

University of Florida
Colleges of Medicine and Public Health & Health Professions
Department of Biostatistics
PHC 6022: Design & Conduct of Clinical Trials (3 credit hours)
Fall 2021
On-Campus
Course Website: <http://elearning.ufl.edu/>

Instructor Names: **Arlene Naranjo**, Ph.D. and **Qinglin Pei**, Ph.D.
6011 NW 1st Place, Gainesville, FL 32607

Room Number: Communicore C1-11

Time: Mondays, 1:55–3:50pm (Periods 7-8)
Wednesdays, 1:55–2:45pm (Period 7)

Phone Numbers: 352-273-0577 and 352-273-0552

Email Addresses: anaranjo@coq.ufl.edu and gpei@coq.ufl.edu

Office Hours: By appointment

Prerequisites

STA 2023 (Introduction to Statistics I) or equivalent, and permission of the instructors. Students are expected to have basic statistical knowledge.

PURPOSE AND OUTCOME

Course Overview

Students will learn about ethics, principles and conduct of clinical trials for medical research. The protection of study participants and the need for equipoise will be covered, including regulatory restrictions and the latest patient privacy regulations for the dissemination and use of data associated with the participants in clinical trials. Various study designs will be discussed, including single-arm, crossover, factorial, sequential multi-stage, and dose-finding designs, plus the means to allocate study participants to appropriate treatment groups using randomization (blocked or stratified) and prognostic factors. Writing the study protocol, data collection, analyses methods and reporting of results of a trial will be discussed. The importance of equipoise, informed consent, and the use of intent-to-treat analysis will be emphasized. Data collection and management for the conduct of clinical trials will be addressed. The course will also include discussions on the application of the appropriate analytic methods for each specific type of study endpoint, approaches to performing interim safety monitoring, and adaptive trial designs. Translational research plays an increasing role in clinical trials, and the identification and rationale for the use of prognostic factors will be covered. Other topics to be touched upon include health-related quality of life measures, longitudinal data analysis, and meta-analysis. The roles of the Institutional Review Board (IRB), Data Safety Monitoring Committee (DSMC) and federal regulatory agencies in the approval and review of ongoing

clinical trials will be discussed. Homework assignments will be extremely applied and will make use of real clinical trials designs and data.

Course Objectives and/or Goals

By the end of this course, the student should be able to:

- (1) Explain key concepts in the design of clinical trials.
- (2) Describe the study designs commonly used.
- (3) Identify key issues in data management for clinical trials.
- (4) Describe the roles of Regulatory Affairs in clinical trials.
- (5) Identify the appropriate data analytic technique to match the study endpoint.
- (6) Describe safety monitoring issues in clinical trials and related data analysis methods.
- (7) Describe the basics of longitudinal data analysis and adaptive designs.
- (8) Understand alternative trial designs.

Instructional Methods

Class sessions will be a combination of presentation of major topics and class discussion of the presentations and additional readings. Attendance and active participation in all class discussions is required, and will be evaluated as part of the student's grade for the course. Students must read the assigned readings prior to each class session. Students are expected to take an active role in initiating and leading discussions and debates.

Blended Learning

What is blended learning and why is it important?

A Blended Learning class uses a mixture of technology and face-to-face instruction to help you maximize your learning. Knowledge content that the instructors would have traditionally presented during a live class lecture is instead provided online before the live class takes place. This lets the instructors focus face-to-face teaching on course activities designed to help you strengthen higher order thinking skills such as critical thinking, problem solving, and collaboration. Competency in these skills is critical for today's health professional.

What is expected of you?

You are expected to actively engage in the course throughout the semester. You must come to class prepared by completing all out-of-class assignments. This preparation gives you the knowledge or practice needed to engage in higher levels of learning during the live class sessions. If you are not prepared for the face-to-face sessions, you may struggle to keep pace with the activities occurring in the live sessions, and it is unlikely that you will reach the higher learning goals of the course. Similarly, you are expected to actively participate in the live class. Your participation fosters a rich course experience for you and your peers that facilitates overall mastery of the course objectives.

