SYLLABUS & COURSE INFORMATION

SCHOOL OF PUBLIC HEALTH
UNIVERSITY OF MINNESOTA

PUBH 6381

Genetics in Public Health in the Era of Precision Medicine
Fall, 2018

COURSE & CONTACT INFORMATION

Credits: 2
Meeting Day(s): Wednesdays
Meeting Time: 11:15 am – 1:10 pm
Meeting Place: Bruininks Hall, Room 131A

Instructor: Ellen W Demerath
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Fax: 4-0315
Office Hours: by appointment
Office Location: WBOB 455

COURSE DESCRIPTION

Our understanding of human genomic variation and its relationship to health is expanding rapidly, and this knowledge is now being translated primarily through the field of “precision medicine” (finding the right drug for the right person at the right time), which is likely to improve clinical care, at least for some diseases and for those with greater resources. Public health, in contrast, seeks to abate the social and environmental factors that lead to disease, and fosters policies and programs that enhance health at the population level to reduce health disparities. Is there a conflict here? This course will provide an introduction to the field of public health genomics at this interesting point in its history. Approximately one-half of the course will be devoted to Genetic Epidemiology. Topics will include different approaches to measuring the association of genes with disease: family history, heritability, and genetic association, epigenetics, and Mendelian Randomization as an approach to causal inference. The second half of the course will cover public health genomics, including “precision public health”, genetic screening programs, and the possibilities and pitfalls of direct to consumer marketing of genetic tests.

COURSE PREREQUISITES

This is a graduate course designed primarily for Epidemiology MPH and PhD, and fulfills the “Epi Of” requirement for the MPH in Epidemiology. Graduate students in other Divisions within the School of Public Health, and students pursuing graduate degrees in the biological or academic health center sciences are very welcome and add to the richness of discussions. Completion of a course in genetics at the undergraduate or graduate level, and an introductory course and familiarity with epidemiology are required. Please contact the instructor if you have questions on prerequisites or would like to ask for special permission.

COURSE GOALS & OBJECTIVES

At the end of this course, you will:

- Gain practice reading the public health genomics literature to describe family history and specific genetic variants as risk factors for major health challenges
- Learn to summarize and interpret tables and figures describing results of genetic epidemiology studies
- Apply epidemiologic concepts to select approaches for population-based testing and screening

- Discuss similarities and contrasts between the tenets and methods of Precision Medicine and the tenets and methods of Public Health
- Advocate for attention to ethical and social implications of genomics and Precision Medicine, including structural bias
- Create educational material appropriate for the general public about the benefits and risks of direct to consumer genetic testing using the Infographic format

METHODS OF INSTRUCTION AND WORK EXPECTATIONS

Each 2 hour class meeting will include an instructor-led lecture, with activities for student learning and class discussion. The class discussion will focus on a "journal club" where each week a different set of students will lead discussion of an assigned reading from the public health genomics literature.

Graduate work requires at least 2 hours OUTSIDE of class for each credit hour in class; therefore, given you are spending 2 hours in class per week, you should expect to spend up to 4 hours per week outside of class reading and preparing for class, completing assignments, and researching and producing your group project.

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

REQUIRED READINGS:

All readings will be available on the Moodle Class site at least one week prior to the class meeting for which it is assigned. To access the course website, go to http://myu.umn.edu, log in with your ID/password, click on the "My Courses" tab, and select "PubH 6381".

Text:
Textbook: Teare MD (editor). *Genetic Epidemiology*. Humana Press. Sheffield, UK. e-ISBN 978-1-60327-416-6

Additional Readings, by week:

Week 1: Introduction of PHG and PM
(Text, Chapter 1)

- Collins FS and Varmus H (2015) A new initiative on precision medicine. *New Engl J Med* 372(9): pp 793-795.
- Khoury MJ , Bowen MS, Burke W, Coates RJ, Dowling NF, Evans JP, Reyes M, St. Pierre J. (2011). Current priorities for public health practice in addressing the role of human genomics in improving population health. *Am J Prev Med* 40(4); 486-93.
- An Introduction to the Human Genome: HMX Genetics YouTube. https://www.youtube.com/watch?v=jEJp7B6u_dY (May 18, 2017)

Week 2: Fam Hx and Heritability
(Text, Chapter 2)

- Anthony JF Griffiths, Jeffrey H Miller, David T Suzuki, Richard C Lewontin, and William M Gelbart. (2000) An Introduction to Genetic Analysis, 7th edition. New York: W. H. Freeman; 2000. ISBN-10: 0-7167-3520-2. (section on "Quantifying Heritability"): https://www.ncbi.nlm.nih.gov/books/NBK21866/. By agreement with the publisher, this book is accessible by the searc feature, but cannot be browsed. NCBI Bookshelf ID: NBK21866
- Walter FM, Prevost AT, Birt L, Grehan N, Restarick K, Morris HC, Sutton S, Rose P, Downing S, Emery JD (2013) Development and evaluation of a brief self-completed family history screening tool for common chronic disease prevention in primary care. *Br J Gen Pract*. 2013 Jun;63(611):e393-400.

