SPPH 516

Methods for Systematic Reviews in Health Research

Course Description
Fall 2017

School of Population and Public Health
University of British Columbia

SPPH 516
Methods for Systematic Reviews in Health Research
Course Outline
2017

Time:	Tuesdays, 9:00 am -12:00 p.m.
Term:	First class: September 12, 2017 Last class: December 5, 2017 *No class Sept 5 (SPPH orientation)*
Class Location:	UBC Point Grey campus School of Population and Public Health Room: B151 2206 Health Sciences Mall
Instructor: **Co-instructor:**	Dr. Lorri Puil, MD PhD Ms. Mimi Doyle-Waters, MA, MLIS
Teaching Assistant	Héctor A. Velásquez García
Office Hours:	Informal lab time 1/2 hour before and 1/2 hour after the class in B151: office hours are also available by appointment
General Information:	Course contact: Dr. Lorri Puil E-mail: lorri.puil@ti.ubc.ca Phone : 604-827-5064 *or* Mimi Doyle-Waters E-mail: Mimi.Doyle-Waters@ubc.ca Phone: 604-875-4111 extension 61176 *or* TA: Dr. Héctor A. Velásquez García E-mail: hector.velasquezgarcia@alumni.ubc.ca

COURSE OUTLINE

Date	Week	Session Topic	Instructor
Sept. 6		***SPPH orientation session – no class***	
Sept 12	*1*	Review syllabus, assignments and course expectations **Unit 1:** What makes a review 'systematic'? Judging the strength of research evidence.	Lorri Puil
Sept 19	2	**Unit 2:** Elements of a systematic review, things to consider; tools to assess the quality of a systematic review **Unit 3:** Developing a research question, setting inclusion and exclusion criteria; scoping the literature. ***Student review teams formed*** ***Assignment # 1 handed out – research questions***	Lorri Puil Lorri Puil Mimi Doyle-Waters
Sept 26	3	**Unit 4:** Literature search techniques; developing a search strategy.	Mimi Doyle-Waters
Oct 3	4	**Unit 5:** Developing a systematic review protocol **Unit 6:** Applying inclusion and exclusion criteria, selecting studies, resolving disagreement. ***Assignment # 2 handed out – draft search strategy***	Lorri Puil
Oct 3		**Draft research question – Assignment # 1 due**	
Oct 10	5	**Unit 7:** Data, Statistics and Meta-Analysis I Continuous and dichotomous outcomes; Data extraction; Meta-analysis concepts; RevMan. ***Assignment # 3 handed out – systematic review protocol***	Lorri Puil
Oct 17	*6*	**Unit 8:** Data, Statistics and Meta-analysis II To pool or not to pool? Fixed-effect and random-effects models; Heterogeneity; Subgroup and sensitivity analyses.	Lorri Puil
Oct 17		**Draft search strategy – Assignment # 2 due**	
Oct 24	7	**Unit 9:** Critical appraisal of clinical trials - risk of bias, other quality assessment of RCTs; Using the Cochrane Risk of Bias tool for RCTs; Incorporating risk of bias assessment into systematic reviews.	Aaron Tejani Lorri Puil
Oct 31	8	**Unit 10:** GRADE and summary of findings tables; Formulating conclusions and completing your review; Exercise: GRADE summary of findings.	Lorri Puil
Nov 7	9	**Unit 11:** Critical appraisal of a systematic review; **Special Topic:** RIAT initiative and other trends.	Penny Brasher Lorri Puil
Nov 7		**Systematic review protocol – assignment # 3 due**	
Nov 14	10	**Unit 12:** Knowledge translation, policy perspective and health economics; **Special Topic:** Gender and equity in systematic reviews.	Stirling Bryan Lorri Puil
Nov 21	11	**Unit 13:** Non-randomized (observational) study designs; Systematic review of observational studies and the Cochrane risk of bias tool for observational studies.	Colin Dormuth Lorri Puil
Nov 28	12	**Review team presentations**	Puil & Doyle-Waters
Dec 5	13	**Special Topic:** Indirect comparisons and network meta-analysis; **Course wrap-up.**	Mir Sohail Fazeli Lorri Puil
Dec 15		**Draft 3-trial preliminary review – Assignment # 4 due**	

CLASS LOCATION: Room B151, School of Population and Public Health, 2206 Health Sciences Mall, UBC.

Interested Participants

- Graduate students
- Physicians and other 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 for Students

- To become familiar with different types of systematic reviews
- To identify health research or clinical questions for which there are no existing high-quality systematic reviews
- To learn appropriate methodology for protocol development and the steps needed to complete a systematic review
- To become familiar with methods for searching the published literature and also for retrieving unpublished literature, and to understand the difference between a scoping search and a primary literature search
- To develop skills in critical appraisal of clinical studies and to apply risk of bias tools within systematic reviews
- To be introduced to statistical techniques required for meta-analysis and data synthesis
- To become familiar with methods for assessing and interpreting evidence within systematic reviews including the GRADE framework.

