ADVANCED EPIDEMIOLOGY - 4 DAY SHORT COURSE

CAUSATION, SYSTEMATIC ERROR, QUANTITATIVE BIAS ANALYSIS and CAUSAL MEDIATION

Convenor and lecturer:  Professor Tony Blakely, University of Otago
Lecturer:   Professor John Lynch, University of Adelaide

Day 1

Causation in Epidemiology
- Models: Causal criteria (Bradford Hill) and Sufficient Component Cause Model (Rothman);
- Individual and population causes

Potential Outcomes Model of Causation
- Counterfactual or Potential Outcomes Model
- Why perfect RCTs work creating “exchangeable” groups
- The inevitable problems with most RCTs and observational studies
- Confounding, Selection, and Information Bias

Directed Acyclic Graphs (DAGs)
- Formalizing assumptions for a causal model

Workshop - What’s your DAG?

Understanding Selection Bias – an application of DAGs
- Conditioning on common effect(s) and dependent on participation by exposure and outcome
- Study design options – complete case versus imputation

Quantitative Bias Analysis (QBA):
- Overview of the principles

Day 2

Selection Bias QBA
- QBA applied to selection bias
- Class exercises using Excel

Understanding Confounding Bias
- Conditioning on common cause(s) or variables on back-door path
- Regression model building strategies thought to achieve appropriate confounder adjustment – the art and science

Propensity Scores and Instrumental variables (IVs)
- Alternative methods for dealing with confounding
- QBA to explore implications of unmeasured and residual confounding

Day 3

Interaction and Effect Measure Modification (EMM)
- Concepts and reporting of EMM

Information Bias
- Misclassification (categorical variables) and measurement error (continuous variables)

Information Bias QBA
- QBA applied to selection bias
Class exercises using Excel

Probabilistic Bias Analysis
- Bringing it all together – simultaneous assessment of selection, confounding and information bias.
- Class exercises using Excel
- Monte Carlo simulation

Workshop - Dealing with “difficult issues”
- Workshop – group discussion of examples provided by course participants

Day 4

Direct and Indirect Effects
- Estimating mediation

Causal Mediation Analysis
- Marginal Structural Models (MSM)

Bringing it all together – DAGs, Sensitivity Analyses and MSMs
- Structured small-group review of paper by Nandi et al., Epidemiology (2014)

Multiple Bias Analysis
- Examples from Rothman Ch 19.

Final Quiz, Feedback and Wrap-up

Course Prerequisites
This course will assume knowledge of study design and analytical methods, the basic principles of systematic error (confounding, selection and information biases) and biostatistics up to multivariable regression. For example, successful completion of a Diploma or Masters of Public Health course in epidemiology and biostatistics (or similar) will usually provide the necessary basis to undertake this course.

Participants
The course has 2 intended audiences
- PhD students, early career researchers, and advanced MPH students who wish to add depth to their understanding of some of the fundamental issues in epidemiology
- More senior investigators who want an efficient “catch up” on some of the new thinking and methods being used in higher quality research publications

Course materials and resources
- Lectures: Powerpoint slides used in teaching will be handed out as a course book at the start of the course. (All readings, however, will be available via DROPBOX – see below.) Often key points are missing from the handouts, as course attendees will be expected to deduce these key points in class and write them into their course-book.
- Texts: The course draws strongly on two key text books.
  1. Rothman, Greenland and Lash (2008). Modern Epidemiology. (3rd Ed.) Lippincott Williams & Wilkins. For attendees wishing to enhance their learning, reading pages 345-63 before the course and pages 363-80 will assist. It is strongly recommended that course attendees either have their own, or have very ready access to, this text. Chapter 19, Bias Analysis, is provided in the readings file on dropbox.
  2. Lash, Fox, Fink (2009). Applying Quantitative Bias Analysis to Epidemiological Data. Springer. A strong point is the range of easy to use Excel spreadsheets for conducting quantitative bias analysis that accompany the text, available at: http://sites.google.com/site/biasanalysis/. These Excel spreadsheets will be provided to attendees, and used for class exercises during the course.
• **Readings:** We have selected a number of readings that correspond to the major topics covered in the course. The readings are available on “DROPBOX” (https://www.dropbox.com/). You will be sent an invitation to the DropBox.

**Causation and Counterfactuals**

**DAGs**

**Confounding**

**Multiple Imputation**
- Sterne et al. Multiple imputation for missing data in epidemiological and clinical research: potential and pitfalls. *BMJ* 2009. 38 doi: 10.1136/bmj.b2393

**Propensity Scores**
Glynn RJ, Schneeweis S, Sturmer T “Indications for propensity scores and review of their use in pharmacoepidemiology” Basic Clin Pharmacol Toxicol 2006; 98(3):253-9

**Instrumental Variables**


**Marginal Structural Models**


**Quantitative Bias Analysis**

## TIMETABLE

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<tr>
<td>0900 to 1030</td>
<td>• Course Overview [TB] • Causation [JL]</td>
<td>• Selection Bias QBA [TB]: o Formulas o QBA Class exercises – Excel</td>
<td>• Interaction and Effect Measure Modification [TB] • What does OR measure (if time) [TB]</td>
<td>Direct and Indirect Effects [TB] Fixed effects</td>
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<td><strong>MORNING BREAK</strong></td>
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<td>1100 to 1230</td>
<td>• Potential Outcomes [JL] • DAGs [JL]</td>
<td>• Confounding [TB]: o Properties, counterfactual, DAGs o Approaches to regression model building</td>
<td>• Information bias [TB]: o Definitions, DAGs, etc • Information bias analysis: • QBA Class exercises – Excel</td>
<td>Causal Mediation Analysis: • Marginal Structural Models 1 • Marginal Structural Models 2</td>
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<td><strong>LUNCH</strong></td>
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<td>1330 to 1500</td>
<td>• Workshop #1: What’s your DAG? (to be handed out by JL)</td>
<td>• Alternative methods for confounding [JL]: o Propensity scores o Instrumental variables</td>
<td>• Probabilistic bias analysis [TB]: o Distributions, Monte Carlo, o Class exercise – Excel</td>
<td>• Bringing it all together – DAGs, sensitivity and MSMs o Class exercise on Nandi (2014) Epidemiology</td>
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<td><strong>AFTERNOON BREAK</strong></td>
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<td>1530 to 1700</td>
<td>• Quantitative bias analysis (QBA) overview [TB] • Selection bias [TB]: o Definitions and DAGs • Study design options – complete case vs imputation • Quiz</td>
<td>• Confounding bias analysis [TB]: o Formulas o QBA Class exercises – Excel</td>
<td>• Workshop #2: challenging issues [TB, LJ] Two students: present, class discussion. See emailed framework that must be followed.</td>
<td>• Multiple bias analysis [TB]: Modern Epi Ch 19 example • Feedback on the course</td>
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<td>• Quiz</td>
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