

School of Public Health

Syllabus and Course Information



UNIVERSITY OF MINNESOTA
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PubH 8341

Advanced Epidemiologic Methods: Concepts

Fall 2016

Credits:	3	
Meeting Days:	Tuesdays, Thursdays	
Meeting Time:	9:45 am – 11:00 am	
Meeting Place:	Mayo A110	
Instructor:	Richard MacLehose, PhD	Susan Mason, PhD
Office Address:	441 West Bank Office Building	340 West Bank Office Building
Office Phone:	4-1932	4-9556
Office Hours:	By appointment	By appointment

I. Course Description

This doctoral seminar introduces students to the conceptual foundations of essential issues in epidemiologic methodology. The focus is on how and why a given method, design, or approach might help us explain population health. The emphasis is on the strengths, limitations, and potential alternatives for a given approach. The origins, use, and potential of both classic and cutting-edge methods are considered. Examples and readings are aimed at both clinical/biologic and social/behavioral track students.

II. Course Prerequisites

None. A general background on basic epidemiologic concepts is recommended.

III. Course Goals and Objectives

Upon completion of this course the student should be able to:

- Understand the concept of causal inference in epidemiology, the different approaches that underpin this concept, and how to ask meaningful research questions for causal inference.
- Understand the concept of identification and how it is different from statistical estimation.
- Define the main types of bias (confounding, selection bias, measurement error), understand alternative approaches to dealing with them, and recognize situations in which those approaches are appropriate.
- Understand the concepts of effect modification and mediation, and implement general approaches for their analysis
- Apply classic epidemiologic study designs (cohort, case-control, cross-sectional) and their variants, knowing their particular strengths and limitations.

IV. Methods of Instruction and Work Expectations

The class will meet twice a week. Most topics will be covered over multiple days. Students are required to attend each class having read the assigned material and prepared for group discussion and debate. Students are required to work through examples from lecture and readings to gain a fuller understanding of the material.

Homework assignments will be posted at the end of most weeks. See the syllabus for dates on which the homework will be assigned. Homework assignments are to be completed individually and are due in class the following Thursday.

V. Course Text and Readings

Two texts are required:

Rothman, Kenneth J., Sander Greenland, and Timothy L. Lash. 2012. *Modern Epidemiology*, 3rd edition (mid-cycle revision). New York: Lippincott Williams & Wilkins. [Note: this 2012 mid-cycle revision is mostly the same as the 3rd edition from 2008]

Hernán MA, Robins JM. *Causal Inference*. Chapman & Hall/CRC, 2015. Available online at: <http://www.hsph.harvard.edu/miguel-hernan/causal-inference-book/>

Additionally, a number of papers and book chapters are also required. These will be made available to students through the course shared folder in Dropbox.

Readings in the course texts are denoted as ME3 and CI

Reading assignments marked with an asterisk (*) are optional; you will not be expected to read this material, though you may benefit by doing so.

Introduction to Epidemiological Inference

Morabia A. Has epidemiology become infatuated with methods? A historical perspective on the place of methods during the classical (1945-1965) phase of epidemiology. *Annu Rev Public Health* 2015; 36: 69-88.

Measures of Disease Frequency

ME3 – Chapter 2 Causation and Causal Inference

ME3 – Chapter 3 Measures of Occurrence

Measures of Disease Association

ME3 – Chapter 4 Measures of Effect and Measures of Association

Greenland, Sander. "Interpretation and choice of effect measures in epidemiologic analyses." *American Journal of Epidemiology* 125.5 (1987): 761-768.

Poole, Charles. "On the origin of risk relativism." *Epidemiology* 21.1 (2010): 3-9.

Counterfactuals and Identifiability Assumptions

CI – Chapter 1 A Definition of Causal Effect

CI – Chapter 2 Randomized Experiments

CI – Chapter 3 Observational Studies

Hernan MA, Taubman SL. Does obesity shorten life? The importance of well-defined interventions to answer causal questions. *International Journal of Obesity* 2008; 32: S8-S14

Messer LC, Oakes JM, Mason S. Effects of socioeconomic and racial segregation on preterm birth: a cautionary tale of structural confounding. *American Journal of Epidemiology* 2010; 171: 664-673.