Faculty Descriptions

Lorri Puil, MD, PhD

Dr. Puil is a senior member of the Therapeutics Initiative Drug Assessment Working Group in the Dept. of Anesthesiology, Pharmacology & Therapeutics, Faculty of Medicine, UBC. She has extensive experience leading systematic reviews of health care interventions for provincial, national and international policy makers (e.g., the federal Common Drug Review; the US Agency for Healthcare Research and Quality). An Editor of Cochrane Hypertension, and a member of the Cochrane Equity Methods Group, Dr. Puil obtained her MD from the University of Toronto and has specialty training in internal medicine, hematology and clinical pharmacology. She holds a PhD from the University of Toronto in signal transduction, an area applicable to the analysis of novel therapeutics such as targeted molecules and biologics. Dr. Puil's research interests include the safety and effectiveness of prescription drugs and complex interventions, pharmaceutical regulatory policy, and research synthesis methods.

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.

Guest Faculty:

Penny Brasher, PhD

Dr. Brasher is a Senior Research Scientist at C2E2 and an associate member of the Department of Statistics at UBC. She is a Statistical Editor for the Canadian Journal of Anesthesia and has served on several grant review committees and ethics boards. Dr. Brasher's research interests include clinical research methodology, secondary use of administrative data and statistical education.

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 Cochrane Hypertension. His interests include critical appraisal of the biomedical literature and knowledge translation activities. 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).

Colin Dormuth, ScD

Dr. Colin Dormuth is an Associate Professor in the Department of Anesthesiology, Pharmacology & Therapeutics, UBC, and co-principal investigator for the BC site of the Canadian Network for Observational Drug Effect Studies (DSEN-CNODES). He has 20 years of experience using administrative health care databases to evaluate drug safety, pharmaceutical policy changes and physician prescribing behaviour. Dr. Dormuth holds Sc.D. and S.M. degrees in epidemiology from Harvard University, an M.A. in economics from the University of Victoria, and a B.A. in economics from the University of Manitoba.

Stirling Bryan, PhD

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.

Mir Fazeli, MD, PhD (c)
Dr. Fazeli is a physician and a PhD candidate in the Experimental Medicine Program in the Department of Pediatrics, UBC. He is trained as a clinical epidemiologist and his main field of expertise includes research methodology and clinical trials with a focus on measuring the activity of the autonomic nervous system, systematic review and meta-analysis of randomized controlled trials, and implementation and evaluation of complementary and alternative medicine interventions.

Teaching Assistant:
Héctor A. Velásquez García, MD MS MPH
Dr. Valasquez Garcia is a primary care physician (Universidad del Rosario, Bogotá, Colombia), with training in Medical Informatics (MS, University of California, Davis) and Public Health (MPH, Epidemiology and Biostatistics, Johns Hopkins Bloomberg School of Public Health). He is currently a PhD Candidate at SPPH; the focus of his research is cancer epidemiology and causal inference in observational studies.

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 meta-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 the following systematic review software: Review Manager (RevMan) (meta-analysis and risk of bias), GRADEpro/GDT (summary of findings tables) and Covidence (study screening). 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 the draft review.

The course is organized into 13 weekly, 3-hour sessions. In addition, the course instructors will be available to meet informally with the students to address questions and discuss their research topic and review protocols. This includes optional lab time from 8:30am to 9am prior to the class (search-related Q's), and 12:00pm to 12:30pm (any Q's) after each class. Additional office time, meetings and tutorials are available on appointment.

Scope of this Course

The focus of this course is systematic reviews involving clinical and policy questions that are addressed primarily through randomized controlled trials (RCTs). Systematic reviews of observational studies will also be covered in the course. Students are encouraged to carry out a review that includes RCT evidence in order to build an experience base before addressing more complex designs but may include other quantitative study designs if appropriate to their topic. Interventions using qualitative methods are briefly discussed but the course is not designed to provide in-depth detail on systematic reviews of qualitative or mixed methods studies.

Each year, the course also covers two or three special topics or innovations. These topics may change from year-to-year or subsequently be incorporated into the core curriculum.

Prerequisites

Students should have basic understanding of health research design / methodology and an introductory understanding of medical statistics. There are no course requisites for students enrolled in SPPH master's and PhD programs. Students in other graduate programs may enroll with permission from the instructor.

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 two to 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.

Assignments

Course assignments will comprise the different stages of a review: 1) development of a research question and scoping search; 2) development of a literature search strategy; 3) development of a systematic review protocol including plans for meta-analysis; and 4) a 3-study draft review with critical appraisal. Students will also present a brief summary of their topic in a class presentation. Full assignment details and guidance will be posted in Canvas during the term.

