HRP 251, Design and Conduct of Clinical Trials
Spring Quarter 2017

Course Directors:	Victor Henderson, MD, MS HRP Redwood Building, Room T203 Phone: 723-5456 Fax: 725-6951 E-mail: vhenderson@stanford.edu Rita Popat, PhD HRP Redwood Bldg., Rm. T209 Phone: 498-5206 Fax: 725-6951 E-mail: rpopat@stanford.edu
Office hours:	By appointment
Administrative support:	Renee Miller, Room T268 reneemm@stanford.edu, 725-5394
Class schedule:	Monday and Wednesday, 9:30–11:00 a.m. First class April 3, 2017.
Location:	LK209 (except June 7, LK306)
Website URL:	https://web.stanford.edu/group/canvas/discovery/ (course homepage, syllabus, course materials, announcements)
Objective:	This course will present the methods and practice of clinical research in humans, specifically on medical interventions. We will cover design of studies, from early clinical development through definitive testing in randomized trials. The emphasis of the course will be on the practice of clinical research, based on the fundamentals of epidemiology and biostatistics.
Textbooks (either or both; recommended; neither required)	Friedman L.M. et al. *Fundamentals of Clinical Trials*, 5th ed. NY: Springer-Verlag, 2015. ISBN-13 978-3319185385. Paperback list price about $80; Amazon.com price about $75. Piantadosi, S. *Clinical Trials. A Methodologic Perspective,* 2nd ed. Hoboken, NJ: John Wiley & Sons, 2005. ISBN-13 978-0471727811. Hardcover list price about $200; Amazon.com price (new) about $150.

Readings, required and optional, may be assigned by individual lecturers. These will be announced and posted on the course website (Canvas)

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Grading and Assignments

HRP 251 is given on a Satisfactory/No Credit basis. "Satisfactory" implies competency with principles and materials covered in this course. Credit is based on 1) attendance and participation (particularly including the Mock Study Section sessions) (20%), 2) timely completion of written assignments (30%), and 3) a final paper (50%). There are no examinations. We appreciate no texting or checking email during class. We ask students to sign-in for each class and look askance at missed classes, but we understand that there are good reasons why a student might miss a class. We will not question your reasons but usually will assign a make-up written assignment intended to help learn materials that were presented during the missed class.

Your final paper is a research proposal for a clinical trial, suitable as the basis for a research grant. The trial can be either hypothetical or an actual plan but needs to be <u>your</u> design. Do not use or closely model an existing trial, your mentor's design, or a clinical trial design prepared for a previous course, such as HRP 226. The format for your trial is that of an NIH Research Project (R01) grant, defined by the NIH as a "discrete, specified, circumscribed project to be performed by the named investigator(s) in an area representing the investigator's specific interest and competencies, based on the mission of the NIH."

Timetable

April 17 – First assignment is due

May 10 – Second assignment is due

May 22 – Third assignment is due

June 7 – Final paper is due (5:00 PM)

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First Assignment: Title, Specific Aims, and the Significance section of the Research Strategy
Second Assignment: All sections of the research proposal, for peer review
Third Assisgnment: Peer review of class proposals.
Final Paper: Final paper, responsive to Mock Study Session critiques

For your assignments, we prefer an electronic submission sent to both Drs. Henderson and Popat (Word format, not PDF).

An NIH-style R01 proposal is the model for the assignments and for the final paper. In this model, the major sections are

1. **Title** (limited to **81 characters**, <u>including</u> spaces), and
   Project Summary or **Abstract** (limited to **30 lines**, if single spaced)
2. **Introduction** (final paper only; limited to **1 page**, if single spaced)
3. **Specific Aims** (the first aim should be your primary outcome) (limited to **1 page**, if single spaced)
4. **Research Strategy**, divided into (a) **Significance**, (b) **Innovation**, and (c) **Approach** (Research Strategy is limited to **12 pages**, if single spaced)

   The Approach may include a section on Preliminary Studies (if applicable) and should mention sample size issues, recruitment and adherence strategies, and the data management plan.
5. **Bibliography** (no page limit)

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Henderson & Popat, LK 209 (June: LK 306), Mon/Wed, 9:30-11:00

Course administrative support: Renee Miller (reneemm@stanford.edu)

