SCHOOL OF PUBLIC HEALTH
UNIVERSITY OF MINNESOTA

PUBH 3415/7415, SECTION 320

Introduction to Clinical Trials - Online
Summer 2019 (8 week term, days of instruction: 10 Jun – 2 Aug, 2019)

COURSE & CONTACT INFORMATION

Credits: 3 credits
Meeting Day(s), Time, and Place: This course is entirely web-based, delivered via Moodle at http://moodle.umn.edu.

Contact Type	Contact Information	Role	When to Contact
Instructors	**Lynn Eberly and Andy Mugglin** leberly@umn.edu (Dr. Eberly) amugglin@umn.edu (Dr. Mugglin) Please contact us via email! Fax: 612-626-0660	Primary instructors for this course	Big-picture questions or concerns about the class and personal matters requiring individual accommodation or adjustments to deadlines. Any issue where you're not comfortable first approaching a TA.
Teaching Assistants	Dillon Corrigan (corri104@umn.edu) Seonguk Jang (jang0065@umn.edu)	Grades and provides feedback on assignments; drafts assignment solution keys; monitors online discussion fora; helps prepare assessments (e.g., assignment, exam, and discussion questions).	Questions or comments about the course material or grading. Your TA will respond promptly and is generally your first line of contact.
Technical Support	Technical support options are available on the SPH website. https://z.umn.edu/sphquickhelp	Troubleshoots technical issues related to the course site or course content.	Technical issues with the course site, media, quizzes or assignments.

Please save this contact information to your computer or print it. That way, you can still contact us in the event that you have difficulty connecting to the Internet or accessing the syllabus.

Communication in Online Courses

Communication is especially important in an online course. The course site announcement forums/discussions and email will be used to communicate with students. You are responsible for reading all course-related emails sent to your University email account and contacting us in a timely manner with any questions you may have. We strongly recommend that you check your U of M email daily. Our goal is to respond to emails within 24 hours, Monday - Friday.

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.

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.

COURSE GOALS & 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.

5. Understand the impacts of randomization and of inclusion/exclusion criteria on each.

6. 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.

7. Determine sample sizes for clinical trials of simple design and understand ingredients in the sample size determination for more complex designs.

8. Identify special requirements of collaborative clinical trials, their organization and operation.

9. Determine the data collection requirements of clinical trials. Recommend different data types and data collection form techniques to ensure quality data.

10. Understand the advantages of intent-to-treat analysis and differentiate its interpretation from that of an on-treatment analysis.

11. Recommend an interim analysis plan for a clinical trial and understand the role of independent data monitoring committees (DSMB) in reviewing interim analysis results.

12. Review critically the published results of clinical trials.

METHODS OF INSTRUCTION AND WORK EXPECTATIONS

Course Workload Expectations

Introduction to Clinical Trials – Online is a 3 credit course. The University expects that for each credit, you will spend a minimum of three hours per week attending class or comparable online activity, reading, studying, completing assignments, etc. over the course of the term. This is a 15-week course packed into an 8-week term. Thus, this course requires a minimum of approximately 3*3*15=135 hours of effort spread over the course of the term in order to earn an average grade.

• Online course content (28 units)

• Published journal article readings

• 7 discussion fora (approximately weekly)

• 6 homework assignments (approximately weekly)

• 2 exams (administered online, one midway through and one at end)

• Students should post questions on lectures, readings, homework 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.

Technology
You will use the following technology tools in this course. Please make yourself familiar with it.

- Course web page: **moodle.umn.edu** (or access it through MyCourses in your MyU Portal)

Learning Community
School of Public Health courses ask students to discuss frameworks, theory, policy, and more, often in the context of past and current events and policy debates. Many of our courses also ask students to work in teams or discussion groups. We do not come to our courses with identical backgrounds and experiences and building on what we already know about collaborating, listening, and engaging is critical to successful professional, academic, and scientific engagement with topics.

In this course, students are expected to engage with each other in respectful and thoughtful ways.

In group discussion, this can mean:

- Respecting the identities and experiences of your classmates.
- Avoid broad statements and generalizations. Group discussions are another form of academic communication and responses to instructor questions in a group discussion are evaluated. Apply the same rigor to crafting discussion posts as you would for a paper.
- Consider your tone and language, especially when communicating in text format, as the lack of other cues can lead to misinterpretation.

Like other work in the course, all student to student communication is covered by the Student Conduct Code (https://z.umn.edu/studentconduct) faculty-with-student communication is covered by the Faculty and Staff Conduct Code (https://regents.umn.edu/sites/regents.umn.edu/files/policies/Code_of_Conduct.pdf).

