



SPPH 516

Systematic Overviews

Methods for Systematic Reviews in Health Research

Course Description

Fall 2015

School of Population and Public Health, UBC
The Centre for Clinical Epidemiology & Evaluation

SPPH 516
Methods for Systematic Reviews in Health Research
Course Outline
2015

Time:	Tuesdays, 9:00-12:00 p.m.
Term:	September 8 – December 1, 2014 <i>No class Sept 8 (orientation)</i>
Class Location:	UBC Point Grey campus School of Population and Public Health Room: B151 2206 Health Sciences Mall
Instructor:	Dr. Darlene Taylor
Co-instructor:	Ms. Mimi Doyle-Waters
Other Instructors:	Dr. Mir Sohail Fazeli Dr. Lorri Puil Dr Aaron Tejani Dr. Tom Perry Dr. Mahyar Etminan Dr. Ed Mills Dr. Stirling Bryan Dr. Jim Wright
Teaching Assistant	Shayesteh Jahanfar
Office Hours:	Informal lab time following the class (12:00pm to 12:30pm) in B151; also available by appointment with the instructor or teaching assistant
General Information:	Dr. Darlene Taylor Phone: (604) 875-2424 extension 6489 E-mail: darlene.taylor@cw.bc.ca or Mimi Doyle-Waters Phone: (604) 875-4111 extension 61176 E-mail: Mimi.Doyle-Waters@ubc.ca or Shayesteh Jahanfar

e-mail: shayesteh.jahanfar@ubc.ca

INTERESTED PARTICIPANTS

- Graduate students
- Clinicians and allied health professionals interested in systematic review methods.

PURPOSE

The purpose of this course is to introduce students to systematic review methodology so that they will develop an understanding of the key components of a review and acquire the key skills needed to carry out their own reviews.

MAIN OBJECTIVES

- To identify clinical questions where there is not a robust well designed systematic review available
- To introduce students to appropriate methodology for protocol development and the steps needed to complete a systematic review
- For students to become aware of the various mechanisms for searching the published literature and also retrieving unpublished literature
- To introduce students to skills in critical appraisal of clinical trials and application of the Cochrane Risk of Bias tool within systematic reviews
- To introduce students to statistical techniques required for data synthesis
- To familiarize students with methods for assessing and interpreting evidence within systematic reviews.

FACULTY DESCRIPTIONS

Dr. Darlene Taylor, RN, PhD

Dr. Taylor is an Instructor in the School of Population & Public Health. She has a doctorate in epidemiology and public health from UBC and has worked at the BC Centre for Disease Control as a senior research manager for 12 years. She also leads the Systematic Review Unit at BCCDC. She has been successful in obtaining CIHR funding to conduct several systematic reviews in the area of sexually transmitted infections and HIV. Her main area of research is in delivering ethical care to marginalized individuals including those who misuse substances and who are homeless or unstably housed.

Ms. Mimi Doyle-Waters, MA, MLIS

Ms. Doyle-Waters is the librarian for the Centre for Clinical Epidemiology and Evaluation (C2E2). She has worked on a variety of systematic reviews over the last 10 years, for example SARS, influenza, herpes zoster, nurse staffing, emerging zoonoses, arthritis and several Cochrane reviews. Through C2E2 she also provides consulting

services to researchers interested in developing measurement instruments, systematic review protocols and searches.

Dr. Lorri Puil, MD, PhD

Dr. Puil is a physician-scientist who has worked with UBC's Therapeutics Initiative since 2001, contributing to its research and educational activities. She is an editor of the Cochrane Collaboration Hypertension Review Group and a member of the Campbell & Cochrane Equity Methods Group. In addition to her MD and specialty training, she has a PhD in signal transduction, an area relevant to novel therapeutics. Her research interests include the effectiveness and safety of prescription drugs, systematic review methodology, and ways to improve systematic review quality.

Dr. Aaron Tejani, PharmD

Dr. Tejani is a clinical assistant professor with UBC's Faculty of Pharmaceutical Sciences and a member of the Fraser Health Research Ethics Board, the BC Medical Association's Guidelines and Protocols Advisory Committee, and an editor for the Cochrane Hypertension Review Group. His interests include critical appraisal of the biomedical literature, knowledge translation activities, and research. He conducts systematic reviews and meta-analyses of health care interventions with the Therapeutics Initiative's Drug Assessment Working Group. Dr Tejani holds a BSc in pharmaceutical sciences from UBC and a PharmD from Creighton University (Omaha, Nebraska).

Dr. Mahyar Etminan, PharmD

Dr. Etminan is an Assistant Professor of Medicine at UBC. He is trained in both clinical pharmacology and epidemiology. His main expertise is in identifying rare adverse drug events using large administrative databases and systematic reviews. He is an expert in methodology of randomized controlled trials and observational studies.

Dr. Stirling Bryan, PhD, Director of C2E2

Dr. Bryan is Head of the Centre for Clinical Epidemiology & Evaluation and Professor in the School of Population and Public Health. For over 20 years he has been a university-based practicing health economist with extensive engagement to the policy and decision making world. He has taught health economics to undergraduate economists and medical trainees, to postgraduate health economics students and to health sector professionals. His research track record reveals a longstanding goal of informing policy and practice and since his relocation to Canada in 2008, he has continued a focus on policy-relevant research. His current position, sponsored by Vancouver Coastal Health, sees him working alongside policy colleagues in one of BC's largest regional health authorities.

