SYLLABUS & COURSE INFORMATION

SCHOOL OF PUBLIC HEALTH
UNIVERSITY OF MINNESOTA

PUBH 6301, SECTION 001

Fundamentals of Clinical Research
Fall 2018

COURSE & CONTACT INFORMATION

Credits: 3 - credits
Meeting Day(s), Thursdays, 11:15am - 1:10pm, Mayo D325:
This is a hybrid course. Web-based materials are delivered via Moodle at http://moodle.umn.edu

Contact Type	Contact Information	Role	When to Contact
Instructors	Russell V. Luepker, MD, MS luepk001@umn.edu [Phone] 612/624-6362 [Fax] 612/624-0315 Kamakshi Lakshminarayan, MD, PhD, MS laksh004@umn.edu [Phone] 612/624-9492 [Fax] 612/624-0315	Primary instructors for this course	
Technical Support	Technical support options are available on the SPH website. https://z.umn.edu/sphquickhelp	Troubleshoots technical issues related to the course site or course content.	Technical issues with the course site, media, quizzes or assignments.

Please save this contact information to your computer or print it. That way, you can still contact us in the event that you have difficulty connecting to the Internet or accessing the syllabus.

COURSE DESCRIPTION

This course is intended to provide a foundation for the more advanced study that is necessary to become an accomplished clinical research investigator. This course will review the concepts that underlie successful clinical research design, implementation, and reporting. This course will also introduce students to the resources and opportunities available to support clinical research at the academic health center.

COURSE PREREQUISITES

This course is a core requirement for Clinical Research MS and Clinical Research Certificate students. Other students with appropriate academic/professional backgrounds (e.g., any post-bachelor health degree) may be admitted with the permission of the instructor.

COURSE GOALS & OBJECTIVES

On completing this course, the student should be able to:

- Utilize a practical knowledge base that can be applied to the variety of approaches to clinical research;
- Understand the stages involved in clinical research, components of design, and types of trials;
- Understand the roles of the FDA, industry sponsors, and the NIH in the clinical research enterprise;
- Understand the study and challenges of research in different population groups;
- Understand the ethical issues with research in humans;
- Be familiar with the resources that are available for clinical research within the Academic Health Center.

METHODS OF INSTRUCTION AND WORK EXPECTATIONS

Course Workload Expectations
PUBH 6301, Fundamentals of Clinical Research, is a 3 - credit course. The University expects that for each credit, you will spend a minimum of three hours per week attending class or comparable online activity, reading, studying, completing assignments, etc. over

the course of a 15-week term. Thus, this course requires approximately 135 hours of effort spread over the course of the term in order to earn an average grade.

Learning Community
School of Public Health courses ask students to discuss frameworks, theory, policy, and more, often in the context of past and current events and policy debates. Many of our courses also ask students to work in teams or discussion groups. We do not come to our courses with identical backgrounds and experiences and building on what we already know about collaborating, listening, and engaging is critical to successful professional, academic, and scientific engagement with topics.

In this course, students are expected to engage with each other in respectful and thoughtful ways.

In group work, this can mean:

- Setting expectations with your groups about communication and response time during the first week of the semester (or as soon as groups are assigned) and contacting the TA or instructor if scheduling problems cannot be overcome.
- Setting clear deadlines and holding yourself and each other accountable.
- Determining the roles group members need to fulfill to successfully complete the project on time.
- Developing a rapport prior to beginning the project (what prior experience are you bringing to the project, what are your strengths as they apply to the project, what do you like to work on?)

In group discussion, this can mean:

- Respecting the identities and experiences of your classmates.
- Avoid broad statements and generalizations. Group discussions are another form of academic communication and responses to instructor questions in a group discussion are evaluated. Apply the same rigor to crafting discussion posts as you would for a paper.
- Consider your tone and language, especially when communicating in text format, as the lack of other cues can lead to misinterpretation.

Like other work in the course, all student to student communication is covered by the Student Conduct Code (https://z.umn.edu/studentconduct).

