TSCI 6061

Patient-Oriented Clinical Research Biostatistics-2

Spring 2018

CLASS DAYS and TIME: Thursdays (January 11 – May 11, 2017), 2:30 – 4:30 pm

CLASSROOM: LIB 2.015

COURSE DIRECTOR: Jonathan Gelfond, MD, PhD

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

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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 – Patient-Oriented Clinical Research Biostatistics-1.
Semester credit hours – 2.0 SCH

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

1. Use graphical tools to discover useful patterns in a data set and to describe statistical results
2. Interpret and present descriptive statistics in oral and written form.
3. Understand the role of random processes in nature and in the conduct of medical research.
4. Apply fundamental principles of statistical analysis to collection, preparation, analysis, and interpretation of data in medical research
5. Analyze, interpret and present results from randomized and non-randomized studies comparing two or more groups.
6. Analyze, interpret and present results from regression analyses with continuous and binary response variables.
7. Understand and use multivariable models to assess risk factors for clinical events measured either as a single time point or as a time to-event endpoint.
8. Understand and use methods of randomization in the design and execution of clinical experiments.
9. Analyze, interpret and present results from randomized clinical experiments, including randomized controlled clinical trials.
10. Understand, use, and interpret univariate and multivariable models to explain patient variation in time-to-event data.

COURSE ORGANIZATION

The main teaching modalities used in this course include:

1. Lectures
2. In-class data analysis
3. In-class discussions

Materials:

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)
- R & RStudio (Open source, free, latest version)
  https://www.rstudio.com/products/RStudio/
  https://www.r-project.org/

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:

1. ***Textbooks (required)***

   Kirkwood BR, Sterne JA. *Essential medical Statistics*. Malden, MA: Blackwell Science Ltd, 2003.

2. ***Textbooks (recommended)***

   Grolemund, G., Wickham, H. *R for data science*. O'Reilly, 2017. (Full text available at http://r4ds.had.co.nz/)

   Kabacoff, Robert. *R in action: data analysis and graphics with R*. Manning Publications Co., 2015.

   Lander, Jared P. *R for Everyone: Advanced Analytics and Graphics*. Pearson Education, 2014.

   Lang TA, Secic M. *How to report statistics in medicine: Annotated guidelines for authors, editors, and reviewers (2nd Ed.).* Philadelphia, PA: American College of Physicians, 2006.

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 data analysis 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 data analysis 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

Include a grading scale used to determine final grades, see example below

S = Satisfactory U = Unsatisfactory

A = 90-100% B = 80-89% C = 70-79% F = < 69%

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.

TENTATIVE CLASS SCHEDULE

TSCI 5072
Patient-Oriented Clinical Biostatistics – 1
Fall2016

Week	Date	Module	Title/Instructor(s)
1	01/11/2018	**Study Design And Linear Regression**	Study Planning and Sample Size Estimation (Lectures given by course instructor)
2	01/18		Linear Regression and Correlation
3	01/25		Multiple linear regression and goodness of fit
4	02/01		Linear regression examples
5	02/08		Introduction to estimating diagnostic accuracy
6	02/15	**Binary and Censored Outcomes**	Logistic regression and diagnostic accuracy
7	02/22		Logistic regression controlling for confounding
8	03/01		Practical examples of logistic regression
9	03/08		Survival analysis: life tables and product-limit estimators
10	03/15		Spring Break No Class
11	03/22		Survival analysis with Cox proportional hazard model
12	03/29		Practical examples of Cox PH model
13	04/05	**Clinical Trials and Longitudinal data**	Completely randomized groups
14	04/12		Introduction to longitudinal data
15	04/19		Modeling longitudinal data
16	04/26		Practical examples of longitudinal data analysis
17	05/03		Meta-Analysis
18	05/10		Review (If needed)

Week: 1
Date: January 11, 2018 (3:00 - 5:00 pm)
Room: LIB 2.015
Instructor(s): Gelfond
Topic: Study Planning and Sample Size Estimation

Learning Objectives and Competencies– Participants will be able to:

1. Compute sample size for binary outcome.
2. Compute sample size for continuous outcomes.
3. Consider multiple testing in power analysis.
4. Write simple power analysis section for a protocol.

Class Assignment: None.