Dr. Mir Fazeli, MD, PhD

Dr. Fazeli is a physician and currently a PhD candidate in Experimental Medicine Program at UBC department of Pediatrics. He is trained as an epidemiologist and his

main field of expertise include research methodology and clinical trials with the main focus on measuring the activity of the autonomic nervous system, systematic review of randomized controlled trials, and implementation and evaluation of complementary and alternative medicine interventions. Mir has been the TA for this course since fall 2013.

TEACHING ASSISTANT – Shayesteh Jahanfar

Shayesteh Jahanfar is a PhD student at SPPH and a Cochrane trainer. She has several Cochrane publications to her credit and is familiar with Revman software. She will be your TA and will be teaching the statistical analysis of systematic review.

INSTRUCTION FORMAT

Students will be introduced to systematic review methods via a variety of topics related to each component of a systematic review, for example, question formulation, the process of developing a search strategy, application of study inclusion and exclusion criteria, data extraction, assessment of risk of bias, and analysis of study results. Once students have completed this course they will have sufficient knowledge to participate in a systematic review. Students will learn to use Review Manager (RevMAN) software. Course assignments include both individual and group work and will build towards team development of a draft systematic review protocol and a partial systematic review. Feedback on each assignment aims to contribute to development of subsequent components of a draft review.

The course instructors will be available to meet informally with the students to address questions regarding the course during a half-hour period of informal optional lab time set aside just before and just after each class, with additional meetings on appointment.

SCOPE OF THIS COURSE

The focus of this course is systematic reviews involving clinical and policy questions that are addressed through a variety of study designs including randomized controlled trials (RCTs). Interventions using qualitative methods are briefly discussed but the course is not designed to provide in depth detail on qualitative systematic reviews.

PREREQUISITES

Students should have basic understanding of health research design / methodology, working knowledge of how to search for literature in the UBC library, and an introductory understanding of medical statistics. Courses in searching the health databases including MEDLINE and the Cochrane Database of Systematic Reviews are available via the UBC library.

STUDENT EVALUATION

Students will receive individual grades on participation and on the section of Assignment #4 on a specific research study. The rest of the assignments will be carried out as research teams, with a single grade for all members of a team.

Evaluation

- | | |
|---|-----|
| ▪ Assignment #1 – Research question [team grade] | 10% |
| ▪ Assignment # 2 – Draft search strategy [team grade] | 10% |
| ▪ Assignment #3 – Protocol [team grade] | 25% |
| ▪ Assignment # 4 – Draft 3-trial results | |
| ○ Individual grade | 20% |
| ○ Team grade | 20% |
| ▪ Assignment # 5 – Team Presentation [individual grade] | 15% |

Research Topic

Students will select an initial research question appropriate to a systematic review. These questions will be used as a basis for the development of ‘review teams’ of three students, who will work together to carry out each stage of a draft systematic review. Each member of a review team will have primary authorship and responsibility for a section of the review, but all team members are expected to provide substantive contributions to the entire review.

Assignment #1 – Research question

Students will work in teams of two to three to identify a research question of interest for a systematic review, for which there is clinical justification and no up-to-date good quality systematic review available.

P.I.C.O.S. format (Patients, interventions, comparators, outcomes, study design) will be used. The teams will carry out a brief scoping review and justification of the choice of research question. The scoping search strategy should be included as an appendix. The assignment will be 2 to 3 pages in length in total. It should be completed as a MS Word document.

Assignment # 2 – Draft conceptualization of a search

Students will work in the same teams of three to carry out the first steps to develop a search strategy for their systematic review question. This will include developing a flow diagram of key concepts addressed in the search, an overview of what resources will be searched for published and unpublished trials, and a draft MEDLINE search strategy. This assignment should be provided in MS Word.

Assignment #3 – Protocol

This assignment should be completed as an MS Word document that is based on a reformatted RevMan file. Student teams are expected to incorporate changes to the research question and search strategy based on feedback on these assignments.

The protocol should be 8 to 10 pages long and include the following elements:

- Research question/s
- Background
- Literature scoping
- Search protocol
- Study selection
- Study quality assessment
- Data extraction
- Synthesis of the extracted evidence

Within each research team, students should agree on primary, second and third authorship for each section. Each author is expected to contribute to all aspects of the protocol development, and the team is expected to work together to develop an equitable division of labour.

Examples of Protocols

Examples of protocols are available through [EBM Reviews - Cochrane Database of Systematic Reviews](#). (Type your topic term into the search box, click search. Click on Limits and then select Protocols)

Assignment #4 - Draft 3-trial results with critical appraisals

This assignment should be completed as a MS Word document. Students are expected to use RevMan when preparing the draft 3-trial review but should not submit a RevMan file.

The sections on each included trial should have a single author (see below for details). For the rest of the review, teams should agree on primary, second and third authorship as for the protocol.

This assignment includes each of the basic elements of a systematic review in abbreviated form, as a full review is beyond the scope of this course. The question,

background and methods sections are expected to incorporate changes based on feedback on previous assignments.