COURSE TEXT & READINGS

Textbook:
Hulley, SB, Cummings, SR, Browner, WS, Grady, DG, Newman, TB. Designing Clinical Research. Fourth Edition. Lippincott, Williams & Wilkins, 2013.

**Please note: the required textbook for this course is available as an eBook for free via the University of Minnesota Libraries. Please check the course Moodle site for the link to access (Link appears under Required Readings in Lesson pages).

This course uses journal articles, which are available via the University Libraries' E-Reserves and will be linked from the course site. It is good practice to use a citation manager to keep track of your readings. More information about citation managers is available at https://www.lib.umn.edu/pim/citation.

Required readings:

1. Agrawal S, Brennan N, Budetti P. The Sunshine Act - Effects on Physicians. N Engl J Med 2013;368(22):2054-2057.
2. Angell, M. Is academic medicine for sale? N. Engl J Med 2000: 342:1516-1518.
3. Angell M. Industry-sponsored clinical research: A broken system. JAMA 2008;300:1069-1071.
4. Atherton H, Banks D, Harbit R, Long L, Chadd F, Hay P, Kerry S, Simms I, Oakeshott P. Recruitment of young women to a trial of Chlamydia screening - as easy as it sounds? Trials 2006;8:1-5.
5. Bennett CL, Nebeker JR, Lyons EA, et al. The research on adverse drug events and reports (RADAR) project. JAMA 2005;293:2131-2140.
6. Berwick DM. The science of improvement. JAMA 2008;299:1182-1184.
7. Bikdeli B, Punnanithinont N, Akram Y, Lee I, Desai NR, Ross JS, Krumholz HM. Two decades of cardiovascular trials with primary surrogate endpoints: 1990-2011. J Am Heart Assoc 2017 Mar 21;6(3).
8. Burns N, Grove S. Outcomes Research. In: Understanding Nursing Research, 4th Edition. Elsevier Science, 2007.
9. Campbell EG, Weissman JS, Ehringhaus S, Rao SR, Moy B, Feibelmann S, Goold SD. Institutional Academic-Industry Relationships. JAMA 2007;298:1779-1786.
10. Chen, PW. Bending the rules of clinical trials. The New York Times, October 29, 2009.
11. Code of Federal Regulations for the Protection of Human Subjects, 45CFR46.
12. Collins FS. Opportunities for Research and NIH. Science 2010;327:36-37.
13. Conway PH, Mostashari F, Clancy C. The future of quality measurement for improvement and accountability. JAMA 2013;309:2215-2216.
14. Deception at Duke, CBS News. https://www.youtube.com/watch?v=eV9dcAGaVU8
15. Drazen JM, Ingelfinger JR. Grants, politics, and the NIH. N Engl J Med 2003;349:2259-2261.
16. Eichenwald, K., Kolata, G. A doctor's drug trial turns into fraud. The New York Times, May 17, 1999.
17. Eichenwald, K., Kolata, G. Drug trials hide conflicts for doctors. The New York Times, May 16, 1999.

