

TSCI 6069
Statistical Issues, Planning, And Analysis of Contemporary Clinical Trials

Spring Semester 2018

CLASS DAYS and TIME: Thursday 3-5 pm

CLASSROOM: LIB 2.088

COURSE DIRECTOR: Joel Michalek PhD FASA

OFFICE LOCATION and HOURS: 314.9 Human Resources Building, Monday 2-3 pm

EMAIL: michalekj@uthscsa.edu

TELEPHONE: 210 567-0886, cell 210 326-6331

READ THIS DOCUMENT CAREFULLY – YOU ARE RESPONSIBLE FOR ITS CONTENTS

COURSE DESCRIPTION AND OBJECTIVES

This elective course will serve as an in-depth survey of the various clinical trial designs, analysis, and regulatory issues. Students will learn to apply statistical principles in designing clinical trials to minimize risk to patients while maximizing generalizable discovery. Specific topics include Phase I-V studies, adaptive designs, longitudinal and survival studies. Students will learn to specify the primary outcome and to estimate the required sample size for common trial designs. Clinical trial design and analysis is often complicated by idiosyncrasies such as missing data, and the methodology for handling these will be covered.

Pre-requisites – Prerequisites: TSCI 5072 and TSCI 6061.

Semester credit hours – 2 credit hours

By the end of this course, each student should be able to:

- Understand and implement standard designs for Phase I, II, and III clinical trials
- Analyze, interpret, and present results
- Write statistical methods paragraphs for clinical trial protocols and grant applications

COURSE ORGANIZATION

The main teaching modalities used in this course include:

1. Lectures
2. In class data analysis
3. In class discussion

Materials:

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).

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 (ALTC 106).

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

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

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

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/eo/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 6069
Statistical Issues, Planning, And Analysis of Contemporary Clinical Trials
Spring Semester 2018

Week	Date	Module	Title/Instructor(s)
1	11 Jan		Introduction
2	18 Jan		Phase III multicenter parallel group – Therapeutic Rheumatology
3	25 Jan		Phase II Simon 2-stage – Therapeutic Cancer
4	1 Feb		Phase I Therapeutic - Cancer
5	8 Feb		Crossover Device – Emergency Medicine
6	15 Feb		Pharmacokinetics - Endocrinology
7	22 Feb		Power Calculations (Dr Choi)
8	1 Mar		Clustering device - Cardiology
9	8 Mar		Replicated N of 1 Therapeutic - Cancer
10	15 Mar		No class, Spring Break
11	22 Mar		Phase III Multicenter therapeutic - Trauma
12	29 Mar		Crossover therapeutic - Raynaud
13	5 Apr		Comparative Accuracy device - Cardiology
14	12 Apr		Stopping Rules
15	19 Apr		Phase III device - Endocrinology
16	26 Apr		ICH Guidelines
17	3 May		Summary

Week: 1
Date: January 11, 2018 (3:00 – 5:00 pm)
Room: LIB 2.088
Instructor(s): Michalek
Topic: Introduction
Learning Objectives and Competencies– Participants will be able to:
<ol style="list-style-type: none"> 1. List the three analysis populations in a Phase III trial 2. Describe a generic safety analysis 3. Describe a generic efficacy analysis
Class Assignment: None
Readings: None

Week: 2
Date: January 18, 2018 (3:00 – 5:00 pm)
Room: LIB 2.088
Instructor(s): Michalek
Topic: Phase III multicenter parallel group (therapeutic)
Learning Objectives and Competencies– Participants will be able to:
<ul style="list-style-type: none"> • List the major elements of a Phase III protocol • Describe a Consort Diagram • Summarize the assigned study
Class Assignment: See assigned reading on Base Camp
Readings:
<ul style="list-style-type: none"> • Kirkwood and Stern: Chapter 34 • Lang A, Secic M. How to report statistics in medicine

Week: 3
Date: January 25, 2018 (3:00 – 5:00 pm)
Room: LIB 2.088
Instructor(s): Michalek
Topic: Phase II Simon 2-stage (therapeutic)
Learning Objectives and Competencies– Participants will be able to:
<ul style="list-style-type: none"> • Describe the hypothesis being tested by the Simon 2 –stage • Describe the Simon 2-stage procedure
Class Assignment: See assigned reading on Base Camp
Readings:
<ul style="list-style-type: none"> • Kirkwood and Stern: Chapter 34 • Lang A, Secic M. How to report statistics in medicine

Week: 4
Date: February 1, 2018 (3:00 – 5:00 pm)
Room: LIB 2.088
Instructor(s): Michalek
Topic: Phase I therapeutic
Learning Objectives and Competencies– Participants will be able to: 1. Describe the goals of a Phase I trial 2. Describe the design of a generic Phase I trial
Class Assignment: See assigned reading on Base Camp
Readings: • Kirkwood and Stern: Chapter 34 • Lang A, Secic M. How to report statistics in medicine

Week: 5
Date: February 8, 2018 (3:00 – 5:00 pm)
Room: LIB 2.088
Instructor(s): Michalek
Topic: Crossover (Device)
Learning Objectives and Competencies– Participants will be able to: 1. Describe a generic 2 treatment 2 period crossover 2. State one advantage of a crossover relative to parallel group
Class Assignment: See assigned reading on Base Camp
Readings: • Kirkwood and Stern: Chapter 34 • Lang A, Secic M. How to report statistics in medicine