- Research question,
- Background
- Methods, including plans for analysis;
- Students will retrieve 100 records and assess studies for inclusion;¹
- Three trials meeting inclusion criteria will be assessed in detail.
- Each student is responsible for evaluation of one trial. This includes:
 - A summary of trial characteristics table
 - Use of the Cochrane Risk of Bias tool to assess internal validity
 - A narrative discussion of external validity
 - Data extraction
- Analysis of the three trial results will be carried out jointly:
 - Meta-analysis as appropriate.
 - A GRADE summary of findings table
 - Interpretation and preliminary conclusions

Examples of Systematic Reviews

Examples of systematic reviews are available through [EBM Reviews - Cochrane Database of Systematic Reviews](#).

Assignment #5 – Team presentations

Each research team will prepare a 5-minute summary presentation to the class about their review (e.g. Assignment 4), followed by 10 minutes of response to questions and discussion. All team members are expected to participate – if someone participated in preparation only, please let the instructors know what your role was.

COURSE TEXTBOOKS AND CORE MATERIALS

1. Two manuals that are available on-line provide core course instructional materials. Individual chapters will be linked to specific course units. Students are encouraged to obtain both of these texts and refer to them throughout the course.

Higgins JPT, Green S. Cochrane Handbook for Systematic Reviews of Interventions. Cochrane Collaboration. Version 5.1.0 [updated 2011 March] <http://www.cochrane-handbook.org/>

¹ Additional records may be needed if < 3 trials meet inclusion criteria

Centre for Reviews and Dissemination. Systematic Reviews. CRD's guidance for undertaking reviews in health care. York, UK: NHS Centre for Reviews and Dissemination; 2009. http://www.york.ac.uk/inst/crd/index_guidance.htm

2. The following textbooks are recommended as an additional resource:

Borenstein M, Hedges LV, Higgins JPT, Rathstein H. Introduction to Meta-Analysis. West Sussex, United Kingdom: John Wiley & Sons Ltd: 2009

Egger M, Smith GD, Altman DG, editors. Systematic reviews in health care : meta-analysis in context. [monograph online]. London: BMJ Publishing Group: 2008. Available on-line via UBC Connect. The 2001 print edition of this book is also being held as a 1-day reserve for this course in Woodward Library. Call number: WA20.5 .S988 2001 C.1.

3. Review manager (RevMan 5.3.4) software will be used in the course (available free of charge):

Download at: <http://ims.cochrane.org/revman/download>

4. General References

Eppi-Centre. Methods for conducting systematic reviews. 2010. Available at: <http://eppi.ioe.ac.uk/cms/LinkClick.aspx?fileticket=hQBu8y4uVwI%3D&tabid=88>

Eppi-Centre. Methods References
<http://eppi.ioe.ac.uk/cms/Default.aspx?tabid=1919>

5. Systematic review quality assessment

Shea BJ, Grimshaw JM, Wells GA, et al. Development of AMSTAR: A measurement tool to assess the methodological quality of systematic reviews. BMC Med Res Methodol. 2007;7:10.

Moja LP, Telaro E, D'Amico R, Moschetti I, Coe L, Liberati A. Assessment of methodological quality of primary studies by systematic reviews: results of the metaquality cross sectional study. BMJ. 2005 May 7;330(7499):1053

Shea B, Boers M, Grimshaw JM, Hamel C, Bouter LM. Does updating improve the methodological and reporting quality of systematic reviews? BMC Med Res Methodol. 2006 Jun 13;6:27.

SPPH COURSE OUTLINE Fall 2015

Date	Week	Session Topic	Instructor
Sept. 8		SPPH orientation session – no class	
Sept. 15	1	Review syllabus, assignments and course expectations Unit 1: What makes a review ‘systematic’? Judging the strength of research evidence Assignment # 1 handed out – research questions	Darlene Taylor Mimi Doyle-Waters
Sept. 22	2	Unit 2: Introductory session – elements of a systematic review, things to consider Unit 3: Scoping the literature, developing a research question, and setting inclusion and exclusion criteria Student review teams formed	Darlene Taylor Mimi Doyle-Waters
Sept 29	3	Unit 4: Literature search techniques; developing a search strategy. Please bring a laptop to class Assignment # 2 handed out – draft search strategy	Mimi Doyle-Waters
Oct 6	4	Unit 5: Introduction to Review Manager (RevMan) software Development of a flow chart Exercise: Use of RevMan. Please bring a laptop.	Mir Sohail Fazeli Darlene Taylor
Oct 6		Draft research question – Assignment # 1 due	
Oct. 13	5	Unit 6: Developing a systematic review protocol Unit 7: Applying inclusion and exclusion criteria, selecting studies, resolving disagreement Exercise: <i>applying inclusion / exclusion criteria</i> Assignment # 3 handed out – systematic review protocol	Darlene Taylor Mimi Doyle- Waters
Oct 20	6	Unit 8: Data and statistics: dichotomous and continuous measures, meta-analysis, meta regression Unit 9: To pool or not to pool? Fixed or random effects model; subgroups and sensitivity analyses Exercise: data extraction and synthesis	Shayesteh Jahanfar Aaron Tejani
Oct 20		Draft search strategy – Assignment # 2 due	
Oct. 27	7	Unit 10: Critical appraisal of clinical trials Using the Cochrane Risk of Bias tool Incorporating risk of bias assessment into systematic reviews Exercise: critical appraisal of a trial	Darlene Taylor Aaron Tejani
Nov 3	8	Unit 11: GRADE and summary of findings tables Formulating conclusions and completing your review Exercise: GRADE summary of findings <i>Outcome assessments in RCTs: not so simple 11:30-12:00pm</i> Assignment # 4 handed out: 3-trial preliminary review	Lorri Puil Darlene Taylor Tom Perry
Nov 3		Systematic review protocol – assignment # 3 due	
Nov 10	9	Unit 12: Critical appraisal of a systematic review <i>Gender and equity in systematic review 11:30 – 12:00pm</i>	Darlene Taylor Lorri Puil
Nov 17	10	Unit 13: Observational study designs 9:00 am to 10:30 am Systematic review of observational studies Introduction to Rapid Reviews	Mahyar Etmiman Darlene Taylor
Nov 24	11	Review teams - 5 minute final presentations	Taylor & Doyle-Waters
Dec 1	12	Unit 15: Knowledge translation – policy perspective Knowledge translation – clinical perspective Introduction to network meta-analysis 11:00 – 12:00 pm	Stirling Bryan Jim Wright Ed Mills
Dec 1		Draft 3-trial preliminary review – Assignment # 4 due	

