

PubH 3415/7415**Introduction to Clinical Trials - Online****Summer 2015 (8 week term, days of instruction: 15 Jun – 10 Aug 2015)**

Credits:	3 credits
Meeting Days:	online
Meeting Time:	online
Meeting Place:	online
Instructors:	Lynn Eberly
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Office Hours:	via Chat or phone or in person, by appointment, with either Dr. Eberly or Xu

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, homework, 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.
3. 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.
4. Understand different randomization techniques and justification for use. Describe basic randomization and blinding implementation strategies.
5. 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.
6. 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.
7. 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.
8. Determine sample sizes for clinical trials of simple design and understand ingredients in the sample size determination for more complex designs.
9. Identify special requirements of collaborative clinical trials, their organization and operation.
10. Determine the data collection requirements of clinical trials. Recommend different data types and data collection form techniques to ensure quality data.
11. Understand the advantages of intent-to-treat analysis and differentiate its interpretation from that of an on-treatment analysis.
12. Recommend an interim analysis plan for a clinical trial and understand the role of independent data monitoring committees (DSMB) in reviewing interim analysis results.
13. 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 (15 topics)
- Published journal article readings
- Discussion fora (1 per topic)
- 6 homework assignments (approximately weekly)
- 2 exams (administered online)
- Students should post questions on lectures, readings, homework assignments, projects, and exams to each week's "General Q & A" discussion forum. Both instructor and Teaching Assistant (TA) 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 the instructor directly.
- In past offerings, both Instructor and TA had regular weekly office hours via Chat within Moodle, but no one ever came. Please contact either of us directly, and **we would be happy to set up a time** to meet in person, speak by telephone, or "chat" 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.
- In general, homework assignments will be made available online each week and will be due via online submission of an electronic document by 23:59 US Central time approximately one week later. See schedule below for details.
- Exams will be made available online by 23:59 US Central time on the schedule-specified day of an exam week, can be accessed up until 23:59 US Central time on the subsequent Sunday, and will be due via online submission of answers within 2 hours of the student's accessing the exam. 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.

VI. Course Outline/Weekly Schedule (continued)

Topic Number	Course Dates	Homework Assignments	Expert Connections	Topics
1	Jun 15 – Jun 17	Homework 1: Topics 1 & 2 (Due Tuesday 23 June)	Kristin Anderson Jim Neaton	Observational Studies Experimental Studies
2	Jun 18 – Jun 20		Russell Luepker Jim Neaton	Early Phase Studies Defining a Research Question Research Considerations & Structure of a Protocol
Tuesday 23 June: Homework 1 due				
3	Jun 22 – Jun 24	Homework 2: Topics 3 & 4 (Due Tuesday 30 June)	Jeff Kahn Michael Oakes John Connett	Ethics I: <i>Guest Lecturer -Michael Oakes:</i> Introduction to Human Subjects Research and IRB Blinding
4	Jun 25 – Jun 27		John Connett Michael Oakes	Treatment Allocation [Implementation] Treatment Allocation [Fixed Methods]
Tuesday 30 June: Homework 2 due				
5	Jun 29 – Jul 1	Homework 3: Topics 5 & 6 (Due Tuesday 7 July)	Don Berry Greg Thompson	Treatment Allocation [Adaptive Methods]
6	Jul 2 – Jul 4		Jim Neaton John Connett Kristin Ensrud	Endpoints [Composite] <i>Guest Lecturer- Dan Sargent:</i> Endpoints [Surrogate] Endpoints [Safety]
Tuesday 6 July: Homework 3 due and Exam I opens (covers HW 1-3, Topics 1-7)				
7	Jul 6 – Jul 8		John Connett Kelvin Lim Russell Luepker Jeffery Kahn Chandy John	Study Population [Eligibility Criteria, Recruitment & Run-ins] Ethics II: International & Vulnerable Populations
8	Jul 9 – Jul 11		Jim Hodges Poem by Andrew Porter	Control Group Selection Regression Towards the Mean
Sunday 12 July: Exam I closes				
9	Jul 13 – Jul 15	Homework 4: Topics 8 & 9 & 10 (Due Tuesday 21 July)	Jeffrey Kahn John Connett	Study Design [Parallel Group] Study Design [Crossover]
10	Jul 16 – Jul 18		Brad Carlin Jim Neaton	Sample Size [Continuous & Binary Outcomes]

