School of Population and Public Health
SPPH 503 – Epidemiologic methods II
January to April 2019

Time: Tuesday, 1330 – 1630
Location: School of Population and Public Health, UBC

Course description
Students will be introduced to a worldview that identifies the role of epidemiologic methods in medical research at the clinical and community levels (the term ‘medical’ is used to describe the aggregate of disciplines concerned with illness in humans). The philosophy of inference will be a core consideration and topics covered will include study design, the meaning of p values and confidence intervals, biases, confounding and adjustment, effect modification, Frequentist versus Bayesian inference and issues related to generalizability. Subsequent sessions will focus on diagnostic, prognostic and etiognostic research. Each topic will be introduced at the basic level and progress to a second level re-examination of the issues.

Course philosophy
The classroom provides a forum where reason and evidence are presented by the instructor in order to enable students to reach an understanding on any particular topic. Although the inferences that students reach need not mirror those of the instructor, the requirement to support one’s position with logic/reason and evidence is an important aspect of the course philosophy.

Students in any class comprise a heterogeneous group in terms of learning abilities and learning needs. All student needs will be respected by presenting topics at the basic level before proceeding to a second or third level re-examination of the issues.

Teaching goals and strategies
Students learn best when they are engaged through a process that is both instructive and intellectually entertaining. The course strategy for achieving this involves the discussion of thought provoking ideas, with illustrations and pertinent examples from the contemporary literature. This strategy also includes challenging, though not necessarily time consuming, assignments.

Course objectives
The objectives of the course are to help students gain an understanding of
1. The philosophy of inference.
2. How epidemiologic research can directly add to the knowledge base of scientific medicine.

Reading list
Course notes will be provided at each session. Additional reading may be listed in the reference section of the course notes.
Recommended (but not required) texts

Pre-requisites
SPPH 502 (Introduction to Epidemiology)
SPPH 400 (Statistics for Health Research)

Method of evaluation
Assignments 20%; mid-term test (40%) and end of term test (40%).
The tests will consists of multiple choice or short answer type questions. Some questions will seek to elicit information on fundamental concepts, while other questions will probe the student’s understanding of the finer points covered in the course. Two examples of potential exam questions are listed below along with the Instructors version of the answers:

Question 1. What purpose(s) do the inclusion and exclusion criteria in a randomized trial serve?

a) inclusion criteria

Answer: Inclusion criteria define the domain within which the question regarding drug (therapy) efficacy is to be answered. They ensure that the study has conceptual and practical meaning in terms of answering the question posed at the outset of the clinical trial.

b) exclusion criteria

Exclusion criteria are typically used to prevent the recruitment of subjects who may interfere with the study’s conduct from an efficacy or safety standpoint. For example, exclusion criteria exclude those who may be hurt through idiosyncratic or other reactions, those who will add “noise” to the study by having the primary outcome through mechanisms not directly related to the study question and those who are likely to be non-compliant with study protocol.

Question 2: A particular technique for measuring the height of a mountain is deployed and 100 readings give a mean height for the mountain as 5,540 meters, SD=30 m, 95% confidence interval= 5,534 to 5,546 m. Which of the following statements is true?

a) The true height of the mountain must be between 5,534 and 5,546 m.
b) The true height has a 95% probability of being between 5,534 and 5,546 m.
c) There is a 95% probability that the range 5,534 to 5,546 m contains the true height of the mountain.
d) The true height of the mountain is either between 5,534 and 5,546 m or it is not.
e) Approximately 95 of the 100 of the measurements made must have fallen between 5,480 and 5,600.
f) If we were to repeat the 100 measurements and calculate the mean and 95% CI over and over again we would still not know the true height of the mountain with certainty.
g) If we were to repeat the 100 measurements and calculate the mean and 95% CI over and over again (based on 100 measurements each) approximately 95% of the CIs we calculated would contain the true height of the mountain but we would not know which.

