



EMORY

ROLLINS
SCHOOL OF
PUBLIC
HEALTH

DEPARTMENT: BIOS

COURSE NUMBER: 520

SECTION NUMBER: 01

CREDIT HOURS: 2

SEMESTER: Spring 2019

COURSE TITLE: Clinical Trials

CLASS HOURS AND LOCATION:

Tuesday, 1:00-2:50pm

INSTRUCTOR NAME: Zhengjia (Nelson) Chen, Ph.D

INSTRUCTOR CONTACT INFORMATION

EMAIL: zchen38@emory.edu

PHONE: (404)-712-8278

SCHOOL ADDRESS OR MAILBOX LOCATION:

Department of Biostatistics & Bioinformatics,
Emory University.

1518 Clifton Road, GCR#342
Atlanta, Georgia 30322, USA

OFFICE HOURS: By appointment

Teaching Assistant(s): Yuzi Zhang

EMAIL: yuzi.zhang@emory.edu

SCHOOL ADDRESS OR MAILBOX LOCATION:

Department of Biostatistics & Bioinformatics,
Emory University.

1518 Clifton Road, GCR
Atlanta, Georgia 30322, USA

OFFICE HOURS: By appointment

COURSE DESCRIPTION

This course is intended to not only provide a basic grounding in all aspects of the conduct of clinical trials from the perspective of a biostatistician, but also teach students

the state-of-the-art knowledge in clinical trials and help them find clinical trial related jobs in pharmaceutical companies, hospitals, oncology research institutes, etc.

Topics of this course include generic drug development, new drug development, pre-clinical trial, the state-of-the-art designs for contemporary Phase I, II, and III clinical trials, protocol writing, hypothesis, methods of randomization, blinding, sample size determination, ethics, subject recruitment, data collection, quality control, monitoring outcomes and adverse events, interim analysis, data analysis, issues with data analysis, reporting, interpreting results, and current advances in clinical trials.

A student completing this course should be able to:

- Identify key operational requirements for a clinical trial before initiating it
- Effectively design a clinical trial and produce a clinical trial proposal
- Produce sample size estimation of a trial
- Design/evaluate safety and outcome monitoring plan
- Produce/evaluate statistical section of a clinical protocol
- Collaborate effectively in the conduct of a trial
- Play critical role in monitoring trial
- Collaborate effectively in the analysis and reporting of a trial
- Identify strengths and weaknesses in the design of a clinical trial from a study proposal
- Critically evaluate clinical trial articles in medical literature

MPH/MSPH FOUNDATIONAL COMPETENCIES:

- Identify statistical issues in contemporary clinical trials.
- Use statistical software for data management and exploratory data analysis.
- Apply regression modeling techniques for continuous, categorical, time-to-event, longitudinal and multilevel data.
- Assess technical accuracy and performance.
- Interpret results of data analysis for clinical trial practice of advanced analytic methods.

CONCENTRATION COMPETENCIES:

- Design clinical trials, including sample size estimation, in collaborative research teams.
- Apply statistical software to implement custom techniques to address unique biomedical or public health problems.
- Explain fundamental concepts of probability and inference used in statistical methodology for clinical trials.
- Communicate the results of statistical analyses to a broad audience.

EVALUATION

Attendance and participation: 5%

Students are required to attend and actively involved in the class.
Need to sign in each class.

Homework: 40%

HW1: Practice on the concept, designs, and data analysis of Phase I clinical trial.

HW2: Practice on the concept, designs, and data analysis of Phase II clinical trial.

HW3: Practice on the concept, designs, and randomization methods of Phase III clinical trial.

HW4: Practice on the power/sample size calculations and interim analysis of Phase III clinical trial.

Students are expected to complete homework assignments in order to practice the materials taught in class. Each assignment will evaluate the students' understanding in three areas: concept, design, and data analysis. Multiple questions for each area will be included in each assignment.

Two clinical data analysis projects: 30%

Project 1: The project is to analyze a dataset from a bioequivalent clinical trial for an abbreviated generic new drug application (ANDA) to FDA.

Project 2: This project is to analyze a typical real data from Phase III clinical trial and report the finding from the trial as a publication.

The two projects require Individual work. It is recommended to use SAS or R to do the projects. Final reports and associated programing codes are required to be submitted together at the due date.

Final in class exam: 25%

A final exam of 2-hour will be administered at the end of the course. The exam will consist of short answers and simple statistical computation. The final exam is intended to have students summarize the important contents of the course and memorize "permanently" the take home points of the clinical trials.

Grade scale:

- A = 93 -- 100%
- A- = 90 -- 93%
- B+ = 87 – 90%
- B = 83 – 85%
- B- = 80 – 83%
- C = 65 – 80%
- F = <65%

COURSE STRUCTURE

The course will be organized into weekly lectures consisting of a combination of electronic slides, whiteboard problem solving, and computational demonstrations. Students are expected to ask and answer questions in class.

