

Comparative Effectiveness Research (M19-5252)

Spring 2019 (1/14/19 – 5/7/19)

Fridays, 1:00-3:00pm

Location: Taylor Avenue Building 2nd floor, Richmond Room**INSTRUCTOR**

Erika A. Waters, PhD, MPH

Division of Public Health Sciences

Department of Surgery

waterse@wustl.edu

Phone: 314-747-5705

Office Hours: By appointment

COURSE DESCRIPTION & OBJECTIVES

This course will provide a comprehensive introduction to comparative effectiveness research (CER). Topics include an overview of CER, stakeholder engagement in CER, designing CER studies, methodologic challenges in doing CER, and recent developments in PCORI and Federal policy. Students will be expected to review and evaluate comparative effectiveness studies as well as actively participate in class discussions. Many class sessions will include a case study. Through examples, class discussion, and homework students will become familiar with CER methods. They will prepare a set of specific aims for a CER project and identify gaps in CER in their field of study.

COMPETENCIES

- Define CER and its basic tenets.
- Understand the broader context of CER
- Identify common methodologies used in CER
- Be able to identify the appropriate research design for the CER question
- Identify methodologic challenges of CER

COURSE FORMAT & EXPECTATIONS

This class is based on a diverse array of activities, including lectures, discussions, reading assignments, study critiques, and in-class case studies. Students must come to each session prepared to be active, thoughtful, and energetic participants. This requires thoughtful and careful reading of assigned course materials prior to each class session.

STUDENT RESPONSIBILITIES

- ✓ Attend each class.
- ✓ Come to class on-time, prepared, and having read all required readings.
- ✓ Participate in class discussions and complete in-class case studies.
- ✓ Complete assignments on time.

- ✓ Seek any necessary clarification regarding course expectations.

Any issues with attendance, deadlines, or completion of assignments should be discussed **before** the deadline/class with the instructor. Email is the best way to contact the instructor. Emails will be answered within two business days with the exception of weekends and holidays.

CLASSROOM ETIQUETTE

- ✓ Please turn all cellphones and pagers to silent or vibrate.
- ✓ If you need to answer a call or page, please leave the room quietly to do so.
- ✓ **Do not use the internet for non-class purposes, social media sites, BJC clinical sites, or check email during class time.**
- ✓ Please be respectful of differences in viewpoints expressed during class discussion.
- ✓ Please keep any sensitive information that arises during discussion confidential.

CANVAS

We will use Canvas to manage our class, access assignment instructions and post course-related questions. Canvas can be accessed at <https://mycanvas.wustl.edu/>. Log in to the **Wash U MyCanvas** version (**NOT** the MD program version) with your WUSTLKey and the class should appear on the homepage.

- All updates and reminders will be posted on Canvas.
- Lecture notes and additional readings and assignment instructions will be posted on Canvas throughout the semester.

We may utilize the Discussion threads for general questions related to lectures and assignments. Students should post all general questions that may be relevant to others in class to the Discussion thread. Student-specific questions (e.g. related to a grade or exam conflict) should be emailed directly to the instructors. Every effort will be made to answer student emails within 48-hours (excluding weekends). Students are encouraged to post materials related to class (e.g. link to a news story) on Canvas for the rest of the class to access.

EVALUATION AND GRADING

Grades will be based on class participation and assignments. Additional specific details for each assignment will be distributed at least 4 week prior to their due date.

1. ***Class participation (15 points):*** The participation portion of the course grade is based upon regular and timely attendance, as well as active, meaningful contributions to class discussion and case studies. Students are expected to read the required readings. Participation points are earned by arriving to class ***on time*** and being an ***active and thoughtful contributor*** to class discussions. More than two absences from class may result in a lowered grade. Please consider not enrolling if you have more than two absences already planned.
2. ***Journal article critique and presentation (25 points):*** You will be required to give a 25 min journal club-style review of an article of your choice in class. The only requirement is that it be an original research article and that it be related to CER. ***The full citation for your selected reading must be emailed to the entire class no later than 12pm the Monday before the day you are scheduled.*** This allows time for the instructor to review materials and to get readings to your classmates in a timely manner. Detailed instructions to follow.

