

**The Ohio State University College of Public Health
PUBHEPI 7412 (3054) – Principles and Procedures of Human Clinical Investigations
3 credit hours – Spring 2026**

Class Time and Location: 3:55-5:15 PM, T Th
LECTURES PRESENTED IN PERSON
Cunz Hall 330

Instructor: **Randall E. Harris, MD, PhD, MS, Professor**
MS, 1971, University of Nebraska, Genetics
PhD, 1974, North Carolina State Univ, Genetics, Statistics
MD, 1983, University of Nebraska, 1983, Medicine
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Course Description: This course presents basic principles and procedures in the design, conduct, and analysis of human clinical investigations (trials). Our intent is to teach basic concepts necessary for the application of human clinical trials in medical research. The lecture schedule will use the recommended text as a template. Lecture content will include (1) historical perspectives of clinical trials, (2) development of hypotheses, objectives, and specific aims, definition of the study population, and eligibility criteria of participants, (3) features of study designs, the randomization process, matching, and issues related to blinding of participants and/or investigators, (4) sample size calculations for main and interaction effects, (5) baseline assessment of participants, ascertainment of accurate information, development of the risk factor questionnaire, molecular biomarkers (6) recruitment strategies, Internal Review Board considerations, (7) prospective monitoring of participants and data collection, monitoring and adjudication of response variables, (8) assessment of adverse events, the Data Safety Monitoring Board, (9) assessment of compliance, adherence, and quality of life of participants, (10) survival and recurrence risk analysis, life tables, stratified analysis, and Cox regression analysis, (11) measurement of random error, confounding, interaction, and bias, (12) closeout and reporting of results, (13) multi-center trials, meta-analysis, and (14) criteria of judgment for evaluation of cause and effect relationships. On completion of the course, students will achieve competency in the essential features of the design, conduct, and analysis of human clinical trials.

Prerequisites: PUBHEPI 7410 and/or 6211 concurrent or permission of instructor. This class is not open to students who have already taken and received credit for PUBHEPI 715.

Course Objectives: The main objective of the course is to teach health professionals essential features of the design, conduct, analysis and interpretative of human clinical trials. The student learning objectives are:

1. Formulate the null and alternative hypotheses for randomized clinical trials.
2. Formulate major objectives and specific aims for randomized clinical trials.
3. Define the study population and eligibility criteria for randomized clinical trials.

4. Understand approaches to recruitment, compliance and retention of participants for randomized clinical trials.
5. Understand and apply sample size calculations for sufficient statistical power in randomized clinical trials.
6. Understand and apply appropriate methods of randomization in the design of randomized clinical trials.
7. Understand the importance of baseline assessment of risk factors and measurement of molecular biomarkers in randomized clinical trials.
8. Be familiar with human subjects consent and approval of the Internal Review Board for randomized clinical trials.
9. Be familiar with procedures for follow-up & adjudication of study outcomes in randomized clinical trials.
10. Implement procedures for determination and evaluation of adverse events and establishment of the Data Safety & Monitoring Board in randomized clinical trials.
11. Be familiar with sources of random and systematic error (bias) in randomized clinical trials.
12. Understand basic principles and procedures of biostatistical analysis of randomized clinical trials.
13. Understand the analysis of life table data.
14. Understand survival analysis (Cox regression).
15. Understand the meta-analysis of multi-center trials.
16. Apply the epidemiologic criteria of judgment in determining cause and effect relationships of biomedical data.

This course covers the following competencies:

MPH Core

- #1 Apply appropriate descriptive and inferential statistical techniques to public health data and interpret results of statistical analyses in the context of public health research and evaluation.
- #2 Apply foundational principles of environmental health science to categorize sources and types of contaminants, matrices involved, pathways for and modes of exposure, associated health effects and societal issues, approaches to control, and major regulations.
- #3 Apply epidemiologic principles to investigate the distribution of risk factors and disease in the population to improve public health.
- #4 Apply evidence-based concepts of health behavior and health promotion to the design of public health messages and strategies.
- #6 Demonstrate effective written and oral skills for communicating with different audiences in the context of professional public health activities.
- #9 Apply basic principles of ethical analysis to issues of public health practice and policy.
- #10 Collaborate with multidisciplinary groups to recognize and evaluate public health issues and develop strategies for intervention.