Unit 1

Overview of Systematic Reviews Levels of Research Evidence

Dr. Darlene Taylor
Ms. Mimi Doyle-Waters

September 15, 2015

Objectives:

- To understand why there is an emerging science of research synthesis
- To know how to distinguish between a narrative and a systematic review, and between a systematic review and a meta-analysis
- To understand the relative strength and applicability of various research designs
- Review syllabus, assignments and course expectations
- Begin to form research teams

Required Readings

1) Egger M, Davey Smith G, O'Rourke K. Rationale, potentials, and promise of systematic reviews. In: Systematic reviews in health care: meta-analysis in context. Pages 3-21. (course textbook; available on-line via UBC Connect website)

2) Greenhalgh T. Assessing the methodological quality of published papers. BMJ. 1997 Aug 2;315(7103):305-8.

3) Richardson WS, Wilson MC, Nishikawa J, Hayward RSA. The well-built clinical question: A key to evidence-based decisions. ACP Journal Club. 1995;123(Nov-Dec, 12).

Supplementary Readings

Cook DJ, Mulrow CD, Haynes RB. Systematic reviews: synthesis of best evidence for clinical decisions. Ann Intern Med. 1997;126:376-80.

Loke YK, Price D, Herxheimer A, Cochrane Adverse Effects Methods Group. Systematic reviews of adverse effects: framework for a structured approach. BMC Med Res Methodol. 2007 Jul 5;7:32.

Altman DG. Systematic reviews of evaluations of prognostic variables. *BMJ*. 2001;323:224-228.

Deeks JJ. Systematic reviews in health care: Systematic reviews of evaluations of diagnostic and screening tests. *BMJ*. 2001;323:157-162.

Unit 2

Elements of a Systematic Review

Dr. Darlene Taylor

September 22, 2015

Objectives:

- To become familiar with the approach used in a systematic review by going through an example in detail
- To obtain an overview of the elements of a systematic review

Required Readings

1) Udell JA, Zawi R, Bhatt DL, et al. Association between influenza vaccination and cardiovascular outcomes in high-risk patients: a meta-analysis. *JAMA*. 2013 Oct 23;310(16):1711-20.

2) Egger M, Davey Smith G. Principles of and procedures for systematic reviews. In: *Systematic Reviews in Health Care: Meta-analysis in context*. Pages 23-42.

Unit 3

Question Development and Background Setting inclusion and exclusion criteria

Dr. Darlene Taylor
Ms. Mimi Doyle-Waters

September 22, 2015

Objectives:

- To understand the PICOS components of a clinical research question
- To explore the appropriate level of precision needed for an informative and relevant systematic review research question
- To explore framing of research questions from a patient health perspective
- To understand how inclusion and exclusion criteria are set in relation to the review question

Class Preparation:

- Find a recent media article on treatment of a health condition (a promising new treatment, inadequate treatment, controversies, etc.) to discuss in class.

Supplementary Readings

PICO and Formulating the Clinical Question: A Guided Exercise. NYU School of Medicine. Ehrman Medical Library.

<http://library.med.nyu.edu/library/instruction/handouts/pdf/picohandout.pdf>

Weinfeld JM, Finkelstein K. How to answer your clinical questions more efficiently. Family Practice Management. 2005;12(7):37-41.

Counsell C. Formulating questions and locating primary studies for inclusion in systematic reviews. Ann Intern Med. 1997 Sept 1;127(5):380-7.

Unit 3

Scoping the Literature

Ms. Mimi Doyle-Waters

September 22, 2015

Objectives:

- To understand the meaning and importance of scoping the literature as it pertains to a systematic review protocol or grant application
- To become familiar with methods on scoping the literature
- To plan a scoping search while considering appropriate databases, subject headings and keywords

Supplementary Readings

Whitlock EP, Lin JS, Chou R, Shekelle P, Robinson KA. Using existing systematic reviews in complex systematic reviews. *Ann Intern Med.* 2008;148:776-782.