3. **Project outline (10 points):** A one page Project Outline to describe key aspects of your planned CER project. Please use the provided Project Outline template on Canvas, and submit your completed outline on Canvas. **The project outline is due March 15, 2019 at 11:59pm.**
4. **Letter of Intent (30 points):** Students will be asked to submit a modified PCORI Letter of Intent (LOI) 3 page limit (excluding references) describing a CER study. The proposed study may be of any type of study design, as long as it meets the criteria for a CER study, as discussed in class and in the LOI instructions. Please submit your completed LOI on Canvas. **The LOI is due April 19, 2019 at 11:59pm.**
5. **Project presentation (20 points):** Students will give a 15-minute PowerPoint presentation describing the CER project they proposed in the LOI. **The presentations will be held either April 26 or May 3, 2019.**

Grading

Participation	15 points
Article critique	25 points
Project outline	10 points
Letter of intent	30 points
Project presentation	20 points

Grading scale:

A:	90-100 points
B:	80-89 points
C:	70-79 points
F:	less than 69 points

Late assignments: Late assignments will result in a deduction of five points for each day late **including weekends** unless prior approval is obtained from the instructor or a compelling situation prevents prior approval (i.e. documented health issues or family emergencies).

ACADEMIC HONESTY

Students are expected to complete all of their assignments in accordance with Washington University in St. Louis' academic rules and regulations regarding honesty and integrity. Any evidence of academic misconduct, including cheating, failure to cite sources, and/or plagiarism will result in appropriate action as dictated by Washington University in St. Louis. Violations of academic honesty will result in notification to the Associate Dean of Academic Affairs at the Washington University School of Medicine, as well as the MPHS Director, Assistant Director(s), and Program Committee. Any hint of violation during an examination or in a written assignment will result in no grade for the exam/assignment. For more information see the University's Student Academic Integrity Policy.

SPECIAL NEEDS

Per University policy, students with learning, sensory, or physical disability or other impairment should contact the Washington University Center for Advanced Learning Disability Resources (DR) at 314-935-4062 or visit <http://disability.wustl.edu/DisabilityResources.aspx>. The DR Office is located in Cornerstone on the Danforth Campus.

Students whose second language is English and/or those in need of assistance in lectures, reading or writing assignments, and/or testing, should contact the University Writing Center at 314-935-4981 or visit <https://writingcenter.wustl.edu/>.

COURSE SCHEDULE

****The syllabus is subject to change at the discretion of the instructor. ****

Session	Date	Topic	Instructor
1	Jan 18	Overview of the Course and CER	Erika Waters
2	Jan 25	Large Databases for Retrospective CER Studies	Anne Mobley Butler
3	Feb 1	Consumer Engagement in CER Studies	Mary Politi
4	Feb 8	Effectiveness and Pragmatic Trials	Shane LaRue
5	Feb 15	Case Study: Pragmatic Trial	Kaharu Sumino
6	Feb 22	CER Systematic Reviews & Meta Analyses	Su-Hsin Chang
7	Mar 1	Cost Effectiveness CER Studies	Su-Hsin Chang
8	Mar 8	Prospective Observational CER Studies	Siobhan Sutcliffe
9	Mar 15	Case Study: Large Database and Cost Effectiveness Research	Varun Puri
10	Mar 22	Case Study: Stakeholder Engagement from the Researcher Perspective	Vetta Thompson
11	Mar 29	Patient-Reported Outcome Measures	Amy McQueen
12	Apr 5	Implementation CER Studies	Stephanie Mazzucca
13	Apr 12	Case Study: Stakeholder Engagement from the Stakeholder Perspective	Elizabeth Kruvand
14	Apr 19	Case Study: Patient Centered Outcomes in Anesthesia	Michael Avidan
15	Apr 26	Student presentations	
16	May 3	Student presentations	

