Foundations in Biostatistics and Epidemiology
Session 5: Observational Study Design; Systematic Review and Meta-analysis

The following provides a summary of the content of this module.

I. Observational Study Design

Terminology:

- Population: large group that study attempts to describe; often impractical to study entire population
- Sample: subgroup from the population; investigators will make generalizations about the entire population from the sample
- Prospective study: Groups recruited and data collected on subsequent events
- Retrospective study: Information is collected on past events or exposures
- Cross-sectional study: Information is collected on subjects at a fixed point in time
- Longitudinal study: Investigate changes over time by taking repeated measurements over a time interval on the same subject
- Observational study: researcher observes subject characteristics, exposures, interventions, etc. and outcomes, but does not control "interventions"

Primary Observational Study Types:

- Cohort Study
  - Design: groups, defined on the basis of some characteristics or exposures are typically prospectively followed to see whether an outcome of interest occurs (could also be retrospectively observed to see whether an outcome of interest occurred prior to some point in time but following exposure)
  - Advantages: time course from exposure to disease is observed (for prospective cohort study); useful for study rare exposures
  - Disadvantages:
    - Long and expensive, even infeasible for rare outcomes;
    - Groups may differ in terms of an important characteristic that is/is not observed,
    - Comment on associations not causation
    - Loss to follow-up is likely
    - May be affected by detection bias (follow-up and assessment methods should be same for all subjects regardless of risk)
- Case-control Study
  - Design: retrospectively compare various characteristics or exposures for cases (subjects with a disease) to those of controls (non-disease comparison group)
  - Advantages: relatively inexpensive and can be completed in a short amount of time; useful for studying rare outcomes
  - Disadvantages:
    - Do not observe entire time course from exposure to disease so causal interpretation is limited,
    - Subjects with disease may be more motivated to recall exposures
    - May miss fatal or short-term cases
    - May be difficult to select comparable group of controls
    - Availability of high quality/complete data may be limited
- Cross-sectional Survey
  - Design: collect data on study subjects at a fixed time, a cross-sectional observation of a group
  - Advantages: simple and inexpensive; useful for estimating number of subjects with existing condition per population at risk in the given period of time

- Disadvantages:
    - Do not observe time course so cannot determine if exposure really came before outcome;
    - Non-responders may be different from responders

II. Systematic Review and Meta-analysis Methods

- Systematic Review: "The application of strategies that limit bias in the assembly, critical appraisal, and synthesis of all relevant studies on a specific topic. Meta-analysis may be, but is not necessarily, used as port of this process. Systematic reviews focus on peer-reviewed publications about a specific health problem and use rigorous, standardized methods for selecting and assessing articles. A systematic review differs from a meta-analysis in not including a quantitative summary of the results."
  Last, *A Dictionary of Epidemiology*. Oxford University Press, 2001.
- Meta-analysis: "A statistical synthesis of the data from separate but similar, i.e., comparable, studies, leading to a quantitative summary of the pooled results."
  Last, *A Dictionary of Epidemiology*. Oxford University Press, 2001.
- Process:
    - Well-defined question
    - Specify study inclusion and exclusion criteria
    - Define search terms
    - Identify sources
    - Implement search and track results
    - Review titles and abstracts for inclusion and identify papers that must be reviewed in full
    - Abstract data
    - Proceed with meta-analysis if appropriate
- Meta-analysis methods:
    - Fixed effects method
        - Assume all studies are estimating the same true (but unknown) fixed effect of an intervention
        - The true effect of treatment is the same value in each study
        - Differences in the treatment effect across studies is due solely to chance
    - Random effects method
        - Assume that the studies are inherently different
        - The treatment effects for the individual studies are assumed to vary around some overall average treatment effect
        - The treatment effects are assumed to be normally distributed with a mean and variance, where the variance is assumed to be non-zero for random effects models
        - Confidence intervals for pooled estimates from random effects analyses will typically be wider than from fixed effects analyses
    - Tests of heterogeneity
- Data summaries
    - Tables of study characteristics and results
    - Graphical summaries
        - Forest plot: summarize individual and pooled estimates
        - Funnel plot: assess potential for publication bias
    - Analyses of data quality

III. Meta-analysis Example