Student Evaluation

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

Evaluation

- Participation and preparation for class (includes class discussions on readings) [individual grade] 10%
- 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-study results
  - Individual grade 20%
  - Team grade 20%
- Assignment # 5 – Team Presentation [team grade] 5%

UBC/SPPH grading details are located in Appendix A at the end of the syllabus.

Course Textbooks and Core Materials

Students are not required to buy textbooks for this course. Two on-line manuals provide core course materials and are available in the *Key Course Resources* module in Canvas. Individual chapters will be linked to specific course weeks and modules. Students are encouraged to access at least one of these on-line or via Canvas and refer to them throughout the course.

1. The Cochrane Handbook.
   - For this semester, the 2017 updated chapters of the Cochrane Handbook (version 5.2.0) are available in Canvas. Higgins JPT, Churchill R, Chandler J, Cumpston MS (editors), Cochrane Handbook for Systematic Reviews of Interventions version 5.2.0 (updated June 2017). Individual chapters that have not yet been updated (2011 version) are also available in Canvas.
   - Alternatively, students may consult the online Cochrane Handbook (2011): Higgins JPT, Green S. Cochrane Handbook for Systematic Reviews of Interventions. Cochrane Collaboration. Version 5.1.0 [updated 2011 March] Available for browsing at: handbook.cochrane.org/

2. 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. www.york.ac.uk/crd/guidance/

The following textbook is recommended as an additional resource and may be referred to in specific sections of the course:

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

3. Software
   - Review manager (RevMan 5.3.5) software will be used in the course (available free of charge):
     - Download at: http://tech.cochrane.org/revman/download
   - GRADEpro will be used for GRADE evidence tables and summary of finding tables.
     - Sign up for a GRADEpro account online (available free of charge) at: https://gradepro.org
   - Access to Covidence (to be used for screening only) will be made available through the class.

Additional General References

The following are two methods references have been made available in Canvas as further resources but are not required reading.

- Borenstein M, Hedges LV, Higgins JPT, Rothstein HR (2009) Introduction to Meta-Analysis, Chichester, UK: John Wiley & Sons Ltd. Available on-line via UBC Connect. [more detail on statistical techniques]
- Agency for Health Care Research and Quality (AHRQ) Methods for Effectiveness and Comparative Effectiveness Reviews (last updated 2015). Chapters 5 to 16 may be useful for specific methods topics.

Other Resources (for interest only unless specified in class)

In Canvas, we have also provided resource material for searching, quality assessment tools and reporting guidance for both systematic reviews and primary studies. Instructors will identify specific items as needed during the course.

The complete syllabus, including class preparation, handouts and assignments, will be made available to students via Canvas. The following provides an overview of each weekly session and is subject to change.

Week 1
Overview of Systematic Reviews; Levels of Research Evidence

Dr. Lorri Puil
September 12, 2017

Objectives:

- To understand why there is an evolving science of research synthesis
- To know how to distinguish between a narrative and a systematic review
- To appreciate the spectrum of different types of systematic reviews
- 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 Canvas)
2) Greenhalgh T. Assessing the methodological quality of published papers. BMJ 1997 Aug 2;315(7103):305-8.

Supplementary Readings and Resources Week 1

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

General classification of systematic reviews:

- Tricco AC, Tetzlaff J, Moher D. The art and science of knowledge synthesis. J Clin Epidemiol 2011 Jan 31;64(1):11-20.
- Straus SE, Kastner M, Soobiah C, Antony J, Tricco AC. Introduction: Engaging researchers on developing, using, and improving knowledge synthesis methods: a series of articles describing the results of a scoping review on emerging knowledge synthesis methods. J Clin Epidemiol 2016 May 31;73:15-8.

Specific types of reviews

- Chou R, Helfand M. Challenges in systematic reviews that assess treatment harms. Ann Intern Med 2005 Jun 21;142(12 Part 2):1090-9.
- 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.
- Elliott JH, Turner T, Clavisi O, Thomas J, Higgins JP, Mavergames C, Gruen RL. Living systematic reviews: an emerging opportunity to narrow the evidence-practice gap. PLOS Med 2014 Feb 18;11(2): e1001603.
- Riley RD, Lambert PC, Abo-Zaid G. Meta-analysis of individual participant data: rationale, conduct, and reporting. BMJ 2010 Feb 5;340:c221.
- Khangura S, Konnyu K, Cushman R, Grimshaw J, Moher D. Evidence summaries: the evolution of a rapid review approach. Syst Rev 2012 Feb 10;1(1):10.

Week 2

1. Introduction to Elements of a Systematic Review
2. Question Development and Background; Setting Inclusion and Exclusion Criteria

Dr. Lorri Puil
September 19, 2017

Objectives:

- To obtain an overview of the elements of a systematic review
- To be aware of features that determine the quality of a systematic review
- 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 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

Required Readings

1) 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. *This provides an overview of the elements of systematic reviews.*

2) 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).

