FUNDAMENTALS OF CLINICAL TRIALS
BIOSTATISTICS 540
YALE UNIVERSITY, SPRING 2025

Lectures	Wednesdays, 1-2.50 PM – 47 College Room 106A
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Office hours	*By arrangement*
Teaching Assistant	Kerry Conlin
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Teaching Assistant	Matthew Ponticiello
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Office hours	Tuesdays 4 – 5pm Zoom ID: 997 398 1259

Course learning objectives:

At the end of this course, students should be able to:

1. Recognize fundamental principles of randomized clinical trials (RCT)
2. Distinguish between various RCT design types
3. Select suitable analytical techniques for an RCT design
4. Conduct a critical evaluation of an RCT
5. Understand appropriate processes of communicating RCT findings

These objectives will be assessed through post-class assignments, the midterm, and final exams.

Prerequisites

- BIS 505 or proficiency in basic biostatistics principles. Enrollment is limited to second-year or greater students unless instructor permission is obtained.

Course Resources

Textbooks

- Peduzzi PN. Principles and Practice of Multi-Site Randomized Controlled Trials in the Phase III Setting CARDET PRESS, a division of the Centre for the Advancement of Research and Development in Educational Technology – CARDET LTD. ISBN: 978-9925-7363-1-7

  PDF version
  https://press.cardet.org/product/principles-and-practice-of-multi-site-randomized-controlled-trials-in-the-phase-iii-setting-electronic/

  ePub version
  https://press.cardet.org/product/principles-and-practice-of-multi-site-randomized-controlled-trials-in-the-phase-iii-setting-electronic-epub/

- Friedman LM, Furberg CD, DeMets DL. Fundamentals of Clinical Trials. Fourth edition. Springer-Verlag, New York; 2010. 400 pp, ISBN 1441915850.
  https://link.springer.com/book/10.1007/978-1-4419-1586-3
  https://yale.idm.oclc.org/login?URL=http://dx.doi.org/10.1007/978-1-4419-1586-3

Other resources

- Warren S Browner MD, MPH, Thomas B Newman MD, MPH, Steven R Cummings MD, Deborah G Grady MD, MPH, Alison J Huang, Alka M. Kanaya, Mark J Pletcher, Designing Clinical Research, ISBN/ISSN: 9781975174408; Publisher - Wolters Kluwer; Publication Date: May 11, 2022.

- Delva Shamley and Brenda Wright, A Comprehensive and Practical Guide to Clinical Trials, ScienceDirect; ISBN: 978-0-12-804729-3; Published 2017, Academic Press

Course Webpage

- Canvas.yale.edu

Assessments and Grading

Post-lecture assessment

- Weekly

Exams

- Midterm (in class): Short answers and multiple choice
- Final (take-home and in class):
    - (a) RCT critique (take home)
    - (b) Short answers and multiple choice (during finals week)

Note: Both exams will be based on material covered during class lecture content and any assigned readings. More detail about the RCT critique will be provided later in the semester.

Grading

- Post-lecture assignments (completed/not completed) (20% of final grade)
- Midterm Exam (30% of final grade)
- Final Exam (50% of final grade)

Class Etiquette

- Please no texting, web surfing, or emailing during class. These activities display a lack of respect for others in the classroom and will not be tolerated. If a student needs to send or read a text message, it is best to leave the room.
- Cellphone ringers should be turned off during class. Students who must be accessible via cellphone due to extenuating circumstance (e.g., family, or clinical responsibilities) should set their phone to vibrate and let the instructor know.
- Please restrict the use of computers and smartphones to class instruction, viewing course-related materials, and taking notes.
- Audio or video recording of class sessions requires prior approval of the course instructor.
- Students are expected to arrive on time for class.

CODE OF ACADEMIC AND PROFESSIONAL INTEGRITY
Honor Code

The Honor Code explicates the highest ethical standards to which we must hold ourselves, our peers, and our colleagues. Honesty, respect, and trust are hallmarks of the science and practice of public health. They must be always nurtured in our classrooms and in our work beyond the classroom. Upon arrival at YSPH, all students will sign an Honor Code that states:

By enrolling in the Yale M.P.H. program, I am accepting the responsibility to promote and uphold the Code of Academic and Professional Integrity.

