



PubH 3415/7415

Introduction to Clinical Trials - Online

Summer 2018 (8 week term, days of instruction: 11 Jun – 3 Aug 2018)

Credits:	3 credits
Meeting Days:	online
Meeting Time:	online
Meeting Place:	online
Instructors:	Lynn Eberly and Andy Mugglin
Teaching Assistants:	Evan Olawsky (olaws004@umn.edu) and Jun Young Park (park1131@umn.edu)
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Office Hours:	via chat or phone or in person, by appointment, with either Dr. Eberly or Dr. Mugglin

I. Course Description

Participating either as a consumer, adviser, or contributor to evidence-based medical and public health decisions requires an understanding of the quality of that evidence. A strong foundation in clinical trials helps prepare scientists to evaluate published medical advances and to implement well-designed pioneering health research. The topics of this Introduction to Clinical Trials class follow the natural sequence in a protocol, and will include: hypotheses and endpoints, choice of intervention and control, ethical considerations, blinding and randomization, data collection and monitoring, sample size, analysis strategies, and writing of the protocol. Motivating examples from published research will be used throughout. All course interactions occur in an on-line environment. Weekly lessons on each topic have an audio lecture presentation, readings in texts and research literature, interactive discussion boards, video delivered by experts, and optional enrichment materials. Students will participate in discussions, assignments, and exams, all delivered on-line.

II. Course Prerequisites

(1) PubH 7415 enrollees must have one semester of graduate level introductory biostatistics or statistics (PUBH 6414, PUBH 6450, STAT 5021, EPSY 5261, or instructor consent)

(2) PubH 3415 enrollees must have one semester of undergraduate level introductory biostatistics or statistics (STAT 3011, EPSY 3264, SOC 3811, BIOL 3272, or instructor consent) AND junior or senior standing or instructor consent.

III. Course Goals and Objectives

1. Identify basic characteristics of a medical/public health investigation and describe the advantages and disadvantages of randomized clinical trials as compared to other epidemiological and clinical investigations.
2. Compare and contrast common designs for randomized clinical trials for addressing medical/public health questions and understand the advantages and disadvantages of different study designs. Explain using examples how the primary and secondary objectives are linked to the endpoint measures of a clinical trial. Distinguish between single, composite, safety and surrogate endpoints, describing strengths/weaknesses. Understand different randomization techniques and justification for use. Describe basic randomization and blinding implementation strategies.
3. Discuss different conflicts and ethical issues that arise from the implementation of clinical trials both domestically and internationally. Describe the purposes of and differences between an Institutional Review Board (IRB) and a Data Safety and Monitoring Board (DSMB) in terms of protection of human subjects in the setting of clinical research.
4. Describe with examples the difference between bias and random error and strategies for minimizing each. Understand the impacts of randomization and of inclusion/exclusion criteria on each.
5. Identify factors important for appropriately defining an intervention group and a control group. Discuss how the definition influences our understanding and interpretation of the results of a clinical trial.
6. Determine sample sizes for clinical trials of simple design and understand ingredients in the sample size determination for more complex designs.
7. Identify special requirements of collaborative clinical trials, their organization and operation.
8. Determine the data collection requirements of clinical trials. Recommend different data types and data collection form techniques to ensure quality data.
9. Understand the advantages of intent-to-treat analysis and differentiate its interpretation from that of an on-treatment analysis.
10. Recommend an interim analysis plan for a clinical trial and understand the role of independent data monitoring committees (DSMB) in reviewing interim analysis results.
11. Review critically the published results of clinical trials.

IV. Methods of Instruction and Work Expectations

- Course web page: moodle.umn.edu (or access it through MyCourses in your MyU Portal)
- Online course content (28 units)
- Published journal article readings
- 7 discussion fora (approximately weekly)
- 6 assignments (approximately weekly)
- 2 exams (administered online, one midway through and one at end)
- Students should post questions on lectures, readings, assignments, projects, and exams to each week's "General Q & A" discussion forum. The teaching team will respond on a regular basis to posted questions.
- Students with questions or concerns they do not wish to share with the entire class may email any instructor or Teaching Assistant directly.
- Please contact anyone on the teaching team directly, and **we would be happy to set up a time** to meet in person, speak by telephone, or chat online with you.

- Students should be aware that the expectations and requirements in this course are no different from the expectations and requirements in a typical classroom offering. In particular, this is not a self-paced course; students are expected to participate regularly in discussion forums, and to complete activities and assignments by posted deadlines, in order to stay on pace with the course content.

