CLRES 2300: Introduction to Systematic Reviews and Meta-Analysis

Instructors: James E. Bost, MS, PhD
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This course is an overview of the concepts necessary for performing systematic reviews and meta-analyses, covered in sufficient detail to enable students to conduct their own systematic reviews/meta-analyses upon completion of the course. Course content will include step-by-step instruction in how to conduct a systematic reviews and meta-analysis, including developing a focused research question, designing a study protocol, defining inclusion/exclusion criteria, identifying relevant literatures databases, developing literature search strategies, data abstraction and management, and statistical methods for meta-analysis. Additional topics covered will include how to determine when meta-analysis may be useful, choosing a meta-analytic method, study quality assessment, exploration of heterogeneity, evaluation of potential sources of bias, and presentation of results. Students will evaluate and update a published systematic review and meta-analysis for their final project.

Course Information:

1.0 credit, pass/fail grading

8 sessions over 4 weeks (9/29/09-10/22/09)

Tuesdays and Thursdays, 10:00AM – noon, Parkvale 222

Office hours by appointment

Course Prerequisites:

Basic biostatistics course, or permission of the instructors

Required Textbook:

Egger M, Davey Smith G, Altman A (eds). Systematic Reviews in Health Care: Meta-Analysis in Context. 2nd Edition. BMJ Books. London, England, 2001.

Other Recommended Books:

1. Sutton AJ, Abrams KR, Jones DR, Sheldon TA, Song F. Methods for Meta-Analysis in Medical Research. John Wiley and Sons. West Sussex, England, 2000.
2. Cooper H, Hedges LV (eds). The Handbook of Research Synthesis. Russell Sage Foundation. New York, 1994.
3. Petitti DB. Meta-Analysis, Decision Analysis, and Cost-Effectiveness Analysis. Oxford University Press, New York, 2000.

Course Requirements:

1. Homework assignments
2. Final Project/Write-up – Update a published systematic review/meta-analysis (provided by instructors)

Session 1	Date	Background about systematic reviews/meta-analysis	Instructor:
	9/29	Formulating a research question and study protocol	Nayak

Topics:

1. Definitions of systematic review and meta-analysis
2. Why do we need systematic reviews and meta-analyses?
3. Difference between systematic reviews and narrative reviews
4. Systematic reviews/meta-analysis of RCTs versus other study designs
5. Introduction to the Cochrane Collaboration
6. Outline of steps in performing a systematic review, including:
    - Defining a research question
    - Defining inclusion/exclusion criteria
    - Developing a study protocol

Required Reading (prior to session):

1. Egger Chapters 1, 2, 12, 25
2. Ross, et al. article (provided on CourseWeb)

In-class Exercise:

Begin to draft a systematic review/meta-analysis study protocol based on the Ross, et al. article you will be updating for the course final project. Specifically: 1) refine the research question, if necessary; 2) specify inclusion and exclusion criteria; and 3) create an inclusion/exclusion criteria form.

Homework Assignment 1:

Using the Ross, et al. article that we have chosen for the course project, review the research question, protocol, and inclusion/exclusion criteria listed in the article. Briefly answer the following questions: Was the research question appropriately defined? Was it clear that a research protocol was developed prior to initiation of the study? Was this protocol explicitly stated? Were inclusion/exclusion criteria clearly stated? Is there anything that you might have done differently regarding defining the research question, planning or presenting the study protocol, or choice of inclusion/exclusion criteria? Additionally, create and hand in an inclusion/exclusion criteria form created *using the same criteria stated by the study authors* (continuation of in-class exercise).

Homework Assignment 1 due Thursday October 1st

Session 2	Date	Goals of literature search	Instructors:
	10/1	How to develop search strategies for online databases	Nayak, HSL Librarians

Topics:

1. Goals of literature search
2. Databases (MEDLINE, EMBASE, etc.) & database-specific search strategies
3. Designing & implementing database search strategies (with demonstration of MEDLINE search)
4. Searching the grey literature, handsearching journals, contacting experts to find additional literature
5. Understanding the Cochrane Collaboration and navigation of the Cochrane website

Required Reading (prior to session):

1. Egger Chapter 4
2. Cooper Chapter 4

Suggested Reading :

1. Petitti Chapter 4

In-class Exercise:

Experiment with the different MEDLINE search features learned in class today (e.g., MESH terms, explode function) to identify search terms that can be used to find articles to update the Ross, et al. meta-analysis. Begin to develop your own MEDLINE search strategy to update the Ross, et al. meta-analysis.

Homework Assignment 2:

Review the search strategies indicated in the Ross, et al. meta-analysis. Briefly answer the following questions: Were the chosen databases appropriate to cover the relevant literature for the research question? Would you have searched any additional databases? Were the search strategies for individual databases sufficiently broad to identify most of the literature on the topic of interest within each of the databases? If there were limits placed on the search (e.g. language limits), were they appropriate? What steps (if any) were taken to find literature beyond the chosen databases? Additionally, *design and hand in* your own MEDLINE search strategy to identify articles to update this review (continuation of in-class exercise).