READINGS AND RESOURCES

A schedule of required and recommended readings will be provided. Additional readings related to student presentations will be distributed a few days before each class. Below are some general resources related to our topic:

Class Background Material:

- Institute of Medicine. What is Comparative Effectiveness Research? In *Initial National Priorities for Comparative Effectiveness Research*. National Academies Press, Washington, DC, p. 29-60.
<https://www.nap.edu/read/12648/chapter/4> [Sign in as guest to download as pdf].
- IOM initial priorities for CER <https://www.nap.edu/read/12648/chapter/1>
- PCORI national priorities (adopted May 21, 2012, latest update August 2014): <https://www.pcori.org/research-results/research-we-support/national-priorities-and-research-agenda> and <https://www.pcori.org/sites/default/files/PCORI-National-Priorities-and-Research-Agenda.pdf>

January 18 (Session 1): Overview of the Course and CER (Waters)

1. Sox HC. Defining comparative effectiveness research: the importance of getting it right. *Med Care* 2010;48(6

Suppl):S7-8.

2. Price-Haywood EG. Clinical Comparative Effectiveness Research through the Lens of Healthcare Decisionmakers. *Ochsner J* 2015;15(2):154-61.
3. Clancy C, Collins FS. Patient-Centered Outcomes Research Institute: the intersection of science and health care. *Sci Transl Med* 2010;2(37):37cm18.
4. Fleurence RL, Curtis LH, Califf RM, et al. Launching PCORnet, a national patient-centered clinical research network. *J Am Med Inform Assoc* 2014;21(4):578-82.
5. PCORI methodology standards (latest update 2018): <https://www.pcori.org/research-results/about-our-research/research-methodology/pcori-methodology-standards> or <https://www.pcori.org/sites/default/files/PCORI-Methodology-Standards.pdf> Although the standards are written as though they are specific to PCORI, they represent generally good research practices overall and therefore can be applied to proposals for multiple funding agencies and for various types of research projects.

January 25 (Session 2): Overview of Large Databases for Retrospective CER Studies (Butler)

1. Berger ML, Mamdani M, Atkins D, et al. Good research practices for comparative effectiveness research: defining, reporting and interpreting nonrandomized studies of treatment effects using secondary data sources: the ISPOR Good Research Practices for Retrospective Database Analysis Task Force Report--Part I. *Value Health* 2009;12(8):1044-52.
2. Roche N, Reddel H, Martin R, et al. Quality Standards for Real-World Research. Focus on Observational Database Studies of Comparative Effectiveness. *Annals of the American Thoracic Society*. 2014; 11(2): Suppl 2:S99-104.
3. Keren R, Shah SS, Srivastava R, et al. Comparative effectiveness of intravenous vs oral antibiotics for postdischarge treatment of acute osteomyelitis in children. *JAMA Pediatrics*. 2015 Feb;169(2):120-8.
4. Presley CJ, Soulos PR, Herrin J, et al. Patterns of use and short-term complications of breast brachytherapy in the national medicare population from 2008-2009. *Journal of Clinical Oncology*. 2012 Dec 10;30(35):4302-7.
5. Cuttino LW, Khan A, Wazer DE, et al. When Retrospective Comparative Effectiveness Research Hinders Science and Patient-Centered Care. *Journal of Clinical Oncology*. 2013;31(17):2226-2227.

February 1 (Session 3): Consumer Engagement in CER Trials (Politi)

1. Hoffman A, Montgomery R, Aubry W, Tunis SR (2010). How best to engage patients, doctors, and other stakeholders in designing comparative effectiveness studies. *Health Affairs*, 10, 1834-41.
2. Daverka, PA, Lavalley, DC, Desai, PJ, Esmail, LC, Ramsey, SD, Veenstra, DL & Tunis, SR (2012). Stakeholder participation in comparative effectiveness research: defining a framework for effective engagement. *Journal of Comparative Effectiveness Research*, 1(2): 181–194.
3. Focus on the rubric itself and its application; the description of its development is less important, although it is also an example of consumer engagement. Sheridan S, Schrandt S, Forsythe L, et al. The PCORI Engagement Rubric: Promising Practices for Partnering in Research. *Ann Fam Med* 2017;15:165-170.
4. PCORI resources: Although these are written to be specific to PCORI, the basic principles (e.g., a written

engagement plan) can be applied to other research projects and funding opportunities.