Readings:

- Chapter 34: Linking Analysis to Study Design
- Chapter 35: Calculation of Required Sample Size
- Chapter 38: Strategies for Analysis

Week: 2

Date: January 18

Room: LIB 2.015

Instructor(s): Gelfond

Topic: Linear regression and correlation

Learning Objectives and Competencies– Participants will be able to:

1. Compute correlation and regression coefficients.
2. Interpret and report correlation and regression coefficients.
3. Create graphical summaries of regression analyses.

Class Assignment: Students will operate R software to perform basic functions.

Readings:

- Kirkwood and Stern: Chapter 10
- Lang A, Secic M. How to report statistics in medicine:

Week: 3

Date: January 25

Room: LIB 2.015

Topic: Multiple linear regression and goodness of fit.

Instructor(s): Jonathan Gelfond, MD, PhD

Learning Objectives – Participants will be able to:

1. Compute estimates for multiple regression.
2. Compute and interpret common measures of model fit.
3. Perform model selection techniques

Class Assignment: Read assigned material and be prepared to discuss.

Readings:

- Kirkwood and Stern: Chapter 11, 12

Week: 4

Date: February 1

Room: LIB 2.015

Topic: Linear regression examples

Instructor(s): Jonathan Gelfond, MD, PhD

Learning Objectives – Participants will be able to:

1. Read in regression data set.
2. Construct multiple regression assessment and report.
3. Create graphics representing multiple regression.

Class Assignment: Read assigned material and come to class prepared to discuss.
Readings: Handouts to be distributed prior to class.

Week: 5
Date: February 8
Room: LIB 2.015
Topic: Introduction to diagnostic accuracy
Instructor(s): Jonathan Gelfond, MD, PhD
Learning Objectives – Participants will be able to: 1. Compute, estimate, report diagnostic measures sensitivity, specificity, PPV, NPV 2. Create AUC graphics
Class Assignment: Read assigned material and be prepared to discuss.
Readings: Chapter 14: Probability, Risk and Odds of Disease Chapter 36.2 The Evaluation of diagnostic Tests

Week: 6
Date: February 15
Room: LIB 2.015
Topic: Logistic regression and diagnostic accuracy
Instructor(s): Jonathan Gelfond, MD, PhD
Learning Objectives – participants will be able to: 1. Perform logistic regression. 2. Use logistic regression models to make predictions. 3. Estimate the accuracy of logistic regression models.
Class Assignment: Read assigned material and be prepared to discuss.
Readings: Chapter 19: Logistic Regression: comparing 2 or more exposure groups

Week: 7

Date: February 22

Room: LIB 2.015

Topic: Logistic regression and controlling for confounding

Instructor(s): Jonathan Gelfond, MD, PhD

Learning Objectives – Participants will be able to:

1. Fit multiple logistic regression models.
2. Test model fit for logistic regression.
3. Explain and distinguish collinearity, confounding, and mediating effects.

Class Assignment: Read assigned material and be prepared to analyze data and discuss.

Readings:

- Chapter 18: Controlling for Confounding: stratification
- Chapter 20: Logistic Regression: Controlling for confounding and other extensions

Week: 8

Date: March 1

Room: LIB 2.015

Topic: Practical Examples of logistic regression

Instructor(s): Jonathan Gelfond, MD, PhD

Learning Objectives – Participants will be able to:

1. Fit, interpret, and report logistic regression models.
2. Perform model selection for logistic regression models.
3. Automate and document logistic regression models.

Class Assignment: Read assigned material and be prepared to analyze data and discuss.

Readings and Bibliography:

Week: 9

Date: March 8

Room: LIB 2.015

Topic: Survival analysis: life tables and product-limit estimators

Instructor(s): Jonathan Gelfond, MD, PhD

Learning Objectives – Participants will be able to:

1. Define censoring.
2. Use patient data with censored event times to improve estimation of event rate.
3. Perform Kaplan-Meier and log-rank analyses.

Class Assignment: Read assigned material and be prepared to analyze data and discuss.

Readings:

1. Chapter 26: Survival Analysis: Displaying and Comparing Survival Patterns

Week: 10

Date: March 15

Room: LIB 2.015

Topic: Spring Break

Instructor(s): Jonathan Gelfond

Learning Objectives – Through homework and class room activities, participants will be able to:

Class Assignment: Read assigned material and be prepared to analyze data and discuss.