3. Scoping the literature

Ms. Mimi Doyle-Waters
September 19, 2017

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

Required Readings

1) Aromataris E, Riitano D. Constructing a search strategy and searching for evidence. A guide to the literature search for a systematic review. Am J Nurs 2014 May;114(5):49-56.
2) Booth A. Unpacking your literature search toolbox: on search styles and tactics. Health Info Libr J 2008 Dec;25(4):313-7.

Supplementary Readings & Additional Resources Week 2

Quality assessment of systematic reviews

- Shea B, Grimshaw J, Wells G, Boers M et al. Development of AMSTAR: A measurement tool to assess the methodological quality of systematic reviews. BMC Med Res Methodol 2007;7:10.
- Wegewitz U, Weikert B, Fishta A, Jacobs A, Pieper D. Resuming the discussion of AMSTAR: What can (should) be made better? BMC Med Res Methodol 2016 Aug 26;16(1):111.
- Shea B, Reeves BC, Wells G, Thuku M, Hamel C, Moran J, Moher D, Tugwell P, Welch V, Kristjansson E, Henry D. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. BMJ 2017;358:j4008
- Whiting P, Savović J, Higgins JP, Caldwell DM, Reeves BC, Shea B, Davies P, Kleijnen J, Churchill R. ROBIS: a new tool to assess risk of bias in systematic reviews was developed. J Clin Epidemiol 2016 Jan 31;69:225-234.
- Risk of Bias in Systematic Reviews (ROBIS) tool. http://www.bristol.ac.uk/ population-health-sciences/projects/robis/
- Scottish Intercollegiate Guidelines Network. Methodology Checklist 1: Systematic Reviews and Meta-analyses. Notes for completion of checklist. Available at: http://www.sign.ac.uk/checklists-and-notes.html
- Higgins JPT, Lasserson T, Chandler J, Tovey D, Churchill R. Methodological Expectations of Cochrane Intervention Reviews. Cochrane: London, 2016.
- 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.

Developing research questions and scoping the literature

- O'Connor D, Green S, Higgins JPT (editors). Chapter 5: Defining the review question and developing criteria for including studies. In: Higgins JPT, Green S (editors), Cochrane Handbook for Systematic Reviews of Interventions. Version 5.1.0 [updated September 2011]. The Cochrane Collaboration, 2011.
- PICO and Formulating the Clinical Question: A Guided Exercise. NYU School of Medicine. Ehrman Medical Library.
- Weinfeld JM, Finkelstein K. How to answer your clinical questions more efficiently. Fam Pract Manag 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):380-387.

Week 3

Literature Search Techniques: Developing a Search Strategy

Ms. Mimi Doyle-Waters

September 27, 2016

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

Required Readings

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

1) Lefebvre C, Manheimer E, Glanville J. Chapter 6: Searching for studies. In: Higgins JPT, Green S (editors). *Cochrane Handbook for Systematic Reviews of Interventions.* Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011.
2) Centre for Reviews and Dissemination. Systematic Reviews. CRD's guidance for undertaking reviews in health care. 2009. http://www.york.ac.uk/crd/guidance/. Chapter 1, Section 1.3 Undertaking the Review (PDF: pages 16-22).

Supplementary Readings & Additional Resources Week 3

- McGill University. Systematic Reviews. Searching for Studies. http://wikisites.mcgill.ca/systematicreview/index.php/Searching_for_Studies
- CADTH. Finding the Evidence: Literature Searching Tools in Support of Systematic Reviews. https://www.cadth.ca/resources/finding-evidence
- CADTH Peer Review Checklist for Search Strategies. https://www.cadth.ca/media/is/Peer_review/CADTH%20Peer%20Review%20Checklist%20for%20Search%20Strategies_e.pdf
- MUHC TAU Members. Guidelines for systematic literature search, version 2.0. Montreal (Canada): Technology Assessment Unit (TAU) of the McGill University Health Centre (MUHC); October 4, 2013 17 pp. Available from: https://www.mcgill.ca/tau/files/tau/muhc_tau_search_v2.0.pdf
- CADTH. Grey Matters: a practical search tool for evidence-based medicine. http://www.cadth.ca/en/resources/finding-evidence-is/grey-matters.

Handouts are available in Canvas for developing your searches. See the module (folder) *Searching Resources*.

Week 4

1. Developing a systematic review protocol

Dr. Lorri Puil
October 3, 2017

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

Required Readings

1) Higgins JPT, Green S (editors). Chapter 4: Guide to the contents of Cochrane protocol and review. In: Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Intervention. Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available from: handbook.cochrane.org/
or
Centre for Reviews and Dissemination. Systematic Reviews. CRD's guidance for undertaking reviews in health care. 2009. http://www.york.ac.uk/crd/guidance/ Chapter 1, Section 1.2 The Review Protocol (PDF: pages 6-15).

2) Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart LA. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. Syst Rev 2015 Jan 1;4(1):1.