DESCRIPTION OF COURSE CONTENT

Topical Outline/Course Schedule

Week	Topic(s)
1	<ul style="list-style-type: none"> ▪ Introduction, Motivation, and Ethics of Clinical Trials ▪ Phases, Contexts, Examples
2	<ul style="list-style-type: none"> ▪ Phases, Contexts, Examples ▪ Study Population & Cohort
3	<ul style="list-style-type: none"> ▪ Study Protocol
4	<ul style="list-style-type: none"> ▪ Research Question and Outcomes ▪ Study/Trial Design
5	<ul style="list-style-type: none"> ▪ Study/Trial Design
6	<ul style="list-style-type: none"> ▪ Treatment Allocation ▪ Privacy
7	<ul style="list-style-type: none"> ▪ Measurement and Data Capture ▪ Hypothesis Testing
8	<ul style="list-style-type: none"> ▪ Hypothesis Testing ▪ Analytic Methods for Specified Endpoints, Assumptions & Diagnostics
9	<ul style="list-style-type: none"> ▪ Analytic Methods for Specified Endpoints, Assumptions & Diagnostics ▪ Random Error & Bias
10	<ul style="list-style-type: none"> ▪ Introduction to Power and Sample Size ▪ Design and Analysis Methods for Translational Research
11	<ul style="list-style-type: none"> ▪ Alternate Trial Designs ▪ Adaptive, Enrichment, and Seamless Designs
12	<ul style="list-style-type: none"> ▪ Adaptive, Enrichment, and Seamless Designs ▪ Issues in Data Analysis
13	<ul style="list-style-type: none"> ▪ Longitudinal Data Analysis ▪ Health-Related Quality of Life
14	<ul style="list-style-type: none"> ▪ Safety Monitoring
15	<ul style="list-style-type: none"> ▪ Regulatory Affairs ▪ IRB ▪ Reporting of Results
16	<ul style="list-style-type: none"> ▪ Student Presentations

Course Materials and Technology

Required Text:

Friedman, Furberg, DeMets, Reboussin, and Granger. *Fundamentals of Clinical Trials (5th Edition)*. Springer, 2015. Text available online at <https://link.springer.com/content/pdf/10.1007%2F978-3-319-18539-2.pdf>.

Optional Texts:

- Machin and Fayers. *Randomized Clinical Trials: Design, Practice and Reporting*. Wiley-Blackwell, 2010.
- Piantadosi S. *Clinical Trials: A Methodologic Perspective (2nd Edition)*. New Jersey: John Wiley & Sons, 2005.
- Meinert CL. *Clinical Trials: Design, Conduct, and Analysis*. Oxford University Press, 1986.
- Pocock SJ. *Clinical Trials: A Practical Approach*. John Wiley & Sons, 1996.

Additional course materials are available via E-Learning at <http://elearning.ufl.edu/>.

For technical support for this class, please contact the UF Help Desk at:

- helpdesk@ufl.edu
- (352) 392-HELP - select option 2
- <https://helpdesk.ufl.edu/>

ACADEMIC REQUIREMENTS AND GRADING

Assignments

There are four requirements:

1. Homework. Based on material covered during Weeks 4, 4-5, 7-8, 8-9, and 9-10 and due via e-mail, E-Learning, or next class session. Assignments must be each student's individual work; plagiarism is prohibited. (5x8%=40%).
2. Quizzes. There will be a quiz covering material from Weeks 1-2, 6, 10-12, and 13-14. (4x5%=20%).
3. Class participation. Class attendance (5%) and reading the required class assignments prior to each class session and active participation in all class discussions (5%) is required. Attendance will be taken every class. Missing three or more unexcused scheduled sessions will result in receiving 0 points for class participation. All students must participate in each class discussion by providing responses to teacher's requests on sharing thoughts or solutions. (2x5%=10%)
4. Written report and presentation at the end of the course. (30%)

Grading

Grades will be based on homework assignments (40%); quizzes (20%); attendance and class participation (10%); written report (15%) and presentation (15%).

