TSCI 6060: Patient Oriented Clinical Research Methods 2

Spring 2018

CLASS DAYS and TIME: Mondays (January 8 – April 30, 2018), 3:00 – 5:00 pm

CLASSROOM: LIB 2.015

COURSE DIRECTORS: Byeongyeob Choi, PhD

OFFICE LOCATION and HOURS: ADM 3.314, Monday – Friday (8:00 am – 5:00 pm by appointment)

EMAIL: ChoiB@uthscsa.edu

TELEPHONE: 210-567-0854

READ THIS DOCUMENT CAREFULLY – YOU ARE RESPONSIBLE FOR ITS CONTENTS

COURSE DESCRIPTION AND OBJECTIVES

This interdisciplinary course is the first in a two-semester sequence designed to train participants in the conduct of patient-oriented clinical research.

Pre-requisites – TSCI 5071 is the only pre-requisite for this course.
Semester credit hours – 2.0 SCH

LEARNING OBJECTIVES and COMPETENCIES

By the end of the course, degree candidates will be able to:

1. Propose study designs for prospectively addressing a translational research question.
2. Assess the strengths and weaknesses of possible prospective study designs for a given translational research questions (cohort studies and clinical trials).
3. Identify existing appropriate measures (assessments of baseline characteristics and outcomes) of translational research.
4. Assess threats to study validity (bias) including problems with sampling, recruitment, randomization, and comparability of study groups.
5. Assess internal validity in any planned or completed clinical or translational study, including selection bias, misclassification, and confounding.
6. Define criteria for inferring causation from observational investigations.
7. Design strategies for subject retention in a study.
8. Design strategies for monitoring progress in a randomized controlled trial.
9. Delineate strategies for minimizing bias in cohort studies and randomized controlled trials.
10. Describe the processes and purposes of using propensity scoring in cohort studies

11. Compare and contrast the uses, strengths, and weaknesses of different clinical trial designs.
12. Critically appraise research reports of cohort studies and randomized controlled trials.
    a. Utilize the STROBE guidelines for assessing an observational study
    b. Utilize the CONSORT statements for assessing a clinical trial
13. Describe the steps in conducting a meta-analysis.
14. Demonstrate knowledge of community-engaged research approaches, including strategies for identification, development, and maintenance of community partnerships.
15. Compare the feasibility, efficiency, and ability to derive unbiased inferences from different translational research study designs (cohort studies and clinical trials).
16. Describe the basic principles and practical importance of random variation, systematic error, sampling error, measurement error, hypothesis testing, type I and type II errors, and confidence limits.
17. Defend the significance of data and safety monitoring plans.
18. Explain the uses, importance, and limitations of early stopping rules in clinical trials.
19. Describe the roles of comparative effectiveness research in the organization of health care and health care policy

COURSE ORGANIZATION

The main teaching modalities used in this course include:

1. Lectures
2. Class discussions requiring active student participation.

Materials:

No special materials are required for this course.

Computer Requirements:

Students are required to have a laptop computer that can connect to and operate over a wireless network.

Software required:

- Microsoft Office Suite (A personal copy of the latest version can be purchased at The UTHSCSA bookstore at student pricing with a student ID)

Laptops with an Apple based Operating System must be able to also operate using a Windows based Operating System. It may be necessary to purchase Windows (student pricing available at The UTHSCSA bookstore with a student ID) and virtualization software.

All laptops will connect to The UTHSCSA network via the HSCwave broadcast wireless connection. Authentication for wireless use is based on The UTHSCSA domain username and password.

Verification of proper operation **prior** to the start of class is highly recommended.

Assistance is available thru the IMS Service Desk

- Telephone:(567-7777
- E-mail (ims-servicedesk@uthscsa.edu)

Assistance is also available at the IMS Student Support Center (4.421T, DTL).

Reading Assignments – Reading assignments will be listed in the individual class sections of this syllabus.

ATTENDANCE

Attendance at scheduled classes and examinations is crucial to meeting course objectives. Therefore, regular attendance in class is expected of each student.

