Overview and Objectives:
This course will define Comparative Effectiveness Research (CER) and highlight the history and current national efforts in promoting CER for drugs, devices and other interventions. The course provides an examination of many of the important issues in CER. The curriculum will include topics on the conceptualization, design, sampling, modeling, data collection and analysis used in CER studies. The curriculum was developed for students learn research methodology, become familiar with problems and controversies, and to develop an appreciation of the complexity of designing CER studies. The teaching methods will be interactive and many sessions will be led by the students.

The course format:
To maximize the utility of classroom discussions and associated exercises, the instructors expect that students complete all assignments ahead of class and are prepared to discuss the assignments. Classroom lectures and activities will only briefly review the key concepts, and instead focus on expanding and applying concepts covered in the assignments.

1. For each topic, assigned readings and videos will provide the background material necessary to learn the topic. Please read and view the material prior to class and be prepared to participate in discussions. You will need the latest version of Flash player to view the assigned video presentations. Please note that you may need to adjust the volume while viewing the video clips in the presentations.

2. The majority of class time will be used for practical application of what has been covered in the assigned readings and videos. This will be done through evaluations; exercises using data; discussions; small group assignments; debates; and other active learning methods.

3. Each class will start with an assessment on material from the previous session and will contribute to the final course grade.

Responsibilities:
Students will review pertinent papers at each session, lead discussions of assigned topics, participate in debates, form small groups for discussions, critique other students work and actively participate in the class.

Course Requirements:
- Attendance: The course is designed to be participatory; students need to be present at each class.
- Pre-class evaluations will consist of multiple choice questions and will be used for grading. They will focus specifically on the previous session and all related activities. Any questions about the evaluation should be directed to the instructor and emailed at least 24 hours before class starts. There will not be an opportunity for questions the day of the assessment.
- Required readings and videos must be completed before class. Knowledge of the required assignments will be necessary for the assessments and to follow class discussion.
- For some of the sessions, in addition to the required readings, short summaries, or other assignments must be prepared in advance as described within each session.
In-class discussions and exercises are needed to learn the material.

Attendance Policy:
Students are expected to sign in to each class (computer provided in suite lobby). If a problem is encountered with the sign-in system, please contact the course instruction(s) as well as Lauren Talotta (talottals@upmc.edu) immediately.

Course Grading Scale: Letter grades
- 15 pre-class evaluations: 60% total
- 5 other short assignments (sessions 2, 4, 6, 7, and 10): 20% total
- Attendance and participation: 20% total

Course Mechanics: 2 Credits (2 hour/session, 2 sessions/week, for 8 weeks)

Required Textbooks: Required readings are listed under each session.

Academic Integrity: Students in this course will be expected to comply with the University of Pittsburgh’s Policy on Academic Integrity (http://www.provost.pitt.edu/info/ai1.html). Any student suspected of violating this obligation for any reason during the semester will be required to participate in the procedural process, initiated at the instructor level, as outlined in the University Guidelines on Academic Integrity. This may include, but is not limited to, the confiscation of the examination of any individual suspected of violating University Policy. Furthermore, no student may bring any unauthorized materials to an exam, including dictionaries, and programmable calculators.
Course Schedule:

Session 1.
What is CER and why is it important?

Session goal:
- Introduce the key concepts of Comparative Effectiveness Research (CER).

Session objectives:
- State the definition of CER and discuss the strengths and limitations of CER studies.
- Review the history of CER in the US and in other countries.
- Describe the needs and challenges associated with national CER priorities (e.g., IOM and PCORI).
- Summarize the use of CER studies in health care.

In-class activities:
- Pre-class assessment

Assignment to be completed before class:
- Required readings
- View CER Lesson #1, slides 11-38 Available at: http://ctsa-cermethodscourse.org/cer-lessons/

Required Readings:
1. Review the AHRQ website: http://www.effectivehealthcare.ahrq.gov/index.cfm/what-is-comparative-effectiveness-research1/

Optional Readings and References:

Session 2.
Overview of CER study designs

Session goal:
- Summarize research methods used in answering comparative effectiveness questions.

