**Course Syllabus**

**Biostatistics 04214**

**Design and Analysis of Clinical Trials**

**Date:** Fall Semester, 2022, August 29 – December 16 (16 weeks)

**Time:** Tuesdays and Thursdays; 11:15 am – 12:40 pm

**Place:** HUB A2545 usually; on October 20, will meet in HRC H1270

**Course Director and Contact Information:**

Michael Martens PhD, Division of Biostatistics, Institute for Health and Equity

Phone: 414-955-8371

Email: [mmartens@mcw.edu](mailto:mmartens@mcw.edu)

Office: HRC 1401

Office hours: Fridays, 10:00am – 12:00pm in HRC 1401/via Webex meeting

**Credit:** 3 credits

**Prerequisites:** Statistical Models and Methods I or concurrent registration.

**Course Description:** This course covers issues in clinical trials including the clinical trial protocol, sources of bias in clinical trials, blinding, randomization, sample size calculation; phase I, phase II, phase III and hybrid trials; interim analysis, stochastic curtailment, and administrative issues in study design.

**Student Learning Objectives/Outcomes:** Students are expected to learn fundamental concepts impacting the design and analysis of clinical trials. Students should be able to critically evaluate and appropriately specify statistical design and analysis techniques for phase I, II, and III clinical trials, including sample size/power determination, analysis methods for trial endpoints, and provisions for data and safety monitoring.

The course emphasizes the following core competencies: Knowledge within program area (conceptual, statistical, and design issues in clinical trials); Research skills (trial design and analysis, reviewing and understanding clinical trials research); Critical and creative thinking (understanding potential biases in clinical trials, evaluating suitability of design and analysis methods, critically reviewing a clinical trial article, protocol, and proposal); Interpersonal and communication skills (participation in discussions, presentation skills).

**Course Structure and Expectations:** The course will meet twice per week for 1.5 hours each session using primarily a lecture format along with some in-class discussion. Homework assignments will be given every 1 - 2 weeks. Reading assignments related to clinical trials will also be assigned regularly and will be discussed in class. At the end of the course, each student will prepare an oral presentation on a paper related to the course. Students should obtain approval from the course director for the chosen paper; the course director can assist in selecting a paper if requested. These paper presentations will take place during the last week of class and should be no longer than 20 minutes. Two examinations will be given during the course, a midterm and a final exam. These will each be administered during regularly scheduled course sessions.

Students are expected to attend all sessions unless specifically excused by the course director - note that part of the course grade is based on participation in discussion. Assignments are expected to be completed on time.

**Grading Policy:** The course grade will be determined by homework assignments (25%), class participation (10%), a midterm exam (20%), a final exam (30%), and a clinical trial paper presentation (15%).

**Resources:**

*Recommended textbook*:

(P) Piantodosi, S. Clinical Trials: A methodologic perspective, 2nd Edition. Wiley, 2005.

*Supplemental textbooks*:

(M) Matthews, J. Introduction to randomized controlled clinical trials, 2nd edition. Chapman and Hall/CRC, 2006.

(FFD) Friedman, Furberg, and DeMets. Fundamentals of clinical trials, 3rd edition. SpringerVerlag, 1998.

(C) Crowley, J. (Ed.) Handbook of Statistics in Clinical Oncology, Marcel Dekker, 2012.

Research articles and clinical trials documents will be provided as needed during the course.

**Technical Requirements:** All students should have access to SAS and R through the Division of Biostatistics computing resources.

**Missed Assignments or Examinations:** Students are referred to the online Graduate School Handbook for the policy on missed assignments or examinations. In brief, vacations and personal travel are not acceptable excuses for missed assignments or examina­tions. If students will be away to attend a scientific meeting, the proposed absence must be discussed with the Course Director in advance of the absence. Absences due to illness should be discussed with the Course Director as soon as possible after recovery. If the final examination is missed due to illness, a note from a licensed health care provider supporting the absence will be required.

**Special Accommodation**: If you will need accommodations in order to meet any of the requirements of this course, please contact the course director as soon as possible.