- Attendance is defined as being present within 15 minutes after the scheduled beginning of the class and until 15 minutes before the scheduled ending of the class.
- Excused absences may be granted by the Course Director in cases such as formal presentations at scientific meetings, illness, or personal emergency.
- Excused absences are considered on an individual basis and require electronic communication with the Course Director to request an excused absence. The e-mail request to the Course Director for consideration of an excused absence must provide details regarding the circumstances and specific dates.
- It is expected that students will provide *advanced notice* of absence for scheduled events.
- If a student has excessive unexcused absences in a given course, they will automatically receive a grade of *unsatisfactory* unless *makeup* has been approved by the Course Director.
- Makeup of absences (both excused and unexcused) is allowed at the discretion of the Course Director.
- Allowable unexcused absences will be determined by the credit hours of the course as follows:

Course Semester Credit Hours	Allowable Unexcused Absences
3.0	3
2.0	2
1.0	1

TEXTBOOKS

Required:

- **"Designing Clinical Research"**, *Fourth Edition*; Hulley SB, Cummings SSR, Browner WS, Grady DG, Newman TB; Lippincott Williams & Wilkins, a Wolters Kluwer Business, Philadelphia, PA 2015; **ISBN/ISSN: 9781608318049**
- **"Causal inference"**; Hernan MA, Robins JM; Boca Raton: Chapman & Hall/CRC, 2018 (forthcoming)

GRADING POLICIES AND EXAMINATION PROCEDURES

1. Class attendance is essential for anyone who wishes to obtain credit for the course. You must attend 14 of the 16 lectures in order to obtain credit for the course. You can make up any sessions missed due to unexpected schedule conflicts, professional travel, or other extenuating circumstances, provided you contact your course director as soon as you know you will need to miss a class. Any student who fails to meet this requirement will receive an UNSATISFACTORY grade for the course.
2. Three assignments are to be completed during the semester. These assignments are posted on Blackboard. Each assignment will be scored on a 100-point scale. ***You must complete and turn-in all 3 assignments on time and receive a minimum score of 70/100 points on each assignment in order to receive credit for the course.***
    a. A student who completes at least 2 of the assignments with 70/100 points, but fails to complete the 3rd assignment with a score of 70/100 points, will receive an incomplete.
    b. A student who completes less than 2 of the assignments with a score of 70/100 points will receive an UNSATISFACTORY grade for the course.
3. A student who receives an INCOMPLETE must meet with the Course Director and develop a plan of action to complete the outstanding work. All outstanding work must be completed within 6 months after the end of the course; otherwise the grade will be changed to UNSATISFACTORY.
4. A student who receives an UNSATISFACTORY grade must retake the course in order obtain a change of grade.

Grading System

The grading will be conducted on a pass fail basis and both assignments need a Satisfactory in order to pass the course.

S = Satisfactory U = Unsatisfactory

REQUESTS FOR ACCOMODATIONS FOR DISABILITIES

In accordance with policy 4.2.3, **Request for Accommodation Under the ADA and the ADA Amendments Act of 2008 (ADAAA)**, any student requesting accommodation must submit the appropriate request for accommodation under the American with Disabilities Act (ADA, form 100). To his/her appropriate Associate Dean of their School and a copy to the ADA Coordinator. Additional information may be obtained at http://uthscsa.edu/eeo/request.asp.

ACADEMIC INTEGRITY AND PROFESSIONALISM

Any student who commits an act of academic dishonesty is subject to discipline as prescribed by the UT System Rules and Regulations of the Board of Regents. Academic dishonesty includes, but is not limited to, cheating, plagiarism, collusion, the submission for credit of any work or materials that are attributable in whole or in part to another person, taking an exam for another person, signing attendance sheets for another student, and any act designed to give unfair advantage to a student or the attempt to commit such an act. Additional information may be obtained at http://catalog.uthscsa.edu/generalinformation/generalacademicpolicies/academicdishonestypolicy/

TITLE IX AT UTHSCSA

Title IX Defined:
Title of the Education Amendments of 1972 is a federal law that prohibits sex discrimination in education. It reads "no person in the United States shall, on the basis of sex, be excluded from participation in, be denied the benefits of, or be subjected to discrimination under any education program or activity receiving Federal financial assistance."

University of Texas Health Science Center San Antonio's Commitment:
University of Texas Health Science Center San Antonio (UTHSCSA) is committed to maintaining a learning environment that is free from discriminatory conduct based on gender. As required by Title IX, UTHSCSA does not discriminate on the basis of sex in its education programs and activities, and it encourages any student, faculty, or staff member who thinks that he or she has been subjected to sex discrimination, sexual harassment (including sexual violence) or sexual misconduct to immediately report the incident to the Title IX Director.