The following grading system will be used:

Points Earned	92.5%-100%	89.5%-92.49%	86.5%-89.49%	82.5%-86.49%	79.5%-82.49%	76.5%-79.49%	72.5%-76.49%	69.5%-72.49%	59.5%-69.49%	Below 59.49%
Letter Grade	A	A-	B+	B	B-	C+	C	C-	D	E

Letter grade to grade point conversions fixed by UF:

Letter Grade	A	A-	B+	B	B-	C+	C	C-	D+	D	D-	E	WF	I	NG	S-U
Grade Points	4.0	3.67	3.33	3.0	2.67	2.33	2.0	1.67	1.33	1.0	0.67	0.0	0.0	0.0	0.0	0.0

More information on UF grading policy may be found at:

<http://gradcatalog.ufl.edu/content.php?catoid=10&navoid=2020#grades>

Exam Policy

No midterm or final exam will be required in this course but there will be 4 quizzes.

Policy Related to Make up Exams or Other Work

Any assignment turned in within 24 hours after the deadline will be penalized 10%. Assignments that are more than 24 hours late will not be accepted and will not receive any credit. Any requests for make-up quizzes or extensions for late or missed work must be accompanied by a documented excuse. Excused absences must be consistent with university policies in the Graduate Catalog (<https://catalog.ufl.edu/graduate/regulations/#text>). Additional information can be found here: <https://catalog.ufl.edu/ugrad/current/regulations/info/attendance.aspx>.

Please note: Any requests for make-ups due to technical issues MUST be accompanied by the UF Computing help desk (<http://helpdesk.ufl.edu/>) correspondence. You MUST e-mail the instructors within 24 hours of the technical difficulty if you wish to request a make-up.

Policy Related to Required Class Attendance

Class attendance is mandatory. Excused absences will follow UF policy (e.g., illness, serious family emergency, military obligations, religious holidays; see below), and should be communicated to the instructors prior to the missed class day when possible. Missing three or more unexcused scheduled sessions will result in receiving 0 points for class participation. Regardless of attendance, students are responsible for all material presented in class and meeting the scheduled due dates for class assignments. Finally, students should read the assigned readings prior to the class meetings and be prepared to be called upon to discuss the material for each session.

Excused absences must be consistent with university policies in the Graduate Catalog (<https://catalog.ufl.edu/graduate/regulations/#text>). Additional information can be found here: <https://catalog.ufl.edu/ugrad/current/regulations/info/attendance.aspx>.

STUDENT EXPECTATIONS, ROLES, AND OPPORTUNITIES FOR INPUT

Expectations Regarding Course Behavior

Students are expected to show up for class prepared and on time. Cell phones are to be silenced during class unless there is an emergency, in which case please inform the instructor.

Communication Guidelines

Students are expected to participate in class discussions. Assignments must be clearly written in reasonably good English.

Academic Integrity

Students are expected to act in accordance with the University of Florida policy on academic integrity. As a student at the University of Florida, you have committed yourself to uphold the Honor Code, which includes the following pledge:

“We, the members of the University of Florida community, pledge to hold ourselves and our peers to the highest standards of honesty and integrity.”

You are expected to exhibit behavior consistent with this commitment to the UF academic community, and on all work submitted for credit at the University of Florida, the following pledge is either required or implied:

“On my honor, I have neither given nor received unauthorized aid in doing this assignment.”

It is your individual responsibility to know and comply with all university policies and procedures regarding academic integrity and the Student Honor Code. Violations of the Honor Code at the University of Florida will not be tolerated. Violations will be reported to the Dean of Students Office for consideration of disciplinary action. For additional information regarding Academic Integrity, please see Student Conduct and Honor Code or the Graduate Student Website for additional details:

<https://www.dso.ufl.edu/sccr/process/student-conduct-honor-code/>
<http://gradschool.ufl.edu/students/introduction.html>

Please remember cheating, lying, misrepresentation, or plagiarism in any form is unacceptable and inexcusable behavior.

Professionalism and COVID

As students pursuing a path in the health professions or public health, it is crucial to demonstrate professional behaviors that reflect integrity and commitment to the health of patients, fellow health professionals, and to populations we serve. To accomplish this, a strong responsibility for the well-being of others must be evident in our decisions, along with accountability for our actions.