Unit 4

Literature Search Techniques Developing a Search Strategy

Ms. Mimi Doyle-Waters

September 29, 2015

Objectives:

- To understand methods for developing a comprehensive search template to find primary studies
- To understand the components of a search protocol which will help you to find all or the majority of relevant primary studies

Class Preparation:

- Ensure that you have some experience searching MEDLINE with keywords and MeSH subject headings

Required Readings

Your two main course readings have sections that are highly relevant to this session on carrying out a literature search.

Higgins JPT, Green S. eds. Cochrane Handbook for Systematic Reviews of Interventions. Version 5.0.2. The Cochrane Collaboration, 2009: www.cochrane-handbook.org.

- Part 2: General methods for Cochrane reviews, Chapter 6: Searching for studies.

Centre for Reviews and Dissemination. Systematic Reviews. CRD's guidance for undertaking reviews in health care. 2009.

http://www.york.ac.uk/inst/crd/index_guidance.htm.

- Chapter 1, Section 1.3 Undertaking the Review (PDF: pages 16-22).

McGill University. Systematic Reviews. Searching for Studies

http://wikisites.mcgill.ca/systematicreview/index.php/Searching_for_Studies

CADTH Peer Review Checklist for Search Strategies.

http://www.cadth.ca/media/is/Peer_review/CADTH%20Peer%20Review%20Checklist%20for%20Search%20Strategies_e.pdf.

Supplementary Readings

CADTH. Grey Matters: a practical search tool for evidence-based medicine.

<http://www.cadth.ca/en/resources/finding-evidence-is/grey-matters>.

Helmer D, Savoie I, Green C, Kazanjian A. Evidence-based practice: Extending the search to find material for the systematic review. *Bull Med Libr Assoc*. 2001;89:346-352.

Yoshii A, Plaut DA, McGraw KA, Anderson MJ, Wellik KE. Analysis of the reporting of search strategies in Cochrane systematic reviews. *Journal of the Medical Library Association*. 2009;97:21-29.

Centre for Reviews and Dissemination. Finding studies for systematic reviews: a resource list for researchers. 2012.

http://www.york.ac.uk/inst/crd/pdf/Finding_studies_for_systematic_reviews.pdf.

Handouts are available in UBC Connect for developing your searches. See the folder *Searching Resources*.

Unit 5

Introduction to Review Manager (RevMan) software Development of a PRISMA flow diagram

Dr. Mir Fazeli

October 6, 2015

Objectives:

- To understand the components of Review Manager (RevMan) and how it may be used to complete various systematic review steps
- To become familiar with the use of RevMan through in-class exercises
- To obtain an overview of the key components in a systematic review protocol and a full systematic review
- To understand the approach needed to ‘counting and accounting’ of studies in systematic reviews to construct a PRISMA flow diagram

Class Preparation:

Please download Review Manager (RevMan 5.3.4) before the September 30 class. You can access it at the following web link: <http://ims.cochrane.org/revman/download>.
And please bring your laptop to class on September 30.

Required Readings

The RevMan User Guide.

http://tech.cochrane.org/sites/tech.cochrane.org/files/uploads/documents/revman/RevMan_5.2_User_Guide.pdf

(no need to read the entire user guide ahead of the class; just familiarize yourself with it).

Supplementary Readings

Documentation Index. <http://ims.cochrane.org/revman/documentation>.

Unit 6

Developing a systematic review protocol

Dr. Darlene Taylor

October 13, 2015

Objectives:

- To frame the systematic review research question
- To understand the rationale for a detailed research protocol before a systematic review is carried out
- To become familiar with each component of a Cochrane review protocol
- To practice carrying out the steps in protocol development

Class Preparation:

- Read and be prepared to discuss the strengths and weaknesses of one of the included protocols available via the UBC Connect website.

Required Readings

Higgins JPT, Green S. eds. Cochrane Handbook for Systematic Reviews of Interventions. Version 5.0.2. The Cochrane Collaboration, 2009: www.cochrane-handbook.org.

- Part 1: Cochrane reviews, Chapter 4: Guide to the contents of a Cochrane protocol and review.

or

Centre for Reviews and Dissemination. Systematic Reviews. CRD's guidance for undertaking reviews in health care. 2009.

http://www.york.ac.uk/inst/crd/index_guidance.htm.

- Chapter 1, Section 1.2 The Review Protocol (PDF: pages 6-15).

Supplementary Readings

Booth A, Clarke M, Gherzi D, Moher D, Petticrew M, Stewart L. An international registry of systematic-review protocols. *Lancet*. 2011 Jan 8;377(9760):108-9.

Chan AW, Hrobjartsson A, Jorgensen KJ et al. Discrepancies in sample size calculations and data analyses reported in randomised controlled trials: comparison of publications with protocols. *BMJ* 2008;337:a2299.

Examples of Protocols

Ferreira de Oliveira AM, Celeste, RKCR, Rodrigues, CRC. Topical fluoride for treating dental caries. Cochrane Oral Health Group Cochrane Database of Systematic Reviews. 4, 2009.

