This course is an overview of the concepts necessary for performing a systematic review and a basic meta-analysis, covered in sufficient detail to enable students to conduct their own systematic review, including a basic meta-analysis if appropriate, upon completion of the course. Course content will include step-by-step instruction on how to conduct a systematic review and meta-analysis, including developing a focused research question, defining inclusion/exclusion criteria, developing literature search strategies, and performing data abstraction-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. Throughout this course you will conduct a mini systematic review. There will be 4 homework assignments and 1 in-class presentation.

Course Information:
1.0 credit, letter grading – A/B/C/F, based on assignments and in class participation. Students have the opportunity obtain 100% of possible points for homeworks handed in on time. If homeworks are handed in after the due date but prior to the beginning of the next class, students have the opportunity to obtain 50% of the possible points. Homeworks handed in after the beginning of the class after the due date will not be accepted. Your final project should be original; if it overlaps significantly with an existing published review points will be taken off (at least 2 new studies should be added).

8 live sessions. Please make every effort to attend class because at least half of each session will be spent on small group/one-on-one work relating to your project.

Course Prerequisites:
Basic biostatistics course and experience with STATA or permission of the instructors. Obtain STATA 14 prior to class, and load the meta-analysis modules (instructions).

Required Textbook (Online):

Competencies Addressed Throughout the Course:

1. Problem Formulation: Propose significant and novel empirical, testable, hypothesis-driven research questions using, where appropriate, different disciplines and community engagement.

2. Problem Formulation: Conduct comprehensive literature reviews from appropriate sources across disciplines.

3. Problem Formulation: Critically review published studies that use various research methodologies and identify possible sources of bias and potential health disparities therein.

4. Methodology: Design basic features of research protocols based on specific research questions, appropriately addressing bias.
5. **Sampling**: Identify appropriate study populations and sample size, control and comparison groups, and possible sources of bias for research problems.

6. **Oral Communication**: Prepare and deliver oral presentations of research at a variety of stages to a range of audiences, and respond to constructive criticism and questions.

7. **Written Communication**: Prepare written presentations of research at a variety of stages to a range of audiences, technical and non-technical, and respond to constructive criticism and questions.

8. **Multidisciplinary Teamwork**: Demonstrate behaviors that facilitate being an effective member of a multidisciplinary team including: generating multiple points of view; contributing to the development of new ideas; and demonstrating conflict management skills.

9. **Applied Analytic Techniques**: Describe appropriate data analysis plans for addressing specific research questions.

10. **Applied Analytic Techniques**: Determine and apply a range of appropriate statistical techniques to answer research questions and explain the implications of missing data on conclusions drawn from statistical results.

**Other Recommended Books:**


4. Cochrane Handbook of Diagnostic reviews: [http://srtda.cochrane.org/handbook-dta-reviews](http://srtda.cochrane.org/handbook-dta-reviews)
Session 1  Formulate a specific research question

**Required preparation (prior to session):**

Email instructor a specific study question on the efficacy of a THERAPY that you would like to investigate via systematic review during this course.

**Questions that best lend themselves to a systematic review with meta-analysis are questions for which at least 4 RCTs will meet inclusion criteria.** It is best if the intervention is a therapy and the outcome is quantitative, either binary (e.g. mortality at 30 days) or continuous (e.g. blood pressure). Binary outcomes will be easier to analyze. For continuous outcomes, a mean and variance must be obtainable. **If a systematic review on your question is already been done, it can be redone ONLY if at least several years (minimum 2 or more) have passed since its publication and if at least 2 additional RCTs on the topic have been published in the interim.**

If you have questions about this prior to the first session, or would like to research a question for which all available data is observational, please contact the instructors.

**Objectives:**

1. Formulate a specific study question
2. Define specific inclusion and exclusion criteria
3. Determine primary and secondary outcome measures

**Lecture:**

1. Definitions of systematic review and meta-analysis
2. Role of systematic reviews
3. Development of a good study question
4. Formulating a specific study question (PICOTS)
5. The importance of specificity
6. Defining inclusion/exclusion criteria

**Competencies**

1. *Problem Formulation:* Propose significant and novel empirical, testable, hypothesis-driven research questions using, where appropriate, different disciplines and community engagement.
2. *Methodology:* Design basic features of research
In class small-group exercise: Formulating a research question

Review each student’s study question. Form small groups and look for ways to refine the questions. Next pick one or two questions and 1) develop inclusion/exclusion criteria and 2) decide on 1° and 2° outcome measures. Report your results in discussion as a large group.

Wrap-up

Introduce the Cochrane Library.

Homework Assignment 1 (10%)

For homework 1, read chapter 5 of the Cochrane Handbook. Refine the study question that you have chosen for the course project.

Do a search on the Cochrane Database of Systematic Reviews, pubmed, clinicaltrials.gov and http://www.crd.york.ac.uk/PROSPERO/ to see if a systematic review or protocol on your topic has already published or registered. If a recent review was completed and you are not likely to have any new data (at least 2 studies) to add to it, pick another topic.

Email your study question and inclusion/exclusion criteria (i.e., complete from “Background” in template up to and including “Secondary Outcomes.” You do not need to start the abstract until Homework 3). It’s ok to use bullets instead of paragraphs.
Session 2 Conduct a systematic search

Objectives
1. Conduct an electronic search using the appropriate terms in an appropriate database
2. Understand basic use of Endnote for systematic review
3. Assess studies using inclusion/exclusion criteria
4. Work effectively with librarians to optimize quality of your search strategy

Lecture:
1. Librarian as co-investigator
2. Search strategies for finding articles in PubMed for systematic review
3. Other specific databases available (CENTRAL, EMBASE, etc.)
4. Gray literature
5. Endnote

Competencies
1. Problem Formulation: Understand the importance of comprehensive literature searching across disciplines
2. Sampling: identify appropriate study populations and sample size, control and comparison groups, and possible sources of bias for research problems.

In-class exercise (finish at home if not done in class)
Generate a short list of keywords and subject headings to use in your search, combining the terms with the appropriate Boolean operators. At a minimum, your list should include 1 subject heading and 3-5 keywords for each concept in your topic. Run the search in PubMed with the help of the librarians. Enter your search strategy into the template provided. For this exercise, please bring to class any good references or PubMed records you have on your topic.

Homework Assignment 2 (30%)
Conduct a literature review on your topic. Select manuscripts that meet your inclusion criteria. Complete all sections marked by an asterisk in the provided template. It’s ok to use bullets instead of paragraphs under each section. Read Cochrane Handbook chapters 7 and 8.

We will discuss analysis plans in class during Session 5, so you should abstract at least a few of your studies prior to that class so you have a sense of what your data look like. Use the abstraction form used in the in-class exercise in Session 4 for binary and/or continuous outcomes as appropriate.
Objectives:
1. Complete a risk of bias table for studies meeting inclusion criteria
2. Determine other covariates (factors other than the ones assessed above) that may be important to collect on the eligible studies

Lecture:
1. Approaches to assessment of risk of bias
2. Differences between bias and quality

Competencies
1. Methodology: Design basic features of research protocols based on specific research questions, appropriately addressing bias.
2. Sampling: Identify appropriate study populations and sample size, control and comparison groups, and possible sources of bias for research problems.

In class exercise:
Each person will assess the risk of bias for provided article. Determine other factors that may influence study results. Complete a risk of bias table for Buster, et al 2008 in groups of 3-4.

Wrap-up:
Discuss issues that come up with ROB assessment with class.
Review of previous session:
Review problems you encountered during your search

Objectives:
1. Abstract dichotomous and continuous data from individual studies
2. Run a basic meta-analysis using STATA
3. Interpret the analysis

Lecture:
1. Overview of common meta-analytic methods
2. Random effects versus fixed effects models
3. How to choose a meta-analytic method

Competencies
1. Applied Analytic Techniques: Determine and apply a range of appropriate statistical techniques to answer research questions and explain the implications of missing data on conclusions drawn from statistical results.
2. Methodology: Compare strengths and weaknesses (feasibility, efficiency, generalizability, validity, and ability to derive unbiased inferences) of different research paradigms and methodologies.
3. Written Communication: Organize and report statistical results.

In class exercise: Abstracting data
Abstract data from studies provided in class using the excel abstraction form provided. This form will be used for data abstraction for your review as well.

Homework Assignment 3, part 1 (10%), due at the beginning of class on Feb 21. Email to Zhongying (Joy) Xu [ZHX17@pitt.edu]

Part 1: Conduct a meta-analysis of the 16 smoking cessation studies provided in smoking.dta. Use the risk ratio as your outcome. The treatment is a minimal smoking intervention from the patient’s family doctor and the control is no intervention. The outcome is cessation from smoking. The variables are the entries in a two by two table of smoking intervention and no intervention (rows) by cease smoking and did not cease smoking (columns). The entries in the table are the variables named “a b c d” as discussed in class. Construct both fixed and random
effects estimates of the pooled risk ratio. Discuss heterogeneity, choose which you think is the correct model (fixed or random effects), and say why you made that choice. Present graphical and tabular data as needed, and interpret the output clinically. What would you do as a clinician as a result of this analysis? Your work should be in a clean and well-documented word file. Your STATA output (cleaned – eliminate extraneous or incorrect output; use column-delimited font such as Courier) should be provided in an appendix. The data are from Silag, C. and S. Ketteridge, 1997. Physician advice for smoking cessation. In Tobacco Addiction Module of the Cochrane Database of Systematic Reviews, ed. T. Lancaster, C. Silagy, and D. Fullerton. Oxford: The Cochrane Collaboration. Chapter 9 of the Cochrane Handbook provides meta-analytic guidance.

Please recall that we will discuss analysis plans in our next class (Session 5), so you should abstract at least a few of your studies prior to that class so you have a sense of what your data look like. Use the abstraction form used in the in-class exercise in Session 4 for binary and/or continuous outcomes as appropriate.
Review of previous session:
Review problems you encountered in Homework #3, part 1.

Objectives:
1. Refine analysis plan
2. Conduct an analysis of heterogeneity in STATA.

Lecture:
1. Overview of approaches to exploring heterogeneity
2. Approaches to sensitivity analysis
3. Meta-regression

Competencies
1. Applied Analytic Techniques: Describe appropriate data analysis plans for addressing specific research questions.
2. Applied Analytic Techniques: Determine and apply a range of appropriate statistical techniques to answer research questions and explain the implications of missing data on conclusions drawn from statistical results.
3. Written Communication: prepare written presentations of research at a variety of stages to a range of audiences, technical and non-technical, and respond to constructive criticism and questions.

In class exercise:
Homework Assignment 3, part 2 (10%), due at the beginning of class on Feb 24. Email to Joy Xu.

Describe your analysis plan a priori, including descriptive and meta-analytic (if appropriate) methods you will apply, and how you will deal with heterogeneity, and subgroups.
Objective:
1. Systematically evaluate the strengths and weaknesses of your results
2. Summarize this evaluation for your readers

Lecture:
1. Summary of findings table
2. GRADE criteria

Competencies
1. Applied Analytic Techniques: Determine and apply a range of appropriate statistical techniques to answer research questions and explain the implications of missing data on conclusions drawn from statistical results.
2. Written Communication: Organize and report statistical results.

In class small-group exercise:
Create a Summary of Findings Table.

Wrap-up discussion:
Discuss issues with creating SOF tables.

Homework Assignment 4, (30%) due at least two hours prior to the beginning of class, i.e., by 8am, on March 3. Email to Drs. Shaikh, Corbelli and Joy Xu.
Hand in your final version of your mini systematic review including a risk of bias and summary of findings tables (use template provided for Homework 3). If your review data are not sufficient for, or are not amenable to, a meta-analysis, explain why not and complete a descriptive analysis. Chapter 4 of the Handbook describes the content that should be included in each section in detail; also refer to the template. Your final project should be original; if it overlaps significantly with an existing published review points will be taken off (at least 2 new studies should be added). Make sure you cite all other systematic review on your topic and explain how your review add to the literature. Include a screenshot of STATA data and the code you used for the analysis. Prepare a 5-minute power-point presentation for the final class with your findings.
Objectives:
1. Apply the PRISMA checklist to evaluate the quality of the reporting of a published meta-analysis
2. Explain how results from meta-analysis can be biased
3. Assess quality of a meta-analysis

Lecture:
1. PRISMA statement
2. Meta-bias
3. Quality assessment of a meta-analysis - AMSTAR

Competencies
1. Problem Formulation: Critically review published studies that use various research methodologies and identify possible sources of bias and potential health disparities therein.
2. Multidisciplinary Teamwork: Demonstrate behaviors that facilitate being an effective member of a multidisciplinary team including: generating multiple points of view; contributing to the development of new ideas; and demonstrating conflict management skills.

In class small-group exercise:
Review the meta-analysis provided to you in small groups using the PRISMA checklist.

Wrap-up discussion:
Review common errors in systematic review/meta-analysis.
How does one differentiate a “good” systematic review/meta-analysis from a “bad” one?
### Session 8

**Date**
03/03 (Tues)

**Presenting results**

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<th>Instructors:</th>
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<td>Shaikh,</td>
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<td>Corbelli</td>
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**Student presentations (10% of final grade)**

Each student will present their findings (5 minute limit). Email your presentations to Drs. Shaikh and Corbelli at least ONE hour before class so that it can be loaded onto the class laptop.

**Competencies**

1. *Oral Communication*: Prepare and deliver oral presentations of research at a variety of stages to a range of audiences, and respond to constructive criticism and questions.