Washington University in St. Louis
SCHOOL OF MEDICINE

Clinical Research Training Center

Syllabus: M17- 589 Spring 2018 Intermediate Methods for Clinical Research

About Intermediate Methods in Clinical Research

Welcome:
Intermediate Methods in Clinical Research is designed for fellows, post-docs, and faculty who want to learn intermediate/advanced methods to conduct clinical research. The prerequisite is Designing Outcomes & Clinical (DOC) Research (or equivalent). Intermediate Clinical Research may be taken as a requirement towards a master's of science in clinical investigation (MSCI) or other graduate degree at Washington University in St. Louis.

Teaching Philosophy:
At the beginning of each class, Julianne and I will provide you with a paper copy of the PowerPoint slides that the lecturer will use that day. We also will post an electronic copy of the slides on blackboard. If you don't understand something the lecturer says, please ask your question during the lecture; you don't have to save questions until the end of class. Although we recommend that you do the readings before class, we understand that sometimes reading gets deferred until after class.

A good way to reinforce the course material is to use your favorite journal as a collection of case studies: After you read the title and background of a study, set the journal down and ask yourself how you would conduct the study. What study design would you have used? Whom would you have enrolled? What methods would you have used to enhance casual inference? How would you analyze the data? This self-reflection will make you a better researcher and help you remember the study.

Required Texts:
The required reading is **Principles and Practice of Clinical Research**, by John Gallin (Editor), Frederick Ognibene (Editor). The textbook is available as an e-book via Bernard-Becker Library. Here's how to access it:
Click https://becker.wustl.edu/
Click "E BOOKS"
At the prompt, "Title begins with" type: **"Principles and Practice of Clinical Research"**
Choose the 2nd option (3rd edition, printed in 2012) by selecting "Ebook Central"
Click "Read online"
To go to page 232, type "232" on the top right.
You can purchase the 3rd edition online for about $105 or the 4th edition cost for about $125. They are very similar. Assigned readings will list the page number for both editions.

Course Materials:
Printouts available at each class; electronic copy on https://bb.wustl.edu.

Course Description:
DOC Research covers how to select a clinical research question, outline a research protocol, and execute a clinical study. Topics include: volunteer selection, observational and experimental study designs, sample size estimation, clinical measurement, bias and confounding, and data management. The course is designed for health care professionals who wish to conduct patient-oriented clinical research. Students incorporate research design concepts into their own research proposal. The course consists of lectures, weekly problem sets, weekly reading assignments, a 2-page protocol, and a final exam.

Target audience:
Students who already have or are pursuing any of the following degrees: MSCI, MPH, MSPH, ANP, MD, DO, DPT, OTD, Pharm D, or a PhD in nursing, rehabilitation/participation science, or medical anthropology. Although there is no formal prerequisite, a clinical background is assumed. No in-depth medical knowledge is required for the homework or final exam, but you may need to use Wikipedia if you've never heard of "carpal tunnel syndrome" or "pulmonary embolism."

Goals of the Course:
By the end of this course, participants will be able to:

- Design an outcomes, clinical, or translational research study
- Execute the research study
- Evaluate the strengths and weakness of alternate study designs
- Read the medical literature critically.

Time Requirements

The time commitment for this course is ~9 hours a week.

About the Coursemaster

Brian F. Gage, MD, MSc is a physician–scientist whose research focuses on antithrombotic therapy and thrombosis. He is a Professor of Medicine at Washington University. He sees patients at Barnes-Jewish Hospital, where he directs the Clinical-Scientist Teaching And Research (C-STAR) program for medical residents. He also directs the Washington University Fellowship in General Medical Sciences (GMS Fellowship) and serves as co-director of the Biostatistics, Epidemiology, and Research Design (BERD) core of the CTSA.

Dr. Gage has a BS (biology) and MSc (health services research) from Stanford University and an MD from the University of California, San Diego. He completed his internship and chief residency at the Good Samaritan/Phoenix VA Medical Center, his internal medicine residency at Barnes-Jewish Hospital, and his fellowship (in general internal medicine) at the Palo Alto VA/Stanford University.

Contact Information:

Name:	Brian F. Gage, MD, MSc.
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Campus office:	GMS, Suite 155 in the Taylor Avenue Building (TAB)

Preferred method of contact: email
In-Person Office Hours: Tuesdays, 9:10-10:45 AM (through May 1) in Dr. Gage's office. To make an appointment at a different time, email him.