CTS Specialization:

- #1 Design a clinical investigation relevant to the student's field of clinical specialty, including the definition of study aims and objectives and the creation of an appropriate study design.
- #2 Identify and employ data collection strategies and instruments appropriate to the student's field of clinical specialty.
- #3 Select appropriate methods for the analysis of clinical research data.

- #4 Collaboratively prepare a grant application to seek funding for a clinical investigation project.
- #5 Use decision analysis and relevant evaluation methods to examine issues of appropriate implementation of treatments or technologies.
- #6 Recognize ethical issues that are likely to arise in clinical investigations and the procedures for handling them appropriately.
- #7 Apply ethical principles to the conduct of clinical investigations, with special emphasis on protection of research subjects.
- #8 Prepare a manuscript suitable for publication and/or for reporting to a sponsor on the conduct and results of a clinical investigation.

Text/Readings: Fundamentals of Clinical Trials (3rd, 4th or 5th Edition) by Lawrence M. Friedman, Curt D. Furberg, and David L. DeMets. Publisher: Springer-Verlag, New York, 2010. Fundamentals of Clinical Trials, 5th Edition Authors: Friedman, L.M., Furberg, C.D., DeMets, D., Reboussin, D.M., Granger C.B.

THE TEXT IS HIGHLY RECOMMENDED BUT NOT REQUIRED.

Grading: Students are expected to participate actively in class discussions, complete weekly assignments, and to make a presentation to the class on a clinical trial published in the current scientific literature. Depending on class size, students may be assigned to groups for discussion and response to questions raised during lecture. Assignments to be completed each week consist of posting three learning statements based upon knowledge gained in the lectures. Grade will be determined by in-class presentations and participation, plus the posted learning statements. Guidelines for grading are given below.

Approximate Weights for Grade Determination

Class Participation:	10%
Class Presentation:	50%
Learning Statements:	40%

Approximate Grade Scale:

A	Significant contributions to in-class discussion, outstanding in-class presentation and completed assignments (learning statements).
A-	Significant contributions to in-class discussions, excellent in-class presentation and completed assignments (learning statements).
B+	Significant contributions to in-class discussions, very good in-class presentation and completed assignments (learning statements)..
B	Some contributions to in-class discussions, very good in-class presentation and completed assignments (learning statements)..
B-	Some contributions to in-class discussions, good in-class presentation and/or incomplete assignments (learning statements)..
C	Lack of contributions to in-class discussions and subpar presentation and/or incomplete assignments (learning statements)..

Guidelines for in-class presentations:

Each student will sign up for an in-class presentation covering the rationale, design, findings and interpretation of a clinical trial published in the scientific literature. Student presentations will begin during week 7 of the semester. Suggested guidelines for presentations are given below.

- In-class presentation: 15-20 min with 10-15 min for Q & A.
- Power point slides: recommended (10-15 slides).
- Maximum of two students per presentation.
- Introduction and Background of Target Disease or Condition
- Rationale for Clinical Trial
- Objective and Specific Aims of Trial
- Experimental Design
- Target Population, Disease & Recruitment
- Power & Sample Size
- Statistical Methods
- Results
- Discussion & Interpretation
- Criteria of Judgment

Guidelines for Learning Statements: Each student is required to post three learning statements based upon material presented in the lectures and discussion of the preceding week. Statements should be brief and reflect basic understanding of the concepts and material presented. Statements should be posted under “Assignments” for each week of the semester.