* Greenland S, Robins JM. Identifiability, exchangeability, and epidemiological confounding. *Int J Epidemiol* 1986;15:413-9.

* Maldonado G, Greenland S. Estimating causal effects. *Int J Epidemiol*. 2002 Apr 1;31(2):422-9.

* Commentaries on Maldonado and Greenland by Dawid, Shafer, Elwert and Winship, and Kaufman and Kaufman

Confounding

CI – Chapter 7 Confounding

ME3 – Chapter 9 Validity in Epidemiologic Studies, pp. 129-134 (Confounding)

Greenland S, Morgenstern H. Confounding in health research. *Annu Rev Public Health* 2001;22:189-212

Hernán MA, Hernández-Díaz S, Werler MM, Mitchell AA. Causal knowledge as a prerequisite for confounding evaluation: an application to birth defects epidemiology. *Am J Epidemiol* 2002;155:176-84.

* Hernán MA, Clayton D, Keiding N. The Simpson's paradox unraveled. *Int J Epidemiol* 2011;40:780-5.

Directed Acyclic Graphs

CI – Chapter 6 Graphical representation of causal effects

ME3 – Chapter 12 Causal diagrams

Robins JM. Data, Design, and Background Knowledge in Etiologic Inference. *Epidemiology* 2001;12:313-320.

* VanderWeele TJ, Hernán MA, Robins JM. Causal directed acyclic graphs and the direction of unmeasured confounding bias. *Epidemiology* 2008;19:720-8.

Selection Bias

CI – Chapter 8 Selection bias

Cole SR, Platt RW, Schisterman EF, Chu H, Westreich D, Richardson D, Poole C. Illustrating bias due to conditioning on a collider. *Int J Epidemiol* 2010;39:417-20.

Hernandez-Diaz S, Schisterman E, Hernan MA. The birth weight “paradox” uncovered? *American Journal of Epidemiology* 2006; 164(11): 1115-1120.

Flanders WD, Klein M. Properties of 2 counterfactual effect definitions of a point exposure. *Epidemiology*. 2007 Jul 1;18(4):453-60.

* Porta M, Vineis P, Bolúmar F. The current deconstruction of paradoxes: one sign of the ongoing methodological “revolution”. *European journal of epidemiology*. 2015 Oct 1;30(10):1079-87.

Measurement Bias

CI – Chapter 9 Measurement bias

ME3 – Chapter 9 Validity in Epidemiologic Studies, pp. 137-146 (Information bias)

Dosemeci M, Wacholder S, Lubin JH. Does nondifferential misclassification of exposure always bias a true effect toward the null value? *Am J Epidemiol* 1990;132:746-8.

Vanderweele T, Hernán MA. Results on differential and dependent measurement error of the exposure and the outcome using signed directed acyclic graphs. *Am J Epidemiol* 2012;175:1303-10.

* Flegal KM, Keyl PM, Nieto FJ. Differential misclassification arising from nondifferential errors in exposure measurement. *Am J Epidemiol* 1991;134:1233-44.

Effect Modification

ME3 – Chapter 5 Concepts of Interaction

CI – Chapter 4 Effect modification

CI – Chapter 5 Interaction

VanderWeele TJ, Knol MJ. A tutorial on interaction. *Epidemiol. Methods* 2014; 3(1): 33–72

* Bhavnani D, Goldstick JE, Cevallos W, Trueba G, Eisenberg JNS. Synergistic effects between rotavirus and coinfecting pathogens on diarrheal disease: Evidence from a community-based study in northwestern Ecuador. *American Journal of Epidemiology* 2012; 176(5): 387-395.

* Vanderweele TJ. Invited commentary: Assessing mechanistic interaction between coinfecting pathogens for diarrheal disease. *American Journal of Epidemiology* 2012; 176(5): 396-399.