COURSE TEXT & READINGS

Optional recommended texts:

- Fundamentals of Clinical Trials (5th edition), by Friedman, Furberg, and DeMets, **ISBN-13:** 978-3319185385
- Clinical Trials: A Methodologic Perspective (3nd Edition), by Piantadosi, **ISBN-13:** 978-1118959206

These texts are also available electronically through the University libraries (Friedman et al on-line and Piantadosi on-line).

This course uses journal articles, which are available via the University Libraries' E-Reserves and will be linked from the course site. It is good practice to use a citation manager to keep track of your readings. More information about citation managers is available at https://www.lib.umn.edu/pim/citation.

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 15 weeks of material packed into an 8-week summer term.** This class moves fast! See schedule below for details.

• In general, all assignments will be due via online submission by 23:55 US Central time on its due date.

• 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 your accessing the exam. (Therefore, if you want a full 2 hours to take the exam, you must access it prior to 21:55 US Central time on the closing date!) You may access each exam only once; it is not possible to partially complete the exam and then return to it later.

Week	Topic	Expert Connections	Activities/Assignments	Unit Number
Week 1 Jun 10 - 12	• Taxonomy of Studies [Observational Studies] • Taxonomy of Studies [Experimental Studies]	• Kristin Anderson • Jim Neaton	• Assignment 1: covers units 1-5 (Due Tuesday 18 June)	• 1 • 2
Week 1 Jun 13 - 16	• Taxonomy of Studies [Early Phase Studies] • Research Preliminaries [Defining a Question] • Research Preliminaries [Getting From the Question to a Protocol]	• Russell Luepker • Jim Neaton	• Discussion forum 1: covers units 1-5 (Due Thursday 20 June)	• 3 • 4 • 5
Tuesday 18 June: Assignment 1 due **Thursday 20 June: Forum 1 due**				
Week 2 Jun 17 - 19	• Research Preliminaries [Ethics I]: *Guest Lecturer* - **Michael Oakes**: Introduction to Human Subjects Research and IRB • Treatment Allocation [Blinding]	• Jeff Kahn • Michael Oakes • John Connett	• Assignment 2: covers units 6-9 (Due Tuesday 25 June)	• 6 • 7

Week 2 Jun 20 - 23	• Treatment Allocation [Implementation] • Treatment Allocation [Fixed Methods]	• John Connett • Michael Oakes	• Discussion forum 2: covers units 6-9 (Due Thursday 27 June)	• 8 • 9
Tuesday 25 June: Assignment 2 due **Thursday 27 June: Forum 2 due**				
Week 3 Jun 24 - 26	• Treatment Allocation [Adaptive Methods]	• Don Berry • Greg Thompson	• Assignment 3: covers units 10-13 (Due Tuesday 2 July)	• 10
Week 3 Jun 27 – Jun 30	• Endpoints [Composite] • Endpoints [Surrogate]: *Guest Lecturer*- **Dan Sargent** • Endpoints [Safety]	• Jim Neaton • John Connett • Kristin Ensrud	• Discussion forum 3: covers units 10-13 (Due Thursday 4 July, but accepted without penalty through Tuesday 9 July)	• 11 • 12 • 13
Tuesday 2 July: Assignment 3 due **Thursday 4 July: Forum 3 due**				
Wednesday 3 July: Exam I opens (covers Homework 1-3, Units 1-13)				
Week 4 Jul 1 – Jul 3	• Study Population [Eligibility Criteria, Recruitment & Run-ins] • Study Population [Ethics II: International & Vulnerable Populations]	• John Connett • Kelvin Lim • Russell Luepker • Jeffery Kahn • Chandy John	• No new assignment • Exam I opens	• 14 • 15
Week 4 Jul 4 – Jul 7	• Study Population [Control Group Selection] • Study Population [Regression Towards the Mean]	• Jim Hodges • Poem by Andrew Porter	• Exam I is open • Discussion forum 4A: covers units 14-17 (Due Thursday 11 July)	• 16 • 17
Tuesday 9 July: Exam I closes **Thursday 11 July: Forum 4A due**				

