School of Population and Public Health  
SPPH 513 – Clinical Epidemiology  
January to April 2024

Time: Tuesdays, 1400 – 1700  
Location: Room SPPH 143

Course description  
This course focuses on epidemiologic methods in clinical research. Diagnosis, prognosis and etiognosis will be discussed with examples used to illustrate both concepts and methods. More general epidemiologic topics will also discussed including study design, the meaning of P values and confidence intervals, causation, biases, confounding and adjustment, effect modification, meta-analysis, Frequentist versus Bayesian inference and issues related to generalizability.

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 with topics presented at a basic level before proceeding to a second 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 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 the  
1. Principles and methods of clinical (epidemiologic) research  
2. Philosophy of inference  
At the end of the course, students will be better equipped to examine the medical literature from a scholarly perspective and also to design and conduct clinical research.

Reading list  
Specific reading material may be listed for some sessions.

Recommended text  
The teaching is based on course notes (provided as Powerpoint documents). The following text is recommended but not required (copy available from Instructor)  
Grobbee DE and Hoes AW. Clinical Epidemiology: Principles, Methods, and Applications for
Method of evaluation
In-class Assignments 30%; mid-term test (35%) and end of term test (35%).

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Course schedule
January 9, 2024
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

January 16, 2024
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

January 23, 2024
Causal prognosis: Clinical trial concepts
Features of a clinical trial: 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

January 30, 2024
Clinical trial details
Clinically relevant questions
Feasibility studies
Pilot trials
Cluster randomized trials
  Non-independent observations
Multi-arm trials
Stepped wedge designs
Non-inferiority trials
Application for funding
Trial management challenges
  Missing data and loss to follow up
Role of clinical trial managers

February 6, 2024
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

February 13, 2024
Bias in epidemiologic studies and effect modification
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
Effect modification

February 20, 2024
Mid-term break
February 27, 2024

**Mid-term examination**

March 5, 2024

Screening

Screening

- Concepts
- Lead time and length time bias
- Assessment of utility

**Miscellaneous topics**

- Models of causation
- Bias towards the null
- Cohort effect
- Regression to the mean
- Ecologic fallacy
- Choice of study population
- Clusters
- Publication bias and detection

March 12, 2024

**Regression modeling for diagnosis and (non-causal) 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

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

March 19, 2024
Etiognosis: 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

March 26, 2024
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

April 2, 2024
Meta-analysis
Information and comparative information
Pooling information
Heterogeneity
Random effects and fixed effects models
Meta-regression
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

April 9, 2024
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

Knowledge translation
Brief history of KT in Canada
Definition
KT and ethics
Double edged sword
Conflict of interest, bias
Vigorous transfer of ‘good ideas’
Rational KT

April 16, 2024
**Final Examination**