M19-550 Randomized Controlled Trials
Fall 2021 (08/30/21 – 12/13/21)
Mondays, 1:00-4:00 pm (see details on class timing below)

INSTRUCTORS
Graham Colditz, MD, DrPH, colditzg@wustl.edu
Esther Lu, PhD, esther@wustl.edu
Carrie Stoll, MPH, MSW Carolyn.stoll@wustl.edu

OFFICE HOURS
Fridays, 11-12 pm starting Sept 3, see Canvas for Zoom link
Or by appointment

CLASS STRUCTURE
For Fall 2021 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. However, please reserve the entire 1:00-4:00 pm period for special workshop classes on Oct 4, Nov 29, and Dec 6. In order to allow for shorter in-person sessions that focus on interactive learning, you are expected to engage with assigned materials (including readings, videos, and assignments) prior to coming 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). Readings will articles that you can download via Canvas, and chapters from the textbook (Fundamentals of Clinical Trials. Friedman, Furberg, and DeMets. 5th edition, available as an ebook via Becker Library).
2. In-person class: Classes will be held on Mondays, 1-2:30 pm.
3. Workshop Classes: There are 3 weeks in which you should reserve Mondays, 1-4 pm for project workshop classes: Oct 4, Nov 29, and Dec 6. Closer to those dates you will be assigned a specific smaller time window within those 3 hrs that you are expected to attend, but for now please reserve the 3 hr 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.
5. Discussion board posts and peer comments: In addition to the larger group assignments, there will be a series of smaller 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.
6. Office hours Carrie will hold weekly Zoom office hours on Fridays, 11-12 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%)

Grading Scale
A+: 97-100; A: 93-96; A-: 90-92; B+: 87-89; B: 83-86; B-: 80-82; C+: 77-79; C: 73-76; C-: 70-72

ATTENDANCE AND PARTICIPATION
Attendance to the Zoom sessions is expected, however up to 2 regular Zoom 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. However, we understand the importance of flexibility in this challenging time and if this expectation is becomes difficult for you to fulfill please reach out to the instructor team and we will address it on a case-by-case basis.

We will judge participation across several methods, which allows students to participate in the ways they feel most comfortable. This can include speaking up on Zoom sessions, participating in whiteboard activities on Zoom, and providing peer feedback on discussion board posts and workshop sessions.

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.

ASSIGNMENTS & DUE DATES
Details of all assignments can be found on Canvas

- Schema draft with peer review
  Due Friday, Sept 17
  Peer comments due Mon, Sept 20

- Schema workshop
  Monday, Oct 4, 1-4 pm

- Sample size assignment
  Due Monday, Oct 18

- Adherence assignment
  Due Fri, Oct 22
  Peer review due Mon, Oct 25

- Consent form assignment
  Due Monday, Nov 1

- Data collection homework
  Due Mon, Nov 8

- Abstract assignment
  Due Mon, Nov 15

- Final Workshops
  Session 1: Monday, Nov 29, 1- 4 pm
  Session 2: Monday, Dec 6, 1-4 pm

- Final Protocol
  Due Dec 13 by 11:59 pm. Submit via Canvas.
**READINGS**
Readings are a combination of articles (available for download from the course site) and chapters from the textbook, Fundamentals of Clinical Trials: Friedman, Furberg, and DeMets. 5th edition. The textbook is available as an ebook from Becker Medical Library and can be found via searching the ebook catalog. When accessing from home you may need to either use a WUSTL VPN or sign into the library proxy first https://login.beckerproxy.wustl.edu/login

**CLASS SCHEDULE**

<table>
<thead>
<tr>
<th>Week</th>
<th>Date</th>
<th>Topics covered</th>
<th>Assignment Due</th>
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<tbody>
<tr>
<td>1</td>
<td>Aug 30</td>
<td>Introduction to the course, the role of RCTs in evaluating interventions</td>
<td>Student introductions</td>
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<tr>
<td>2</td>
<td>Sept 7-Sept 13</td>
<td>Defining the research question and choosing an appropriate design: Phase III trials, superiority vs non-inferiority, efficacy vs effectiveness</td>
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<td>3</td>
<td>Sept 14 – Sept 20</td>
<td>Outcomes: primary endpoints, biomarker endpoints, surrogate endpoints</td>
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<td>4</td>
<td>Sept 21 – Sept 27</td>
<td>Bias and error, randomization</td>
<td>Schema draft, + peer review</td>
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<td>5</td>
<td>Sept 27 – Oct 4</td>
<td>SCHEMA WORKSHOP</td>
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<tr>
<td>6</td>
<td>Oct 4 – Oct 11</td>
<td>Sample size, stopping rules</td>
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<tr>
<td>7</td>
<td>Oct 12 – Oct 18</td>
<td>Defining and enrolling patients</td>
<td>Sample size assignment due</td>
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<td>Oct 18</td>
<td>RCT for prevention</td>
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<td>8</td>
<td>Oct 19 – Oct 25</td>
<td>Data quality, issues in data collection and management Adherence to intervention</td>
<td>Adherence assignment</td>
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<td>9</td>
<td>Oct 26 – Nov 1</td>
<td>Ethical considerations, health literacy, participant recruitment issues, informed consent</td>
<td>Consent form assignment</td>
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<td>10</td>
<td>Nov 2 – Nov 8</td>
<td>Analysis-main hypothesis, secondary subgroup analysis</td>
<td>Data collection homework due</td>
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<td>11</td>
<td>Nov 9 – Nov 15</td>
<td>Per protocol analysis Reporting: CONSORT, Cochrane Risk of Bias</td>
<td>Abstract assignment</td>
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<td>12</td>
<td>Nov 16 – Nov 22</td>
<td>Follow up, data monitoring, interim analysis, adverse events</td>
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<td>13</td>
<td>Nov 23 – Nov 29</td>
<td>FINAL WORKSHOP</td>
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<td>14</td>
<td>Nov 29 – Dec 6</td>
<td>FINAL WORKSHOP</td>
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<tr>
<td>15</td>
<td>Dec 7 – Dec 13</td>
<td>Implementation of clinical trials, considerations for multicenter trials Emerging issues/new statistical designs Budgets, timelines, feasibility Applying results of RCTs to clinical practice</td>
<td>Final protocol due</td>
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**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/