18. Gerber Y, Jacobsen SJ, Killian JM, Weston SA, Roger VL. Participation bias assessement in a community-based study of myocardial infarction, 2002-2005. Mayo Clin Proc 2007;82:933-938.
19. Glickman SW, Anstrom KJ, Lin L, et al. Challenges in enrollment of minority, pediatric, and geriatric patients in emergency and acute care clinical research. Ann Emerg Med 2008;51:775-780.
20. Green LW. Making research relevant: if it is an evidence-based practice, where's the practice-based evidence? Family Practice-An International Journal 2008;i20-i24.
21. Harris, G. Roberts, J. After sanctions, doctors get drug company pay. The New York Times, June 3, 2007.
22. Hudson KL, Collins FS. Sharing and Reporting the Results of Clinical Trials. JAMA 2015;313(4):355-356.
23. Hudson KL, Lauer MS, Collins FS. Toward a New Era of Trust and Transparency in Clinical Trials. JAMA 2016;316(13):1353-1354.
24. Johnston SC, Hauser SL, Desmond-Hellmann S. Enhancing ties between academia and industry to improve health. Nature Medicine 2011;17(4):434-436.
25. Kolata, G., Johns Hopkins death brings halt to U.S.-financed human studies. The New York Times, July 20, 2001.
26. Lakshminarayan K, Borbas C, McLaughlin B, Morris NE, Vazquez G, Luepker RV, Anderson DC. A cluster-randomized trial to improve stroke care in hospitals. Neurology 2010;74:1634-1642.
27. Lakshminarayan K, Rostambeigi N, Fuller CC, Peacock JM, Tsai AW. Impact of an electronic medical record-based clinical decision support tool for dysphagia screening on care quality. Stroke 2012;43:3399-3401.
28. Moore TJ, Cohen MR, Furberg CD. Serious adverse drug events reported to the Food and Drug Administration, 1998-2005. Arch Intern Med 2007;167:1752-1759.
29. Naik, G. Mistakes in Scientific Studies Surge. The Wall Street Journal, August 10, 2011.
30. Nixdorf DR, Law AS, Look JO, Rindal DB, Durand EU, Kang W, Agee BS, Fellows JL, Gordan VV, Gilbert GH, for the National Dental PBRN Collaborative Group. Large-scale Clinical Endodontic Research in the National Dental Practice-Based Research Network: Study Overview and Methods. J Endod 2012;38:1470-1478.
31. Office of Human Research Protections (OHRP), Department of Health and Human Services (HHS). Guidance on reviewing and reporting unanticipated problems involving risks to subjects or others and adverse events, January 15, 2007.
32. Patrick Hurd. The Sunshine Act: How to Avoid Getting Burned From the Family Practice Management at the American Academy of Family Physicians 2013.
33. Physician Financial Transparency Reports (Sunshine Act), AMA, 2017.
34. Pronk JT, Lee SY, Lievense J, Pierce J, Palsson B, Uhlen M, Jens Nielsen J. How to set up collaborations between academia and industrial biotech companies. Nature Biotechnology 2015;33(3):237-240.
35. Ramsey BW, Nepom GT, Lonial S. Academic, Foundation, and Industry Collaboration in Finding New Therapies. N Engl J Med 2017;376:1762-1769. DOI: 10.1056/NEJMra1612575.
36. Redberg RF, Jacoby AF, Sharfstein JM. Power morcellators, postmarketing surveillance, and the US Food and Drug Administration. JAMA 2017;318:325-326.
37. Slutsky AS, Lavery JV. Data safety and monitoring boards. N Engl J Med 2004;350:1143-1147.
38. Suvarna V. Phase IV of drug development. Perspect Clin Res 2010;1:57-60.
39. The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. 1979. The Belmont Report.
40. Trouble at the lab. The Economist, October 19, 2013.
41. U.S. Department of Health & Human Services (January 18, 2017). Final Rule Enhances Protections for Research Participants, Modernizes Oversight System
42. U.S. Department of Health and Human Services. Guidance for clinical trial sponsors: Establishment and operation of clinical trial data monitoring committees. March 2006;OBM Control No. 0910-0581.
43. Viera AJ, Garrett JM. Understanding Interobserver Agreement: The Kappa Statistic. Fam Med 2005;37(4):360-363.

Optional readings:

1. Akard TF1, Wray S, Gilmer MJ. Facebook Advertisements Recruit Parents of Children With Cancer for an Online Survey of Web-Based Research Preferences. Cancer Nurs. 2014 Jun 18. [Epub ahead of print]
2. Bavdekar SB. Pediatric clinical trials. Perspect Clin Res. 2013 Jan;4(1):89-99. doi: 10.4103/2229- 3485.106403.
3. Schumacher KR1, Stringer KA2, Donohue JE3, Yu S3, Shaver A3, Caruthers RL3, Zikmund-Fisher BJ4, Fifer C3, Goldberg C3, Russell MW3. Social media methods for studying rare diseases. Pediatrics. 2014 May;133(5):e1345-53. doi: 10.1542/peds.2013-2966. Epub 2014 Apr 14.