Estimation and Hypothesis Testing

ME3 – Chapter 10 Precision and Statistics in Epidemiologic Studies

CI – Chapter 10 Random Variability

Poole C. Low P-values or narrow confidence intervals: which are more durable? *Epidemiology* 2001;12:291-4.

Greenland, Sander, et al. "Statistical tests, P values, confidence intervals, and power: a guide to misinterpretations." *European journal of epidemiology*(2016): 1-14.

Rothman KJ. Curbing type I and type II errors. *Eur J Epidemiol* 2010;25:223-4.

Stang A, Poole C, Kuss O. The ongoing tyranny of statistical significance testing in biomedical research. *Eur J of Epidemiol* 2010;25:225-230

Randomized Trials

ME3 Chapter 6 (read through subsection 'Experimental Studies' pp 87-93)

DeMets DL. Statistical issues in interpreting clinical trials. *J Intern Med* 2004;255:529-37.

Mansournia MA, Higgins JP, Sterne JA, Hernán MA. Biases in randomized trials: a conversation between trialists and epidemiologists. *Epidemiology*. 2017 Jan 1;28(1):54-9.

* Kaufman JS, Kaufman S, Poole C. Causal inference from randomized trials in social epidemiology. *Soc Sci Med* 2003;57:2397-409.

Cohort Studies

ME3 – Chapter 7 (Cohort Studies, pp 100-110)

Bao Y, Bertoia ML, Lenart EB, Stampfer MJ, Willett WC, Speizer FE, Chavarro JE. Origin, methods, and evolution of the three Nurses' Health Studies. *American journal of public health*. 2016 Sep;106(9):1573-81.

Kolata G. Hormone studies: What went wrong? *New York Times*. April 22, 2003

Hernan MA, Alonso A, Logan R, Grodstein F, Michels KB, Willett W, Mason JE, Robins JM. Observational Studies Analyzed Like Randomized Experiments: An Application to Postmenopausal Hormone Therapy and Coronary Heart Disease. *Epidemiology* 2008; 19(6): 766-779.

* Ioannidis JP, Haidich AB, Pappa M, Pantazis N, Kokori SI, Tektonidou MG, Contopoulos-Ioannidis DG, Lau J. Comparison of evidence of treatment effects in randomized and nonrandomized studies. *JAMA* 2001; 286(7): 821-30.

Case-Control Studies

ME3 – Chapter 8 (Case-control Studies, pp. 111-122)

Langholz, Bryan. "Case-control studies= odds ratios: blame the retrospective model." *Epidemiology* 21.1 (2010): 10-12.

Knol MJ, Vandenbroucke JP, Scott P, Egger M. What do case-control studies estimate? Survey of methods and assumptions in case-control research. *Am J Epidemiol* 2008;168:1073-81.

Vandenbroucke JP, Pearce N. Case-control studies: basic concepts. *Int J Epidemiol* 2012;41:1480-9.

ME3 – pp. 171-182 [Matching]

Mediation

Cole SR, Hernán MA. Fallibility in estimating direct effects. *Int J Epidemiol* 2002;31:163-5.

Robins JM, Greenland S. Identifiability and exchangeability for direct and indirect effects. *Epidemiology* 1992;3:143-55.

VanderWeele, Tyler J., and Whitney R. Robinson. "On causal interpretation of race in regressions adjusting for confounding and mediating variables." *Epidemiology (Cambridge, Mass.)* 25.4 (2014): 473.

* VanderWeele TJ. A unification of mediation and interaction: a 4-way decomposition. *Epidemiology* 2014;25:5:749-61.