Teaching Assistant (TA):

Name:	Julianne Sefko, MPH
Phone number:	314 747-2496
Email address:	jsefko@wustl.edu

Preferred method of contact: email

Course Schedule (may be revised)

Dates	Topic	Reading (Pages from Gallin & Ognibene 3rd and 4th editions are shown)	Assignments Due
Jan 17	4:00 Placebo & Nocebo Effects B. Gage, MD	3rd ed: 232-239 or 4th ed: 258-266 R. Al-Lamee et al. Percutaneous coronary intervention in stable angina (ORBITA): a double-blind, randomised controlled trial Lancet 2017.	*Get Problem Set 1*
	5:00 Mendelian Randomization B. Gage, MD	https://www.uptodate.com/contents/mendelian-randomization	
Jan 24	4:00 Personalized Medicine B. Gage, MD	3rd ed: 629* to 635 (stop at "the Role of the FDA") 4th ed: 649* to 654 (stop at "the Role of the Regulatory Agency") * Start at "Contribution of Clinical Pharmacology"	**Due Problem Set 1;** *Get Problem Set 2*
	4:30 Pharmacogenetics and Warfarin as a Case Study B. Gage, MD	L. Wang et al. Genomics and Drug Response NEJM 2011	
Jan 31	4:00 Developing & Evaluating Survey Measures Amy McQueen, PhD	Kimberlin & Winterstein. Validity and reliability of measurement instruments used in research AJHP 2008 3rd ed: 327-329 4th ed: 311-312 (Start at "Selection a Functional Measure" & stop at "Case Example: Chronic Liver Disease Questionnaire")	**Due Problem Set 2;** *Get Problem Set 3*
	5:10 ClinicalTrials.gov & CONSORT diagram B. Gage, MD	3rd ed: 101-104 (stop at Examples); 176-180 4th ed: 111-123	
Feb 7	4:00 : IRBs, the Common Rule, Regulations, and Mistakes when using MyIRB Jonathan Green, MD	3rd ed: 53-63 or 4th ed 47-59	**Due Problem Set 3;** *Get Problem Set 4*
	5:05 Propensity Scores Margaret Olsen, PhD	3rd ed: p. 316-317 or 4th ed: 283-284 Sturmer T. Propensity scores for confounder adjustment when assessing the effects of medical interventions using nonexperimental study designs. J Int Med 2014 (OK to skip Figures 5-7). Ferraris VA et al. Surgical outcomes and transfusion of minimal amounts of blood in the operating room. Arch Surg 2012.	
Feb 14	4:00 PROMIS and other Quality-of-life metrics Ryan Calfee, MD	3rd ed: p. 321-327 or 4th ed: 303-311	**Due: Problem Set 4;** *Get Problem Set 5*
	5:10 Prediction modeling: Competing risk models, landmark analyses, & assigning points to clinical prediction rules B. Gage, MD	3rd ed: p. 311-312* or 4th ed: 400-403* *Start at "Special Considerations in Survival Analysis & Stop at "Missing Data."	

Feb 21	4:00 Instrumental Variables Lei Liu, PhD 5:05 B. Gage, MD		**Due: Problem Set 5;** *Get Problem Set 6*
Feb 28	4:00 Mediation & Structural Equation Modeling (SEM) Amy McQueen, PhD 5:05 Imputation for Missing Data Ben Cooper, MPH		**Due: Problem Set 6;** *Get Problem Set 7*
Mar 7	4:00 N-of-1 trials Christopher Schmid, PhD 5:05 Latent class analysis Ziyad Al-Aly, MD	N. Duan et al. Single-patient (n-of-1) trials: a pragmatic clinical decision methodology for patient-centered comparative effectiveness research J Clin Epi 2013.	**Due: Problem Set 7;** *Get Problem Set 8*
Mar 14	Spring break (no class)	- -	
Mar 21	4:00 Budgets Phyllis Klein, RN 5:10 Informatics Philip Payne, PhD	3rd ed: 491-499 4th ed: 571-586; 604 (budget section)	**Due: Problem Set 8:**
Mar 28	4:00 Population Interventions Anne Marie Dale, PhD, OTR 5:05 Research integrity and impact: The practices and mindsets of research exemplars Alison Antes Schuelke, PhD		**Due: Problem Set 9** Get Problem Set 10
Apr 4	4:00-4:45 Directed acyclic graphs Ann Marie Dale, PhD, OTR 5:05 Health Economics Kathleen Gillespie, PhD		**Due: Problem Set 10;** *Get problem Set 11 and practice final*
Apr 11	4:00 Interim monitoring & stopping rules for trials Esther Lu, PhD 5:15 ? Liz	3rd ed: p. 295-303 or 4th ed: 384-391 (stop at "unequal sample sizes")	**Due: Problem Set 11;** *Get problem set 12*
Apr 18	4:00 Competing Risks Elizabeth Yanik, PhD 5:10 Clustered RCTs B. Gage	Nephrology Dialysis Transplantation	**Due: Problem Set 12;** *Get practice final*
TBA	Optional final date		
Apr 25	4:00 B. Gage	Review Practice final	

Apr 25	3:30-5:30 Final Exam review	
May 1	Extended office hours	
May 2	Final Exam	You will *not* need a calculator nor your notes.