COURSE OUTLINE/WEEKLY SCHEDULE

This course has specific deadlines. All coursework must be submitted via the course site before the date and time specified on the site. **Note: assignments are due by 11:55pm CST unless indicated otherwise.**

Week	Lesson		Lecturer	Readings	Activities/Assignments
Week 1 9/4/18 – 9/9/18	1a	Course Introduction	• Course Introduction (Luepker)		• **Post discussion questions (due Mon. 9/10)** • *Begin working on Assignment 1 (due Thurs. 9/20)*
	1b	Current Context of Clinical Research	• Current Context of Clinical Research (Luepker)	• Chapters 1, 2 • Additional readings - see the Moodle site	
		History of Clinical Research	• History of Clinical Research (Luepker)		
Week 2 9/10/18 – 9/16/18	2a	Study Designs	• Study Designs (Luepker)	• Chapters 7, 8	• **Post discussion questions (due Mon. 9/17)** • *Begin working on Assignment 2 (due Thurs. 9/27)*
	2b	Recruitment and Retention	• Recruitment and Retention (Luepker)	• Additional readings - see the Moodle site	
Week 3 9/17/18 – 9/23/18	3a	Clinical Trials I & II	• Clinical Trials I & II (Luepker)	• Chapters 4, 10-12 • Additional readings - see the Moodle site	• **Submit Assignment 1: Online Module – Good Clinical Practice in Clinical Research (due Thurs. 9/20)** • **Post discussion questions (due Mon. 9/24)** • *Begin working on Assignment 3 (due Thurs. 10/4)*
	3b	Working with the Elderly in Clinical Research	• Working with the Elderly in Clinical Research (Pacala)		
Week 4 9/24/18 – 9/30/18	4a	Research in Resource-Poor Settings: Challenges and Issues	• Research in Resource Poor Settings: Challenges and Issues (Lifson)		• **Submit Assignment 2: Special Populations Exercise (due Thurs. 9/27)** • **Post discussion questions (due Mon. 10/1)** • *Begin working on Assignment 4 (due Thurs. 10/11)*

	4b	Utility of Biomarkers in Clinical Research	• Utility of Biomarkers in Clinical Research (Thyagarajan)		
Week 5 10/1/18 – 10/7/18	5a	Management of the Clinical Research Team	• Management of the Clinical Research Team (Begun)		• **Submit Assignment 3: Abstracts (due Thurs. 10/4)** • **Post discussion questions (due Mon. 10/8)**
	5b	Practice-Based Research: A Dental Example	• Practice-Based Research: A Dental Example (Nixdorf)	• Additional readings - see the Moodle site	
Week 6 10/8/18 – 10/14/18	6a	Clinical Research with Pharmaceutical Companies: Practical Issues	• Clinical Research with Pharmaceutical Companies: Practical Issues (Eid)	• Additional readings - see the Moodle site	• **Submit Assignment 4: Clinical Trial Exercise (due Thurs. 10/11)** • **Post discussion questions (due Mon. 10/15)** • *Begin working on Assignment 5 (due Thurs. 11/1)*
	6b	IND Application, Process, and Responsibility	• IND Application, Process, and Responsibility (Arbit)		
Week 7 10/15/18 – 10/21/18	7a	Role of the NIH in Clinical Research	• Role of the NIH in Clinical Research (Lakshminarayan)	• Additional readings - see the Moodle site	• **Post discussion questions (due Mon. 10/22)**
	7b	How to Develop a Medical Device	• How to Develop a Medical Device (Wilson)		
Week 8 10/22/18 – 10/28/18	8a	Safeguarding Trust: The Ethics of Research Involving Human Participants	• Safeguarding Trust: The Ethics of Research Involving Human Participants (DeBruin)	• Chapter 14 • Additional readings - see the Moodle site	• **MID-TERM EXAM - in class** • **Submit Assignment 5: Investigator-Initiated Research Contract Exercise (due Thurs. 10/25)** • **Post discussion questions (due Mon. 10/29)**
	8b	Precision and Accuracy	• Precision and Accuracy (Luepker)	• Additional readings - see the Moodle site	