VI. Course Outline/Weekly Schedule

WEEK	DATE	TOPIC	INSTRUCTOR	HOMEWORK
1	Sep 5	Introduction to Epidemiologic Inference	R+S	
	Sep 7	Measures of Disease Frequency	S	
2	Sep 12	Measures of Association	S	
	Sep 14	Counterfactuals and Identifiability Assumptions	S	HW 1 Assigned
3	Sep 19	Exchangeability and Confounding (I)	R	
	Sep 21	Confounding (II)	R	HW 2 Assigned
4	Sep 26	Confounding (III)	S	
	Sep 28	Confounding (IV) and DAGs	S	HW 3 Assigned
5	Oct 3	Selection Bias (I)	S	
	Oct 5	Selection Bias (II)	S	HW 4 Assigned
6	Oct 10	Measurement Bias (I)	R	
	Oct 12	Measurement Bias (II)	R	
7	Oct 17	Review	R&S	
	Oct 19	MIDTERM		
8	Oct 24	Effect Modification (I)	S	
	Oct 26	Effect Modification (II)	S	HW 5 Assigned
9	Oct 31	Estimation and Hypothesis Testing (I)	R	
	Nov 2	Estimation and Hypothesis Testing (II)	R	HW 6 Assigned
10	Nov 7	Estimation and Hypothesis Testing (III)	R	
	Nov 9	Estimation and Hypothesis Testing (IV)	R	HW 7 Assigned
11	Nov 14	Randomized Trials	S	
	Nov 16	Cohort Studies	S	
12	Nov 21	Case-Control Studies (I)	R	
	Nov 23	THANKSGIVING		
13	Nov 28	Case-Control Studies (II)	R	
	Nov 30	Case-Control Studies/Matching (III)	S	HW 8 Assigned
14	Dec 5	Mediation	R	

	Dec 7	Review	R+S	
15	Dec 12	FINAL EXAM		

VII. Evaluation and Grading

Letter grades and associated points are awarded in this course as follows below. These will appear in the student's official transcript. See <http://www1.umn.edu/usenate/policies/gradingpolicy.html> for details.

Pass/Fail Grading: An alternative to traditional A-F scale grades is the S/N grading scale. The "S" grade does not carry points but credit will count toward completion of student's degree if permitted by college or program. An "N" is given for student's exercising the S/N grading option but who fail to meet minimum course requirements. Students may change grading options without written permission as specified by the University and without penalty during the initial registration period or during the first two weeks of the semester. The grading option may not be changed after the second week of the term.

The total grade for the course is a weighted average of homework assignments, the midterm exam and the final exam:

- Homework assignments (8) comprise 60% of the total grade
- Midterm exam is 20% of the total grade
- Final exam is 20% of the total grade

Numeric grades map to letter grades as per the table to the right.

A 4.000 - Represents achievement that is outstanding relative to the level necessary to meet course requirements

A- 3.667

B+ 3.333

B 3.000 - Represents achievement that is significantly above the level necessary to meet course requirements

B- 2.667

C+ 2.333

C 2.000 - Represents achievement that meets the course requirements in every respect

C- 1.667

D+ 1.333

D 1.000 - Represents achievement that is worthy of credit even though it fails to meet fully the course requirements

S Represents achievement that is satisfactory, which is equivalent to a C- or better.

For additional information, please refer to:

<http://policy.umn.edu/Policies/Education/Education/GRADINGTRANSCRIPTS.html>.

Grade Mapping	
Class Points	Letter Grade
>94	A
90-94	A-
87-89	B+
83-86	B
80-82	B-
77-79	C+
73-76	C
70-72	C-
70+	S
-	N/F
-	I

Course Evaluation

The SPH will collect student course evaluations electronically using a software system called CourseEval: www.sph.umn.edu/courseeval. The system will send email notifications to students when they can access and complete their course evaluations. Students who complete their course evaluations promptly will be able to access their final grades just as soon as the faculty member renders the grade in SPHGrades: www.sph.umn.edu/grades. All students will have access to their final grades through OneStop two weeks after the last day of the semester regardless of whether they completed their course evaluation or not. Student feedback on course content and faculty teaching skills are an important means for improving our work. Please take the time to complete a course evaluation for each of the courses for which you are

registered.