Week: 6
Date: February 15, 2018 (3:00 – 5:00 pm)
Room: LIB 2.088
Instructor(s): Michalek
Topic: Pharmacokinetics
Learning Objectives and Competencies– Participants will be able to: 1. Describe a generic pharmacokinetic trial 2. List two pharmacokinetic parameters
Class Assignment: See assigned reading on Base Camp
Readings: • Kirkwood and Stern: Chapter 34 • Lang A, Secic M. How to report statistics in medicine

Week: 7
Date: February 22, 2018 (3:00 – 5:00 pm)
Room: LIB 2.088
Instructor(s): Choi
Topic: Power Calculations
Learning Objectives and Competencies– Participants will be able to: <ol style="list-style-type: none">1. Calculate power for a t-test2. Calculate sample size for a Simon 2-stage3. Calculate sample size for a chis-square on a 2 by 2 table
Class Assignment: See assigned reading on Base Camp
Readings: <ul style="list-style-type: none">• Kirkwood and Stern: Chapter 34• Lang A, Secic M. How to report statistics in medicine

Week: 8
Date: March 1, 2018 (3:00 – 5:00 pm)
Room: LIB 2.088
Instructor(s): Michalek
Topic: Clustering (Device)
Learning Objectives and Competencies– Participants will be able to: <ol style="list-style-type: none">1. Describe clustering2. Describe how to adjust for clustering
Class Assignment: See assigned reading on Base Camp
Readings: <ul style="list-style-type: none">• Kirkwood and Stern: Chapter 34• Lang A, Secic M. How to report statistics in medicine

Week: 9
Date: March 8, 2018 (3:00 – 5:00 pm)
Room: LIB 2.088
Instructor(s): Michalek
Topic: Replicated N of 1 (Therapeutic)
Learning Objectives and Competencies– Participants will be able to: 1. Describe a generic replicated N of 1 trial 2. Why is this sometimes ranked higher than a RCT?
Class Assignment: See assigned reading on Base Camp
Readings: <ul style="list-style-type: none">• Kirkwood and Stern: Chapter 34• Lang A, Secic M. How to report statistics in medicine

Week: 10
Date: March 15, 2018 (3:00 – 5:00 pm)
Room: LIB 2.088
Instructor(s): Michalek
Topic: Noi Class, Spring Break
Learning Objectives and Competencies– Participants will be able to:
Class Assignment:
Readings:

Week: 11
Date: March 22, 2018 (3:00 – 5:00 pm)
Room: LIB 2.088
Instructor(s): Michalek
Topic: Phase III multicenter (trauma)
Learning Objectives and Competencies– Participants will be able to: 1. Describe the goal of this trial 2. Describe some limitations of this trial
Class Assignment: See assigned reading on Base Camp
Readings: <ul style="list-style-type: none">• Kirkwood and Stern: Chapter 34• Lang A, Secic M. How to report statistics in medicine

Week: 12
Date: March 29, 2018 (3:00 – 5:00 pm)
Room: LIB 2.088
Instructor(s): Michalek
Topic: Crossover (Therapeutic)
Learning Objectives and Competencies– Participants will be able to: 1. Summarize this trial, what is the primary hypothesis
Class Assignment: See assigned reading on Base Camp
Readings: <ul style="list-style-type: none">• Kirkwood and Stern: Chapter 34• Lang A, Secic M. How to report statistics in medicine

Week: 13
Date: April 5, 2018 (3:00 – 5:00 pm)
Room: LIB 2.088
Instructor(s): Michalek
Topic: Comparative accuracy (therapeutic) - Cardiology
Learning Objectives and Competencies– Participants will be able to: 1. State the goal of this trial 2. State the statistical method
Class Assignment: See assigned reading on Base Camp
Readings: • Kirkwood and Stern: Chapter 34 • Lang A, Secic M. How to report statistics in medicine

Week: 14
Date: April 12, 2018 (3:00 – 5:00 pm)
Room: LIB 2.088
Instructor(s): Michalek
Topic: Stopping Rules
Learning Objectives and Competencies– Participants will be able to: 1. Describe a stopping rule 2. State two benefits of a stopping rule
Class Assignment:
Readings: Readings: • Kirkwood and Stern: Chapter 34 • Lang A, Secic M. How to report statistics in medicine

Week: 15
Date: April 19, 2018 (3:00 – 5:00 pm)
Room: LIB 2.088
Instructor(s): Michalek
Topic: Phase III (Device) - Endocrinology
Learning Objectives and Competencies– Participants will be able to: 1. Describe this trial 2. Describe the primary end point
Class Assignment: See assigned reading on Base Camp
Readings: • Kirkwood and Stern: Chapter 34 • Lang A, Secic M. How to report statistics in medicine

Week: 16
Date: April 26, 2018 (3:00 – 5:00 pm)
Room: LIB 2.088
Instructor(s): Michalek
Topic: ICH Guidelines
Learning Objectives and Competencies– Participants will be able to: 1. Summarize the ICH Guidelines briefly
Class Assignment: None
Readings: <ul style="list-style-type: none">• ICH Guidelines

Week: 17
Date: May 3, 2018 (3:00 – 5:00 pm)
Room: LIB 2.088
Instructor(s): Michalek
Topic: Summary
Learning Objectives and Competencies– Participants will be able to: 1. Discuss the different kinds of trials we have considered
Class Assignment: See assigned reading on Base Camp
Readings: None