Westby DM, Kennedy D, Jones D, Jones A, Doyle-Waters MM, Backman C. Post-acute physiotherapy for primary total knee arthroplasty. Cochrane Musculoskeletal Group Cochrane Database of Systematic Reviews. 4, 2009.

Pinto-Sanchez MI, Yuan Y, Bercik P, Moayyedi P. Proton pump inhibitors for functional dyspepsia. Cochrane Database of Systematic Reviews 2014, Issue 7. Art. No.: CD011194.

Templates of Systematic Review Protocols

Instructions for Authors. Protocol articles. Systematic Reviews

<http://www.systematicreviewsjournal.com/authors/instructions/protocol>

Developing a Protocol CMSG Review Author Resource Pack.

http://musculoskeletal.cochrane.org/sites/musculoskeletal.cochrane.org/files/uploads/completeprotocolpackage_v6.pdf

EBBP - Introduction to Systematic Reviews.

http://www.ebbp.org/course_outlines/systematic_review/#2

How to write a protocol. Cochrane Renal Group, A Review Group of the Cochrane Collaboration [http://www.cochrane-](http://www.cochrane-renal.org/docs/how%20to%20write%20a%20protocol.pdf)

[renal.org/docs/how%20to%20write%20a%20protocol.pdf](http://www.cochrane-renal.org/docs/how%20to%20write%20a%20protocol.pdf)

Methodological checklist: Protocol. Cochrane Pregnancy and Childbirth Group.

<http://pregnancy.cochrane.org/author-resources-protocols>

Unit 7

Inclusion and exclusion criteria Selecting Studies; Measuring and Resolving Disagreement

Dr. Darlene Taylor
Ms. Mimi Doyle-Waters

October 13, 2015

Objectives:

- To be familiar with how to ‘operationalize’ inclusion criteria for a review
- To consider and measure the reproducibility of decisions about what research to include in your overview
- To consider the potential impact of publication and reporting bias
- To consider ways of improving the reliability of the data you collect and analyze for your team protocols and systematic reviews.

Class Preparation:

- Consider the following questions:
 - What is the potential for publication bias in your area and what, if anything, will you do to protect against a possible publication bias?
 - What groups or individuals will you contact, if any to locate research?
 - What efforts will you make to identify studies not reported in English?
 - How will you record the search strategies used, yields, costs (including your time), personal contacts, and rejected studies?

Required Readings

1) Higgins JPT, Green S. eds. Cochrane Handbook for Systematic Reviews of Interventions. Version 5.0.2. The Cochrane Collaboration, 2009: www.cochrane-handbook.org.

- Part 2: General methods for Cochrane reviews, Chapter 7: Selecting studies and collecting data.

or

Centre for Reviews and Dissemination. Systematic Reviews. CRD's guidance for undertaking reviews in health care. 2009.

http://www.york.ac.uk/inst/crd/index_guidance.htm

- Chapter 1, Section 1.3 Undertaking the Review, 1.3.2 Study selection (PDF pages 23-27).

2) Doshi P, Jones M, Jefferson T. Rethinking credible evidence synthesis. *BMJ* 2012;344:d7898.

Supplementary Readings

Meade MO, Richardson WS. Selecting and appraising studies for a systematic review. *Ann Intern Med.* 1997 Oct 1;127(7):531-7.

Unit 8

Data and statistics: dichotomous and continuous measures, meta-analysis

Dr. Darlene Taylor
Dr. Aaron Tejani

October 20, 2015

Objectives:

- To know why meta-analysis is used rather than simple data pooling
- To understand key measures of effect for dichotomous and continuous outcomes and how to choose which measure to apply
- To be able to describe the difference between risk and odds
- To understand weighting of mean differences
- To become familiar with the main measures of relative and absolute risk used to analyze dichotomous and continuous data
- To become familiar with how a data collection form is developed for extracting information from study reports

Class Preparation:

Read the following article and be prepared to discuss how individual trials were combined:

- Kaiser L, Wat C, Mills T et al. Impact of Oseltamivir Treatment on Influenza-Related Lower Respiratory Tract Complications and Hospitalizations. Arch Intern Med. 2003;163:1667-1672.

Required Readings

1) Scott I, Interpreting risks and ratios in therapy trials. Aust Prescriber 2008; 31(1): 12-16.

2) Higgins JPT, Green S. eds. Cochrane Handbook for Systematic Reviews of Interventions. www.cochrane-handbook.org.

- Part 2: General methods for Cochrane reviews, Chapter 9: Analysing data and undertaking meta-analysis.

or

Centre for Reviews and Dissemination. Systematic Reviews.

http://www.york.ac.uk/inst/crd/index_guidance.htm.

- Chapter 1, Section 1.3 Undertaking the Review, Section 1.3.5 Data Synthesis (PDF: pages 45-76).

Unit 9

Data Extraction and Synthesis To pool or not to pool? Subgroup and sensitivity analyses

Dr. Darlene Taylor
Dr. Aaron Tejani

October 20, 2015

Objectives:

- To understand concepts of statistical and clinical heterogeneity
- To understand the difference between fixed and random effects models
- To consider potential sources of error and bias in extracting and pooling data
- To understand when subgroup and sensitivity analyses are appropriate
- To practice using RevMan for subgroup and sensitivity analyses
- To understand how funnel plots may be used to assess publication bias

Required Readings

Higgins JPT, Green S. eds. Cochrane Handbook for Systematic Reviews of Interventions.
www.cochrane-handbook.org.

Part 2: General methods, Chapter 9: Analysing data and undertaking meta-analysis.

Centre for Reviews and Dissemination. Systematic Reviews. 2009

http://www.york.ac.uk/inst/crd/index_guidance.htm.

Chapter 1, Section 1.3.5 Data synthesis (including the narrative and quantitative sections of the chapter) (PDF: pages 45-76).

Sterne JA, Egger M, Smith GD. Systematic reviews in health care: Investigating and dealing with publication and other biases in meta-analysis. *BMJ*. 2001;323:101-5.

Supplementary Readings

Thornton A, Lee P. Publication bias in meta-analysis: its causes and consequences. *J Clin Epidemiol*. 2000 Feb;53(2):207-16.

Examples of data extraction forms

See UBC Connect website

Unit 10

Introduction to critical appraisal Using the Cochrane Risk of Bias tool

Dr. Darlene Taylor
Dr. Aaron Tejani

October 27, 2015

Objectives:

- To become familiar with methodological details that are required to judge quality of the studies included in a systematic review
- To know the main elements of internal and external validity to consider when assessing and applying clinical trial results
- To develop familiarity with applying the Cochrane risk of bias tool
- To understand why quality assessment is needed in systematic reviews

Class Preparation:

Please read and be prepared to discuss this trial in detail:

Calverley PM, Anderson JA, Celli B, Ferguson GT, Jenkins C, Jones PW, et al. Salmeterol and fluticasone propionate and survival in chronic obstructive pulmonary disease. *N Engl J Med* 2007; 356: 775–789.

Required Readings

Critical appraisal methods - background

1) Juni P, Altman DG, Egger M. Chapter 5. Assessing the quality of randomised controlled trials. In: *Systematic Reviews in health Care: Meta-analysis in context*. (Course text; available on-line via Connect website)

2) Rothwell P. External validity of randomised controlled trials: “To whom do the results of this trial apply?” *Lancet* 2005; 365: 82-93

Practical methods guides

1) Higgins JPT, Green S. eds. *Cochrane Handbook for Systematic Reviews of Interventions*. Version 5.0.2. The Cochrane Collaboration, 2009: www.cochrane-handbook.org.

- Part 2: General methods for Cochrane reviews, Chapter 8: Assessing risk of bias in included studies.

2) CASP Randomised controlled trial checklist. <http://www.casp-uk.net/wp-content/uploads/2011/11/CASP-Randomised-Controlled-Trial-Checklist-31.05.131.pdf>

3) an example of in-depth critical appraisal of a trial:

Erviti J. Denosumab in osteoporosis related fractures. A critical appraisal of the FREEDOM trial. *Drugs and therapeutics bulletin*, Navarra Spain. 2012 March April;20(2):1-8.

http://www.navarra.es/NR/rdonlyres/9DD8ACF2-1F79-4880-A2D0-3235C273AC4C/231795/Bit_v20n2_e1.pdf

Supplementary Readings

Egger M, Juni P, Bartlett C, Holenstein F, Sterne J. How important are comprehensive literature searches and the assessment of trial quality in systematic reviews? Empirical study. *Health Technol Assess*. 2003;7(1):1-76.

Greenhalgh T. Assessing the methodological quality of published papers. *BMJ*. 1997 Aug 2;315(7103):305-8. [review – reading from unit 1]

Lundh A, Sismondo S, Lexchin J et al. Industry sponsorship and research outcome. *Cochrane Database of Systematic Reviews* 2012, Issue 12. Art. No.: MR000033. DOI: 10.1002/14651858.MR000033.pub2.

Juni P, Altman DG, Egger M. Systematic reviews in health care: Assessing the quality of controlled clinical trials. *BMJ*. 2001;323:42-6.

Scott IA, Greenberg PB. Cautionary tales in the clinical interpretation of therapeutic trial reports. *Intern Med J*. 2005 Oct;35(10):611-21.

Unit 11

GRADE and summary of findings tables Formulating conclusions and completing your review

Dr. Lorri Puil

November 3, 2015

Objectives:

- To become familiar with use of the GRADE summary of findings table
- To learn to apply outcome specific evidence ratings
- To consider how to translate systematic review results into relevant conclusions

Required Readings

1) Higgins JPT, Green S. eds. Cochrane Handbook for Systematic Reviews of Interventions. Version 5.0.2. The Cochrane Collaboration, 2009: www.cochrane-handbook.org.

- Part 2: Chapter 11: Presenting results and ‘summary of findings’ tables
- Part 2: Chapter 12: Interpreting results and drawing conclusions

2) Guyatt GH, Oxman AD, Vist GE et al. GRADE: what is “quality of evidence” and why is it important to clinicians? *BMJ*. 2008;336:995-998.