Incomplete Contracts

A grade of incomplete "I" shall be assigned at the discretion of the instructor when, due to extraordinary circumstances (e.g., documented illness or hospitalization, death in family, etc.), the student was prevented from completing the work of the course on time. The assignment of an "I" requires that a contract be initiated and completed by the student before the last official day of class, and signed by both the student and instructor. If an incomplete is deemed appropriate by the instructor, the student in consultation with the instructor, will specify the time and manner in which the student will complete course requirements. Extension for completion of the work will not exceed one year (or earlier if designated by the student's college). For more information and to initiate an incomplete contract, students should go to SPHGrades at: www.sph.umn.edu/grades.

University of Minnesota Uniform Grading and Transcript Policy - A link to the policy can be found at onestop.umn.edu.

VIII. Other Course Information and Policies

Grade Option Change (if applicable)

For full-semester courses, students may change their grade option, if applicable, through the second week of the semester. Grade option change deadlines for other terms (i.e. summer and half-semester courses) can be found at onestop.umn.edu.

Course Withdrawal

Students should refer to the Refund and Drop/Add Deadlines for the particular term at onestop.umn.edu for information and deadlines for withdrawing from a course. As a courtesy, students should notify their instructor and, if applicable, advisor of their intent to withdraw.

Students wishing to withdraw from a course after the noted final deadline for a particular term must contact the School of Public Health Office of Admissions and Student Resources at sph-ssc@umn.edu for further information.

Student Conduct Code

The University seeks an environment that promotes academic achievement and integrity, that is protective of free inquiry, and that serves the educational mission of the University. Similarly, the University seeks a community that is free from violence, threats, and intimidation; that is respectful of the rights, opportunities, and welfare of students, faculty, staff, and guests of the University; and that does not threaten the physical or mental health or safety of members of the University community.

As a student at the University you are expected adhere to Board of Regents Policy: *Student Conduct Code*. To review the Student Conduct Code, please see:

http://regents.umn.edu/sites/default/files/policies/Student_Conduct_Code.pdf.

Note that the conduct code specifically addresses disruptive classroom conduct, which means "engaging in behavior that substantially or repeatedly interrupts either the instructor's ability to teach or student learning. The classroom extends to any setting where a student is engaged in work toward academic credit or satisfaction of program-based requirements or related activities."

Use of Personal Electronic Devices in the Classroom

Using personal electronic devices in the classroom setting can hinder instruction and learning, not only for the student using the device but also for other students in the class. To this end, the University establishes the right of each faculty member to determine if and how personal electronic devices are allowed to be used in the classroom. For complete information, please reference:

<http://policy.umn.edu/Policies/Education/Education/STUDENTRESP.html>.

Scholastic Dishonesty

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. (Student Conduct Code:

http://regents.umn.edu/sites/default/files/policies/Student_Conduct_Code.pdf) If it is determined that a student has cheated, he or she may be given an "F" or an "N" for the course, and may face additional sanctions from the University. For additional information, please see:

<http://policy.umn.edu/Policies/Education/Education/INSTRUCTORRESP.html>.

The Office for Student Conduct and Academic Integrity has compiled a useful list of Frequently Asked Questions pertaining to scholastic dishonesty: <http://www1.umn.edu/oscai/integrity/student/index.html>. If you have additional questions, please clarify with your instructor for the course. 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.

Makeup Work for Legitimate Absences

Students will not be penalized for absence during the semester due to unavoidable or legitimate circumstances. Such circumstances include verified illness, participation in intercollegiate athletic events, subpoenas, jury duty, military service, bereavement, and religious observances. Such circumstances do not include voting in local, state, or national elections. For complete information, please see:

<http://policy.umn.edu/Policies/Education/Education/MAKEUPWORK.html>.

Appropriate Student Use of Class Notes and Course Materials

Taking notes is a means of recording information but more importantly of personally absorbing and integrating the educational experience. However, broadly disseminating class notes beyond the classroom community or accepting compensation for taking and distributing classroom notes undermines instructor interests in their intellectual work product while not substantially furthering instructor and student interests in effective learning. Such actions violate shared norms and standards of the academic community. For additional information, please see: <http://policy.umn.edu/Policies/Education/Education/STUDENTRESP.html>.

Sexual Harassment

"Sexual harassment" means unwelcome sexual advances, requests for sexual favors, and/or other verbal or physical conduct of a sexual nature. Such conduct has the purpose or effect of unreasonably interfering with an individual's work or academic performance or creating an intimidating, hostile, or offensive working or academic environment in any University activity or program. Such behavior is not acceptable in the University setting. For additional information, please consult Board of Regents Policy:

<http://regents.umn.edu/sites/default/files/policies/SexHarassment.pdf>

Equity, Diversity, Equal Opportunity, and Affirmative Action

The University will provide equal access to and opportunity in its programs and facilities, without regard to race, color, creed, religion, national origin, gender, age, marital status, disability, public assistance status, veteran status, sexual orientation, gender identity, or gender expression. For more information, please consult Board of Regents Policy: http://regents.umn.edu/sites/default/files/policies/Equity_Diversity_EO_AA.pdf.

Disability Accommodations

The University of Minnesota is committed to providing equitable access to learning opportunities for all students. Disability Services (DS) is the campus office that collaborates with students who have disabilities to provide and/or arrange reasonable accommodations.

If you have, or think you may have, a disability (e.g., mental health, attentional, learning, chronic health, sensory, or physical), please contact DS at 612-626-1333 to arrange a confidential discussion regarding equitable access and reasonable accommodations.

If you are registered with DS and have a current letter requesting reasonable accommodations, please contact your instructor as early in the semester as possible to discuss how the accommodations will be applied in the course.

For more information, please see the DS website, <https://diversity.umn.edu/disability/>.

Mental Health and Stress Management

As a student you may experience a range of issues that can cause barriers to learning, such as strained relationships, increased anxiety, alcohol/drug problems, feeling down, difficulty concentrating and/or lack of motivation. These mental health concerns or stressful events may lead to diminished academic performance and may reduce your ability to participate in daily activities. University of Minnesota services are available to assist you. You can learn more about the broad range of confidential mental health services available on campus via the Student Mental Health Website: <http://www.mentalhealth.umn.edu>.

The Office of Student Affairs at the University of Minnesota

The Office for Student Affairs provides services, programs, and facilities that advance student success, inspire students to make life-long positive contributions to society, promote an inclusive environment, and enrich the University of Minnesota community.

Units within the Office for Student Affairs include, the Aurora Center for Advocacy & Education, Boynton Health Service, Central Career Initiatives (CCE, CDes, CFANS), Leadership Education and Development –Undergraduate Programs (LEAD-UP), the Office for Fraternity and Sorority Life, the Office for Student Conduct and Academic Integrity, the Office for Student Engagement, the Parent Program, Recreational Sports, Student and Community Relations, the Student Conflict Resolution Center, the Student Parent HELP Center, Student Unions & Activities, University Counseling & Consulting Services, and University Student Legal Service.

For more information, please see the Office of Student Affairs at <http://www.osa.umn.edu/index.html>.

Academic Freedom and Responsibility: for courses that do not involve students in research

Academic freedom is a cornerstone of the University. Within the scope and content of the course as defined by the instructor, it includes the freedom to discuss relevant matters in the classroom. Along with this freedom comes responsibility. Students are encouraged to develop the capacity for critical judgment and to engage in a sustained and independent search for truth. Students are free to take reasoned exception to the views offered in any course of study and to reserve judgment about matters of opinion, but they are responsible for learning the content of any course of study for which they are enrolled.*

Reports of concerns about academic freedom are taken seriously, and there are individuals and offices available for help. Contact the instructor, the Department Chair, your adviser, the associate dean of the college, or the Vice Provost for Faculty and Academic Affairs in the Office of the Provost.

* Language adapted from the American Association of University Professors "Joint Statement on Rights and Freedoms of Students".

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