Week 5 Jul 8 - 10	• Study Design [Parallel Groups] • Study Design [Crossover]	• Jeffrey Kahn • John Connett	• Assignment 4: covers units 14-20 (Due Tuesday 16 July)	• 18 • 19
Week 5 Jul 11 - 14	• Sample Size [Continuous & Binary Outcomes]	• Brad Carlin • Jim Neaton	• Discussion forum 4B: covers units 18-20 (Due Thursday 18 July)	• 20
Tuesday 16 July: Assignment 4 due **Thursday 18 July: Forum 4B due**				
Week 6 Jul 15 - 17	• Sample Size [Complications Part I] • Sample Size [Complications Part II]	• James Hodges	• Assignment 5: covers units 21-24 (Due Tuesday 23 July)	• 21 • 22
Week 6 Jul 18 - 21	• Analysis [Intention-to-Treat & Per-Protocol] • Analysis [Interim]	• James Hodges • Jeffrey Kahn	• Discussion forum 5: covers units 21-24 (Due Thursday 25 July)	• 23 • 24
Tuesday 23 July: Assignment 5 due **Thursday 25 July: Forum 5 due**				
Week 7 Jul 22 - 24	• Data [Collection] • Data [Quality]	• John Connett • Kelvin Lim • James Hodges	• Assignment 6: covers units 25-28 (Due Tuesday 30 July)	• 25 • 26
Week 7 Jul 25 - 28	• Data [Ethics III: Scientific Fraud and Misconduct]	• John Connett • Jeffrey Kahn	• Discussion forum 6: covers units 25-28 (Due Thursday 1 August)	• 27
Tuesday30 July: Assignment 6 due **Wednesday 31 July: Exam II opens (covers Homework 4-6, Units 14-28)** **Thursday 1 August: Forum 6 due**				
Week 8 Jul 29 – Jul 31	• Reporting [CONSORT guidelines]		• No new homework • Exam II opens	• 28
Week 8 Aug 1 – 4	• No new material		• No new discussion fora	
Tuesday 6 August: Exam II closes				

SPH AND UNIVERSITY POLICIES & RESOURCES

The School of Public Health maintains up-to-date information about resources available to students, as well as formal course policies, on our website at www.sph.umn.edu/student-policies/. Students are expected to read and understand all policy information available at this link and are encouraged to make use of the resources available.

The University of Minnesota has official policies, including but not limited to the following:

- Grade definitions
- Scholastic dishonesty
- Makeup work for legitimate absences
- Student conduct code
- Sexual harassment, sexual assault, stalking and relationship violence
- Equity, diversity, equal employment opportunity, and affirmative action
- Disability services
- Academic freedom and responsibility

Resources available for students include:

- Confidential mental health services
- Disability accommodations
- Housing and financial instability resources
- Technology help
- Academic support

EVALUATION & GRADING

Assignments (6 at 25 points each for 150 possible points)
Discussion fora (7 at 16 points each for 112 possible points)
Exam I (100 possible points)
Exam II (100 possible points)

- Each homework 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 posting guidelines, tips, and expectations. Points will be added across the fora for total possible points of 112.

- 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 462.

Grading Scale
The University uses plus and minus grading on a 4.000 cumulative grade point scale in accordance with the following, and you can expect the grade lines to be drawn as follows:

% In Class	Grade	GPA
93.00 – 100.00%	A	4.000
90.00 - 92.99%	A-	3.667
87.00 - 89.99%	B+	3.333
83.00 - 86.99%	B	3.000
80.00 - 82.99%	B-	2.667
77.00 - 79.99%	C+	2.333
73.00 - 76.99%	C	2.000
70.00 - 72.99%	C-	1.667
67.00 - 69.99%	D+	1.333
60.00 – 66.99%	D	1.000
< 60.00%	F	

- A = achievement that is outstanding relative to the level necessary to meet course requirements.
- B = achievement that is significantly above the level necessary to meet course requirements.
- C = achievement that meets the course requirements in every respect.
- D = achievement that is worthy of credit even though it fails to meet fully the course requirements.
- F = failure because 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 (Incomplete).
- S = achievement that is satisfactory, which is equivalent to a C- or better
- N = achievement that is not satisfactory and signifies that the work was either 1) completed but at a level that is not worthy of credit, or 2) not completed and there was no agreement between the instructor and student that the student would receive an I (Incomplete).