2. Applying eligibility criteria and selecting studies

Dr. Lorri Puil
October 3, 2017

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 review
- To become familiar with one type of software that can be used to screen (Covidence)
- To understand the approach needed to 'count and account' for studies in systematic reviews and to construct a PRISMA flow diagram (either in Covidence or RevMan)
- 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.

Required Readings

1) Higgins JPT, Deeks JJ (editors). Chapter 7: Selecting studies and collecting data. In: Higgins JPT, Green S (editors), *Cochrane Handbook for Systematic Reviews of Interventions.* Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available from: handbook.cochrane.org/
   or
   Centre for Reviews and Dissemination. Systematic Reviews. CRD's guidance for undertaking reviews in health care. 2009. http://www.york.ac.uk/crd/guidance/
   Chapter 1, Section 1.3 Undertaking the Review, 1.3.2 Study selection (PDF pages 23-27).

Supplementary Readings & Additional Resources Week 4

Protocol development

- Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart LA. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ 2015 Jan 2;349:g7647.
- Booth A, Clarke M, Dooley G, Ghersi D, Moher D, Petticrew M, Stewart L. The nuts and bolts of PROSPERO: an international prospective register of systematic reviews. Syst Rev 2012 Feb 9;1(1):1.
- Booth A. PROSPERO's progress and activities 2012/13. Syst Rev 2013 Dec 11;2(1):1.
- Analytic frameworks: Anderson LM, Petticrew M, Rehfuess E, Armstrong R, Ueffing E, Baker P, Francis D, Tugwell P. Using logic models to capture complexity in systematic reviews. Res Synth Methods 2011 Mar 1;2(1):33-42.
- Also provided in Canvas is a folder of protocol samples.

Applying eligibility criteria and selecting studies

- Doshi P, Jones M, Jefferson T. Rethinking credible evidence synthesis. BMJ 2012;344:d7898.
- Meade MO, Richardson WS. Selecting and appraising studies for a systematic review. Ann Intern Med 1997 Oct 1;127(7):531-7.

Week 5

1. Data, Statistics and Meta-analysis I - Introduction

Dichotomous and continuous measures; data extraction; meta-analysis concepts

Dr. Lorri Puil

October 10, 2017

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 become familiar with how a data collection form is developed for extracting information from study reports

Class Preparation: Students will be asked to read a review and be prepared to discuss how individual trials were combined. The article to read will be provided in Canvas.

Required Readings

1) Deeks JJ, Higgins JPT, Altman DG (editors) on behalf of the Cochrane Statistical Methods Group. Chapter 9: Analysing data and undertaking meta-analyses. In: Higgins JPT, Churchill R, Chandler J, Cumpston MS (editors), Cochrane Handbook for Systematic Reviews of Interventions version 5.2.0 (updated June 2017), Cochrane, 2017. Available from www.training.cochrane.org/handbook.
   or
   Centre for Reviews and Dissemination. Systematic Reviews. http://www.york.ac.uk/crd/guidance/. Chapter 1, Section 1.3 Undertaking the Review, Section 1.3.5 Data Synthesis (PDF: pages 45-76).

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

2. RevMan Introduction

Dr. Lorri Puil
October 10, 2017

RevMan will be introduced throughout the course, starting in this session, via in-class exercises.

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 and assignments
- To obtain an overview of the key components in a systematic review protocol and a full systematic review

No Required Readings

Supplementary Reading & Additional Resources Week 5

- Examples of data extraction forms are in Canvas.
- A handout on analyzing continuous outcomes is in Canvas.
- The RevMan User Guide: http://community.cochrane.org/sites/default/files/uploads/inline-files/RevMan_5.3_User_Guide.pdf
- RevMan Calculator: http://training.cochrane.org/resource/revman-calculator (useful to be aware of).
- Deeks J, Higgins J. 2010. Statistical Algorithms in RevMan - in Canvas.

Week 6

Data, Statistics and Meta-Analysis II

To pool or not to pool? Heterogeneity; Subgroup and sensitivity analyses; Unit of analysis issues

Dr. Lorri Puil

October 17, 2017

Objectives:

- To understand underlying assumptions of fixed-effect and random-effects models of meta-analysis
- To be familiar with the concepts of statistical and clinical heterogeneity, and how heterogeneity may be explored (subgroup and sensitivity analyses; meta-regression)
- To consider potential sources of error and bias in extracting and pooling data
- To understand how funnel plots may be used to assess 'small study effects' and potential publication bias

Required Readings

1) Deeks JJ, Higgins JPT, Altman DG (editors). Chapter 9: Analysing data and undertaking meta-analyses. In: Higgins JPT, Green S (editors). *Cochrane Handbook for Systematic Reviews of Interventions*. Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available from: handbook.cochrane.org/
   or
   Centre for Reviews and Dissemination. Systematic Reviews. 2009 http://www.york.ac.uk/crd/guidance/. Chapter1, Section 1.3.5 Data synthesis (including the narrative and quantitative sections of the chapter) (PDF: pages 45-76).