***** Reading should be done prior to lectures (except lectures 1 & 2). Readings in parentheses are optional.

Assessment/Grading

Grade Composition:

The final is ~40% of the course grade; the problem sets ~60%. If your average falls between two grades in the table below, in-class participation will be used to determine whether your grade should be rounded up or down.

Grade (Percent of Points)
A+ (98.5% to 100%) A (93.0% to 98.4%) A- (90.0% to 92.9%)
B+ (88.5% to 89.9%) B (83.0% to 88.4%)* B- (80.0% to 82.9%)
C+ (78.5% to 79.9%) C (73.0% to 78.4%) C- (70.0% to 72.9%)

***** Minimum for Core courses for MSCI students

Late Assignments:

Assignments are due at the beginning of class. For each day (calculated at 12:01 AM) that an assignment (except for assignment 1) is late the score is multiplied by 0.93. For example, a perfect assignment submitted 3 days late would score 80.4%. To avoid a late penalty if you will be away when an assignment is due, email it to Julianne Sefko, MPH with this subject line: **DOC Research Problem Set N**, (where **N** is the problem set #).

Attendance Requirement for Face-to-Face Course:

In-class participation is an important part of the coursework taken as part of the MSCI or AHBR programs and the clinical research training programs within the CRTC. Students are expected to physically attend at least 75% of class sessions. Watching the videotaped class presentations, if available, is helpful to keep up with missed sessions, but is not a substitute for class attendance. Students whose professional duties or personal circumstances prevent them from meeting this program attendance requirement must receive prior written approval of the coursemaster, and agree on an alternate plan to achieve course objectives and earn academic credit.

Technology Usage During Class:

When class starts, please turn down the volume of ringers and pagers. If you plan to use your laptop during class, don't sit in the front row.

Feedback and Grading Timeline:

Problem sets will be returned 1 week after they are submitted.

Technical Support

If you have any technical problems accessing Blackboard please e-mail crtc@email.wustl.edu. Note that this mailbox is not monitored in the evening or on weekends. If you need immediate help after hours please put a service request into https://wusm.service-now.com.

Course Policies

Participation (Expectations):

- It is critical that our classroom environment promotes the respectful exchange of ideas. This entails being sensitive to the views and beliefs expressed during discussions.
- Your success in this course will depend on your ability to communicate, engage and participate in all course activities. Successful completion of this course requires that a student keep up with assignments.

Drop Dates:

If you want or need to drop this class, please contact me. You can drop for any reason during the course of the semester. However, you may only receive a partial or no tuition reimbursement depending upon how far into the semester you drop the course. See the Academic Calendar for your program for specific dates and reimbursement policies. Late withdrawals will appear on your transcript as a withdrawal.

CRTC Academic Policy Guidelines:

Guidelines regarding CRTC course registration and enrollment, grades, tuition obligation, and academic leave are consolidated in the CRTC Academic Policy Guidelines. Please review this document.

CRTC Guidelines for Academic and Non-Academic Transgressions:

By registering for this course you have agreed to the terms of the CRTC Guidelines for Academic and Non-Academic Transgressions. If you have not already reviewed this policy, please do so.

Academic Integrity/Plagiarism:

- Academic dishonesty is a serious offense that may lead to probation, suspension, or dismissal from the University. One form of academic dishonesty is plagiarism – the use of an author's ideas, statements, or approaches without crediting the source. Academic dishonesty also includes copying information from another student.
- Academic dishonesty will be reported to the Office of the Registrar for possible action. The coursemaster will make an academic judgment about the student's grade. The CRTC process regarding academic dishonesty is described in the CRTC Guidelines for Academic and Non-Academic Transgressions

Writing Assistance:

For additional help on your writing, consult the expert staff of The Writing Center in Olin Library (first floor). It can be helpful to ask someone to read your prose and to provide feedback on strength of argument, clarity, organization, etc.

Disability Resources:

Washington University is committed to providing accommodations and/or services to students with documented disabilities. Washington University's Cornerstone: Center for Advanced Learning Disability Resources is the University's official resource for students with disabilities and students with suspected disabilities. DR assists students with disabilities by providing guidance and accommodations to ensure equal access to our campus, both physically and academically. To learn more about its services, initiate the process of formal documentation and/or to arrange for accommodations, please contact Disability Resources at the start of the course.

Mental Health Resources:

Mental Health Services' professional staff members work with students to resolve personal and interpersonal difficulties, many of which can affect the academic experience. These include conflicts with or worry about

friends or family, concerns about eating or drinking patterns, and feelings of anxiety and depression. See: http://shs.wustl.edu/MentalHealth.

Reporting Policies:
Please also review the CRTC website for policies regarding sexual assault reporting and reporting concerns about bias, prejudice or discrimination.