Below are Selected Published Clinical Trials (examples to be discussed in class):

1. Low-Fat Dietary Pattern and Risk of Invasive Breast Cancer: The Women's Health Initiative Randomized Controlled Dietary Modification Trial

Ross L. Prentice, PhD; Bette Caan, DrPH; Rowan T. Chlebowski, MD; Ruth Patterson, PhD; Lewis H. Kuller, MD; Judith K. Ockene, PhD; Karen L. Margolis, MD; Marian C. Limacher, MD; JoAnn E. Manson, MD; Linda M. Parker, DSc; Electra Paskett, PhD; Lawrence Phillips, MD; John Robbins, MD; Jacques E. Rossouw, MD; Gloria E. Sarto, MD; James M. Shikany, DrPH; Marcia L. Stefanick, PhD; Cynthia A. Thomson, PhD; Linda Van Horn, PhD; Mara Z. Vitolins, DrPH; Jean Wactawski-Wende, PhD; Robert B. Wallace, MD; Sylvia Wassertheil-Smoller, PhD; Evelyn Whitlock, MD; Katsuhiko Yano, MD; Lucile Adams-Campbell, PhD; Garnet L. Anderson, PhD; Annlouise R. Assaf, PhD; Shirley A. Beresford, PhD; Henry R. Black, MD; Robert L. Brunner, PhD; Robert G. Brzyski, MD; Leslie Ford, MD; Margery Gass, MD; Jennifer Hays, PhD; David Heber, MD; Gerardo Heiss, MD; Susan L. Hendrix, DO; Judith Hsia, MD; F. Allan Hubbell, MD; Rebecca D. Jackson, MD; Karen C. Johnson, MD; Jane Morley Kotchen, MD; Andrea Z. LaCroix, PhD; Dorothy S. Lane, MD; Robert D. Langer, MD; Norman L. Lasser, MD; Maureen M. Henderson, MD
JAMA. 2006; 295:629-642.

2. Cardiovascular Events Associated with Rofecoxib in a Colorectal Adenoma Chemoprevention Trial

Robert S. Bresalier, M.D., Robert S. Sandler, M.D., Hui Quan, Ph.D., James A. Bolognese, M.Stat., Bettina Oxenius, M.D., Kevin Horgan, M.D., Christopher Lines, Ph.D., Robert Riddell, M.D., Dion Morton, M.D., Angel Lanás, M.D., Marvin A. Konstam, M.D., John A. Baron, M.D., for the Adenomatous Polyp Prevention on Vioxx (APPROVe) Trial Investigators
New England Journal of Medicine, 2005; Volume 352 (11): 1092-1102.

3. Cardiovascular Risk Associated with Celecoxib in a Clinical Trial for Colorectal Adenoma Prevention

Scott D. Solomon, M.D., John J.V. McMurray, M.D., Marc A. Pfeffer, M.D., Ph.D., Janet Wittes, Ph.D., Robert Fowler, M.S., Peter Finn, M.D., William F. Anderson, M.D., M.P.H., Ann Zauber, Ph.D., Ernest Hawk, M.D., M.P.H., Monica Bertagnolli, M.D., for the Adenoma Prevention with Celecoxib (APC) Study Investigators

New England Journal of Medicine, 2005; Volume 352 (11): 1071-1080.

4. Celecoxib for the prevention of sporadic colorectal adenomas.

Bertagnolli MM, Eagle CJ, Zauber AG, Redston M, Solomon SD, Kim K, Tang J, Rosenstein RB, Wittes J, Corle D, Hess TM, Woloj GM, Boissierie F, Anderson WF, Viner JL, Bagheri D, Burn J, Chung DC, Dewar T, Foley TR, Hoffman N, Macrae F, Pruitt RE, Saltzman JR, Salzberg B, Sylwestrowicz T, Gordon GB, Hawk ET; APC Study Investigators.

New England Journal of Medicine. 2006; 355(9): 73-84.