In an emergency, victims of sexual abuse should call 911. For non-emergencies, they may contact UPD at 210-567-2800. Additional information may be obtained at http://students.uthscsa.edu/titleix/

EMAIL POLICY

All correspondence will be sent to the student using the student's LiveMail address and CANVAS. All correspondence from the student to the course director should be sent to the course director's e-mail as listed on the first page of this syllabus.

USE OF RECORDING DEVICES

Only with course director's or instructor's permission.

ELECTRONIC DEVICES

Cell phones must be turned off during all class meetings and exams. Computers and electronic tablets are allowed only for participating in classroom activities (*e.g.*, viewing slides presented in lecture or conference materials). No texting, tweeting, e-mailing, web-surfing, gaming, or any use of electronic devices that is not directly connected with classroom activities is permitted.

All Classes Held in ROOM 2.015

Week	Date	Title
1	1/8/2018	A Definition of Causal Effect (Choi)
2	1/15/2018	**NO CLASS – Martin Luther King Day**
3	1/22/2018	Retention of Subjects and Minimizing Bias in Prospective Studies (Hazuda)
4	1/29/2018	Randomized experiments (Choi)
5	2/5/2018	Group Interventions – Community Studies (Valerio)
6	2/12/2018	Clinically based cohort studies (Espinoza)
7	2/19/2018	Observational studies (Choi)
8	2/26/2018	Propensity score (Choi)
9	3/5/2018	Drug Development – Phase I Trials (Gelfond)
10	3/12/2018	Instrumental variable analysis (Choi)
11	3/19/2018	**NO CLASS – Spring Break**
12	3/26/2018	Randomized Controlled Trials (Michalek)
13	4/2/2018	Comparative Effectiveness Research (Turner)
14	4/9/2018	Multi-center Clinical Trials and Stopping Rules (Michalek)
15	4/16/2018	Reading the Literature – Randomized Controlled Trials (Gelfond)
16	4/23/2018	Meta-analysis (Shah)
17	4/30/2018	Student presentation

Patient Oriented Clinical Research Methods 2
Week: 1
Date: January 8, 2018
Topic: A Definition of Causal Effect
Instructors: Byeongyeob Choi, PhD
Learning Objectives and Competencies: 1. Understand a counterfactual outcome framework for causal inference 2. Understand a difference between a causal effect and an associational effect
Class Assignment:
Readings: Hernan and Robins: **Causal inference** – Chapter 1

Patient Oriented Clinical Research Methods 2
Week: 2
Date: January 15, 2018
Instructors:
Topic: **NO CLASS – Martin Luther King Day**

Patient Oriented Clinical Research Methods 2
Week: 3
Date: January 22, 2018
Instructors: Helen Hazuda, Ph.D.
Topic: Retention of Subjects and Minimizing Bias in Prospective Studies
Learning Objectives and Competencies – Participants will be able to: 1. Create plans for tracking subjects within a cohort study or randomized controlled trial. 2. Identify key strategies for retaining subjects enrolled within a cohort study or clinical trial 3. Discuss methods for assessing potential bias attributable to dropping out from prospective studies 4. Describe procedures for ascertaining mortality in cohort studies, especially use of the National Death Index. 5. Describe methods of assessing co-interventions during randomized controlled trials. 6. Discuss the effects of cross-over between study arms of randomized controlled trials.
Class Assignment: Using table 7.3 in Hulley and Cummings as a framework, be prepared to discuss the necessary resources needed to put a tracking system in place for a cohort study, techniques for staying in touch with participants, and how you would prepare and justify a budget to support these resources.
Readings and Bibliography: 1. Hulley and Cummings: **Designing Clinical Research** - Chapter 7, table 7.3 – page 95 2. Hulley and Cummings: **Designing Clinical Research**, Chapter 11 – Alternative Clinical Trial Designs and Implementation Issues, pp. 151-170 3. Review National Death Index Information at: http://www.cdc.gov/nchs/ndi.htm

Patient Oriented Clinical Research Methods 2
Week: 4
Date: January 29, 2018
Topic: Randomized experiments
Instructors: Byeongyeob Choi, PhD
Learning Objectives and Competencies: 1. Understand the concept of exchangeability for causal inference 2. Learn statistical methods to obtain causal effects
Class Assignment:
Readings: Hernan and Robins: **Causal inference** – Chapter 2

Patient Oriented Clinical Research Methods 2
Week: 5
Date: February 5, 2018
Topic: Group Interventions – Community Studies
Instructors: Melissa Valerio, DrPH
Learning Objectives and Competencies – Participants will be able to: 1. Describe the steps necessary to garner community support for group intervention studies 2. Discuss strategies for assessing the effect of community interventions 3. Identify data sources that may be used to monitor outcomes in community studies
Class Assignment: Read assigned material and be prepared to discuss.
Readings and Bibliography: Handouts to be circulated prior to class. Hulley and Cummings: **Designing Clinical Research**, Chapter 18, Community and International Studies, pp 268-276.

