SYLLABUS & COURSE INFORMATION

SCHOOL OF PUBLIC HEALTH
UNIVERSITY OF MINNESOTA

PUBH 7420, SECTION 001

Clinical Trials: Design, Implementation, and Analysis
Spring 2019

COURSE & CONTACT INFORMATION

Credits: 3
Meeting Day(s): TTh
Meeting Time: 9:45-11:00
Meeting Place: Mayo 3-125

Instructor: Jim Neaton
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Office Hours: By Appointment
Office Location: 2221 University Ave SE, Suite 200

COURSE DESCRIPTION

This course covers basic concepts in the design, conduct and analysis of clinical trials. The Moodle site for the course can be found at: https://ay17.moodle.umn.edu/course/view.php?id=18510. Notes and slide provided each week.

COURSE PREREQUISITES

Introduction to Biostatistics

COURSE GOALS & OBJECTIVES

1. Identify basic characteristics of a clinical trial and describe the advantages and disadvantages or randomized clinical trials as compared to other epidemiological and clinical investigations.
2. Construct randomization schedules and develop procedures for carrying out randomization.
3. Determine when pre-stratified designs should be used and differentiate pre from post-stratification.
4. Determine what level of blinding (masking) of treatments is warranted for trials.
5. Understand considerations in defining control groups for clinical trials, including the use of placebos.
6. Identify the advantages and disadvantages of different types of endpoints for trials, and the importance of pre-specifying trial estimands of interest.
7. Understand issues in the definition of target populations for trials (inclusion and exclusion criteria); identify the essential elements of informed consent.
8. Recognize the regression to the mean phenomenon and how to minimize its effect.
9. Recognize the advantages and disadvantages of different types of trial designs, including crossover and factorial studies, pragmatic versus explanatory trials, and superiority and non-inferiority designs.
10. Discuss examples of misconduct and fraud and their implications in clinical research.
11. Determine sample sizes for trials of simple design and understand ingredients in the sample size determination for more complex designs, including clinical outcome trials and non-inferiority studies.

12. Write the statistical design and data analysis section of a protocol and identify special requirements of collaborative trials, their organization and operation.
13. Determine data collection requirements and quality assurance procedures for clinical trials, including procedures to minimizing missing outcome data.
14. Understand the advantages of intent-to-treat analysis and to differentiate it from analyses such as “on treatment” and “per protocol” analyses.
15. Summarize and interpret subgroup analyses and assess possible pitfalls.
16. Recommend a plan for interim analyses for trials and understand the role of independent Data Monitoring Committees.

METHODS OF INSTRUCTION AND WORK EXPECTATIONS

Course Workload Expectations

PubH 7-420 is a 3 credit course. You will spend an estimated 3 hours per week attending class and 3-4 hours per week outside of class reading, studying, completing assignments, and in small group work. Slides and reading materials will be provided each week. The slides will be the focus of lectures and discussion.

Learning Community

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

In group work, this can mean:

- Setting expectations with your groups about communication and response time during the first week of the semester (or as soon as groups are assigned) and contacting the TA or instructor if scheduling problems cannot be overcome.
- Setting clear deadlines and holding yourself and each other accountable.
- Determining the roles group members need to fulfill to successfully complete the project on time.
- Developing a rapport prior to beginning the project (what prior experience are you bringing to the project, what are your strengths as they apply to the project, what do you like to work on?)

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).

COURSE TEXT & READINGS

Fundamentals of Clinical Trials (5th Edition), Friedman, Furberg, DeMets, Reboussin, and Granger (available as an ebook). The link is: Link: http://link.springer.com.ezp1.lib.umn.edu/book/10.1007%2F978-3-319-18539-2

See notes and web site for other readings.

COURSE OUTLINE/WEEKLY SCHEDULE (SEE COURSE CALENDAR ON WEB SITE FOR READINGS, ACTIVITIES AND ASSIGNMENTS)

Week	Topic	Readings	Activities/Assignments
Week 1 Date-Date	• **Methods of Clinical Research**	• **Readings**	• **Assignment** •
Week 2 Date-Date	• **Randomization and Stratification**	•	•
Week 3 Date-Date	• **Intention to Treat and Blinding**	•	•
Week 4 Date-Date	• **Endpoints**	•	•
Week 5 Date-Date	• **Treatment and Control Groups**	•	•
Week 6 Date-Date	• **Endpoints**	•	•
Week 7 Date-Date	• **Eligibility Criteria and Scientific Misconduct/Ethical Issues**	•	•
Week 8 Date-Date	• **Mid-Term Exam and Parallel Group Trials**	•	•
Week 9 Date-Date	• **Crossover Trials and Sample Size**	•	•
Week 10 Date-Date	• **Sample Size**	•	•
Week 11 Date-Date	• **Superiority and Non-inferiority designs and Subgroup Analysis**	•	•
Week 12 Date-Date	• **Data and Safety Monitoring Boards and Interim Analyses**	•	•
Week 13 Date-Date	• **Protocol Presentations**	•	•
Week 14 Date-Date	• **Protocol Presentations**	•	•
Week 15 Date-Date	• **Protocol Presentations**	•	•

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

- Homework (3 assignments – 20%); in the homework you will construct randomization schedules for trials with and without stratification, implement adaptive stratification methods, recommend procedures for implementing randomization to ensure that assignments cannot be anticipated, develop procedures for implementing single- and double-blind studies, analyze factorial and crossover studies, estimate the impact of regression to the mean on the interpretation of results, compute sample size for complex trials, carry out and interpret subgroup analyses, and develop monitoring boundaries for interim analyses.
- Group debate (5%): two groups will debate a controversial topic. Each group will be given 10 minutes to make a slide presentation. This will involve reading 2-3 papers to prepare arguments.
- Group literature review (5%): Each group will be asked in 10 minutes summarize a key design/analysis topic of a published clinical trial.
- Protocol project (30%); a part of a multi-disciplinary team of 7-8 people, you will write a protocol for a clinical trial. The protocol will include the following sections: 1) background and rationale; 2) primary and secondary objectives, include subgroup hypotheses; 3) inclusion and exclusion criteria; 4) treatment definitions, including procedures for randomization and blinding; 5) sample size justification; 6) data collection plan and follow-up schedule; and 7) interim and final analysis plans.
- Mid-term (20%) and final (20%); these will be closed book exams that test comprehension of high level issues critical to the design, implementation and analysis of clinical trials, e.g., methods for randomization and blinding, when to stratify in the design versus analysis, when to consider placebo versus active controls, inclusion criteria and regression to the mean, considerations in use of factorial and crossover studies, factors influencing sample size in long-term trials, superiority and non-inferiority trials, intention to treat, subgroup analysis, type 1 error and futility considerations in interim analyses of trials, and reporting trial results.

Homework and mid-term grade results will generally be distributed within 2 weeks.

S Represents achievement that is satisfactory, which is equivalent to a C- or better. Please also refer to the University's Uniform Grading Policy and Grading Rubric Resource at https://z.umn.edu/gradingpolicy]

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 - 100%	A	4.000
90 - 92%	A-	3.667
87 - 89%	B+	3.333

83 - 86%	B	3.000
80 - 82%	B-	2.667
77 - 79%	C+	2.333
73 - 76%	C	2.000
70 - 72%	C-	1.667
67 - 69%	D+	1.333
63 - 66%	D	1.000
< 62%	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	Please notify instructor
Attendance Requirements	NA
Extra Credit	NA

CEPH COMPETENCIES

Competency	Learning Objectives	Assessment Strategies
1-4 (Evidence-based approaches to public health)	See goals and objectives of course.	See evaluation and grading.