5. Effect of Celecoxib on Cardiovascular Events and Blood Pressure in Two Trials for the Prevention of Colorectal Adenomas

Scott D. Solomon, MD; Marc A. Pfeffer, MD, PhD; John J.V. McMurray, MD; Rob Fowler, MS; Peter Finn, MD; Bernard Levin, MD; Craig Eagle, MD; Ernest Hawk, MD; Mariajosé Lechuga, MD; Ann G. Zauber, PhD; Monica M. Bertagnolli, MD; Nadir Arber, MD; Janet Wittes, PhD, for the APC and PreSAP Trial Investigators

Circulation. 2006;114:1028-1035.

6. A Randomized Trial of Intensive versus Standard Blood-Pressure Control.

SPRINT Research Group, Wright JT Jr, Williamson JD, Whelton PK, Snyder JK, Sink KM, Rocco MV, Reboussin DM, Rahman M, Oparil S, Lewis CE, Kimmel PL, Johnson KC, Goff DC Jr, Fine LJ, Cutler JA, Cushman WC, Cheung AK, Ambrosius WT. *N Engl J Med*. 2015 Nov 26;373(22):2103-16. doi: 10.1056/NEJMoa1511939. Epub 2015 Nov 9

7. Oral Nirmatrelvir for High-Risk, Nonhospitalized Adults with Covid-19.

Hammond J, Leister-Tebbe H, Gardner A, Abreu P, Bao W, Wisemandle W, Baniecki M, Hendrick VM, Damle B, Simón-Campos A, Pypstra R, Rusnak JM; EPIC-HR Investigators. *N Engl J Med*. 2022 Apr 14;386(15):1397-1408. doi: 10.1056/NEJMoa2118542. Epub 2022 Feb 16. PMID: 35172054; PMCID: PMC8908851.

Carmen: Power point presentations will be posted on Carmen approximately one week prior to the scheduled lectures for the course. A tentative lecture schedule is presented in the table below.

Class Policies: Students are expected to attend all lectures and participate actively in class discussions of clinical trials and Q & A sessions following student presentations.

Office of Disability Services: Any student who feels s/he may need an accommodation based on the impact of a disability should contact me privately to discuss your specific needs. Please contact the Office for Disability Services at 614-292-3307 in room 150 Pomerene Hall to coordinate reasonable accommodations for students with documented disabilities.

Academic integrity: Academic integrity is essential to maintaining an environment that fosters excellence in teaching, research, and other educational and scholarly activities. Thus, The Ohio State University, the College of Public Health, and the Committee on Academic Misconduct

(COAM) expect that all students have read and understood the University’s *Code of Student Conduct* and the School’s *Student Handbook*, and that all students will complete all academic and scholarly assignments with fairness and honesty. The *Code of Student Conduct* and other information on academic integrity and academic misconduct can be found at the COAM web pages (<http://oaa.osu.edu/coam.html>). Students must recognize that failure to follow the rules and guidelines established in the University’s *Code of Student Conduct*, the *Student Handbook*, and in the syllabi for their courses may constitute “Academic Misconduct.”

The Ohio State University’s *Code of Student Conduct* (Section 3335-23-04) defines academic misconduct as: “Any activity that tends to compromise the academic integrity of the University, or subvert the educational process.” Examples of academic misconduct include (but are not limited to) plagiarism, collusion (unauthorized collaboration), copying the work of another student, and possession of unauthorized materials during an examination. Please note that the use of material from the Internet without appropriate acknowledgement and complete citation is plagiarism just as it would be if the source were printed material. Further examples are found in the *Student Handbook*. Ignorance of the *Code of Student Conduct* and the *Student Handbook* is never considered an “excuse” for academic misconduct. If I suspect a student of academic misconduct in a course, I am obligated by University Rules to report these suspicions to the University’s Committee on Academic Misconduct. If COAM determines that the student has violated the University’s *Code of Student Conduct* (committed academic misconduct), the sanctions for the misconduct could include a failing grade in the course and suspension or dismissal from the University. If you have any questions about the above policy or what constitutes academic misconduct in this course, please contact me.