Outcome Assessments in RCTs: not so simple

Dr. Tom Perry jr, MD, FRCP

Clinical Assistant Professor, Department of Medicine, UBC
Clinical Pharmacologist, General Internist
Chair, Education Working Group, Therapeutics Initiative

When does a documented outcome in a clinical trial not mean what you or I might think it means? This presentation uses a recent high-profile trial to raise questions about outcome assessment in trials and how they affect our understanding and application of results.

Required Reading: Connolly SJ, Ezekowitz MD, Yusuf S et al. Dabigatran versus warfarin in patients with atrial fibrillation. *NEJM* 2009; 361(12): 1139-1151.

Unit 12

Critical Appraisal of a Systematic Review

Dr. Darlene Taylor

November 10, 2015

Objectives:

- To be familiar with assessment of the quality and risk of bias in a systematic review and meta-analysis.
- To be of assistance to you both as background to your own systematic reviews and the assessment of the research literature.

Preparation for this class:

Students will be asked to read and critique a systematic review and one of the trials included in that review. The articles will be listed later in the term.

Required Readings

1) Abalos E, Carroli G, Mackey ME, Bergel E. Critical appraisal of systematic reviews: The WHO Reproductive Health Library, No 4, Geneva, The World Health Organization, 2001 (WHO/RHR/01.6).

<http://apps.who.int/rhl/Critical%20appraisal%20of%20systematic%20reviews.pdf>

Supplementary Readings

Critical Appraisal Checklists for Systematic Reviews.

United Lincolnshire Hospitals, NHS. Critical appraisal toolkit for systematic reviews

http://www.hello.nhs.uk/documents/CAT7-Systematic_Review.pdf

Scottish Intercollegiate Guidelines Network. Critical appraisal: Notes and checklists

<http://www.sign.ac.uk/methodology/checklists.html>

Centre for Evidence-Based Medicine. Critical appraisal tools

<http://www.cebm.net/index.aspx?o=1157>

Critical Skills Appraisal Programme. CSAP checklists

<http://www.casp-uk.net/wp-content/uploads/2011/11/casp-randomised-controlled-trial-checklist-31.05.131.pdf#!casp-tools-checklists/c18f8>

Sex, Gender and Equity in Systematic Reviews

Dr. Lorri Puil

This is an introduction into methods used to consider sex, gender and equity in systematic reviews. The aim is to consider to whom the evidence applies, concepts of 'sex' and 'gender' and incorporating equity concerns.

Required Readings

Doull, M., Runnels V., Tudiver, S., Boscoe, M. Appraising the evidence: applying sex and gender based analysis (SGBA) to Cochrane systematic reviews on cardiovascular diseases. *J Womens Health*. 2010;19(5):997-1003.

<http://www.liebertonline.com/doi/abs/10.1089/jwh.2009.1626>

Unit 13

Systematic reviews of Observational Studies

Dr. Mahyar Etminan

November 17, 2015

Objectives:

- To be familiarized with major concepts in observational meta-analysis including data extraction, data analysis, bias, heterogeneity

Required Readings

1) Egger M, Schneider M, Davey Smith G. Spurious precision? Meta-analysis of observational studies. *BMJ*. 1998;316(7125):140-4.

2) Stroup DF, Berlin JA, Morton SC, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. *JAMA*. 2000 Apr 19;283(15):2008-12.

Supplementary Readings

Sanderson S, Tatt ID, Higgins JP. Tools for assessing quality and susceptibility to bias in observational studies in epidemiology: A systematic review and annotated bibliography. *Int J Epidemiol*. 2007;36:666-676.

Unit 14

Knowledge Translation

Dr. Stirling Bryan

December 1, 2015

Objectives:

- To consider models of knowledge use
- To explore what types of knowledge should change policy and practice
- To understand how systematic reviews are used in economics

Required Readings

1) Tugwell P, Robinson V, Grimshaw J, Santesso N. Systematic reviews and knowledge translation. Bull World Health Organ. 2006 Aug;84(8):643-51.

<http://www.who.int/bulletin/volumes/84/8/05-026658.pdf>

2) Chambers D, Wilson PM, Thompson CA, Hanbury A, Farley K, Light K. Maximizing the impact of systematic reviews in health care decision making: a systematic scoping review of knowledge-translation resources. Milbank Q. 2011 Mar;89(1):131-56.

Supplementary Readings

Moat KA, Lavis JN, Wilson MG et al. Twelve myths about systematic reviews for health systems policymaking rebutted. J Health Serv Res Policy 2013; 18: 44–50.

Website

KT Clearinghouse. Available from: <http://ktclearinghouse.ca/>

Introduction to Network Meta-analysis

Dr. Edward Mills, PhD

Partner, Redwood Outcomes; Visiting Association Professor, Stanford University

Network meta-analysis has become a popular analytical tool to use in order to draw conclusions about comparative effectiveness based on both direct and indirect evidence. This introduction provides an overview on when and how network meta-analysis is used, what is involved, strengths, and limitations.

Required reading: Mills EJ, Ioannidis JP, Thorlund K, et al. How to use an article reporting a multiple treatment comparison meta-analysis. JAMA 2012; 308 (12): 1246-1253.

Knowledge Translation – Clinical Perspective

Dr. Jim Wright