**Course Evaluation:** All students completing the course for credit are required to complete an online Course Evaluation in OASIS at the end of the course. This includes feedback on teaching of individual instructors in each course. Participation by all students is important for the Graduate School’s course evaluation process and for our continued accreditation. The Graduate School will provide instructions on how to complete the evaluation at the beginning of each semester, and you will have until 2 weeks after the end of the course to complete the evaluation. Students who fail to complete the evaluation are no longer in good standing. The Graduate School will not provide transcripts, confirm enrollment, allow enrollment in additional courses, allow graduation, or support payment of stipends for students who are not in good standing. The Graduate School may impose a $100 fine for each course evaluation not completed on time.

**Instructor Feedback:** All students enrolled in the course for credit are required to complete a 4 item form in OASIS for each instructor. You will receive email prompts to direct you to OASIS and to facilitate the task.

**Copyright Protected:**

Educational materials, including exams, lecture notes, outlines, instructions for homework assignments, Power Point presentations, study guides, audio, video and/or digital files and/or any materials authored or created by MCW faculty for use in courses may not be used for any other purpose without the written permission of the course director.

<https://www.mcw.edu/-/media/MCW/Education/Graduate-School/Documents/2016-Graduate-School-Handbook.pdf>

(Page 41)

[*http://infoscope.mcw.edu/research/GeneralPolicies/PatentandCopyright.htm*](http://infoscope.mcw.edu/research/GeneralPolicies/PatentandCopyright.htm)

**Course Schedule:**

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| --- | --- | --- | --- |
| **Week** | **Class date** | **Topic** | **Chapter in textbook\*** |
| 1 | Aug 30 | Introduction to clinical trials | P: 1-8,12; FFD: 1-3,6 |
|  | Sep 1 | Introduction to clinical trials | P: 1-8,12; FFD: 1-3,6 |
| 2 | Sep 6 | Phase I trials | P: 10; C: 1-3 |
|  | Sep 8 | Phase I trials | P: 16.2; C: 1-3 |
| 3 | Sep 13 | Phase II trials | P: 11; C: 7 |
|  | Sep 15 | Phase II trials | P: 16.3; C: 8-9 |
| 4 | Sep 20 | Phase III trials | P: 13; FFD: 5; M: 4 |
|  | Sep 22 | Randomization techniques | P: 13; FFD: 5; M: 4 |
| 5 | Sep 27 | Simple univariate analysis | P: 16; M: 6 |
|  | Sep 29 | Simple univariate analysis | P: 16; M: 6 |
| 6 | Oct 4 | Simple univariate analysis | P: 16; FFD: 14; M: 7 |
|  | Oct 6 | Sample size calculations | P: 11; FFD: 7; M: 3 |
| 7 | Oct 11 | Sample size calculations | P: 11; FFD: 7; M: 3 |
|  | Oct 13 | Adjusting analysis for covariates | P: 17; FFD: 16; M: 6,7 |
| 8 | Oct 18 | Adjusting analysis for covariates | P: 17; FFD: 16; M: 6,7 |
|  | Oct 20 | Midterm exam |  |
| 9 | Oct 25 | Interim analysis and group sequential methods | P: 14; FFD: 15; M: 8 |
|  | Oct 27 | Interim analysis and group sequential methods | P: 14; FFD: 15; M: 8 |
| 10 | Nov 1 | Error spending | P: 14; FFD: 15; M: 8 |
|  | Nov 3 | Stochastic curtailment and safety monitoring | P: 14; FFD: 15; M: 8 |
| 11 | Nov 8 | Subgroup analysis | P: 16.7; FFD: 16; M: 9 |
|  | Nov 10 | Multiple outcomes | P: 16.7; FFD: 16; M: 9 |
| 12 | Nov 15 | Analysis populations | P: 15; FFD: 16; M: 10 |
|  | Nov 17 | Missing data | P: 15; FFD: 16; M: 10 |
| 13 | Nov 22 | Crossover trials | P: 19; FFD: 4; M: 11 |
|  | Nov 24 | No class - Happy Thanksgiving! |  |
| 14 | Nov 29 | Factorial designs | P: 20; FFD: 4 |
|  | Dec 1 | Adaptive designs |  |
| 15 | Dec 6 | Presentations |  |
|  | Dec 8 | Presentations |  |
| 16 | Dec 13 | Presentations and course review |  |
|  | Dec 15 | Final exam |  |

\* P, FFD, M, C refer to the textbooks listed in the Resources section