Supplementary Readings & Additional Resources Week 6

Forest plots

- Sedgwick P. How to read a forest plot in a meta-analysis. BMJ 2015 Jul 24;351:h4028.

Subgroup Analyses

- Sun X, Briel M, Busse JW, You JJ, Akl EA, Mejza F, Bala MM, Bassler D, Mertz D, Diaz-Granados N, Vandvik PO. Credibility of claims of subgroup effects in randomised controlled trials: systematic review. BMJ 2012 Mar 15;344:e1553.

Funnel plots

- Sterne, JA, Egger M, Smith GD. Systematic reviews in health care: Investigating and dealing with publication and other biases in meta-analysis. BMJ 2001; 323:101-105.
- Sterne JA, Sutton AJ, Ioannidis JP, Terrin N, Jones DR, Lau J, Carpenter J, Rücker G, Harbord RM, Schmid CH, Tetzlaff J. Recommendations for examining and interpreting funnel plot asymmetry in meta-analyses of randomised controlled trials. BMJ 2011 Jul 22;343:d4002.
- Thornton A, Lee P. Publication bias in meta-analysis: its causes and consequences. J Clin Epidemiol 2000 Feb;53(2):207-216.

Week 7
Introduction to critical appraisal of individual studies
Using the Cochrane Risk of Bias tool

Dr. Aaron Tejani and Dr. Lorri Puil
October 24, 2017

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 for RCTs
- To understand why quality assessment is needed in systematic reviews

Preparation for this class: Students will be asked to read a trial and to be prepared to discuss it in detail. The trial will be assigned later in the term.

Required Readings

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.
2) Rothwell P. External validity of randomised controlled trials: "To whom do the results of this trial apply?" Lancet 2005; 365: 82-93
3) Higgins JPT, Altman DG, Sterne JAC (editors). Chapter 8: Assessing risk of bias in included studies. In: Higgins JPT, Churchill R, Chandler J, Cumpston MS (editors), Cochrane Handbook for Systematic Reviews of Interventions version 5.2.0 (updated June 2017), Cochrane, 2017. Available from www.training.cochrane.org/handbook.

Supplementary Readings & Additional Resources Week 7

Risk of bias assessment for randomized controlled trials

- CASP Randomised controlled trial checklist. http://media.wix.com/ugd/dded87_40b9ff0bf53840478331915a8ed8b2fb.pdf
- Higgins JP, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD, Savović J, Schulz KF, Weeks L, Sterne JA. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ. 2011 Oct 18;343:d5928.

Empirical evidence of bias

- Lundh A, Lexchin J, Mintzes B, Schroll JB, Bero L. Industry sponsorship and research outcome. Cochrane Database of Systematic Reviews 2017, Issue 2. Art. No.: MR000033. DOI: 10.1002/14651858.MR000033.pub3
- Berkman ND, Santaguida PL, Viswanathan M, Morton SC. The Empirical Evidence of Bias in Trials Measuring Treatment Differences. Methods Research Report.

(Prepared by the RTI-UNC Evidence-based Practice Center under Contract No. 290-2007-10056-I.) AHRQ Publication No. 14-EHC050-EF. Rockville, MD: Agency for Healthcare Research and Quality; September 2014.

- 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.
- Wood L, Egger M, Gluud LL, Schulz KF, Juni P, Altman DG, Gluud C, Martin RM, Wood AJ, Sterne JA. Empirical evidence of bias in treatment effect estimates in controlled trials with different interventions and outcomes: meta-epidemiological study. BMJ 2008 Mar 13;336(7644):601-605.

Examples of critical appraisal of individual trials

- 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.
- Scott IA, Greenberg PB. Cautionary tales in the clinical interpretation of therapeutic trial reports. Intern Med J 2005

Week 8
GRADE and summary of findings tables
Formulating conclusions and completing your review

Dr. Lorri Puil
October 31, 2017

Objectives:

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

Required Readings

1) Schünemann HJ, Oxman AD, Higgins JPT, Vist GE, Glasziou P, Akl E, Guyatt GH on behalf of the Cochrane GRADEing Methods Group and the Cochrane Statistical Methods Group. Chapter 11: Completing 'Summary of Findings' tables and grading the confidence in or quality of the evidence. In: Higgins JPT, Churchill R, Chandler J, Cumpston MS (editors), Cochrane Handbook for Systematic Reviews of Interventions version 5.2.0 (updated June 2017). Cochrane, 2017. Available from www.training.cochrane.org/handbook.

2) Schünemann HJ, Oxman AD, Vist GE, Higgins JPT, Deeks JJ, Glasziou P, Akl E, Guyatt GH on behalf of the Cochrane Applicability and Recommendations Methods Group. Chapter 12: Interpreting results and drawing conclusions. In: Higgins JPT, Churchill R, Chandler J, Cumpston MS (editors), Cochrane Handbook for Systematic Reviews of Interventions version 5.2.0 (updated June 2017). Cochrane, 2017. Available from www.training.cochrane.org/handbook.