Session objectives:
- Provide an overview of study designs used in CER.
- Identify and discriminate the differences and similarities between different CER study designs.
- Analyze strengths and weaknesses of each research method.
**In-class activities:**
- Pre-class evaluation of session #1 class activities, required reading and CER video lessons.
- Small group discussions of CER research questions

**Assignment to be completed before class:**
- Required readings
- Identify 1-2 research questions in your area that could optimally be answered using a CER study design. Prepare a ½ page summary that defines the problem, provides some background of the problem, and highlights why this problem is significant to your field.

**Required Readings:**

**Optional Readings and References:**

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**Session 3.**
*CER using observational studies I*

**Session goal:**
- Explain observational study designs, their limitations and analytic issues.

**Session objectives:**
- Discuss the central features of observational study designs in CER.
- Identify the potential strengths and weaknesses in CER studies that use observational designs.
- Summarize methods used to adjust for confounding and bias in observational study designs.
- Identify existing datasets at Pitt that are available for CER.

**In-class activities:**
- Pre-class evaluation of session #2 class activities and required reading.
- Small group discussions and presentations of assigned readings.
- Post-class assessment on methods to reduce confounding in observational studies.

**Assignment to be completed before class:**
- Required readings
- View CER Lesson #14 and # 15 Available at: [http://ctsa-cermethodscourse.org/cer-lessons/](http://ctsa-cermethodscourse.org/cer-lessons/)
- Be prepared to 1) describe how the Ahmed and Beck studies (required readings) benefited from propensity scores or instrumental variables and 2) describe the limitations and assumptions of each study.

**Required Readings:**

**Optional Readings and References:**

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**Session 4.**

*CER using observational studies II*

**Session goal:**
- Analyze the strengths and limitations of different statistical methods used to minimize bias and confounding in observational studies.

**Session objectives:**
- Demonstrate the use of statistical methods in STATA to minimize bias and confounding in observational data.
- Apply the skills learned through the assignment to analyze a dataset using 1) propensity score adjustment methods, 2) propensity matching, 3) instrumental variables, and 4) regression adjustment for confounding.

**In-class activities:**
- Pre-class evaluation of session #3 video lessons, required readings and class activities.
- Lab session to run STATA commands and interpret output.
- Small group discussion of STATA results.
- Post-class assessment of interpreting analyses of observational data.

**Assignment to be completed before class:**
- Required readings
- Review STATA handout for propensity scores, instrumental variables, and standard regression adjustment for confounding. This document will provide the commands needed for class activities.
- Using an assigned data set, print out a summary of the data using the codebook command. Write a 2–3 sentence summary of how other variables in the data set might influence treatment.

**Required Readings:**

Optional Readings and References:

**Session 5.**
Registries and CER

**Session goal:**
- Describe how registries and networks are used in observational studies.

**Session objectives:**
- Identify questions that are most appropriate for research registries
- Evaluate strengths and weaknesses of registries
- Summarize limitations in the use of registries in CER

**In-class activities:**
- Pre-class evaluation of session #4 required readings and class activities.
- Small group discussions and presentations of different studies that used various methods and registries to answer CER questions.

**Assignment to be completed before class:**
- Required readings

**Required Readings:**

**Session 6.**
Heterogeneity of treatment effects and personalized medicine in CER

**Session goal:**
- Summarize the challenges of applying CER findings to individual patients or subgroups.

**Session objectives:**
- Identify key aspects and challenges of assessing and incorporating heterogeneity.
- Illustrate how results of standard analyses do or do not apply to individual patients and/or differential response among patient subgroups.
• Select the appropriate STATA commands for analysis of heterogeneity of treatment effects (HTE) and interpret results.
• Describe possible relationship between CER and personalized medicine.

In-class activities:
• Pre-class evaluation of session #5 required readings and class activities
• Small group discussion of STATA results from in-class exercise
• Start with an existing data set used to assess heterogeneity of treatment effects (HTE) in an analysis of cardiac-related treatments.
• Apply STATA commands to fit interactions, estimate and test subgroup effects and predict outcomes for an individual.
• Interpret findings and contrast results with standard main effects models.