Professionalism in the health disciplines requires adherence to high standards of conduct that begin long before graduation. This is particularly true during times of health emergencies such as the COVID pandemic, given our professional habits can have a direct impact upon the health of persons entrusted to us.

If you are not vaccinated, get vaccinated. Vaccines are readily available at no cost and have been demonstrated to be safe and effective against the COVID-19 virus. Visit this link for details on where to get your shot, including options that do not require an appointment:

<https://coronavirus.ufhealth.org/vaccinations/vaccine-availability/>. Students who receive the first dose of the vaccine somewhere off-campus and/or outside of Gainesville can still receive their second dose on campus.

In response to COVID-19, the following professional practices are in place to maintain your learning environment, to enhance the safety of our in-classroom interactions, and to protect the health and safety of ourselves, our patients, our neighbors, and our loved ones.

- You are required to wear approved face coverings at all times while in Health Science Center classrooms and within Health Science Center buildings even if you are vaccinated.
- If you are sick, stay home and self-quarantine. Please visit the UF Health Screen, Test & Protect website about next steps, retake the questionnaire and schedule your test for no sooner than 24 hours after your symptoms began. Please call your primary care provider if you are ill and need immediate care or the UF Student Health Care Center at 352-392-1161 (or email covid@shcc.ufl.edu) to be evaluated for testing and to receive further instructions about returning to campus. UF Health Screen, Test & Protect offers guidance when you are sick, have been exposed to someone who has tested positive or have tested positive yourself. Visit the UF Health Screen, Test & Protect website for more information.
- Continue to follow healthy habits, including best practices like frequent hand washing.
- Avoid crowded places (including gatherings/parties with more than 10 people)

Sanitizing supplies are available in the classroom if you wish to wipe down your desks prior to sitting down and at the end of the class. Hand sanitizing stations will be located in every classroom.

Course materials will be provided to you with an excused absence, and you will be given a reasonable amount of time to make up work. If you are withheld from campus by the Department of Health through Screen, Test & Protect you are not permitted to use any on campus facilities. Students attempting to attend campus activities when withheld from campus will be referred to the Dean of Students Office.

Continue to regularly visit coronavirus.UFHealth.org and coronavirus.ufl.edu for up-to-date information about COVID-19 and vaccination.

COVID-19 Symptoms

See <https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/symptoms.html> for information about COVID-19 symptoms, which may include fever, cough, shortness of breath or difficulty breathing, fatigue, chills, muscle or body aches, headache, sore throat, congestion or runny nose, nausea or vomiting, diarrhea, and loss of taste or smell.

Recording Within the Course

Students are allowed to record video or audio of class lectures. However, the purposes for which these recordings may be used are strictly controlled. The only allowable purposes are (1) for personal educational use, (2) in connection with a complaint to the university, or (3) as evidence in, or in preparation for, a criminal or civil proceeding. All other purposes are prohibited. Specifically, students may not publish recorded lectures without the written consent of the instructor.

A “class lecture” is an educational presentation intended to inform or teach enrolled students about a particular subject, including any instructor-led discussions that form part of the presentation, and delivered by any instructor hired or appointed by the University, or by a guest instructor, as part of a University of Florida course. A class lecture does not include lab sessions, student presentations, clinical presentations such as patient history, academic exercises involving solely student participation, assessments (quizzes, tests, exams), field trips, private conversations between students in the class or between a student and the faculty or lecturer during a class session.

Publication without permission of the instructor is prohibited. To “publish” means to share, transmit, circulate, distribute, or provide access to a recording, regardless of format or medium, to another person (or persons), including but not limited to another student within the same class section. Additionally, a recording, or transcript of a recording, is considered published if it is posted on or uploaded to, in whole or in part, any media platform, including but not limited to social media, book, magazine, newspaper, leaflet, or third party note/tutoring services. A student who publishes a recording without written consent may be subject to a civil cause of action instituted by a person injured by the publication and/or discipline under UF Regulation 4.040 Student Honor Code and Student Conduct Code.