Supplementary Readings & Additional Resources Week 8

- 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.
- Guyatt G, Oxman AD, Akl EA, Kunz R, Vist G, Brozek J, Norris S, Falck-Ytter Y, Glasziou P, Jaeschke R, Rind D. GRADE guidelines: 1. Introduction—GRADE evidence profiles and summary of findings tables. J Clin Epidemiol 2011 Apr 30;64(4):383-94.
- GRADE guideline series in the Journal of Clinical Epidemiology 2011-2015. Available at: https://gradepro.org/guidelines-development (scroll down to JCE series).
- McMaster University on-line GRADE video series. Available at: https://cebgrade.mcmaster.ca/

Week 9

1. Critical Appraisal of a Systematic Review

Dr. Penny Brasher
November 7, 2017

Objectives:

- To be familiar with assessment of the quality and risk of bias in the conduct of a systematic review and meta-analysis.
- To review a randomized trial for risk of bias and extract the data pertinent to the quantitative synthesis for the review's primary outcome.
- 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 and pairs of students will be assigned to each trial.

Required Readings

The systematic review and trials for the review will be provided later in the term.

2. Special Topic: RIAT - Restoring Invisible and Abandoned Trials and other Recent Trends

Dr. Lorri Puil
November 7, 2017

Objectives:

- To be aware of recent initiatives to restore trials and other trends
- To be aware of the differences between clinical study reports and publications and to discuss examples of reporting bias
- To know the reasons why systematic review authors look for data sources beyond publications

No Required Readings

Supplementary Readings & Additional Resources Week 9

Critical appraisal of a systematic review

- Scottish Intercollegiate Guidelines Network (SIGN) Critical Appraisal Notes and Checklists and Notes http://www.sign.ac.uk/methodology/checklists.html
- Critical Appraisal Skills Programme (CASP) Systematic Review checklist http://www.hello.nhs.uk/documents/CAT7-Systematic_Review.pdf

RIAT initiative and other recent trends

- Doshi P, Jones M, Jefferson T. Rethinking credible evidence synthesis. BMJ 2012;344:d7898
- Sharma T, Guski LS, Freund N, Gøtzsche PC. Suicidality and aggression during antidepressant treatment: systematic review and meta-analyses based on clinical study reports. BMJ 2016 Jan 27;352:i65.
- Le Noury J, Nardo JM, Healy D, Jureidini J, Raven M, Tufanaru C, Abi-Jaoude E. Restoring Study 329: efficacy and harms of paroxetine and imipramine in treatment of major depression in adolescence. BMJ 2015 Sep 16;351:h4320.

Week 10

1. Knowledge Translation, Policy Perspective and Health Economics

Dr. Stirling Bryan
November 14, 2017

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.

2. Special topic: Sex, Gender and Equity in Systematic Reviews

Dr. Lorri Puil
November 14, 2017

Objectives:

- To understand the interrelated concepts of 'sex', and 'gender', and their importance in the context of health care
- To be aware of methods that can be used to consider sex, gender and equity in systematic reviews
- To consider "to whom does the evidence apply"?

Required Readings

1) 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 Women's Health. 2010;19(5):997-1003.

Supplementary Reading & Additional Resources Week 10

Knowledge translation, policy perspective and health economics

- 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: http://ktcanada.net/

Gender and equity in systematic reviews

- Krieger N. Genders, sexes, and health: what are the connections—and why does it matter? International Journal of Epidemiology. 2003 Aug 1;32(4):652-
- An additional reading list will be made available in class.

Week 11
Observational Studies in Systematic Reviews

Dr. Colin Dormuth
Dr. Lorri Puil
November 21, 2017

Dr. Dormuth will cover the first two objectives below. Dr. Puil will further discuss when to use non-randomized studies in systematic reviews (objective 2) and will cover the assessment of risk of bias in non-randomized studies (objective 3).

Objectives:

- To become familiar with major concepts in observational studies and their meta-analysis including data extraction, data analysis, bias, and heterogeneity
- To consider when to use non-randomized studies in a systematic review
- To become familiar with tools to assess risk of bias in non-randomized studies, including ROBINS-I, the Cochrane Risk of Bias Tool for Non-randomized Studies of Interventions

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 reading & Additional Resources Week 11

Observational studies and meta-analysis

- Dormuth CR, Hemmelgarn BR, Paterson JM, James MT, Teare GF et al., Canadian Network for Observational Drug Effect Studies (CNODES). Use of high potency statins and rates of admission for acute kidney injury: multicenter, retrospective observational analysis of administrative databases. BMJ 2013; 346:f880 doi: 10.1136/bmj.f880.
- Dormuth C, Filion K, Paterson JM, James MT, Teare GF et al., for the Canadian Network for Observational Drug Effect Studies (CNODES) Investigators. High potency statins and the risk of new diabetes: multicentre, observational study of administrative databases. BMJ 2014; 348:g3244 doi: 10.1136/bmj.g3244.
- Filion KB, Azoulay L, Platt RW, Dahl M, Dormuth CR et al., for the CNODES Investigators. A multicenter observational study of incretin-based drugs and heart failure. New Engl J Med 2016; 374:1145-1154.
- Dormuth CR, Filion KB Platt RQ. Likelihood ratio meta-analysis: new motivation and approach for an old method. Contemporary Clinical Trials 2016; 47: 259-265.

