they attempt to test hypotheses or explain causal relations through comparisons using inferential statistics.

- Example:
  - Case-control study: generally concerned with determining etiology of disease.
    - Use data from case patients (who are known to have the characteristic or disease of interest at outset of the study) and control patients (who do not).
    - Test theories about disease occurrence by looking at past exposures and risk factors, and thus are retrospective.
Primary Studies: Analytic

- Cohort study: Concerned with determining etiology of disease.
  - Carefully-defined population that has been/may become exposed to factor/factors thought to contribute to the occurrence of disease or other outcome.
  - Subsets of population (cohorts) grouped according to their exposure status.
  - Most are **prospective** (and cohorts are followed over time).
  - Useful for establishing risk factors for disease.

Primary Studies: Experimental

- AKA Interventional: controlled intervention performed on a group of patients (clinical trials) or small numbers of volunteers (experiments).

- Example: Randomized Control Trial
  - Large interventional study in which participants (with a defined set of characteristics) are randomly assigned to two or more treatment groups and followed for a specified period.
  - Should ensure that the treatment groups are equal at the outset to allow the best chance of studying the effect of a single (treatment) variable.
  - Considered the gold standard of medical research, but not all questions can be studied in this fashion.
Secondary Studies

- Studies or reports that summarize and draw conclusions from a review of multiple primary studies.
  - Systematic reviews (a careful review of each of the primary studies in accordance with pre-established criteria).
    - Meta-analysis: the synthesis of numerical results from several studies that investigated the same question.
      - By combining the data from several studies, can usually make conclusions that are more powerful than a single study.
Hierarchy of Evidence

Relative weight given to evidence from each type of study (from best evidence to least best evidence):

1. Meta-analyses and Systematic Reviews
2. Randomized Control Trials
3. Cohort Studies
4. Case Control Studies
5. Prevalence Studies
6. Case Reports and Case Series
Assessing Methodological Quality

- Note the study design and whether it was appropriate for the question.
- Who was the study population?
  - Do they represent the general population?
- Was the study well designed?
- Was systematic bias avoided?
- Was the study large enough and long enough? (What was the power?)
Sampling

- Who was studied? Are they representative of the target population?
  - Target population: that group to which we would like to generalize the findings.
- Was the study population a convenience sample or random sample?
  - Convenience sample: those who agree to participate.
Were certain people excluded?

Exclusions based on age and co-morbidities may result in greater differences between the study group and the target population.
Bias

☐ Anything that produces a systematic error in the research findings and threatens the validity of the study.

☐ Possible causes:
  ☐ Selection of study participants.
    ☐ Volunteer effect
    ☐ Healthy worker effect
    ☐ Non-response effect
  ☐ Treatment/study procedures performed.
    ☐ Attention bias
    ☐ Therapeutic effect
    ☐ Non-compliance effect

Bias

- Possible causes (contd.)
  - Measurement and data collection.
    - Recall bias
    - Insensitive measures
    - Diagnostic suspicion
    - Un-blinded assessment bias
  - Methods of data analysis.
    - Efficacy analysis vs. intent to treat
    - Sub-group analyses

- Some study designs are more prone to bias than others.
  - Randomized controlled trials vs. non-randomized controlled trials.
  - Cohort studies vs. case control studies.

Confounding

- Occurs when the effects of several variables cannot be distinguished.
  - May not be possible to determine if the observed effect is due to the variable in question or some other confounding variable.

- Multivariate analysis (logistic regression) may allow you to separate confounding variables from true predictors of effect.
The likelihood of detecting a specified difference between two groups if it truly exists.

- If a study had 80% power then there is a 20% chance that you won’t find a significant relationship even if that relationship exists (20% chance of beta error).

Should be determined prior to the actual conduct of the trial.

Two pieces of information are needed:

1. What is considered a clinically significant effect?
2. The mean and standard deviation of the outcome variable.
Power

- When a clinical trial has negative results (findings were not statistically significant), the study may not have had adequate power to detect the desired effect. It may be erroneous to conclude that the intervention has no efficacy.
Summary

- Ask the right question.
- Search for the right articles.
- Note appropriateness of the study design.
- Is the study valid? Look at the methods:
  - Sampling
  - Source bias
  - Possible confounding variables
  - Adequate power
- What are the results and are they significant?
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