Assignment to be completed before class:
• Required readings
• View CER Lesson #4 Available at http://ctsa-cermethodscourse.org/cer-lessons/
• Review handout on STATA commands for assessing THE.
• Using an assigned data set, print out a summary of data using the codebook command. Write a 2-3 sentence summary of how other variables in the data set might influence treatment.

Required Reading:

Session 7.
CER using pragmatic clinical trials

Session goal:
• Describe design and implementation of pragmatic trials.

Session objectives:
• Assess the components of a pragmatic trial and contrast this design to the design of explanatory trials.
• Identify the strengths and limitations of implementing a pragmatic design in practice.
• Discuss the methodological challenges in designing pragmatic trials.

In-class activities:
• Pre-class evaluation of session #6 video lesson, required readings and class activities
• Summary of when to consider clinical trials and when not
• Small group discussion of case studies presented in readings
Assignment to be completed before class:
- Required readings
- View CER Lesson #2 and #3 Available at: http://ctsa-cermethodscourse.org/cer-lessons/
- Complete short answer questions

Required Readings:

Optional Readings and References:

Session 8.
CER using meta-analysis and systematic reviews

Session goal:
- Summarize systematic reviews and meta-analyses methods and their role in CER.

Session objectives:
- Articulate the differences between meta-analyses and systematic reviews.
- Discuss the role of analytic frameworks in systematic review and the approach to formulate answerable questions.
- Describe the limitations of meta-analysis and systematic reviews in CER.

In-class activities:
- Pre-class evaluation of session #7 video lesson, required readings and class activities.

Assignment to be completed before class:
- Required readings
- View CER Lesson #16 and #18 Available at http://ctsa-cermethodscourse.org/cer-lessons/

Required Readings:
**Session 9.**  
*CER using modeling and simulation*

**Session goal:**  
- Summarize how modeling and simulation techniques can answer specific CER questions

**Session objectives:**  
- Review the rationale for use of modeling in CER  
- Analyze the types of modeling approaches useful in CER  
- Summarize the type of questions that can be answered by modeling  
- Discuss uses of simulation to answer a CER question  
- Consider the limitations and challenges of modeling and simulation in CER

**In-class activities:**  
- Pre-class evaluation of session #8 video lesson, required readings and class activities  
- Facilitated discussion: scenarios where modeling might be considered, what modeling approaches could be appropriate, and how the modeling process could move forward.  
- Students will be provided with 3 papers to review in three groups and one member from each team will present and discuss the paper.

**Assignment to be completed before class:**  
- Required readings

**Required Readings:**

**Session 10.**  
*The role of stakeholders in CER*

**Session goal:**  
- Define the role stakeholders in CER and discuss how their involvement can occur in all phases of research.

**Session objectives:**  
- Differentiate the role of research subject, advisor, and stakeholder.  
- Summarize ways that stakeholder input is important in designing CER studies.  
- Recognize the role of stakeholders in the implementation stage of CER.  
- Analyze methods of obtaining, incorporating, and evaluating stakeholder input in CER.

**In-class activities:**  
- Pre-class evaluation of session #9 required reading and class activities  
- Small group discussions and presentations on identifying stakeholders
Assignment to be completed before class:
- Required readings
- Identify 1-2 stakeholder groups that you could engage to study the problem that you identified in Session #2. Prepare a ½ page summary that describes and justifies the role of the stakeholders, compare their perspectives of the problem with yours as the study’s principal investigator (PI), and how you propose to engage them to study your identified problem.

Required Readings:

Optional Readings and References:

**Session 11.**
*CER, health care quality and translating evidence into practice and policy*

Session goal:
- Summarize the how CER evidence is translated into practice and used to improve the quality of health care.

Session objectives:
- Describe how evidence is used to develop quality measures.
- Evaluate how evidence is translated and implemented into practice
- Summarize gaps in health care quality.
- Outline a toolbox and framework for dissemination and implementation of CER findings into practice.