Online Faculty Course Evaluation Process

Students are expected to provide professional and respectful feedback on the quality of instruction in this course by completing course evaluations online via GatorEvals. Guidance on how to give feedback in a professional and respectful manner is available at <https://gatorevals.aa.ufl.edu/students>. Students will be notified when the evaluation period opens, and can complete evaluations through the email they receive from GatorEvals, in their Canvas course menu under GatorEvals, or via <https://ufl.bluera.com/ufl/>. Summaries of course evaluation results are available to students at <https://gatorevals.aa.ufl.edu/public-results/>.

SUPPORT SERVICES

Accommodations for Students with Disabilities

If you require classroom accommodation because of a disability, it is strongly recommended you register with the Dean of Students Office <http://www.dso.ufl.edu> within the first week of class or as soon as you believe you might be eligible for accommodations. The Dean of Students Office will provide documentation of accommodations to you, which you must then give to the instructors of the course to receive accommodations. Please do this as soon as possible after you receive the letter. Students with disabilities should follow this procedure as early as possible in the semester. The College is committed to providing reasonable accommodations to assist students in their coursework.

Counseling and Student Health

Students sometimes experience stress from academic expectations and/or personal and interpersonal issues that may interfere with their academic performance. If you find yourself facing issues that have the potential to or are already negatively affecting your coursework, you are encouraged to talk with an instructor and/or seek help through University resources available to you.

- The **Counseling and Wellness Center** 352-392-1575 offers a variety of support services such as psychological assessment and intervention and assistance for math and test anxiety. Visit their web site for more information: <http://www.counseling.ufl.edu>. Online and in person assistance is available.
- **U Matter We Care** website: <http://www.umatter.ufl.edu/>. If you are feeling overwhelmed or stressed, you can reach out for help through the You Matter We Care website, which is staffed by Dean of Students and Counseling Center personnel.
- The **Student Health Care Center** at Shands is a satellite clinic of the main Student Health Care Center located on Fletcher Drive on campus. Student Health at Shands offers a variety of clinical services. The clinic is located on the second floor of the Dental Tower in the Health Science Center. For more information, contact the clinic at 392-0627 or check out the web site at: <https://shcc.ufl.edu/>
- Crisis intervention is always available 24/7 from:
Alachua County Crisis Center
(352) 264-6789
<http://www.alachuacounty.us/DEPTS/CSS/CRISISCENTER/Pages/CrisisCenter.aspx>
- **University Police Department:** [Visit UF Police Department website](#) or call 352-392-1111 (or 9-1-1 for emergencies).
- **UF Health Shands Emergency Room / Trauma Center:** For immediate medical care call 352-733-0111 or go to the emergency room at 1515 SW Archer Road, Gainesville, FL 32608; [Visit the UF Health Emergency Room and Trauma Center website.](#)

Do not wait until you reach a crisis to come in and talk with us. We have helped many students through stressful situations impacting their academic performance. You are not alone so do not be afraid to ask for assistance.

Inclusive Learning Environment

Public health and health professions are based on the belief in human dignity and on respect for the individual. As we share our personal beliefs inside or outside of the classroom, it is always with the understanding that we value and respect diversity of background, experience, and opinion, where every individual feels valued. We believe in, and promote, openness and tolerance of differences in ethnicity and culture, and we respect differing personal, spiritual, religious and political values. We further believe that celebrating such diversity enriches the quality of the educational experiences we provide our students and enhances our own personal and professional relationships. We embrace The University of Florida's Non-Discrimination Policy, which reads, "The University shall actively promote equal opportunity policies and practices conforming to laws against discrimination. The University is committed to non-discrimination with respect to race, creed, color, religion, age, disability, sex, sexual orientation, gender identity and expression, marital status, national origin, political opinions or affiliations, genetic information and veteran status as protected under the Vietnam Era Veterans' Readjustment Assistance Act." If you have questions or concerns about your rights and responsibilities for inclusive learning environment, please see your instructor or refer to the Office of Multicultural & Diversity Affairs website: www.multicultural.ufl.edu.