V. Course Text and Readings

Optional recommended texts:

- Fundamentals of Clinical Trials (3rd or 4th Edition), by Friedman, Furberg, and DeMets, **ISBN-13: 978-1441915856**
- Clinical Trials: A Methodologic Perspective (2nd Edition), by Piantadosi, **ISBN-13: 978-0471727811**

VI. Course Outline/Weekly Schedule

- The course week runs from Monday through Sunday. We attempt to make each week's materials available by the end of the Friday before the week begins. **This class contains 16 weeks of material packed into an 8 week summer term.** This class moves fast!
- In general, assignments will be due via online submission by 23:55 US Central time on its due date. See schedule below for details.
- Exams will be made available online by 09:00 US Central time on the schedule-specified day of opening, can be accessed up until 23:55 US Central time on the schedule-specified date of closing, and will be due via online submission of answers within 2 hours of the student's accessing the exam. (Therefore, if you want a full 2 hours to take the exam, you must access the exam prior to 21:55 US Central time on the closing date!) Students may access each exam **only once**; it will not be possible to partially complete the exam and then return to it later. See schedule below for details.

Week Number	Course Dates	Assignments	Expert Connections	Unit Names	Unit Number
1	Jun 11 – Jun 13	Assignment 1: covers units 1-5 (Due Tuesday 19 June)	Kristin Anderson Jim Neaton	Taxonomy of Studies [Observational Studies] Taxonomy of Studies [Experimental Studies]	1 2
1	Jun 14– Jun 17	Discussion forum 1: covers units 1-5 (Due Thursday 21 June)	Russell Luepker Jim Neaton	Taxonomy of Studies [Early Phase Studies] Research Preliminaries [Defining a Question] Research Preliminaries[Getting From the Question to a Protocol]	3 4 5
Tuesday 19 June: Assignment 1 due					
2	Jun 18 – Jun 20	Assignment 2: covers units 6-9 (Due Tuesday 26 June)	Jeff Kahn Michael Oakes John Connett	Research Preliminaries [Ethics I]: <i>Guest Lecturer -Michael Oakes</i> : Introduction to Human Subjects Research and IRB Treatment Allocation [Blinding]	6 7
2	Jun 21 – Jun 24	Discussion forum 2: covers units 6-9 (Due Thursday 28 June)	John Connett Michael Oakes	Treatment Allocation [Implementation] Treatment Allocation [Fixed Methods]	8 9

Tuesday 26 June: Assignment 2 due					
3	Jun 25 – Jun 27	Assignment 3: covers units 10-13 (Due Thursday 5 July)	Don Berry Greg Thompson	Treatment Allocation [Adaptive Methods]	10
3	Jun 28 – Jul 1	Discussion forum 3: covers units 10-13 (Due Monday 9 July)	Jim Neaton John Connett Kristin Ensrud	Endpoints [Composite] Endpoints [Surrogate]: <i>Guest Lecturer- Dan Sargent</i> Endpoints [Safety]	11 12 13
Tuesday 3 July: Exam I opens (covers Assignment 1-3, Units 1-13)					
Thursday 5 July: Assignment 3 due					
4	Jul 2 – Jul 4	No new Assignment	John Connett Kelvin Lim Russell Luepker Jeffery Kahn Chandy John	Study Population [Eligibility Criteria, Recruitment & Run-ins] Study Population [Ethics II: International & Vulnerable Populations]	14 15
4	Jul 5 – Jul 8	Exam I opens. Discussion forum 4: covers units 14-17 (Due Thursday 12 July)	Jim Hodges Poem by Andrew Porter	Study Population [Control Group Selection] Study Population [Regression Towards the Mean]	16 17
Monday 9 July: Exam I closes					
5	Jul 9 – Jul 11	Assignment 4: covers units 14-20 (Due Tuesday 17 July)	Jeffrey Kahn John Connett	Study Design [Parallel Groups] Study Design [Crossover]	18 19
5	Jul 12 – Jul 15	Discussion forum 5: covers units 18-20 (Due Thursday 19 July)	Brad Carlin Jim Neaton	Sample Size [Continuous & Binary Outcomes]	20
Tuesday 17 July: Assignment 4 due					
6	Jul 16 – Jul 18	Assignment 5: covers units 21-24 (Due Tuesday 24 July)	James Hodges	Sample Size [Complications Part I] Sample Size [Complications Part II]	21 22
6	Jul 19 – Jul 22	Discussion forum 6: covers units 21-24 (Due Thursday 26 July)	James Hodges Jeffrey Kahn	Analysis [Intention-to-Treat & Per-Protocol] Analysis [Interim]	23 24
Tuesday 24 July: Assignment 5 due					
7	Jul 23 – Jul 25	Assignment 6: covers units 25-28 (Due Tuesday 31 July)	John Connett Kelvin Lim James Hodges	Data [Collection] Data [Quality]	25 26
7	Jul 26 – Jul 29	Discussion forum 7: covers units 25-28 (Due Thursday 2 August)	John Connett Jeffrey Kahn	Data [Ethics III: Scientific Fraud and Misconduct]	27
Tuesday 31 July: Assignment 6 due and Exam II opens (covers Assignment 4-6, Units 14-28)					