- a. <http://www.pcori.org/funding-opportunities/what-we-mean-engagement>
- b. <http://www.pcori.org/assets/2013/11/PCORI-Sample-Engagement-Plans.pdf>
- c. <http://www.pcori.org/sites/default/files/PCORI-Compensation-Framework-for-Engaged-Research-Partners.pdf>

February 8 (Session 4): Effectiveness and Pragmatic Trials (LaRue)

1. Chalkidou K, Tunis S, Whicher D, et al. The role for pragmatic randomized controlled trials (pRCTs) in comparative effectiveness research. *Clin Trials* 2012;9(4):436-46.
2. Loudon K, Treweek S, Sullivan F, et al. The PRECIS-2 tool: designing trials that are fit for purpose. *BMJ* 2015;350:h2147.
3. Ezenwa MO, Suarez ML, Carrasco JD, et al. Implementing the PAINRelieveIt Randomized Controlled Trial in Hospice Care: Mechanisms for Success and Meeting PCORI Methodology Standards. *West J Nurs Res* 2016.
4. Lauer MS. Commentary: How the debate about comparative effectiveness research should impact the future of clinical trials. *Stat Med* 2012;31(25):3051-3.

February 15 (Session 5): Case Study – Pragmatic Trials (Sumino)

1. Frobert O, Lagerqvist B, Olivecrona GK, et al. Thrombus aspiration during ST-segment elevation myocardial infarction. *N Engl J Med* 2013;369(17):1587-97.
2. *This article is not precisely CER because it doesn't compare two treatments with demonstrated effectiveness, but it includes a variety of design features that may be of interest. It is also relevant to the cost effectiveness session.* Smith JR, Musgrave S, Payerne E, et al. At-risk registers integrated into primary care to stop asthma crises in the UK (ARRISA-UK): study protocol for a pragmatic, cluster randomised trial with nested health economic and process evaluations. *Trials*. 2018;19(1):466. Published 2018 Aug 29. doi:10.1186/s13063-018-2816-z
3. Kramer CB, LeRoy L, Donahue S, Apter AJ, Bryant-Stephens T, Elder JP, Hamilton WJ, Krishnan JA, Shelef DQ, Stout JW, Sumino K. Enrolling African-American and Latino patients with asthma in comparative effectiveness research: lessons learned from 8 patient-centered studies. *Journal of Allergy and Clinical Immunology*. 2016 Dec 1;138(6):1600-7.

February 22 (Session 6): CER Systematic Reviews & Meta Analyses (Chang)

1. Brouwers MC, Thabane, L, Moher, D & Straus, SE (2012). Comparative Effectiveness Research Paradigm: Implications for Systematic Reviews and Clinical Practice Guidelines. *Journal of Clinical Oncology*, 30(34):4202-7.
2. Chang SH, Stoll CR, Song J, Varela JE, Eagon CJ, Colditz GA. Bariatric surgery: an updated systematic review and meta-analysis, 2003–2012. *JAMA surgery*. 2014 Mar 1;149(3):275-87.
3. Chang SH, Freeman NL, Lee JA, Stoll CR, Calhoun AJ, Eagon JC, Colditz GA. Early major complications after

bariatric surgery in the USA, 2003–2014: a systematic review and meta-analysis. *Obesity Reviews*. 2018 Apr;19(4):529-37.