Tentative Schedule of Lectures and Student Presentations:

Week	Lecture Schedule	Lecture Topic (See Footnote)	Text Reading 3 rd , 4 th , 5 th Ed.
1 1/13	Lecture One	COVID 19 & Vaccine Trials Introduction & Historical Perspectives, Phase I, Phase II, & Phase III Trials	Internet pp. 1-15, pp. 16-48
1 1/15	Lecture Two	Hypothesis, Objectives & Specific Aims	pp. 16-29 pp. 37-54 pp. 40-71
2 1/20	Lecture Three	Study Populations & Basic Study Designs	pp. 30-40, pp. 55-66
2 1/22	Lecture Four	Basic Study Designs	pp. 41-60, pp. 67-96 pp. 73-121
3 1/27	Lecture Five	Randomization	pp. 61-81, pp. 97-118 pp. 123-145
3 1/29	Lecture Six	Matching & Blinding	pp. 82-93, pp. 119-132 pp. 147-163
4 2/3	Lecture Seven	Sample Size Calculations	pp. 94-113, pp. 133-156 pp. 165-200
4 2/5	Lecture Eight	Sample Size Calculations	pp. 114-129, pp. 157-168 pp. 165-200

5 2/10	Lecture Nine	Baseline assessment, Risk factor questionnaire	pp. 130-139, pp. 169-182 pp. 201-214
5 2/12	Lecture Ten	Recruitment of Study Participants	pp. 140-155, pp. 183-198 pp. 215-232
6 2/17	Lecture Eleven	Data Collection & Quality Control	pp. 156-169, pp. 199-214 pp. 233-253
6 2/19	Lecture Twelve	Data Safety Monitoring Board & Adverse Events	pp. 170-184, pp. 215-232 pp. 255-277
7 2/24	Lecture Thirteen	Assessment of Health-related Quality of Life	pp. 185-203, pp. 233-250 pp. 279-295
7 2/26	Lecture Fourteen	Participant Adherence and Compliance	pp. 204-222, pp. 251-268 pp. 297-318
8 3/3	Lecture Fifteen	Survival & Recurrence Risk Analysis	pp. 223-245, pp. 269-292 pp. 319-341
8 3/5	Lecture Sixteen	Monitoring Response Variables	pp. 246-283, pp. 293-344 pp. 343-372
9 3/10	Lecture Seventeen	Data Analysis	pp. 284-296, pp. 345-381 pp. 373-401
9 3/12	Lecture Eighteen	Data Analysis	pp. 284-296, pp. 345-381 pp. 403-461
WEEK 10, SPRING BREAK, MARCH 16-20			
11 3/24	Lecture Nineteen	Data Analysis & Student Presentations	pp. 304-307, pp. 345-381 pp. 403-461
11 3/26	Lecture Twenty	Meta-analysis & Student Presentations	pp. 308-322, pp. 382-398 pp. 403-461
12 3/31	Lecture Twenty-One	Closeout & Student Presentations	pp. 323-332, pp. 399-410 pp. 452-477
12 4/2	Lecture Twenty-Two	Reporting Results & Student Presentations	pp. 333-344, pp. 411-426 pp. 479-499
13 4/7	Lecture Twenty-Three	Multicenter Trials, Regulatory Issues & Student Presentations	pp. 345-356, pp. 437-442 pp. 501-542

13 4/9	Lecture Twenty-Four	Scientific Fraud, Systematic Error (Bias), Criteria of Judgment & Student Presentations	TBA
14 4/14	Lecture Twenty-Five	Student Presentations	TBA
14 4/16	Lecture Twenty-Six	Student Presentations	TBA
15 4/21	Lecture Twenty-Seven	Student Presentations	TBA
15 4/23	Lecture Twenty-Eight	Student Presentations	TBA

Lecture topics are aligned with pages in the 3rd, 4th & 5th editions of the recommended text. I will announce the topics to be presented in class during the semester and post the corresponding lecture files of power point slides on Carmen. Students are only responsible for the topics addressed in class.