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
Doll & Hill teaching room. 2nd Floor, Taylor Ave Building – 600 S Taylor Ave
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.

Students (working in groups) will present their work according to the following schedule:
A. Study protocol: precise topic, search strategy, inclusion/exclusion criteria.
B. Search results, extraction form, statistical issues.
Last 2 days of class: Final presentation of results and conclusions.

Evaluation
Working in groups of 2-3 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. A 6-month trial version will be provided for each student.

Grading Scale
A+: 97-100; A: 93-96; A-: 90-92; B+: 87-89; B: 83-86; B-: 80-82; C+: 77-79; C: 73-76; C-: 70-72

Assignments and Grading
- Homework 1: Preliminary topic presentation (10%)
- Homework 2: Library assignment (10%)
- Homework 3: Analysis in STATA (10%)
- Homework 4 Data extraction (10%)
- Final Presentation (10%)
- Final Paper (50%)

Assignment due dates
Details of all assignments can be found on Canvas

- **HW 1: Topic and search protocol**
  Presented in class on February 1.
  Slides are due via Canvas by January 30 at 11:59 pm

- **HW 2: Library assignment**
  Due February 8 by 11:59 pm, submit via Canvas AND email to dathomas@wustl.edu

- **HW 3: Analysis in STATA**
  Due March 8 by 11:59 pm, submit via Canvas.

- **HW 4: Data extraction form**
  Presented in class on March 22.
  Slides due via Canvas by March 20 at 11:59 pm.

- **Final Presentation**
  In class on April 26 and May 3. Students will sign up for a date in February.
  Presentation slides are due April 24 and May 1 by 11:59 pm, respectively, via Canvas.

- **Final Paper**
  Due May 5 by 11:59 pm via Canvas.

**Attendance and Participation**

Class attendance is required. As a courtesy to other students, you are expected to arrive on time. More than two unexcused absences from class may result in a lowered grade. Readings assigned for each class should be read ahead of the class and students should be prepared to discuss the material from readings.

**Policy on Late Assignments**

Late assignments will result in a deduction of one grade point (A+ down to A) for each day late (including weekends) unless prior approval is obtained from the instructor or a compelling situation prevents prior approval (i.e. documented health issues or family emergencies).

**Readings**


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 Canvas.

**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 and handbook http://handbook.cochrane.org/

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/

PLOS template for systematic review – meta-analysis article preparation
www.plosone.org/static/tpl_plos_meta.doc
Many students go on to publish based on the work they performed in this class. Since 2011, the following publications have been produced by participants in this class:


<table>
<thead>
<tr>
<th>Date</th>
<th>Topic</th>
<th>Key Reading</th>
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<tbody>
<tr>
<td>January 18</td>
<td><strong>Introduction</strong></td>
<td>Egger 2001</td>
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<tr>
<td>Week 1</td>
<td>CER issues</td>
<td>Mosteller and Colditz 1996</td>
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<td>Berlin and Colditz 1999</td>
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<td>Stampfer 1982 (classic article)</td>
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<td>January 25</td>
<td><strong>Defining the research question</strong></td>
<td>Counsell 1997</td>
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<td>Week 2</td>
<td>Searching the literature; <em>Michelle Doering, Angela Hardi</em> – <em>Resources at Becker</em></td>
<td>Egger 2001</td>
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<td>Lemeshow 2005</td>
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<td>Tuuli 2011</td>
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<td>Dickersin 1994 (classic article)</td>
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<td>February 1</td>
<td><strong>STUDENT PRESENTATIONS</strong></td>
<td>Egger 2001</td>
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<td>Week 3</td>
<td><em>Homework 1: Preliminary topic</em></td>
<td>Normand S-L 1999</td>
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<td>Laird 1990</td>
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<td>February 8</td>
<td><strong>Statistical methods: effect sizes, basic meta-analysis calculations; BCG</strong></td>
<td>Egger 2001</td>
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<td>Week 4</td>
<td>Guest Speaker: Anne Drewry, MD <em>Homework 2: Library assignment DUE</em></td>
<td>Normand S-L 1999</td>
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<td>Laird 1990</td>
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<td>February 15</td>
<td><strong>Statistical methods, continued:</strong> regression, cumulative meta-analysis, BCG,</td>
<td>Egger 2001</td>
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<td>Week 5</td>
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<td>Tuuli 2011</td>
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<td>February 22</td>
<td><strong>Heterogeneity I: I², subgroup analysis;</strong></td>
<td>Egger 2001</td>
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<td>Week 6</td>
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<td>Colditz 1995</td>
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<td>Berlin 1995</td>
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<td>Higgins 2003</td>
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<td>Gonzales 2007</td>
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<td>March 1</td>
<td><strong>Computer lab 1.</strong></td>
<td>Intro to STATA</td>
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<td>Week 7</td>
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<td>March 8</td>
<td><strong>Homework 3: Analysis DUE</strong></td>
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<td>Week 8</td>
<td><strong>Data extraction – examples &amp; in class exercise</strong></td>
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<td><strong>Quality scores: application to research synthesis</strong></td>
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<td>March 15</td>
<td><strong>SPRING BREAK</strong></td>
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<td>Week 10</td>
<td><strong>STUDENT PRESENTATIONS</strong></td>
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<td>March 29</td>
<td>Week 11</td>
<td><strong>Computer lab 2</strong></td>
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<td>April 5</td>
<td>Week 12</td>
<td><strong>Analysis combining individual level patient data</strong></td>
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<td><strong>Critique:</strong></td>
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<td><em>Cholesterol Treatment Trialists’ 2010</em></td>
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<td>April 12</td>
<td>Week 13</td>
<td><strong>Drug safety and adverse events Network Analysis</strong></td>
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<td>April 19</td>
<td>Week 14</td>
<td><strong>Combining diagnostic test results</strong></td>
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<td>April 26</td>
<td>Week 15</td>
<td><strong>Student presentations:</strong></td>
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<td><em>Summary and final results</em></td>
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<td>May 3</td>
<td>Week 16</td>
<td><strong>Student presentations:</strong></td>
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<td><em>Summary and final results</em></td>
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<td><strong>Final assignment DUE</strong></td>
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Readings