In-class activities:
- Pre-class evaluation of session #10 required reading and class activities

Assignment to be completed before class:
- Required readings
- View Module #13 Translating CER Evidence into Practice, Policy and Public Health and Module #14 Translational Toolbox Available at http://media.cph.ohio-state.edu/Mediasite/Play/6c50a6e7bb4d4b1290737a5ac04871d01d
Required Readings:

Session 12.
CER and health care cost I

Session goal:
- Summarize how health care is finance in the US and compare to other countries.

Session objectives:
- Describe methods of payment for health care in the US.
- Compare health care coverage in other countries to the US.
- Discuss how cost of care has led to emergence of CER.

In-class activities:
- Pre-class evaluation of session #11 video lessons, required readings and class activities
- Students will be divided into 5 groups. Each will take up one of the following questions and then report to the class their deliberations discussing pros and cons of policies regarding the following and whether they will affect rising cost of health care:
  - Promote payment rates within global targets
  - Accelerate alternatives to fee-for-service payment
  - Use competitive bidding for all commodities
  - Simplify administrative systems for all payers
  - Require full price transparency
  - Ban physician self-referral
  - Reduce cost of defensive medicine

Assignment to be completed before class:
- Required readings

Required Readings:
3. Gluck M. Incorporating costs into CER. AcademyHealth Research Insights
4. Gawande A. Testing, testing: The health-care bill has no master plan for curbing costs. Is that a bad thing? The New Yorker December 14, 2009 Available at: http://www.newyorker.com/reporting/2009/12/14/091214fa_fact_gawande

Session 13.
CER and health care cost II

Session goal:
Discuss the role of CER in health care policy, cost-effectiveness, and decisions about what is covered by insurance.

Session objectives:
- Describe cost of care and compare to other nations.
- Summarize the arguments for and against using cost in CER studies
- Discuss IOM and PCORI stands using cost in CER

In-class activities:
- Pre-class evaluation of session #12 required readings and class activities
- Debate: Should cost be used in CER studies?

Assignment to be completed before class:
- Required readings
- View CER Lesson #19 and #22 Available at http://ctsa-cermethodscourse.org/cer-lessons/

Required Readings:
3. Saha S. Giving teeth to comparative effectiveness research-The Oregon experience. NEJM February 18, 201.

Session 14.
PCOR funding opportunities—current and future

Session goals:
- Summarize funding opportunities in CER and how the elections will affect it.

Session objectives:
- Summarize funding opportunities through PCORI, AHRQ, NIH and other sources
- Describe some of the elements needed for successful PCOR and CER grant applications
- Guesses about the future

In-class activities:
- Pre-class evaluation of session #13 video lessons, required readings and class activities
- Review an RFA from PCORI and develop an outline of response. Available at: http://www.pcori.org/assets/PFA-Assessment-of-Options-05222012.pdf

Assignment to be completed before class:
- Required readings
- View video: Seeing through the eyes of patients: The Patient-Centered Outcomes Research Institute Funding Announcements http://annals.org/article.aspx?articleID=1262303
• Review the Patient-Centered Outcomes Research Institute Website. Available at: http://www.pcori.org/

Required Readings:

Session 15.
Advanced Analytics and Design Issues in CER

Session goal:
• Introduce complex designs and analysis methods used in CER.

Session objectives:
• Describe study designs that incorporate nesting, and adaptive and personalized (e.g. biomarker based) treatment strategies.
• Describe analysis methods for causal models, prognostic modeling, or estimating individualized treatment effects.
• Provide an overview of how to apply the most appropriate methods.

In-class activities:
• Pre-class evaluation of session #14 video lesson, required readings and class activities
• Team and class discussion of pros and cons for several different designs and analysis methods.

Assignment to be completed before class:
• Required readings

Required Readings:

Session 16.
Review of the course and Q and A

Session goal:
• Review main course objectives and explore further questions about CER.

In-class activities:
• Pre-class evaluation of session #15 required readings and class activities

Assignment to be completed before class:
• None

Required Readings:
• None