Systematic Reviews and Meta-Analysis - Course Syllabus
2011-2012

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Course Description
Introduction to the use of meta-analysis and related methods used to synthesize and evaluate epidemiological and clinical research in public health and clinical medicine. Concepts introduced and illustrated through case studies of public health and medical issues.

Course Objectives
To learn how to use a variety of formal and informal methods for synthesizing epidemiological information on public health risks, to understand how to use these methods to assess the strength of the evidence in policy development and clinical contexts, and to appreciate how research synthesis can contribute to rational policy making in controversial areas.

Competencies
Principles consistent with epidemiology and biostatics competencies for the MPHS (www.mphs.wustl.edu)
Ability to design research synthesis and meta-analysis
- Define research question
- Define literature search strategy
- Conduct literature search and document the process
- Apply eligibility criteria, data extraction, and data quality scoring
- Develop data analysis plan
- Understand and interpret fixed-effects, random-effects, and meta-regression methods and results
- Recognize heterogeneity and approaches to quantification and reporting of among-study variation

Skills and experience to conduct analysis
- Master data analysis and model fitting in context of meta-analysis
- Quantitatively evaluate publication bias
- Be able to estimate combined results from reports of randomized trials, observational studies, and diagnostic test

Master the core reporting strategies
- Master reporting standards for RCTs and observational data in context of meta-analysis
- Master forest plot, summary tables, and publication bias presentations

Draw inferences from data to inform clinical and public health practices
- Correctly use reasoning for design and methodologies employed
- Present oral and written reports from analyses
- Place inference in context of clinical and public health implications for action and future research
**Time and Location**  
Friday 9:00 AM to noon  
Class location to be determined

**Instructors**  
Graham A. Colditz, MD, colditzg@wudosis.wustl.edu  
Methodius Tuuli, MD, tuulim@wudosis.wustl.edu  
Office hours: By appointment and after class

**Target audience**  
Clinicians interested in conducting research synthesis or meta-analysis to inform practice or policy, clinical training program participants, students enrolled in Genetic Epidemiology Master of Science program, students in MPH addressing application of epidemiologic data to prevention. Prior clinical or community research experience is helpful but not required.

**Prerequisite**  
Introductory epidemiology and biostatistics 1 (or permission of the course master)

**Credits**  
3

**Class schedule**  
Most classes will involve case discussions, and students are expected to come to class prepared to discuss the readings. On one day to be determined --, the class will meet in the computer lab (STAT available in the Becker library) to review the use of Comprehensive Meta Analysis, a specialized computer program (or we could use Stata).

Students (working individually or in groups) will present their work according to the following schedule:  

**A. Study protocol:** precise topic, search strategy, inclusion/exclusion criteria.  
**B. Search results, evidence table, statistical issues.**  
**Last 2 days of class:** Final presentation of results and conclusions.

**Evaluation**  
Working individually or in groups of 2 individuals, students will be expected to carry out a written research synthesis of a public health or clinical topic of their own choosing. Intermediate results will be presented and discussed in class. Grades will be based on the written paper, presentations, and on class participation. The content of the written paper should be based on the QUORUM or MOOSE consensus statement as appropriate.


**Software:** We will be using STATA with the meta-analysis supplementary routines. It is available for purchase but can be used at the library where it is on 4 computers.  
http://becker.wustl.edu/services/researchpod.html

**Assignments and Grading**  
- Homework 1 = 15%  
- Homework 2 = 15%  
- Final Paper = 55%  
- Class Participation = 15%  
- Readings
The primary text for the course is Systematic Reviews in Health Care: Meta-analysis in Context, 2nd Edition, Mattias Egger, George Davey Smith, and Douglas Altman, eds., BMJ Books, 2001. Supplemental readings from Introduction to Meta-Analysis, Michael Borenstein, Larry V Hedges, Julian PT Higgins, and Hannah R Rothstein, Wiley, 2009, are also given. Additional readings are indicated below and will be available through blackboard.

Additional Resources
BMJ methods http://www.bmj.com/search?submit=yes&tocsectionid=Research%20Methods*
Cochrane library http://www.thecochranelibrary.com/view/0/index.html

Cochrane methods group

UK NICE (National Institute for Health and Clinical Excellence) http://www.nice.org.uk/
Australia Handbook. How to use the evidence. NHMRC.
Berkeley Systematic Reviews Group, http://www.medepi.net/meta/