Readings: To be announced.

Week: 11

Date: March 22

Room: LIB 2.015

Topic: Survival analysis with Cox proportional hazards model

Instructor(s): Jonathan Gelfond, MD, PhD

Learning Objectives- Participants will be able to:

1. Describe proportional hazards assumption.
2. Interpret hazard ratios.
3. Fit Cox proportional hazard model.

Class Assignment: Read assigned material and be prepared to discuss.

Readings:

- Kirkwood and Stern: Chapter 27 Regression analysis of survival data

Week: 12

Date: March 29

Room: LIB 2.015

Topic: Practical examples of Cox proportional hazards model

Instructor(s): Jonathan Gelfond, MD, PhD

Learning Objectives – Participants will be able to:

1. Fit multivariable Cox model.
2. Perform diagnostic tests of proportional hazards assumption.
3. Interpret and report Cox models.

Class Assignment: Read assigned material and be prepared to analyze data and discuss.

Readings: To be announced

Week: 13

Date: April 5

Topic: Completely randomized groups

Room: LIB 2.015

Instructor(s): Jonathan Gelfond, MD, PhD

Learning Objectives – Participants will be able to:

1. Explain the role of randomization and stratification in clinical trials.
2. Perform tests of the primary hypothesis using t-tests, chi-square, and Cox models.
3. Assess patient flow in a clinical trial

Class Assignment: Read assigned material and be prepared to analyze data and discuss.

Readings:

Kirkwood and Stern: Chapters 8 and 9

Week: 14

Date: April 12

Topic: Introduction to longitudinal data

Room: LIB 2.015

Instructor(s): Jonathan Gelfond, MD, PhD

Learning Objectives – Participants will be able to:

1. Explain correlation between repeated measures.
2. Test time by treatment interactions.

3. Explain covariance matrix models such as compound symmetric and unstructured.

Class Assignment: Read assigned material and be prepared to analyze data and discuss.

Readings:

- Chapter 31: Analysis of Clustered Data
- Vickers. Use of Percentage Change (pdf)

Week: 15

Date: April 19

Room: LIB 2.015

Topic: Modeling longitudinal data

Instructor(s): Jonathan Gelfond, MD, PhD

Learning Objectives – Participants will be able to:

1. Fit linear mixed effect models.
2. Test various covariance model assumptions.
3. Perform model diagnostics for mixed effect models.

Class Assignment: Read assigned material and be prepared to analyze data and discuss.

- **Readings:** Chapter 31: Analysis of Clustered Data
- Vickers. Use of Percentage Change (pdf)
- Gueorguieva, Krystal. Move Over Anova (pdf)

Week: 16

Date: April 26

Room: LIB 2.015

Topic: Practical examples of longitudinal data analysis

Instructor(s): Jonathan Gelfond MD, PhD

Learning Objectives – Participants will be able to:

1. Fit linear mixed effect models.
2. Test various covariance model assumptions.
3. Perform model diagnostics for mixed effect models.

Class Assignment: Read assigned material and be prepared to analyze data and discuss.

Readings: To be announced.

Week: 17

Date: May 3

Room: LIB 2.015

Topic: Meta-analysis

Instructor(s): Jonathan Gelfond, MD, PhD

Learning Objectives – Participants will be able to:

1. Explain key difficulties in meta-analysis (PICO).
2. Describe multiple methods for meta-analysis.
3. Describe systematic review component within a meta-analysis.

Class Assignment: Read assigned material and be prepared to analyze data and discuss.

Readings:

- Chapter 32: Systematic Reviews and Meta-analysis
- Cornell JE, Mulrow C. Meta-analysis (pp. 285-323).
- In HJ Adèr and GJ Mellenbergh (Eds.), Research Methodology in the Social, Behavioral, and Life Sciences.

London: SAGE Publications,1999

Week: 18 (if needed)

Date: May 10

Room: LIB 2.015

Topic: Review of course

Instructor(s): Jonathan Gelfond, MD, PhD

Learning Objectives – Participants will be able to:

1. Describe linear, logistic, and Cox proportional hazards regression models.
2. Describe measures of diagnostic test accuracy
3. Explain covariance matrices and mixed effect models.

Class Assignment: Read assigned material and be prepared to analyze data and discuss.

Readings: