

M19-550 Randomized Controlled Trials

Fall 2022 (08/29/22 – 12/12/22)

Mondays, 1:00-4:00 pm (see details on class timing below)

This syllabus is currently being edited for Fall 2022. Canvas will always have the most up-to-date information.

INSTRUCTORS

Graham Colditz, MD, DrPH, colditzg@wustl.edu

Esther Lu, PhD, esther@wustl.edu

Carrie Stoll, MPH, MSW Carolyn.stoll@wustl.edu

OFFICE HOURS (VIRTUAL)

Wednesdays, 12-1 pm, OR by appointment

CLASS STRUCTURE

For Fall 2022 we will return to in-person instruction. Although the class is scheduled from 1:00-4:00 pm, most classes will only run 1:00-2:30 (see below for exceptions). In order to allow for shorter in-person sessions that focus on interactive learning, students are expected to engage with assigned materials (readings, videos, assignments, etc) prior to class.

CLASS COMPONENTS

1. Asynchronous materials: Every week, asynchronous materials (a combination of videos, slide sets, discussion board posts, readings) will be posted on Canvas by Wednesday. You are expected to complete these weekly tasks prior to class on Monday. Each week there will be a list of *key readings* (ones you are expected to be familiar with prior to class) and *recommended readings* (helpful readings but will not necessarily be used in synchronous class).
2. In-person class: Classes will be held on **Mondays, 1-2:30 pm** in the Taylor Avenue Building (600 S. Taylor).
3. Workshops: There are 3 weeks in which you should reserve **Mondays, 1-4 pm** for project workshop classes: **Oct 3, Nov 28, and Dec 5**. Closer to those dates you will be assigned a specific smaller time window within those 3 hours that you are expected to attend, but for now please reserve the 3 hour block on your schedule.
4. Group assignments and projects: Throughout the semester you will apply the concepts from to design a randomized controlled trial on a research question of your choosing. There will be a series of assignments that build to your final protocol. We highly encourage you to work in a group (2-4 students), although you are allowed to work individually. We especially encourage students from the biostatistics program to team up with clinicians/medical students.
5. Weekly assignments: In addition to the larger group assignments, there are a series of smaller weekly assignments in which you will apply class material to your project topic. In addition to submitting these assignments, you will sometimes be expected to critique/comment on assignments from your classmates. These assignments are typically due prior to class so that we can use them during class.
6. Office hours Carrie will hold weekly Zoom office hours on Wednesdays, 12-1 pm. You can join the office hour Zoom meeting anytime during that hour to ask questions about content, assignments, projects, etc. You are also welcome to email instructors directly to request a meeting outside of the weekly office hours

PREREQUISITES

Introductory epidemiology and biostatistics 1 simultaneously to this course (or permission of the course master)

TARGET AUDIENCE

Clinicians interested in conducting research, clinical training program participants, students undergoing training in public health. Prior clinical or community research experience is helpful but not required.

COURSE DESCRIPTION & OBJECTIVES

This course provides a comprehensive introduction to randomized controlled clinical trials. Topics include types of clinical trials research (efficacy and effectiveness trials), study design, treatment allocation, randomization and stratification, quality control, analysis, sample size requirements, patient consent, data safety and monitoring plans, reporting standards, and interpretation of results. The role of randomized trials in comparative effectiveness research

and also the evaluation of prevention strategies is also addressed. Application of results of trials to inform practice is emphasized throughout.

Evaluation: Students design a randomized controlled trial protocol in their own field of interest, write a proposal for it, and critique recently published medical literature.

COMPETENCIES

1. Ability to design randomized controlled trial
 - Define research question
 - Understand efficacy and effectiveness trials, their differences and implications for clinical practice
 - Define study population and estimate sample size
 - Define approaches for recruitment strategy, randomization, and blinding
 - Apply eligibility criteria and recording of recruitment adequate for trial reports (trials.gov mandated reporting and journal requirements)
 - Develop data collection plan for primary endpoint, secondary endpoint, covariates and adverse events and implement data quality monitoring
 - Apply strategies for monitoring intervention adherence
2. Skills and experience to conduct analysis of RCT
 - Master data analysis and model fitting in context of RCT
 - Conduct survival analysis
 - Apply principles of interim analysis and stopping rules
 - Apply principles for subgroup analysis
 - Apply principles for per protocol analysis
 - Understand design and implementation issues in conduct of multicenter trials
3. Master the core reporting strategies
 - Master reporting standards for RCTs following Consort and Extended Consort approaches
 - Master development of reports for data safety monitoring board
 - Understand issues pertaining to FDA standards for reporting (drugs, devices, apps, decision aids)
4. Draw inferences from data to inform clinical and public health practices
 - Correctly use reasoning for design and methodologies employed
 - Interpret Adverse Events in context of biology and study design
 - Interpret subgroup analyses in context of biology, disease process and public health practices
 - Present oral and written reports from analyses
 - Place inference in context of clinical and public health implications for action and future research

GRADING

Your grade will be based on:

- Class participation (5%)
- Course pulse survey (1%)
- Primary outcome and sample size calculation assignment (12%)
- Data collection and analysis plan assignment (10%)
- Workshop classes: Schema (10%) and Final protocol (15%)
- Discussion posts/assignments with peer review (17%- 4 assignments, 4% each, 1%- introduction assignment)
- Final protocol paper (30%)

ATTENDANCE AND PARTICIPATION

Attendance to the in-person sessions is expected, and the class is designed with this in mind. However, virtual attendance to individual classes may be allowed on a case-by-case basis. In order to attend a session virtually you must request the zoom link from before class.

Up to 2 classes (NOT workshops) may be missed without affecting your grade, however you must notify us either before the class or within 24 hours after class. Attending virtually (with prior permission) counts as attending class.

Exceptions to these policies will be considered on a case-by-case basis. Please contact Carrie with any requests.

CLASS SCHEDULE- see Canvas for most up-to-date information

Week	Date	Topics covered	Assignment Due
1	Aug 29	Introduction to the course, role of RCTs in evaluating interventions	Student introductions
	Sep 5	LABOR DAY- NO CLASS	
2 Sept 6-Sept 12	Sept 12	Defining the research question and choosing an appropriate design: Phase III trials, superiority vs non-inferiority, efficacy vs effectiveness	
3 Sept 13 – Sept 19	Sept 19	Outcomes: primary endpoints, biomarker endpoints, surrogate endpoints	
4 Sept 20 – Sept 26	Sept 26	Bias and error, randomization	Schema draft, + peer review
5 Sept 27 – Oct 3	Oct 3	SCHEMA WORKSHOP 1-4 PM	Schema workshop slides
6 Oct 4 – Oct 10	Oct 10	Sample size, stopping rules	Course pulse survey
7 Oct 11 – Oct 17	Oct 17	Defining and enrolling patients	Sample size assignment
8 Oct 18 – Oct 24	Oct 24	Analysis-main hypothesis, secondary subgroup analysis	
9 Oct 25 – Oct 31	Oct 31	Data quality, issues in data collection and management Adherence to intervention RCT for prevention	Adherence assignment
10 Nov 1 – Nov 7	Nov 7	Ethical considerations, health literacy, participant recruitment issues, informed consent	Consent form assignment
11 Nov 8 – Nov 14	Nov 14	Follow up, data monitoring, interim analysis, adverse events	Data collection assignment
12 Nov 15 – Nov 21	Nov 21	Per protocol analysis Reporting: CONSORT, Cochrane Risk of Bias	
13 Nov 22 – Nov 28	Nov 28	FINAL WORKSHOP	Final workshop slides
14 Nov 29 – Dec 5	Dec 5	FINAL WORKSHOP	Final workshop slides
15 Dec 6 – Dec 12	Dec 12	Implementation of clinical trials; Emerging issues/new statistical designs; Budgets, timelines, feasibility; Applying results of RCTs to clinical practice; Reporting	Abstract assignment Final protocol due

ASSIGNMENTS & DUE DATES- See Canvas for most up-to-date information

Details of all assignments can be found on Canvas

- **Student introduction discussion board**
Due Monday, Aug 29
- **Schema draft with peer review**
Due Monday, Sept 26
Peer comments due Wed, Sept 28
- **Schema workshop**
Slides due Sunday, Oct 2 by midnight
Workshops, Monday, Oct 3, 1-4 pm
- **Course pulse survey**
Due Monday, Oct 10
- **Sample size assignment**
Due Monday, Oct 17
- **Adherence assignment**
Due Fri, Oct 28
Peer review due Mon, Oct 31
- **Consent form assignment**
Due Monday, Nov 7
- **Data collection homework**
Due Mon, Nov 14
- **Final Workshops**
Slides due the night before each session
Session 1: Monday, Nov 28, 1- 4 pm
Session 2: Monday, Dec 5, 1-4 pm
- **Abstract assignment**
Due Mon, Dec 12
- **Final Protocol**
Due Dec 14 by 11:59 pm

POLICY ON LATE ASSIGNMENTS

Late assignments will result in a deduction of one grade point (A+ down to A) for each day late (including weekends) unless prior approval is obtained from the instructor or a compelling situation prevents prior approval. Extensions will be given on a case-by-case basis. Please reach out to Carrie (Carolyn.stoll@wustl.edu) if you need an extension.

READINGS

Readings are a combination of articles (available for download from the course site) and chapters from the textbooks, (a) Fundamentals of Clinical Trials: Friedman, Furberg, and DeMets. 5th edition; (b) Principles and Practice of Clinical Trials: Piantadosi and Meinert. The textbooks are available as ebooks through Becker Medical Library. See Canvas for access details.

DROP DATES

You may drop for any reason during the course of the semester. However, you may only receive a partial or no tuition reimbursement depending upon how far into the semester you drop the course. See the [MPHS Student Handbook](#). Late withdrawals will appear on your transcript as a withdrawal.

MPHS ACADEMIC POLICY GUIDELINES:

Guidelines regarding MPHS course registration and enrollment, grades, tuition obligation, and academic leave are consolidated in the [MPHS Student Handbook](#). Please review this document.

MPHS Guidelines for Academic and Non-Academic Transgressions:

By registering for this course you have agreed to the terms of the **MPHS Academic Integrity Policy, outlined below and in more detail in the [MPHS Student Handbook](#)**. Please review this policy before submitting your first graded assignment.

Academic Integrity/Plagiarism Policy:

- Academic dishonesty is a serious offense that may lead to probation, suspension, or dismissal from the University. Academic dishonesty includes plagiarism (the use of someone else's ideas, statements, or approaches without proper citation). Academic dishonesty also includes copying information from another student, submitting work from a previous class for a new grade without prior approval from your instructor, cheating on exams, etc. You are responsible for reviewing [WashU's academic integrity resources](#) to become aware of all the actions that constitute academic dishonesty.
- All instances of academic dishonesty will be reported to the Office of the Registrar for investigation and potential disciplinary action. In addition, the instructor will make an independent decision about the student's grade on any assignment in question. The MPHS process regarding academic dishonesty is described in the [MPHS Student Handbook](#)

DISABILITY RESOURCES

It is the goal of Washington University to assist students with disabilities in removing the barriers their disabilities may pose and provide support in facing the challenge of pursuing an education at Washington University. Washington University recognizes and accepts its professional, legal and moral responsibility to avoid discrimination in the acceptance and education of qualified students with disabilities and to provide reasonable accommodations to such students consistent with the principles embodied in the law. These guidelines apply to students seeking admittance as well as to those who become disabled while they are enrolled. Washington University makes every effort to insure that all qualified applicants and students can participate in and take full advantage of all programs and opportunities offered within the university. Washington University encourages and gives full consideration to all applicants for admission. Washington University does not discriminate in access to its programs and activities on the basis of age, sex, sexual orientation, race, disability, religion, color or national origin. To learn more about services provided to students with disabilities, initiate the process of formal documentation and/or to arrange for accommodations, please review the [Disability Resources](#) for the Med School at the start of the course.

MENTAL HEALTH RESOURCES

Mental Health Services' professional staff members work with students to resolve personal and interpersonal difficulties, many of which can affect the academic experience. These include conflicts with or worry about friends or family, concerns about eating or drinking patterns, and feelings of anxiety and depression. See: shs.wustl.edu/MentalHealth.

SEXUAL ASSAULT RESOURCES

You can also speak confidentially and learn about available resources by contacting [Dr. Gladys Smith, PhD](#), Sexual Violence Prevention Therapist and Licensed Psychologist at the Medical Campus, (314) 362-2404. Additionally, you can report incidents to the Office of Student Affairs or by contacting WUSM Protective Services 314-362-4357 or your local law enforcement agency.

BIAS RESOURCES

The University has a process through which students and staff who have experienced or witnessed bias, prejudice or discrimination against a student can report their experiences to the University's Bias Report and Support System (BRSS) team. For details see: diversityinclusion.wustl.edu/brss/

Office of the Associate Vice Chancellor for Diversity, Equity and Inclusion (DEI)

The DEI Training Team designs, facilitates and leads diversity education programming for faculty, staff and students on a wide range of topics including: creating a climate of respect, the value of diversity and the role of biases in our day-to-day lives. diversity.med.wustl.edu/training/

The Office of Diversity Programs promotes diversity among and prepares medical students to lead in a global society. A priority for the Office of Diversity Programs is to cultivate and foster a supportive campus climate for students of all backgrounds, cultures and identities. mddiversity.wustl.edu/

The Diversity and Inclusion Student Council promotes an inclusive campus environment for all School of Medicine students. sites.wustl.edu/disc/

The Office for International Students and Scholars embraces the university's mission of welcoming promising students from around the world. wumma.wustl.edu/