MPH/MSPH Foundational Competency assessed	Representative Assignment
Identify statistical issues in contemporary clinical trials.	Homework assignments and exams will involve clinical trial paper reading and criticism
Use statistical software for data management and exploratory data analysis	Homework assignments and two projects will require programming in SAS, R or a similar language.
Apply regression modeling techniques for continuous, categorical, time-to-event, longitudinal and multilevel data	Homework assignments and two projects will involve analysis of real data sets using different regression models.
Interpret results of data analysis for clinical trial practice.	Homework assignments and two projects will involve interpretation and report of hypothesis tests and finding in the clinical trials.
Assess technical accuracy and performance of advanced analytic methods.	Lectures will introduce and compare different designs and advanced analytic methods for each Phase of clinical trials. Homework questions will be assigned that requires students to practice selecting the best designs and approaches for specific purpose of clinical trials.
BIOS Concentration Competencies assessed	Representative Assignment
Design clinical trials, including sample size estimation, in collaborative research teams.	Homework assignments in the sections on power will require simulation-based power calculations.
Apply statistical software to implement custom techniques to address unique biomedical or public health problems	Homework assignments will require students to install and use cutting-edge statistical software to design and conduct clinical trials according to their specific purpose.
Explain fundamental concepts of probability and inference used in statistical methodology.	Homework assignments and projects will require interpreting results of a statistical analysis, including interpreting confidence intervals, p-values, Bayesian inference, etc
Communicate the results of statistical analyses to a broad audience.	Homework and projects will require interpreting the data analysis results in a layman way that is appropriate for different audiences.

COURSE POLICIES

Students are expected to attend lectures and ask questions during class. For computational assignments, students are encouraged, but not required, to bring a laptop to class to follow along with code demonstrations.

What you need:

- Course is kind of technical and requires a background in statistical methods.
- Experience in SAS or R software is strongly recommended.
- Attend the classes and actively involve.
- Finish and turn in home works and projects on time.

Recommended text book and software:

- Fundamentals of Clinical Trials; Third Edition, Friedman, Furberg, and Demets
- PASS 2011: Power Analysis and Sample Size Software (<http://www.ncss.com/download.html>)
- SAS and R.

Other books helpful:

- Clinical Trials: A Methodologic Perspective; Piantadosi
- Clinical Trials: A Practical Approach; Pocock
- Adaptive Design Theory and Implementation Using SAS and R; Chang

As the instructor of this course I endeavor to provide an inclusive learning environment. However, if you experience barriers to learning in this course, do not hesitate to discuss them with me and the Office for Equity and Inclusion, 404-727-9877.

RSPH POLICIES

Accessibility and Accommodations

Accessibility Services works with students who have disabilities to provide reasonable accommodations. In order to receive consideration for reasonable accommodations, you must contact the Office of Accessibility Services (OAS). It is the responsibility of the student to register with OAS. Please note that accommodations are not retroactive and that disability accommodations are not provided until an accommodation letter has been processed.

Students who registered with OAS and have a letter outlining their academic accommodations are strongly encouraged to coordinate a meeting time with me to discuss a protocol to implement the accommodations as needed throughout the semester. This meeting should occur as early in the semester as possible.

Contact Accessibility Services for more information at (404) 727-9877 or accessibility@emory.edu. Additional information is available at the OAS website at <http://equityandinclusion.emory.edu/access/students/index.html>

Honor Code

You are bound by Emory University's Student Honor and Conduct Code.

RSPH requires that all material submitted by a student fulfilling his or her academic course of study must be the original work of the student. Violations of academic honor include any action by a student indicating dishonesty or a lack of integrity in academic ethics. *Academic dishonesty refers to cheating, plagiarizing, assisting other students without authorization, lying, tampering, or stealing in performing any academic work, and will not be tolerated under any circumstances.*

The RSPH Honor Code states: "Plagiarism is the act of presenting as one's own work the expression, words, or ideas of another person whether published or unpublished (including the work of another student). A writer's work should be regarded as his/her own property."

http://www.sph.emory.edu/cms/current_students/enrollment_services/honor_code.html

COURSE CALENDAR AND OUTLINE

Topics and dates are subject to change as the semester progresses.

Date	Topics	Evaluations
Jan 15	Introduction: Characteristics of Clinical trials; Drug Development (Generic Drug vs New Drug). Clinical Trial by Phase;	Baseline quiz.
Jan 22	NDA vs ANDA; Bioavailability and Bioequivalence studies. Introduction to Pre-clinical trial (Phase 0).	Project 1 given
Jan 29	Pre-clinical trial (Phase 0): Invited guest (Dr. Yun Bai) lecture on PK/PD.	
Feb 5	Regulations: Protocol; IRB; Ethics and consent; DSMC. Phase I clinical trials: Adverse events; DLT; MTD; Dose escalation; etc.	
Feb 12	Phase I clinical trials: Fibonacci series; Algorithm-based designs, Standard 3+3 Design Etc.	HW 1 given
Feb 19	Phase I clinical trials: Model-based designs (CRM and EWOC); Demo of CRM and EWOC software.	

	Analysis of Phase I clinical trial data.	
Feb 26	Phase II clinical trials: Concept; Tumor response measurement (RECIST and WHO); One stage Phase II design; Gehan's two stage design; Simon's two stage design.	HW 2 given
March 5	Phase II clinical trials: Randomized phase II design; Randomized discontinuation Phase II design; Selection Phase II design; Screening Phase II design. Analysis of Phase II clinical trial data.	HW 1 due, Project 2 given.
March 12	SPRING BREAK	
March 19	Phase III clinical trials: Overview; Use of control; Different designs; etc.	HW 2 due, Project 1 due, HW 3 given.
March 26	Phase III clinical trials: Different randomization methods; Blinding; etc.	
April 2	Phase III clinical trials: Power and sample size calculations for different designs.	HW 4 given
April 9	Phase III clinical trials: Monitoring, Interim analysis; Futility Analysis.	HW 3 due,
April 16	Phase III clinical trials: Review the analysis methods of Phase III clinical trial data (t-test, Chi-Square test, ANOVA, GLM, Logistic regression, ROC analysis, Survival Analysis, etc.)	
April 23	Analysis and report of Phase III clinical trial using Project 2 as an example. Course review for final exam.	HW 4 due.
April 30	Final Exam	Project 2 Due.