Answer: c, d, e, f, and g. Please refer to course notes for details.
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Topics to be addressed
1. Science, medicine and epidemiology
   Definition of medicine
   Classification of medical disciplines
      Clinical
      Community
   The art and science of medicine
   Essence of the art of medicine
   Public health
   Types of medical research
   Types of knowledge (general, particular)
   Scientific medicine, medical professionalism
   Foundation of scientific medicine
   Epidemiologic research
   Role of statistics
   Evidence-based medicine versus knowledge-based medicine
   The subjective nature of inference and the inter-subjective nature of knowledge
   Critical thinking

2. Epidemiologic study design
   Types of epidemiologic studies
      Cohort
      Case-control
      Cross-sectional
   Indices of disease frequency
      Incidence vs prevalence
      Proportion type rates
      Density type rates
      Rate ratios
      Rate differences
      Odds ratios
Epidemiologic study design - the axes for categorization
Directionality
Timing
Sample selection
Study design revisited
Cohort vs case-control studies
Cohort vs dynamic population
Survival analysis
Actuarial
Kaplan-Meier

3. Clinical trials
Features of a clinical trial: conceptual sequence
Equipoise
Framing the question
Inclusion and exclusion criteria
Assurance of validity
Randomization
Stratification (and blocking)
Blinding (differential co-intervention/information)
Intention-to-treat principle
Assurance of relevance
Compliance, crossover
Clinical algorithms and decision nodes
Issues related to generalizability
Conflicting imperatives
Status of the randomized trial

4. Bias in epidemiologic studies
Types of bias
Selection bias
Information bias
Confounding
Definition, conditions for confounding and types
Addressing confounding
Prevention through design
Restriction and stratification
Matching
Adjustment during analysis
External weighting schemes (direct and indirect standardization)
Internal weighting schemes (M-H, inverse of variance)
Studies of intended vs unintended effects
Confounding by indication
Confounding by contraindication
Residual confounding

5. Effect-modification and miscellaneous topics
   Effect modification
   Bias towards the null
   Cohort effect
   Regression to the mean
   Ecologic fallacy
   Choice of study population
   Clusters
   Publication bias and detection

6. Case-control studies
   Historical note
   The cohort vs case-control dichotomy
   Cohort vs dynamic populations
   Case-referent studies
   Primary study base, secondary scheme for case-ascertainment
   Primary scheme for case ascertainment, secondary study base
   Ensuring comparability of information
   Time issues related to determinant effects
   Etiognostic probability

7. P values and 95% confidence intervals
   The logic of statistical inference: a clinical analogy
   Statistical (Frequentist) inference
   Parametric tests
   Non-Parametric tests
   P values
   Confidence intervals
   P values vs confidence intervals
   Interpreting 95% Confidence intervals in terms of P values
   Clinical significance vs statistical significance
   P values and 95% confidence intervals from small versus large studies
   P value functions

8. Frequentist versus Bayesian approaches to inference
   Frequentist theory continued
   Optimization of study size
   Multiple hypothesis testing
   Sequential/repeated testing, interim analyses in clinical trials
   Data generated vs hypothesis driven P values
Subgroup analyses in clinical trials
Bias vs chance
P value function
Bayesian inference
Prior probability, likelihood ratio and posterior probability
Subjective vs objective inference
Prior belief
Study data as the likelihood ratio
Implications for study size, multiple hypothesis testing, etc

9. **Introduction to diagnosis**
   Indices of validity
     Sensitivity
     Specificity
   Clinically relevant indices
     Positive predictive value
     Negative predictive value
   Prevalence dependence of predictive values
   Receiver Operating Characteristic curves
   Likelihood ratios
   Bayes theorem
   Sequential application of Bayes theorem
   Problems with the sequential application of Bayes theorem

10. **Regression modeling for diagnosis and prognosis**
    General linear models
        Multiple linear regression
    Generalized linear models
        Log linear regression
        Logistic regression
        Cox proportional hazards regression
    Choice of model
    Designing variables from determinants
        Indicator variables
        Multinomial or ordinal determinants
        Determinants measured on a continuous scale
        Effect modification
    Model building
    Creating prevalence functions (for diagnosis/prognosis)
    Creating scoring systems for (for diagnosis/prognosis)
    Misguided focus on single predictors

11. **Causal models versus predictive models**
Form and function
Criteria for causality
Features of a causal model
Features of predictive models
Assessing performance of predictive models
  Calibration ability
  Stratification capacity
  Classification accuracy

12. Causal diagrams

13. Publication, validation and contribution to science
   Practical issues
   General issues
     Authorship
     Choice of journal
     Status of peer review
     Determinants of success
     Publication and validation
     Contribution to science
     Citation
     Impact factors
     Sociology of science
       Normal science, paradigm shift
       Mathew effect
       Medawar’s curve
     Open access publishing
     Future directions