4. AHRQ Methods guide for Effectiveness and Comparative Effectiveness Reviews: <http://effectivehealthcare.ahrq.gov/search-for-guides-reviews-and-reports/?pageaction=displayproduct&mp=1&productID=318>
5. AHRQ also has a slide library for training for systematic reviews with their focus on comparative effectiveness: <http://www.effectivehealthcare.ahrq.gov/index.cfm/tools-and-resources/slide-library/#slidetrainingmodules>

March 1 (Session 7): Cost Effectiveness CER Studies (Chang)

1. Chandra A, Jena AB, Skinner JS. The pragmatist's guide to comparative effectiveness research. *J Econ Perspect*. 2011;25(2):27-46.
2. Neumann PJ, Cohen JT, Weinstein MC. Updating cost-effectiveness—the curious resilience of the \$50,000-per-QALY threshold. *New England Journal of Medicine*. 2014 Aug 28;371(9):796-7.
3. Review the relevant portions of the Smith et al., *Trials*, 2018 article from class session 5.
4. This article provides an example of how the comparator in CER research can be treatment options or patient subgroups. Tosteson AN, Tosteson TD, Lurie JD, et al. Comparative effectiveness evidence from the spine patient outcomes research trial: surgical versus nonoperative care for spinal stenosis, degenerative spondylolisthesis, and intervertebral disc herniation. *Spine (Phila Pa 1976)*. 2011;36(24):2061-8.

March 8 (Session 8): Prospective Observational CER Studies (Sutcliffe)

1. Berger ML, Dreyer N, Anderson F, et al. Prospective Observational Studies to Assess Comparative Effectiveness: The ISPOR Good Research Practices Task Force Report. *Value in Health* 2012;217-230.
2. Fleurence RL, Naci H, Jansen JP. The critical role of observational evidence in comparative effectiveness research. *Health Aff (Millwood)* 2010;29(10):1826-33.
3. Glynn RJ. Use of propensity scores to design observational comparative effectiveness studies. *JNCI: Journal of the National Cancer Institute*. 2017 Aug 1;109(8):1-3.
4. Xian Y, O'Brien EC, Fonarow GC, et al. Patient-Centered Research into Outcomes Stroke Patients Prefer and Effectiveness Research: Implementing the patient-driven research paradigm to aid decision making in stroke care. *Am Heart J* 2015;170(1):36-45, 45 e1-11.
5. OPTIONAL: Austin PC. An Introduction to Propensity Score Methods for Reducing the Effects of Confounding in Observational Studies. *Multivariate Behav Res* 2011;46(3):399-424.

March 15 (Session 9): Case Study – Large Database and Cost Effectiveness (Puri)

1. Semenkovich TR, Panni RZ, Hudson JL, Thomas T, Elmore LC, Chang SH, Meyers BF, Kozower BD, Puri V.

Comparative effectiveness of upfront esophagectomy versus induction chemoradiation in clinical stage T2N0 esophageal cancer: A decision analysis. *The Journal of thoracic and cardiovascular surgery*. 2018 May 1;155(5):2221-30.

2. Hu Y, Puri V, Shami VM, Stukenborg GJ, Kozower BD. Comparative effectiveness of esophagectomy versus endoscopic treatment for esophageal high-grade dysplasia. *Annals of surgery*. 2016 Apr 1;263(4):719-26.
3. Guss, Zachary David, et al. Validity of using cancer registry data for comparative effectiveness research. *Journal of Clinical Oncology*. 2018; 36 (15): 6574-6574.

March 22 (Session 10): Case Study – Stakeholder Engagement from the Researcher Perspective (Sanders Thompson)

1. Goodman MS, Sanders Thompson VL. The science of stakeholder engagement in research: classification, implementation, and evaluation. *Translational Behavioral Medicine*. 2017;7(3):486-491.
2. Hamilton AB, Yano EM. The importance of symbolic and engaged participation in evidence-based quality improvement in a complex integrated healthcare system: response to “The science of stakeholder engagement in research.” *Translational Behavioral Medicine*. 2017;7(3):492-494.
3. Komaie G, Ekenge CC, Sanders Thompson VL, Goodman MS. Increasing Community Research Capacity to Address Health Disparities. *J Empir Res Hum Res Ethics*. 2017 Feb;12(1):55-66.
4. Concannon TW, Fuster M, Saunders T, Patel K, Wong JB, Leslie LK, Lau J. A systematic review of stakeholder engagement in comparative effectiveness and patient-centered outcomes research. *Journal of general internal medicine*. 2014 Dec 1;29(12):1692-701.