Week 1
Introduction and CER issues and perspectives


Classic article

Week 2
Defining the Question
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

Classic article

Week 3
Student presentations: Study protocol precise topic, search strategy, inclusion/exclusion criteria.
Week 4
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 5
Statistical methods, continued: cumulative meta-analysis, tools for publication bias


Week 6
Heterogeneity: I^2, subgroup analysis
Examples: ETS, HIV counseling & testing, NAC


Colditz GA, Burdick E, Mosteller F. Heterogeneity in Meta-analysis of Data from Epidemiologic Studies: Reviews and Commentary. AJE 1995;371-81.Colditz


Week 7
Computer lab
See STATA handout
Week 8

**Quality scores application to research synthesis**


Assessing the quality of randomized control trials. Current issues and future directions. Moher D, Jadad AR, Tugwell P. Int'l J of Technology Assessment in Health Care 1996;12-1;196-208 (see Canvas)


*Additional readings:*
Borenstein, Chapter 44

Week 9 **SPRING BREAK**

Week 10

**Present data extraction form and one study extraction**

Week 11

**Computer lab**
See STATA handout – on course web site

Week 12

**Individual patient data combined across studies.**

Cholesterol Treatment Trialists [Efficacy and safety of more intensive lowering of LDL cholesterol: a meta-analysis of data from 170,000 participants in 26 randomized trials](https://www.thelancet.com/viewarticle/10). Lancet 2010;376:1670-81

[Breast cancer and hormonal contraceptives: collaborative reanalysis of individual data on 53,297 women with breast cancer and 100,238 women without breast cancer from 54 epidemiological studies](https://www.thelancet.com). Lancet 1996;347:1713-27

Week 13

**Drug Safety and adverse events**

*Examples: Vioxx, Avandia, vaccines, antidepressants*


Golder S, Loke YK, Bland M. Meta-analysis of adverse effects data derived from Randomised controlled trials as compared to observational studies: Methodologic overview. PLOS medicine 2011; 8 e1001026


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 14

Combining Diagnostic Tests

Example:


Further reading on this topic see Rutter CM, Gatsonis CA http://onlinelibrary.wiley.com/doi/10.1002/sim.942/abstract


Examples:

Kwok Y et al., Meta-analysis of exercise testing to detect coronary artery disease in women, American Journal of Cardiology 1999; 83: 660-666.

Additional reading:

Applying results to policy and practice

Ioannidis J, Karassa F. The need to consider the wider agenda in systematic reviews and meta-analysis. BMJ 2010;341:762-65


**Weeks 15 and 16**

**Student presentations:**

Final presentation of overall SRMA including some results and conclusions.