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 class room 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
1. Rothman KJ, Greenland S, Lash TL. Modern Epidemiology. 3rd edition. Lippincott Williams & Wilkins.

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 5,480and 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.

Teaching assistant

Weiran Yuchi
Email: weiran.yuchi@ubc.ca

Course instructor

K.S. Joseph MD, PhD (primary instructor)
Professor
Department of Obstetrics & Gynaecology
School of Population and Public Health
University of British Columbia and the
Children's and Women's Hospital of British Columbia
Tel: 604-875-2000 ext 4811 E-mail: ksjoseph@bcchr.ca

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