	8c	Mid-Term Exam (in class)			
Week 9 10/29/18 – 11/4/18	9a	Challenges in Emergency and Acute Care Research	• Challenges in Emergency and Acute Care Research (Biros)		• **Post discussion questions (due Mon. 11/5)**
	9b	Surgical Research: Unique Problems and Potential Solutions	• Surgical Research: Unique Problems and Potential Solutions (Tuttle)		
Week 10 11/5/18 – 11/11/18	10a	Introduction to Health Outcomes Research	• Introduction to Health Outcomes Research (Lakshminarayan)	• Additional readings - see the Moodle site	• **Post discussion questions (due Mon. 11/12)**
	10b	Working with Racial/Ethnic Minorities and Marginalized Populations in Clinical Research	• Working with Racial/Ethnic Minorities and Marginalized Populations in Clinical Research (Allen)		
	10c	Group Presentation (1)			
Week 11 11/12/18 – 11/18/18	11a	An Overview of Mental Health Research	• An Overview of Mental Health Research (Wozniak)		• **Post discussion questions (due Mon. 11/26)**
	11b	Conflict of Interests in Clinical Medicine and Research	• Conflict of Interests in Clinical Medicine and Research (Oakes)		
	11c	Group Presentation (2)			
11/19/18 – 11/25/18	**Thanksgiving (no class)**				

Week 12 11/26/18 – 12/2/18	12a	Adverse Events in Clinical Research Data and Safety Monitoring Boards	• Adverse Events in Clinical Research (Lakshminarayan) • Data & Safety Monitoring Boards (Lakshminarayan)	• Additional readings - see the Moodle site	• **Post discussion questions (due Mon. 12/3)** • *Begin working on Assignment 6 (due Thurs. 12/6)*
	12b	Clinical Research in Children	• Clinical Research in Children (Steinberger)		
	12c	Group Presentation (3)			
Week 13 12/3/18 – 12/9/18	13a	Clinical Research in Private Practice	• Clinical Research in Private Practice (Tadros)		• **Submit Assignment 6: Adverse Effects (due Thurs. 12/6)**
	13b	Meta-analysis	• Meta-analysis (Duval)		
	13c	Group Presentation (4)			
Week 14 12/10/18 – 12/16/18		**Study Day**			
Week 15 12/17/18 – 12/23/18		FINAL EXAM Emphasizes last half of course (Lessons 8-13) but includes material from entire course			• **FINAL EXAM - in class**

SPH AND UNIVERSITY POLICIES & RESOURCES

The School of Public Health maintains up-to-date information about resources available to students, as well as formal course policies, on our website at www.sph.umn.edu/student-policies/. Students are expected to read and understand all policy information available at this link and are encouraged to make use of the resources available.

The University of Minnesota has official policies, including but not limited to the following:

- Grade definitions
- Scholastic dishonesty
- Makeup work for legitimate absences
- Student conduct code
- Sexual harassment, sexual assault, stalking and relationship violence
- Equity, diversity, equal employment opportunity, and affirmative action
- Disability services
- Academic freedom and responsibility

Resources available for students include:

- Confidential mental health services
- Disability accommodations
- Housing and financial instability resources
- Technology help
- Academic support

EVALUATION & GRADING

Point values for determining the final course grade are assigned as follows:

Activity	Point value
Mid-Term Exam	20
Final Exam	20
Homework Assignment 1	5
Homework Assignment 2	5
Homework Assignment 3	10
Homework Assignment 4	10
Homework Assignment 5	10
Homework Assignment 6	10
Attendance/Participation	10 (missing >5 = loss of 10 points; >3 = loss of 5 points)

Grading Scale
The University uses plus and minus grading on a 4.000 cumulative grade point scale in accordance with the following, and you can expect the grade lines to be drawn as follows:

% In Class	Grade	GPA
93 - 100%	A	4.000
90 - 92%	A-	3.667
87 - 89%	B+	3.333
83 - 86%	B	3.000
80 - 82%	B-	2.667
77 - 79%	C+	2.333