Homework Assignment 2 due Tuesday, October 6th

Session 3	Date	Managing references	Instructors:

	10/6	Applying inclusion/exclusion criteria to select articles Study quality assessment Abstracting data Data management	HSL Librarians, Nayak

Topics:

1. Managing and sharing references
2. Applying inclusion/exclusion criteria to identify relevant articles
3. Approaches to quality assessment
4. Categories of data to abstract
5. Data abstraction
6. Data management/recordkeeping

Required Reading (prior to session):

1. Egger Chapters 3, 5, 7

Suggested Reading:

1. Petitti Chapter 5

In-class Exercise:

Begin to develop a data abstraction form to extract data from the articles you will find to update the Ross, et al. meta-analysis. Use the data abstraction template provided in class today to develop your own form.

Homework Assignment 3:

Complete and submit your data abstraction form to capture relevant information from articles found in your search to update the Ross, et al. meta-analysis.

Homework Assignment 3 due Thursday October 8th

Session 4	Date	Introduction to Statistical Methods for Meta-Analysis	Instructor:

10/8	Nayak

Topics:

1. How to determine if studies found in systematic reviews are appropriate for meta-analysis
2. Statistical tests of homogeneity
3. Random effects versus fixed effects models
4. Overview of commonly used meta-analytic methods
5. How to choose a meta-analytic method

Required Reading (prior to session):

1. Egger Chapters 15, 16
2. Keren, et al. Article (provided on CourseWeb)

Suggested Reading:

2. Sutton Chapters 3, 4 and 5

In-class Exercise:

Using the STATA commands discussed in class today, and the data set that we provided you, perform a statistical test of homogeneity and random and fixed effects meta-analyses. Plot the meta-analysis results using a forest plot.

Homework Assignment 4:

Using the list of articles found with the librarians' search strategy (provided to you on CourseWeb), review the articles assigned to you to determine if any meet inclusion criteria. Use the inclusion/exclusion criteria form that you created to identify additional articles. Keep a record of total number of articles found in your search, the number of articles excluded, and the number and titles of articles that meet inclusion criteria. *Using the data abstraction form provided to you by the class instructors,* abstract data from any studies that meet inclusion criteria. Hand in the data abstraction forms for the articles you found that meet inclusion criteria (if any). Additionally, hand in a brief write-up summarizing how many of the titles/articles you reviewed were included vs. excluded, some of the most common reasons for exclusion, and the titles of the articles that you found that met inclusion criteria.

Homework Assignment 4 (last HW assignment) due Tuesday October 13th

Session 5	Date	Exploring data	Instructor:
	10/13		Bost

Topics:

1. Publication bias and other potential sources of bias
2. Overview of approaches to exploring heterogeneity
3. Subgroup analysis

Required Reading (prior to session):

1. Egger Chapters 8, 9, 11

Suggested Reading:

3. Sutton Chapters 6 and 7

In-class Exercise:

Using the STATA commands taught in class today, and the dataset that we provide you, perform subgroup analysis and search for evidence of publication bias.

Course Final Project:

On Friday October 16th you will be provided with the dataset (both in Excel and Stata) and all the Stata output needed for you to update the Ross, et al. meta-analysis. Begin work on the final project write-up, a no more than 10 page double-spaced summary of your update of the published meta-analysis. Your write-up should be organized into background (brief, no more than one to two paragraphs), methods, results, and discussion sections. In addition to discussing what your conclusions are and whether they agree with Ross et al.'s conclusions in the discussion section, also critique Ross, et al.'s methods. What did the authors do well? What might you have done differently?

Final Project due Friday November 6

Session 6	Date 10/15	Exploring combined data, Part 2	Instructor: Bost

Topics:

1. Continuation of topics covered in session 5 on Heterogeneity
2. Meta-Regression
3. Assessing Study Quality
4. Sensitivity analysis

Required Reading (prior to session):

Egger Chapter 15 and 16

Suggested Reading:

4. Sutton Chapters 8 and 9

In-class Exercise:

Using the dataset that we provided you, perform meta-regression, cumulative meta-analysis and sensitivity analysis to evaluate the influence of individual studies on the meta-analysis results. Did removal of any of the individual studies significantly change the results?

Session 7	Date 10/20	Lab: Meta-Analysis using STATA	Instructor: Bost

Topics:

1. Overview of STATA commands for meta-analysis
2. Step by step tutorial using STATA to test for homogeneity, combine data, perform sensitivity analysis, explore for evidence of publication bias, present results

Required Reading (prior to session):

1. Egger Chapter 18
2. Chan, et al. article (provided on CourseWeb)

In-class Exercise:

Step by step tutorial of how to analyze your data in STATA.

Session 8	Date 10/22	Applications of systematic reviews/meta-analysis	Instructors: Nayak and Bost

Topics:

1. Writing the Meta-Analysis Report
2. Brief Introduction to Other Contexts for Meta-Analysis

Required Reading (prior to session):

Egger Chapters 19,21,22,23

Suggested Reading:

5. Sutton Chapter 10

In-class Exercise:

Time will be available to consult with your instructors on the course final project.

Course Final Project:

Submit a no more than 10 page double-spaced summary of your update of the published meta-analysis. Your write-up should be organized into background (brief, no more than one to two paragraphs), methods, results, and discussion sections. In addition to discussing what your conclusions are and whether they agree with Ross et al.'s conclusions in the discussion section, also critique Ross, et al.'s methods. What did the authors do well? What might you have done differently?

Final Project Write-up due Friday November 6th.