Day	*Date*	*Instructor*	*Topic*	*Location/ Assignments*
M	April 3	***V. Henderson***	**Introduction to clinical trials**	LK 209
W	April 5	***V. Henderson***	**Design issues**	LK 209
M	April 10	***S. Kummar***	**Design and conduct of early phase trials**	LK 209
W	April 12	***V. Henderson***	**Outcomes**	LK 209
M	April 17	***V. Henderson***	**Study design**	LK 209 **Assignment #1**
W	April 19	***M. Desai***	**Missing data**	LK 209
M	April 24	***M-C Shih***	**Adaptive trials**	LK 209
W	April 26	***R. Popat***	**Sample size and power issues in clinical trials**	LK 209
M	May 1	***R. Popat***	**Data analysis overview**	LK 209
W	May 3	***H. Greely***	**FDA law**	LK 209
M	May 8	***M-C Shih***	**Interim monitoring, 1 (Statistical issues)**	LK 209
W	May 10	***Goodman***	**Interim monitoring, 2 (DSMB)**	LK 209 **Assignment #2**
M	May 15	***Popat***	**Trial critique examples, Mock section information**	LK 209
W	May 17	***Gardener***	**Recruitment**	LK 209
M	May 22	***Stefanick***	**Large multicenter trials: WHI as a paradigm**	LK 209 **Assignment #3**
W	May 24	***Henderson/ Popat***	**Mock Study Section 1**	LK 209
M	May 29	*no class*	*Memorial Day*	LK 209
W	May 31	***Popat/ Henderson***	**Mock Study Section 2**	LK 209
M	June 5	***P. Yock***	**Clinical trials involving medical devices**	LK 209
W	June 7	***J. Ioannidis***	**Pitfalls in design and interpretation**	LK 306 **Assignment #4**

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Additional Information about Course Directors and Lecturers

COURSE DIRECTORS

Victor Henderson, MD, MS. Professor of Health Research & Policy (Epidemiology) and of Neurology & Neurological Sciences. Research interests in age-associated cognitive decline and dementia.

Rita Popat, PhD. Clinical Associate Professor of Health Research & Policy (Epidemiology). Research interests in neuroepidemiology, including the epidemiology of Parkinson's disease and amyotrophic lateral sclerosis.

OTHER COURSE LECTURERS

Manisha Desai, PhD. Professor (Research) of Medicine (BMIR), of Biomedical Data Science, and (by courtesy) of Health Research & Policy. Research interests in applications of biostatistical methods to medicine and epidemiology.

Christopher Gardner, PhD. Professor (Research) of Medicine (Stanford Prevention Research Center). Research interests in nutrition and preventive medicine, including weight loss diets, phytochemicals, cardiovascular disease and cancer prevention.

Steven Goodman, MD, PhD. Professor of Medicine (General Medical Disciplines) and of Health Research & Policy (Epidemiology). Research interests in evidence in medical research.

Henry T. Greely, JD. Deane F. and Kate Edelman Johnson Professor of Law and (by courtesy) of Genetics. Research interests in the ethical, legal, and social implications of new biomedical technologies related to neuroscience, genetics, or stem cell research.

John Ioannidis, MD, DSc. C.F. Rehnborg Professor of Disease Prevention in the School of Medicine; Professor of Health Research & Policy (Epidemiology) and (by courtesy) of Statistics. Research interests in large-scale evidence and in appraisal and control of biases in biomedical research.

Shivaani Kummar, MD. Professor of Medicine (Oncology) and of Radiology (Molecular Imaging Program); Director, Phase I Clinical Research Program, Division of Oncology. Research interests focus on developing novel therapies for cancer. She specializes in conducting pharmacokinetic and pharmacodynamic driven first-in-human trials.

Mei-Chiung Shih, PhD. Adjunct Professor of Biomedical Data Science. Research interests in biostatistics; group sequential designs and adaptive designs for clinical trials.

Marcia Stefanick, PhD. Professor (Research) of Medicine (Stanford Prevention Research Center) and of Obstetrics & Gynecology.

Paul Yock, MD. Martha Meier Weiland Professor in the School of Medicine; Professor of Bioengineering and (by courtesy) of Mechanical Engineering. Research interests: Device development and testing in interventional cardiology.

Students with Documented Disabilities: Students who may need an academic accommodation based on the impact of a disability must initiate the request with the Office of Accessible Education (OAE). Professional staff will evaluate the request with required documentation, recommend reasonable accommodations, and prepare an Accommodation Letter for faculty dated in the current quarter in which the request is made. Students should contact the OAE as soon as possible since timely notice is needed to coordinate accommodations. The OAE is located at 563 Salvatierra Walk (phone: 723-1066, web: http://studentaffairs.stanford.edu/oae).