Evaluation/Grading Policy	Evaluation/Grading Policy Description
Scholastic Dishonesty, Plagiarism, Cheating, etc.	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 (As defined in the Student Conduct Code). For additional information, please see https://z.umn.edu/dishonesty The Office for Student Conduct and Academic Integrity has compiled a useful list of Frequently Asked Questions pertaining to scholastic dishonesty: https://z.umn.edu/integrity. If you have additional questions, please clarify with your instructor. 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. Indiana University offers a clear description of plagiarism and an online quiz to check your understanding (http://z.umn.edu/iuplagiarism).
Late Assignments	Assignments that are late will generally not be accepted for credit. Students anticipating late submission should first seek permission from the instructors.
Attendance Requirements	Not applicable.
Makeup Work for Legitimate Reasons	If you experience an extraordinary event that prevents you from completing coursework on time and you would like to make arrangements to make up your work, contact your instructor within 24 hours of the missed deadline if an event could not have been anticipated and at least 48 hours prior if it is anticipated. University policy recognizes that there are a variety of legitimate circumstances in which students will miss coursework, and that accommodations for makeup work will be made. This policy applies to all course requirements, including any final examination. Students are responsible for planning their schedules to avoid excessive conflicts with course requirements. 1. Instructors may not penalize students for absence during the academic term due to the following unavoidable or legitimate circumstances: illness, physical or mental, of the student or a student's dependent; medical conditions related to pregnancy; participation in intercollegiate athletic events; subpoenas; jury duty; military service; bereavement, including travel related to bereavement; religious observances; participation in formal University system governance, including the University Senate, Student Senate, and Board of Regents meetings, by students selected as representatives to those bodies; and activities sponsored by the University if identified by the senior academic officer for the campus or the officer's designee as the basis for excused absences. 2. Voting in a regional, state, or national election is not an unavoidable or legitimate absence. 3. Instructors are expected to accommodate students who wish to participate in party caucuses, pursuant to Board of Regents resolution (see December 2005 Board of Regents Minutes, p 147.) 4. For circumstances not listed in (1), the instructor has primary responsibility to decide on a case-by-case basis if an absence is due to unavoidable or legitimate circumstances and grant a request for makeup work. Because this course is entirely online and all materials are available to students from the first day of the term, we expect students to plan accordingly if travels or access to internet will cause them to miss a deadline. Note that our deadlines are generally set for 11:55 p.m. CST, so traveling to a different time zone will require additional planning. Further, circumstances that qualify for making up missed work will be handled by the instructor on a case-by-case basis; they will always be considered but not always granted. For complete information, view the U of M's policy on Makeup Work for Legitimate Absences (http://z.umn.edu/sphmakeupwork).
Saving & Submitting Coursework	**Documents that students submit are considered final;** students may not submit more than one version or draft of each assignment.

Technical Issues with Course Materials	You are expected to submit all coursework on time and it is your responsibility to ensure that your work is submitted properly before the deadline.
	
	If you experience technical difficulties while navigating through the course site or attempting to submit coursework:
	
	• Go to Quick Help: http://z.umn.edu/sphquickhelp.
	• Connect with the appropriate person or office within 30 minutes of the problem's occurrence.
	  o Provide as much information as possible, so the tech team can best help you as soon as possible.
	  o You can expect a response within 1-2 business days to help resolve the problem.

CEPH COMPETENCIES

Competency	Learning Objectives	Assessment Strategies
2. Select quantitative and qualitative data collection methods appropriate for a given health context.	Distinguish among the different quantitative and qualitative types of studies that may be used to gather information on safety and/or efficacy of a proposed treatment or intervention. 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.	Homework assignments and the group discussions will cover this learning objective.
3. Analyze quantitative and qualitative data using biostatistics, informatics, computer-based programming and software.	Understand the role of sample size and power calculations in study design, how to get the necessary inputs for those calculations (e.g., estimated group mean difference, variability, and error probabilities), and how to implement the calculations for various clinical trial study designs.	Homework assignments and the group discussions will cover this learning objective.
4. Interpret results of data analysis for public health research, policy or practice.	Review critically the published results of clinical trials. Discern, from reading a research article on a clinical trial's design or its results, which study design was used for that trial. Interpret the results of research studies (for various types of study designs involving treatment(s) or intervention(s)) within the context of the stated hypothesis and the scientific/public health relevance.	Homework assignments and the group discussions will cover this learning objective.
6. Discuss the means by which structural bias, social inequities, and racism undermine health and create challenges to achieving health equity at the organizational, community, and societal levels. and 8. Apply awareness of cultural values and practices to the design or implementation of public health programs.	Discuss historical background and how it informs current issues in, and ethical practices for, human subjects research and involving vulnerable populations in clinical trials. Understand challenges inherent in conducting a clinical trial in a developing country. Discuss different conflicts and ethical issues that arise from the implementation of clinical trials both domestically and internationally.	Homework assignments and the group discussions will cover this learning objective.
18. Select communication strategies for different audiences and sectors.	Be aware of the need to assess an audience's cultural and scientific backgrounds and research interests; practice tailoring written communications to be understandable and relevant to those backgrounds and interests.	Because the students in this class encompass diverse cultural and scientific-training backgrounds, communication by each student within the group discussions will cover this learning objective.

http://www.isph.umn.edu/sph/instructor-resources/