Assessment of risk of bias of non-randomized studies

- Sterne JAC, Hernan MA, Reeves BC, Savovic J, Berkman ND et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. BMJ 216; 355:i4919 doi: 101136/bmj.i4919.
- ROBINS-I tool – Available at: https://sites.google.com/site/riskofbiastool/
- 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.
- Other tools to assess the quality of observational studies are available in the Quality Assessment Tools module in Canvas.

Week 12
Student Review Team Presentations

November 28, 2017

Each team will present their research topic in a brief class presentation. Details and the presentation schedule will be provided in Canvas.

Week 13

1. Special Topic: Indirect Comparisons and Introduction to Network Meta-analysis

Dr. Mir Fazeli
December 5, 2017

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

Objectives:

- To be aware of the underlying assumptions of network meta-analysis, and their limitations and strengths
- To be able to read a network meta-analysis and critique it.

Required readings

1) 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.

Supplementary readings & Additional Resources Week 13

- Salanti G. Indirect and mixed-treatment comparison, network, or multiple-treatments meta-analysis: many names, many benefits, many concerns for the next generation evidence synthesis tool. Res Synth Methods 2012 Jun 1;3(2):80-97.
- Cipriani A, Higgins JP, Geddes JR, Salanti G. Conceptual and technical challenges in network meta-analysis. Ann Intern Med 2013 Jul 16;159(2):130-7.

- Salanti G, Del Giovane C, Chaimani A, Caldwell DM, Higgins JP. Evaluating the quality of evidence from a network meta-analysis. PLOS One 2014 Jul 3;9(7):e99682
- Hutton B, Salanti G, Caldwell DM, Chaimani A, Schmid CH, Cameron C, Ioannidis JP, Straus S, Thorlund K, Jansen JP, Mulrow C. The PRISMA Extension Statement for Reporting of Systematic Reviews Incorporating Network Meta-analyses of Health Care Interventions: Checklist and Explanations PRISMA Extension for Network Meta-analysis. Ann Intern Med 2015 Jun 2;162(11):777-84.

2. Course Wrap-up and Discussion

Dr. Lorri Puil
December 5, 2017

Some of the main concepts of the course will be highlighted and discussed in the context of the class assignments.

Appendix A
SPPH Course Grading adapted from: Pratt, D. Graduate Course Grading Policy, UBC Department of Education Studies.

Numeric and letter grades will be assigned as follows:

A Level (80% to 100%)
This category of achievement is typified by work that meets the highest expectations as outlined below.
A+ is from 90% to 100%: It is reserved for exceptional work that greatly exceeds course expectations. In addition, achievement must satisfy all the conditions below.
A is from 85% to 89%: A mark of this order suggests a very high level of performance on all criteria used for evaluation. Contributions deserving an A are distinguished in virtually every aspect. They show that the individual significantly shows initiative, creativity, insight, and probing analysis where appropriate. Further, the achievement must show careful attention to course requirements as established by the instructor.
A- is from 80% to 84%: It is awarded for generally high quality of performance, no problems of any significance, and fulfillment of all course requirements.

B Level (68% to 79%)
This category of achievement is typified by adequate but unexceptional performance. It is distinguished from A level work by one or more problems, for example: a significant error in understanding, superficial representation or analysis of key concepts, or lack of coherent organization or explanation of ideas. The level of B work is judged in accordance with the nature of problems demonstrated. B+ is from 76% to 79%, B is from 72% to 75%, and B- is from 68% to 71%.

C Level (55% to 67%)
This category of achievement is typified by less than adequate performance at the graduate level, and is distinguished from B level work by multiple problems, including: significant errors in understanding, superficial representation or analysis of key concepts, and/or lack of coherent organization or explanation of ideas. The level of C work is judged in accordance with the severity of the problems demonstrated. C+ is from 64% to 67%, C is from 60% to 63%, and C- is from 55% to 59%.

Note: All assignments are due on the dates noted. In the absence of a pre-arranged extension to the due date or documented medical circumstances, students handing in a late assignment will incur a penalty of 10% of the allotted assignment grade for each day after the due date. Also, late assignments may mean delays in marking.

Further information on UBC policy will be provided in Canvas.