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<tr>
<th>Date</th>
<th>Topic</th>
<th>Key Reading</th>
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<tr>
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<td>Stampfer 1982 (classic article)</td>
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<td>Cousell 1997</td>
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<td>Dickersin 1994 (classic article)</td>
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<td>February 3</td>
<td>Statistical methods: effect sizes, basic meta-analysis calculations; BCG</td>
<td>Egger 2001                      Normand S-L 1999 Laird 1990</td>
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<td>February 10</td>
<td>Statistical methods, continued: cumulative meta-analysis, tools for publication bias; BCG</td>
<td>Egger 2001                      Tuuli 2011 Borenstein Chapter 11, Publication Bias</td>
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<td>February 17</td>
<td>Student presentations: Homework 1: Topic and search protocol</td>
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<td>Date</td>
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<td>March 2</td>
<td>Quality scores: application to research synthesis</td>
<td>Moher 1995&lt;br&gt;Moher 1996&lt;br&gt;Grade BMJ, 2004&lt;br&gt;Intro to STATA</td>
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<td>GRADE</td>
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<td>Computer lab</td>
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<td>March 9</td>
<td>Heterogeneity II: Meta-regression; BCG, ETS, Alcohol and stroke, Vitamin E</td>
<td>Egger 2001&lt;br&gt;Reynolds 2003&lt;br&gt;Miller 2005</td>
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<td>Homework 2 : data extraction write up</td>
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<td>March 23</td>
<td>Student presentations: Results of literature search and preliminary results</td>
<td>Egger 2001&lt;br&gt;Ioannidis 2010&lt;br&gt;Kendrick 2009&lt;br&gt;Glasziou 2010&lt;br&gt;Bastian 2010&lt;br&gt;Grade 2008</td>
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<td>Applying results to policy and practice</td>
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<td>March 30</td>
<td>Drug safety</td>
<td>Jüni 2008&lt;br&gt;Bridge 2007&lt;br&gt;Kaizar 2006&lt;br&gt;Berlin and Colditz 1999</td>
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<td>Pros and Cons of meta-analysis</td>
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<td>Class debate: meta-analysis vs. large trials</td>
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<td>Class teams will debate this topic using aspirin for prevention of preeclampsia as the topic</td>
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<td>April 6</td>
<td>Computer lab</td>
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<td>April 13</td>
<td><strong>Combining diagnostic test results</strong></td>
<td>Egger 2001&lt;br&gt;Shapiro 1995&lt;br&gt;Rutter and Gatsomis 1995&lt;br&gt;Irwig 1994&lt;br&gt;Hovels 2008&lt;br&gt;Kwok 1999</td>
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Comparing meta-analysis of published results with pooled analysis of individual level data

Beral 2008
Whittemore 1992
Breast Cancer Collaborate 1996
Steinberg 1997
Hankinson 1992
Cholesterol Treatment Trialists’ 2010

Student presentations:
Summary and final results

Student presentations:
Summary and final results

Readings

Week 1

*Introduction and Defining the Question*


*Classic article*


Week 2

*Searching the literature*

Example: BCG vaccine efficacy

Staples vs suture


Lemeshow AR, Blum RE, Berlin JA, Stoto MA, Colditz GA. Searching one or two databases was insufficient for meta-analysis of observational studies. J Clin Epidemiol 2005; 58:867-73 [lemeshow-searching-05.pdf](lemeshow-searching-05.pdf)

Classic article
Dickersin K. Scherer R, Lefebvre C. Systematic Reviews: Identifying relevant studies for systematic reviews BMJ 1994;309:1286-91. [Identifying relevant studies bmj 00465-0048.pdf](Identifying relevant studies bmj 00465-0048.pdf)

Week 3
**Statistical methods**
**Example: BCG vaccine efficacy (continued)**


*Additional readings:*
Borenstein, Chapters 3-14
*Using meta-analysis for research synthesis: pooling data from several studies. Biostatistics in Clinical Medicine, Chapter 14, 332-360.*

Week 4
**Statistical methods, continued: cumulative meta-analysis, tools for publication bias**


*Additional readings:*

Week 5
**Student presentations:** Study protocol precise topic, search strategy, inclusion/exclusion criteria.

Week 3-Class B
**Heterogeneity I: \( I^2 \), subgroup analysis**

**Examples:** ETS, HIV counseling & testing, NAC


Week 6
**Quality scores application to research synthesis**


**Computer lab**

Comprehensive Meta Analysis Version 2.0: Introduction to the program
**Additional readings:**
Borenstein, Chapter 44

**Week 8**

**Heterogeneity II: Meta-regression; BCG, ETS, Alcohol and stroke, Vitamin E**


**Additional readings:**

**Week 9**

**Epidemiology**

*Examples: Environmental tobacco smoke, electromagnetic fields, physical activity*


**Week 10**
Student presentations
Search results, evidence table, statistical issues.

Applying results to policy and practice


Bastian PLOS 2010


Week 11
Drug Safety
Examples: Vioxx, Avandia, vaccines, antidepressants


Additional reading:
Stoto MA, Research synthesis for public health policy: Experience of the Institute of Medicine, in Meta-Analysis in Medicine and Health Policy, Stangl D and Berry D., eds., New York: Marcel Dekker, 2000, pp 321-357.

Week 12
**Computer lab**

**Week 13**

**Combining Diagnostic Tests, Bayesian meta-analysis**

**Example: Exercise testing to detect coronary artery disease, mammography**


Regression methods for meta-analysis of diagnostic test data.


Examples:


Additional reading:

**Week 14**

**Comparing meta-analysis of published results with pooled analysis of individual level data**


A Quantitative Assessment of Oral Contraceptive Use and Risk of Ovarian Cancer. 


Weeks 15 and 16

**Student presentations:**
Final presentation of results and conclusions.