73 - 76%	C	2.000
70 - 72%	C-	1.667
67 - 69%	D+	1.333
63 - 66%	D	1.000
< 62%	F	

- A = achievement that is outstanding relative to the level necessary to meet course requirements.
- B = achievement that is significantly above the level necessary to meet course requirements.
- C = achievement that meets the course requirements in every respect.
- D = achievement that is worthy of credit even though it fails to meet fully the course requirements.
- F = failure because work was either (1) completed but at a level of achievement that is not worthy of credit or (2) was not completed and there was no agreement between the instructor and the student that the student would be awarded an I (Incomplete).
- S = achievement that is satisfactory, which is equivalent to a C- or better
- N = achievement that is not satisfactory and signifies that the work was either 1) completed but at a level that is not worthy of credit, or 2) not completed and there was no agreement between the instructor and student that the student would receive an I (Incomplete).

Evaluation/Grading Policy	**Evaluation/Grading Policy Description**
Scholastic Dishonesty, Plagiarism, Cheating, etc.	You are expected to do your own academic work and cite sources as necessary. Failing to do so is scholastic dishonesty. Scholastic dishonesty means plagiarizing; cheating on assignments or examinations; engaging in unauthorized collaboration on academic work; taking, acquiring, or using test materials without faculty permission; submitting false or incomplete records of academic achievement; acting alone or in cooperation with another to falsify records or to obtain dishonestly grades, honors, awards, or professional endorsement; altering, forging, or misusing a University academic record; or fabricating or falsifying data, research procedures, or data analysis (As defined in the Student Conduct Code). For additional information, please see https://z.umn.edu/dishonesty The Office for Student Conduct and Academic Integrity has compiled a useful list of Frequently Asked Questions pertaining to scholastic dishonesty: https://z.umn.edu/integrity. If you have additional questions, please clarify with your instructor. Your instructor can respond to your specific questions regarding what would constitute scholastic dishonesty in the context of a particular class-e.g., whether collaboration on assignments is permitted, requirements and methods for citing sources, if electronic aids are permitted or prohibited during an exam. Indiana University offers a clear description of plagiarism and an online quiz to check your understanding (http://z.umn.edu/iuplagiarism).
Late Assignments	1 point deducted for late assignments of a week or less.
Attendance Requirements	No more than 2 unexcused absences.

Makeup Work for Legitimate Reasons	If you experience an extraordinary event that prevents you from completing coursework on time and you would like to make arrangements to make up your work, contact your instructor within 24 hours of the missed deadline if an event could not have been anticipated and at least 48 hours prior if it is anticipated. Per University policy, legitimate reasons for making up work may include: • illness • serious accident or personal injury • hospitalization • death or serious illness within the family • bereavement • religious observances • subpoenas • jury duty • military service • participation in intercollegiate athletic events Because this course is entirely online and all materials are available to students from the first day of the term, we expect students to plan accordingly if travels or access to internet will cause them to miss a deadline. Note that our deadlines are generally set for 11:55 p.m. CST, so traveling to a different time zone will require additional planning. Further, circumstances that qualify for making up missed work will be handled by the instructor on a case-by-case basis; they will always be considered but not always granted. For complete information, view the U of M's policy on Makeup Work for Legitimate Absences (http://z.umn.edu/sphmakeupwork).

Saving & Submitting Coursework	**Documents that students submit are considered final;** students may not submit more than one version or draft of each assignment.

Technical Issues with Course Materials	You are expected to submit all coursework on time and it is your responsibility to ensure that your work is submitted properly before the deadline.
	
	If you experience technical difficulties while navigating through the course site or attempting to submit coursework:
	
	• Go to Quick Help: http://z.umn.edu/sphquickhelp.
	• Connect with the appropriate person or office within 30 minutes of the problem's occurrence.
	  ○ Provide as much information as possible, so the tech team can best help you as soon as possible.
	  ○ You can expect a response within 1-2 business days to help resolve the problem.