Patient Oriented Clinical Research Methods 2
Week: 6
Date: February 12, 2018
Topic: Clinically Based Cohort Studies
Instructors: Sara Espinoza, MD, M.Sc.
Learning Objectives and Competencies – Participants will be able to: 1. Develop procedures for identifying and recruiting subjects from clinical settings. 2. Discuss effects of differing stages of disease on entry into cohort and generalizability. 3. Describe procedures for maintaining confidentiality of subject records for research purposes in a clinical setting.
Class Assignment: Read assigned material and be prepared to discuss.
Readings and Bibliography: Handouts to be circulated prior to class.

Patient Oriented Clinical Research Methods 2
Week: 7
Date: February 19, 2018
Topic: Observational studies
Instructors: Byeong Choi, PhD

Learning Objectives and Competencies – Participants will be able to: 1. Learn key concepts needed to make causal inference from observational studies.
Class Assignment: Read assigned material and be prepared to discuss.
Readings: Hernan and Robins: **Causal inference** – Chapter 3

Patient Oriented Clinical Research Methods 2
Week: 8
Date: February 26, 2018
Topic: Propensity Scores in Cohort Studies
Instructor: Byeong Choi, PhD
Learning Objectives and Competencies – Participants will be able to: 1. Articulate the utility of propensity scores in the analysis of observational cohort studies 2. Compare and contrast the relative strengths and weaknesses of propensity scores for cohort studies compared to the conduct of a randomized controlled trial
Class Assignment: Read the assigned material and be prepared to discuss in class
Readings and Bibliography: 1. Handouts and assigned reading prior to class

Patient Oriented Clinical Research Methods 2
Week: 9
Date: March 5, 2018
Topic: Drug Development – Phase I Studies
Instructors: Jonathan Gelfond, MD, PhD
Learning Objectives and Competencies – Participants will be able to: 1. Describe the purposes of a Phase I study of a new therapeutic agent 2. Define maximum tolerated dose 3. Discuss the potential benefits, if any, for a subject participating in a Phase I study. 4. Describe methods for enrolling subjects at different dosing levels, and the rationale for moving to the next dosing level.
Class Assignment: Read assigned material and be prepared to discuss
• Readings and Bibliography: – PDF File available on Blackboard: • Roberts TG, Jr., Goulart BH, Squitieri L, et.al., Trends in the Risks and Benefits to Patients with Cancer Participating in Phase 1 Clinical Trials. JAMA 2004; 292:2130-2140.

Patient Oriented Clinical Research Methods 2
Week: 10
Date: March 12, 2018

Topic: Instrumental Variable Analysis
Instructor: Byeong Choi, PhD
Learning Objectives and Competencies 1. Learn conditions and examples of an instrumental variable 2. Computation of an instrumental variable estimator
Class Assignment: Read the assigned material and be prepared to discuss in class
Readings and Bibliography: 1. Handouts and assigned reading prior to class

Patient Oriented Clinical Research Methods 2
Week: March 19
Date: March 13, 2018
Instructors:
Topic: **NO CLASS – Spring Break**

Patient Oriented Clinical Research Methods 2
Week: 12
Date: March 26, 2018
Topic: Randomized Controlled Trials
Instructors: Joel Michalek, PhD
Learning Objectives and Competencies – participants will be able to: 1. Contrast the strengths and weaknesses of an experimental vs. observational study. 2. Describe the purpose and rationale for randomization 3. Develop inclusion criteria and describe rationales for excluding persons from entry into a study. 4. Describe the importance of and methods for masking (blinding) the outcome assessment.
Class Assignment: Read assigned material and be prepared to discuss.
Readings and Bibliography: 1. Hulley and Cummings: **Designing Clinical Research**, Chapter 10 – Designing a Randomized Blinded Trial, pp. 147-162