8	Jul 30 – Aug 1	No new Assignment; Exam II opens		Reporting [CONSORT guidelines]	28
8	Aug 2 – Aug 5	No new discussion fora		(no new material)	
Sunday 5 August: Exam II closes					

VII. Evaluation and Grading

Assignments (6 at 25 points each for 150 possible points)
 Discussion fora (7 at 16 points each for 102 possible points)
 Exam I (100 possible points)
 Exam II (100 possible points)

- Each assignment is graded on a scale of 0 – 25 points. Points will be added across the assignments for total possible points of 150.
- Discussion fora are graded on a scale of 0 - 8 - 16 points: 8 points for your own discussion posting and an additional 8 points for responding to a classmate's post. Check the class Moodle site for guidance on posting guidance and expectations. Points will be added across the fora for total possible points of 102.
- Two exams will be given at approximately 4 weeks and 8 weeks during the term. The exams are focused on the most recent information presented. Each exam is graded on a scale of 0 – 100 points.
- The total number of possible points is 452.

The University utilizes plus and minus grading on a 4.000 cumulative grade point scale in accordance with the following: A/F letter grade will be determined by total effort as follows:

A = 93.00-100.00%	(4.0) Represents achievement that is outstanding relative to the level necessary to meet course requirements.
A- = 90.00-92.99%	(3.667)
B+ = 87.00-89.99%	(3.333)
B = 83.00-86.99%	(3.0) Represents achievement that is significantly above the level necessary to meet course requirements.
B- = 80.00-82.99%	(2.667)
C+ = 77.00-79.99%	(2.333)
C = 73.00-76.99%	(2.0) Represents achievement that meets the minimum course requirements.
C- = 70.00-72.99%	(1.667)
D+ = 67.00 – 69.99	(1.333)
D = 60.00-66.99	(1.000) Represents achievement that is worthy of credit even though it fails to meet fully the course requirements
F = 0 – 59.99	Represents failure (or no credit) and signifies that the work was either (1) completed but at a level of achievement that is not worthy of credit or (2) was not completed and there was no agreement between the instructor and the student that the student would be awarded an I.

For additional information, please refer to:

<http://policy.umn.edu/Policies/Education/Education/GRADINGTRANSCRIPTS.html>.

Course Evaluation

The SPH will collect student course evaluations electronically using a software system called CoursEval: www.sph.umn.edu/courseval. The system will send email notifications to students when they can access and

complete their course evaluations. Students who complete their course evaluations promptly will be able to access their final grades just as soon as the faculty member renders the grade in SPHGrades: www.sph.umn.edu/grades. All students will have access to their final grades through OneStop two weeks after the last day of the semester regardless of whether they completed their course evaluation or not. Student feedback on course content and faculty teaching skills are an important means for improving our work. Please take the time to complete a course evaluation for each of the courses for which you are registered.

Incomplete Contracts

A grade of incomplete "I" shall be assigned at the discretion of the instructor when, due to extraordinary circumstances (e.g., documented illness or hospitalization, death in family, etc.), the student was prevented from completing the work of the course on time. The assignment of an "I" requires that a contract be initiated and completed by the student before the last official day of class, and signed by both the student and instructor. If an incomplete is deemed appropriate by the instructor, the student in consultation with the instructor, will specify the time and manner in which the student will complete course requirements. Extension for completion of the work will not exceed one year (or earlier if designated by the student's college). For more information and to initiate an incomplete contract, students should go to SPHGrades at: www.sph.umn.edu/grades.

University of Minnesota Uniform Grading and Transcript Policy

A link to the policy can be found at onestop.umn.edu.