March 29 (Session 11): Patient-Reported Outcome Measures (McQueen)

1. Basch E. Patient-Reported Outcomes - Harnessing Patients' Voices to Improve Clinical Care. *N Engl J Med* 2017;376(2):105-08.
2. Bingham CO, 3rd, Bartlett SJ, Merkel PA, et al. Using patient-reported outcomes and PROMIS in research and clinical applications: experiences from the PCORI pilot projects. *Qual Life Res* 2016;25(8):2109-16.
3. Francis DO, Patel DA, Sharda R, et al. Patient-Reported Outcome Measures Related to Laryngopharyngeal Reflux: A Systematic Review of Instrument Development and Validation. *Otolaryngol Head Neck Surg* 2016;155(6):923-35.
4. Patient-Reported Outcomes Measurement Information System (PROMIS). <http://www.healthmeasures.net/explore-measurement-systems/promis>

April 5 (Session 12): Implementation CER Studies (Mazzucca)

1. General overview of implementation designs Curran, Geoffrey M et al. “Effectiveness-implementation hybrid designs: combining elements of clinical effectiveness and implementation research to enhance public health impact” *Medical care* vol. 50,3 (2012): 217-26.
2. Glasgow RE, Rabin BA. Implementation science and comparative effectiveness research: a partnership capable of improving population health. *Journal of comparative effectiveness research*. 2014 May;3(3):237-40.

3. Proctor EK, Powell BJ, McMillen JC. Implementation strategies: recommendations for specifying and reporting. *Implement Sci.* 2013;8:139. Published 2013 Dec 1. doi:10.1186/1748-5908-8-139
4. Seers K, Rycroft-Malone J, Cox K, Crichton N, Edwards RT, Eldh AC, Estabrooks CA, Harvey G, Hawkes C, Jones C, Kitson A. Facilitating Implementation of Research Evidence (FIRE): an international cluster randomised controlled trial to evaluate two models of facilitation informed by the Promoting Action on Research Implementation in Health Services (PARIHS) framework. *Implementation Science.* 2018 Dec;13(1):137.
5. Mills KT, Obst KM, Shen W, et al. Comparative Effectiveness of Implementation Strategies for Blood Pressure Control in Hypertensive Patients: A Systematic Review and Meta-analysis. *Ann Intern Med.* 2017;168(2):110-120.

April 12 (Session 13): Case Study – Stakeholder Engagement from the Stakeholder Perspective (Kruvand)

1. Weissman JS, Westrich K, Hargraves JL, Pearson SD, Dubois R, Emond S, Olufajo OA. Translating comparative effectiveness research into Medicaid payment policy: views from medical and pharmacy directors. *Journal of comparative effectiveness research.* 2015 Mar;4(2):79-88.
2. Frerichs L, Kim M, Dave G, Cheney A, Hassmiller Lich K, Jones J, Young TL, Cene CW, Varma DS, Schaal J, Black A. Stakeholder perspectives on creating and maintaining trust in community–Academic research partnerships. *Health Education & Behavior.* 2017 Feb;44(1):182-91.
3. Tapp H, Derkowski D, Calvert M, Welch M, Spencer S. Patient perspectives on engagement in shared decision-making for asthma care. *Family practice.* 2016 Dec 29;34(3):353-7.
4. Saunders T, Mackie TI, Shah S, Gooding H, de Ferranti SD, Leslie LK. Young adult and parent stakeholder perspectives on participation in patient-centered comparative effectiveness research. *Journal of comparative effectiveness research.* 2016 Aug;5(5):487-97.

April 19 (Session 14): Case Study – Patient Centered Outcomes in Anesthesia (PROMIS) (Avidan)

No readings for this class session.

April 26 (Session 15): Student Presentations

May 3 (Session 16): Student Presentations