Tuesday 21 July: Homework 4 due				
11	Jul 20 – Jul 22	Homework 5: Topics 11 & 12 (Due Tuesday 28 July)	James Hodges	Sample Size [Complications Part I] Sample Size [Complications Part II]
12	Jul 23 – Jul 25		James Hodges Jeffrey Kahn	Analysis [Intention-to-Treat & Per-Protocol] Analysis [Interim]
Tuesday 28 July: Homework 5 due				
13	Jul 27 – Jul 29	Homework 6: Topics 13 & 14 (Due Tuesday 4 August)	John Connett Kelvin Lim James Hodges	Data Collection Data Quality
14	Jul 30 – Aug 1		John Connett Jeffrey Kahn	Ethics III: Scientific Fraud and Misconduct
Tuesday 4 August: Homework 6 due and Exam II opens (covers HW 4-6, Topics 8-15)				
15	Aug 3 – Aug 5			Reporting: CONSORT guidelines
16	Aug 6 – Aug 8			(no new material)
Sunday 9 August: Exam II closes				

VII. Evaluation and Grading

Homework (6 at 20 points each for 120 possible points)
Discussion fora (14 at 10 points each for 140 possible points)
Exam I (100 possible points)
Exam II (100 possible points)

- Each homework assignment is graded on a scale of 0 – 20 points. Points will be added across the homeworks for total possible points of 120.
- Discussion fora are graded on a scale of 0 - 5 - 10 points: 5 points for your own discussion posting and an additional 5 points for responding to a classmate's post. Points will be added across the fora (1 forum in each of the first 14 topics) for total possible points of 140.
- 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.

A/F letter grade will be determined by total effort as follows:

A = 93-100%	(4.0) Represents achievement that is outstanding relative to the level necessary to meet course requirements.
A- = 90-92%	
B+ = 87-89%	
B = 83-86%	(3.0) Represents achievement that is significantly above the level necessary to meet course requirements.
B- = 80-82%	

C+ = 77-79%	
C = 73-76%	(2.0) Represents achievement that meets the minimum course requirements.
C- = 70-72%	
F =	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.

Course Evaluation

Beginning in fall 2008, the SPH will collect student course evaluations electronically using a software system called CourseEval: www.sph.umn.edu/courseeval. 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 Student Services Center at sph-ssc@umn.edu for further information.

Student Conduct, Scholastic Dishonesty and Sexual Harassment Policies

Students are responsible for knowing the University of Minnesota, Board of Regents' policy on Student Conduct and Sexual Harassment found at www.umn.edu/regents/polindex.html.

Students are responsible for maintaining scholastic honesty in their work at all times. Students engaged in scholastic dishonesty will be penalized, and offenses will be reported to the SPH Associate Dean for Academic Affairs who may file a report with the University's Academic Integrity Officer.

The University's Student Conduct Code defines scholastic dishonesty as "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; or altering, forging, or misusing a University academic record; or fabricating or falsifying of data, research procedures, or data analysis."

Plagiarism is an important element of this policy. It is defined as the presentation of another's writing or ideas as your own. Serious, intentional plagiarism will result in a grade of "F" or "N" for the entire course. For more information on this policy and for a helpful discussion of preventing plagiarism, please consult University policies and procedures regarding academic integrity: <http://writing.umn.edu/tww/plagiarism/>.

Students are urged to be careful that they properly attribute and cite others' work in their own writing. For guidelines for correctly citing sources, go to <http://tutorial.lib.umn.edu/> and click on "Citing Sources".

In addition, original work is expected in this course. Unless the instructor has specified otherwise, all assignments, papers, reports, etc. should be the work of the individual student. It is unacceptable to hand in assignments for this course for which you receive credit in another course unless by prior agreement with the instructor. Building on a line of work begun in another course or leading to a thesis, dissertation, or final project is acceptable.

Disability Statement

It is University policy to provide, on a flexible and individualized basis, reasonable accommodations to students who have a documented disability (e.g., physical, learning, psychiatric, vision, hearing, or systemic) that may affect their ability to participate in course activities or to meet course requirements. Students with disabilities are encouraged to contact Disability Services to have a confidential discussion of their individual needs for accommodations. Disability Services is located in Suite 180 McNamara Alumni Center, 200 Oak Street. Staff can be reached by calling 612/626-1333 (voice or TTY).