I understand that the work I submit must represent my own efforts; that I will conduct myself with dignity, integrity, and honesty in my studies; that I will uphold the directions of my faculty and complete all my work in the spirit it was assigned. I understand I must honestly represent my credentials, abilities, and situation as I further my career as a public health professional.

I agree to be held accountable for maintaining the atmosphere of honesty and professionalism at Yale University and within the greater academic community. In the spirit of my professional development—where I should not tolerate misconduct in my professional setting—I also agree to contact the appropriate faculty member, or the associate dean for student affairs, if I witness a violation of this Code of Academic and Professional Integrity by any of my peers.

Upon completion of all written assignments and examinations, students will sign the following statement:

I have not given, received, or witnessed inappropriate exchange of information on this assignment, and I certify that this is my own original work.

https://catalog.yale.edu/ysph/academic-policies/ysph-committee-academic-professional-integrity-capi/ *Accessed 14 January 2025*

AI Tool Use policy for the course

This course will assess your understanding of the material through assignments that will require your own critical thinking and the supportive arguments that go along with such. I would strongly encourage you to adhere to this didactic approach.

However, we do acknowledge that artificial intelligence (AI) tools are abundantly used, and this area is fast-changing for all areas including teaching and learning. Hence, the AI tool use policy for this course is outlined below.

Note that the University's policy states that *"Inserting AI-generated text into an assignment without proper attribution is a violation of academic integrity, and using AI tools in a manner that was not authorized by your instructor may also be considered a breach of academic integrity*". In general, this means using AI to generate arguments and writing without proper attribution is considered plagiarism.

In this course, any written work that you submit must be your own ideas and writing, and not copied or AI generated.

AI may be used to support your work (i.e. gathering sources, reviewing literature, etc): If you use any AI tool to support work on an assignment it must be acknowledged in a citation that includes 1) the prompt you submitted to the bot, 2) the date of access, and 3) the URL of the program.

For more details, please consult the Poorvu Center's guidelines on using sources.

Course Schedule

Session	Date	Topic
1.	01/15/25	Course description Introduction to RCTs I o *Historical Overview of Clinical Trials* o *Definition, Objectives, and Importance of Clinical Trials*
2.	01/22/25	Introduction to RCTs II o *Lifecycle: from Research Question to Final Report*
3.	01/29/25	Ethical and Regulatory Framework: Human Subjects Protection o *Regulations and Guidelines governing Clinical Trials* o *Informed Consent Process* o *Institutional Review Boards and Ethics Committee*
4.	02/05/25	RCT Design Principles I o *The Research Question* o *Selection of endpoint(s)* o *Selection and Recruitment of Study Participants*
5.	02/12/25	RCT Design Principles II o *Types of trials and trial designs* o *Randomization and Blinding* o *Bias and Methods to Minimize It*
6.	02/19/25	RCT Design Principles III o *Sample size determination*
7.	02/26/25	Data Management and Trial Monitoring* o *CRF Design and Development* o *Data Entry, Cleaning and Validation* o *Monitoring Visits and Responsibilities* o *Source Document Verification* o *GCP Compliance* o *Regulatory Inspections and Audits* o **Real-life RCT experience: Course Contributor: Kerry Conlin*
8.	**03/05/25**	**MIDTERM EXAM – *in class during usual class time***
	03/12/25	**RECESS- No Class**
	03/19/25	**RECESS- No Class**

9.	03/26/25	Trial Conduct, Coordination and Management ○ *Investigator Selection and Training* ○ *Site Selection and Initiation* ○ *Clinical Trial Operations* ○ *Data Collection and Management* ○ *Adverse Event Reporting and Safety Monitoring* ○ *Quality Control and Assurance*
10.	04/02/25	Data Analysis Principles I ○ *Statistical Analysis and Interpretation*
11.	04/09/25	Data Analysis Principles II ○ *Statistical Analysis and Interpretation*
12.	04/16/25	Data Analysis Principles III ○ *Statistical Analysis and Interpretation*
13.	04/23/25	Trial closeout and Reporting ○ *Data Analysis and Final Report* ○ *Dissemination of results*
	04/30/25	**Reading Period-No Class**
14.	**05/07/25**	**FINAL EXAM** ***Take-home component: Due by 1pm on this day*** ***In-class component: on this day***