VIII. Other Course Information and Policies

Grade Option Change (if applicable):

For full-semester courses, students may change their grade option, if applicable, through the second week of the semester. Grade option change deadlines for other terms (i.e. summer and half-semester courses) can be found at onestop.umn.edu.

Course Withdrawal:

Students should refer to the Refund and Drop/Add Deadlines for the particular term at onestop.umn.edu for information and deadlines for withdrawing from a course. As a courtesy, students should notify their instructor and, if applicable, advisor of their intent to withdraw.

Students wishing to withdraw from a course after the noted final deadline for a particular term must contact the School of Public Health Office of Admissions and Student Resources at sph-ssc@umn.edu for further information.

Student Conduct Code:

The University seeks an environment that promotes academic achievement and integrity, that is protective of free inquiry, and that serves the educational mission of the University. Similarly, the University seeks a community that is free from violence, threats, and intimidation; that is respectful of the rights, opportunities, and welfare of students, faculty, staff, and guests of the University; and that does not threaten the physical or mental health or safety of members of the University community.

As a student at the University you are expected adhere to Board of Regents Policy: *Student Conduct Code*. To review the Student Conduct Code, please see: http://regents.umn.edu/sites/default/files/policies/Student_Conduct_Code.pdf.

Note that the conduct code specifically addresses disruptive classroom conduct, which means "engaging in behavior that substantially or repeatedly interrupts either the instructor's ability to teach or student learning. The classroom extends to any setting where a student is engaged in work toward academic credit or satisfaction of program-based requirements or related activities."

Use of Personal Electronic Devices in the Classroom:

Using personal electronic devices in the classroom setting can hinder instruction and learning, not only for the student using the device but also for other students in the class. To this end, the University establishes the right of each faculty member to determine if and how personal electronic devices are allowed to be used in the classroom. For complete information, please reference: <http://policy.umn.edu/Policies/Education/Education/STUDENTRESP.html>.

Scholastic Dishonesty:

You are expected to do your own academic work and cite sources as necessary. Failing to do so is scholastic dishonesty. Scholastic dishonesty means plagiarizing; cheating on assignments or examinations; engaging in unauthorized collaboration on academic work; taking, acquiring, or using test materials without faculty permission; submitting false or incomplete records of academic achievement; acting alone or in cooperation with another to falsify records or to obtain dishonestly grades, honors, awards, or professional endorsement; altering, forging, or misusing a University academic record; or fabricating or falsifying data, research procedures, or data analysis. (Student Conduct Code:

http://regents.umn.edu/sites/default/files/policies/Student_Conduct_Code.pdf) If it is determined that a student has cheated, he or she may be given an "F" or an "N" for the course, and may face additional sanctions from the University. For additional information, please see:

<http://policy.umn.edu/Policies/Education/Education/INSTRUCTORRESP.html>.

The Office for Student Conduct and Academic Integrity has compiled a useful list of Frequently Asked Questions pertaining to scholastic dishonesty: <http://www1.umn.edu/oscai/integrity/student/index.html>. If you have additional questions, please clarify with your instructor for the course. Your instructor can respond to your specific questions regarding what would constitute scholastic dishonesty in the context of a particular class-e.g., whether collaboration on assignments is permitted, requirements and methods for citing sources, if electronic aids are permitted or prohibited during an exam.

Makeup Work for Legitimate Absences:

Students will not be penalized for absence during the semester due to unavoidable or legitimate circumstances. Such circumstances include verified illness, participation in intercollegiate athletic events, subpoenas, jury duty, military service, bereavement, and religious observances. Such circumstances do not include voting in local, state, or national elections. For complete information, please see:

<http://policy.umn.edu/Policies/Education/Education/MAKEUPWORK.html>.

Appropriate Student Use of Class Notes and Course Materials:

Taking notes is a means of recording information but more importantly of personally absorbing and integrating the educational experience. However, broadly disseminating class notes beyond the classroom community or accepting compensation for taking and distributing classroom notes undermines instructor interests in their intellectual work product while not substantially furthering instructor and student interests in effective learning. Such actions violate shared norms and standards of the academic community. For additional information, please see: <http://policy.umn.edu/Policies/Education/Education/STUDENTRESP.html>.