Patient Oriented Clinical Research Methods 2
Week: 13
Date: April 2, 2018
Topic: Comparative Effectiveness Research (CER)
Instructor: Barbara Turner, MD
Learning Objectives and Competencies – Participants will be able to: 1. Describe the difference between efficacy and effectiveness studies 2. Design studies using a non-inferiority design when appropriate to the question 3. Explain the role of registries in CER 4. Explain key features of pragmatic trial design and is able to design a pragmatic trial 5. Identify sources of existing data for observational research including electronic health records and administrative claims 6. State the strengths and limitations of different data and the sources of bias and threats to internal validity in each 7. Identify the strengths and limitations of the study designs used in CER
Class Assignment: Read the assigned material and be prepared to discuss
Readings and Bibliography: 2. Handouts and assigned reading prior to class

Patient Oriented Clinical Research Methods 2
Week: 14
Date: April 9, 2016
Topic: Multi-Center Clinical Trials, Monitoring Trial Progress and Stopping Rules
Instructors: Joel Michalek, PhD
Learning Objectives and Competencies – Participants will be able to: 1. Describe procedures for organizing and conducting multi-center clinical trials. 2. Develop methods for monitoring clinical trial progress 3. Describe techniques for decisions to stop clinical trials 4. Discuss the effects of repeated interim analyses on study power to detect primary outcomes.
Class Assignment: Read assigned material and be prepared to discuss

Readings and Bibliography:

1. Hulley and Cummings: **Designing Clinical Research**, Chapter 11 – Alternative Trial Designs and Implementation Issues, pp. 163-182
2. Handouts to be circulated prior to class.

Patient Oriented Clinical Research Methods 2
Week: 15
Date: April 16, 2018
Topic: Reading the Literature – Randomized Controlled Trials
Instructors: Jon Gelfond, MD, PhD
Learning Objectives and Competencies – Participants will be able to: 1. Critically assess a published report of a randomized controlled clinical trial 2. Assess the eligibility and exclusion criteria for subjects and their relation to ones own work. 3. Determine whether the randomization process was successful 4. Determine whether the outcome assessments were appropriately and completely ascertained. 5. Assess the clinical and statistical impact of the reported outcomes. 6. Identify criteria for what should be expected to be included in a published report of a randomized controlled clinical trial.
Class Assignment: • Read assigned material and be prepared to discuss in class. • Review the CONSORT STATEMENT. • Then take the randomized trial of palliative medicine in non-small cell lung cancer and rate the report against the CONSORT guidelines.
Readings and Bibliography: 1. Randomized Controlled Trial: • Granger, C.B., Alexander, J.H., McMurray, J.J., Lopes, R.D., Hylek, E.M., Hanna, M., Al-Khalidi, H.R., Ansell, J., Atar, D., Avezum, A. and Bahit, M.C., 2011. Apixaban versus warfarin in patients with atrial fibrillation. *New England Journal of Medicine*, *365*(11), pp.981-992. 2. The CONSORT Statement: • Moher D, Schulz KF, Altman DG, for the CONSORT Group. The CONSORT Statement: Revised Recommendations for Improving the Quality of Reports of Parallel-Group Randomized Trials. Ann Intern Med 2001; 134:657-662. • Altman DG, Schulz KF, Moher D, Egger M, Davidoff F, Elbourne D, Gotzsche PC, Lang T, for the CONSORT Group. The Revised CONSORT Statement for Reporting Randomized Trials: Explanation and Elaboration. Ann Intern Med 2001; 134:663-694. • Ioannidis JPA, Evans SJW, Gotzshe PC, et.al. Better Reporting of Harms in Randomized Trials: An Extension of the CONSORT Statement. Ann Intern Med 2004; 141:781-788.

Patient Oriented Clinical Research Methods 2
Week: 16
Date: April 23, 2018
Topic: Meta-Analysis
Instructors: Dimpy Shah
Learning Objectives and Competencies – Participants will be able to: 1. Identify and apply assessment tools for determining the quality of published randomized controlled trials. 2. Describe the underlying mathematical principles for pooling results in a meta-analysis. 3. Take data from several randomized controlled trials, pool them, and calculate summary statistics of the resulting odds ratio.
Class Assignment: Read assigned material and be prepared to discuss
Readings and Bibliography: 1. Hulley and Cummings: **Designing Clinical Research**, Chapter 13 – Research Using Existing Data, pp. 192-207. 2. Handouts to be circulated prior to class.