

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 be 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)

Grobbée DE and Hoes AW. Clinical Epidemiology: Principles, Methods, and Applications for

Clinical Research. Second Edition. Jones & Bartlett Learning. 2014.

Method of evaluation

In-class Assignments 30%; mid-term test (35%) and end of term test (35%).

Course instructor

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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