Sexual Harassment:

"Sexual harassment" means unwelcome sexual advances, requests for sexual favors, and/or other verbal or physical conduct of a sexual nature. Such conduct has the purpose or effect of unreasonably interfering with an individual's work or academic performance or creating an intimidating, hostile, or offensive working or academic environment in any University activity or program. Such behavior is not acceptable in the University setting. For additional information, please consult Board of Regents Policy:

<http://regents.umn.edu/sites/default/files/policies/SexHarassment.pdf>

Equity, Diversity, Equal Opportunity, and Affirmative Action:

The University will provide equal access to and opportunity in its programs and facilities, without regard to race, color, creed, religion, national origin, gender, age, marital status, disability, public assistance status, veteran status, sexual orientation, gender identity, or gender expression. For more information, please consult Board of Regents Policy:

http://regents.umn.edu/sites/default/files/policies/Equity_Diversity_EO_AA.pdf.

Disability Accommodations:

The University of Minnesota is committed to providing equitable access to learning opportunities for all students. The Disability Resource Center Student Services is the campus office that collaborates with students who have disabilities to provide and/or arrange reasonable accommodations.

If you have, or think you may have, a disability (e.g., mental health, attentional, learning, chronic health, sensory, or physical), please contact DRC at 612-626-1333 or drc@umn.edu to arrange a confidential discussion regarding equitable access and reasonable accommodations.

If you are registered with DS and have a current letter requesting reasonable accommodations, please contact your instructor as early in the semester as possible to discuss how the accommodations will be applied in the course.

For more information, please see the DS website, <https://diversity.umn.edu/disability/>.

Mental Health and Stress Management:

As a student you may experience a range of issues that can cause barriers to learning, such as strained relationships, increased anxiety, alcohol/drug problems, feeling down, difficulty concentrating and/or lack of motivation. These mental health concerns or stressful events may lead to diminished academic performance and may reduce your ability to participate in daily activities. University of Minnesota services are available to assist you. You can learn more about the broad range of confidential mental health services available on campus via the Student Mental Health Website: <http://www.mentalhealth.umn.edu>.

The Office of Student Affairs at the University of Minnesota:

The Office for Student Affairs provides services, programs, and facilities that advance student success, inspire students to make life-long positive contributions to society, promote an inclusive environment, and enrich the University of Minnesota community.

Units within the Office for Student Affairs include, the Aurora Center for Advocacy & Education, Boynton Health Service, Central Career Initiatives (CCE, CDes, CFANS), Leadership Education and Development – Undergraduate Programs (LEAD-UP), the Office for Fraternity and Sorority Life, the Office for Student Conduct and Academic Integrity, the Office for Student Engagement, the Parent Program, Recreational Sports, Student and Community Relations, the Student Conflict Resolution Center, the Student Parent HELP Center, Student Unions & Activities, University Counseling & Consulting Services, and University Student Legal Service.

For more information, please see the Office of Student Affairs at <http://www.osa.umn.edu/index.html>.

Academic Freedom and Responsibility: *for courses that do not involve students in research:*

Academic freedom is a cornerstone of the University. Within the scope and content of the course as defined by the instructor, it includes the freedom to discuss relevant matters in the classroom. Along with this freedom comes responsibility. Students are encouraged to develop the capacity for critical judgment and to engage in a sustained and independent search for truth. Students are free to take reasoned exception to the views offered in any course of study and to reserve judgment about matters of opinion, but they are responsible for learning the content of any course of study for which they are enrolled.*

OR:

Academic Freedom and Responsibility, for courses that involve students in research

Academic freedom is a cornerstone of the University. Within the scope and content of the course as defined by the instructor, it includes the freedom to discuss relevant matters in the classroom and conduct relevant research. Along with this freedom comes responsibility. Students are encouraged to develop the capacity for critical judgment and to engage in a sustained and independent search for truth. Students are free to take reasoned exception to the views offered in any course of study and to reserve judgment about matters of opinion, but they are responsible for learning the content of any course of study for which they are enrolled.* When conducting research, pertinent institutional approvals must be obtained and the research must be consistent with University policies.

Reports of concerns about academic freedom are taken seriously, and there are individuals and offices available for help. Contact the instructor, the Department Chair, your adviser, the associate dean of the college, (Dr Kristin Anderson, SPH Dean of Student Affairs), or the Vice Provost for Faculty and Academic Affairs in the Office of the Provost.

** Language adapted from the American Association of University Professors "Joint Statement on Rights and Freedoms of Students".*

Student Academic Success Services (SASS): <http://www.sass.umn.edu>:

Students who wish to improve their academic performance may find assistance from Student Academic Support Services. While tutoring and advising are not offered, SASS provides resources such as individual consultations, workshops, and self-help materials.