Week 3: Genetic Association and MR
(Text, Chapter 8)

- Benn, Marianne ; Nordestgaard, Borge G. ; Grande, Peer ; Schnohr, Peter ; Tybjaerg - Hansen, Anne PCSK9R46L, Low-Density Lipoprotein Cholesterol Levels, and Risk of Ischemic Heart Disease. Journal of the American College of Cardiology, June 22, 2010, Vol.55(25), p.2833(10).
- Lawlor, Debbie A. ; Harbord, Roger M. ; Sterne, Jonathan A. C. ; Timpson, Nic ; Davey Smith, George Mendelian randomization: Using genes as instruments for making causal inferences in epidemiology. Statistics in Medicine, 15 April 2008, Vol.27(8), pp.1133-1163

Week 4 : GWAS and intro to Genetic Tests
(Text, Chapter 7)

- Manolio, Teri A (2010) Genomewide Association Studies and Assessment of the Risk of Disease. The New England Journal of Medicine, 2010, Vol.363(2), pp.166-176
- Burke W. (2014) Genetic Tests: Clinical Validity and Clinical Utility. Curr Protoc Hum Genet. 2014; 81: 9.15.1–9.15.8. PMID: 24763995

Week 5: CVD Genomics

- O'Donnell CJ and Nabel EG. Genomics of Cardiovascular Disease. New Engl J Med, 2011, Vol.365(22), pp.2098-2109
- Swerdlow, D, Holmes M, Harrison, S, Humphries SE. The genetics of coronary heart disease. British Medical Bulletin, 2012, Vol. 102(1), pp.59-77.
- Tang, W. ; Teichert, M. ; Chasman, D.I. ; Heit, J.A. ; Morange, P.E. ; Li, G. ; Pankratz, N. ; Leebeek, F.W. ; Pare, G. ; Andrade, M. de ; Tzourio, C. ; Psaty, B.M. ; Basu, S. ; Ruiter, R. de ; Rose, L. ; Armasu, S.M. ; Lumley, T. ; Heckbert, S.R. ; Uitterlinden, A.G. ; Lathrop, M. ; Rice, K.M. ; Cushman, M. ; Hofman, A. ; Lambert, J.C. ; Glazer, N.L. ; Pankow, J.S. ; Witteman, J.C. ; Amouyel, P. ; Bis, J.C. ; Bovill, E.G. ; Kong, X. ; Tracy, R.P. ; Boerwinkle, E. ; Rotter, J.I. ; Tregouet, D.A. ; Loth, D.W. ; Stricker, B.H. ; Ridker, P.M. ; Folsom, A.R. ; Smith, N.L. A genome-wide association study for venous thromboembolism: the extended cohorts for heart and aging research in genomic epidemiology (CHARGE) consortium. Genetic Epidemiology, 2013, Vol.37, pp.512-521
- Khera AV, Emdin CA, Drake I, Natarajan P, Bick AG, Cook NR, Chasman DI, Baber U, Mehran R, Rader DJ, Fuster V, Boerwinkle E, Melander O, Orho-Melander M, Ridker PM, Kathiresan S. Genetic Risk, Adherence to a Healthy Lifestyle, and Coronary Disease. N Engl J Med. 2016 Dec 15;375(24):2349-2358. Epub 2016 Nov 13. PMID: 27959714

Week 6: Cancer Genomics

- Yang JJ, Landier W, Yang W, Liu C, Hageman L, Cheng C, Pei D, Chen Y, Crews KR, Kornegay N, Wong FL. Inherited NUDT15 variant is a genetic determinant of mercaptopurine intolerance in children with acute lymphoblastic leukemia. Journal of clinical oncology. 2015 Apr 10;33(11):1235
- Roberts KG, Li Y, Payne-Turner D, Harvey RC, Yang YL, Pei D, McCastlain K, Ding L, Lu C, Song G, Ma J. Targetable kinase-activating lesions in Ph-like acute lymphoblastic leukemia. New England journal of medicine. 2014 Sep 11;371(11):1005-15.

Week 7: Epigenomics and Health Disparities
(Text, Chapter 14)

- Relton, Caroline L ; Davey Smith, George. (2010) Epigenetic Epidemiology of Common Complex Disease: Prospects for Prediction, Prevention, and Treatment. PLoS Medicine, 2010, Vol.7(10), p.e1000356
- Olden, Kenneth ; Olden, Heather ; Lin, Yu-Sheng (2015) The Role of the Epigenome in Translating Neighborhood Disadvantage Into Health Disparities. Current Environmental Health Reports, 2015, Vol.2(2), pp.163-170

Week 8:Polygenic Risk Scores

- Ostergren JE1, Gornick MC, Carere DA, Kalia SS, Uhlmann WR, Ruffin MT, Mountain JL, Green RC, Roberts JS; PGen Study Group. How Well Do Customers of Direct-to-Consumer Personal Genomic Testing Services Comprehend Genetic Test Results? Findings from the Impact of Personal Genomics Study. Public Health Genomics. 2015;18(4):216-24. doi: 10.1159/000431250. Epub 2015 Jun 16.
- Nilanjan Chatterjee1–3, Jianxin Shi3 and Montserrat García-Closas3 (2016) Developing and evaluating polygenic risk prediction models for stratified disease prevention. Nat Rev Genet. 2016 Jul;17(7):392-406. doi: 10.1038/nrg.2016.27.
- Mihaescu, Raluca ; Meigs, James ; Sijbrands, Eric ; Janssens, A Cecile (2011) Genetic risk profiling for prediction of type 2 diabetes. PLoS currents, 11 January 2011, Vol.3, pp.RRN1208
- ROC Curves and Area Under the Curve (AUC) Explained: https://www.youtube.com/watch?v=OAl6eAyP-yo

Week 9;Pharmacogenomics

- Diane M. Korngiebel,1 Kenneth E. Thummel,2 and Wylie Burke3,* Implementing Precision Medicine: The Ethical Challenges. Trends in Pharmacological Sciences, January 2017, Vol. 38, No. 1, pp 8-14.
- Marylyn D. Ritchie (2012) The success of pharmacogenomics in moving genetic association studies from bench to bedside: study design and implementation of precision medicine in the post-GWAS era. Hum Genet (2012) 131:1615–1626

Week 10 Newborn Screening

TBD

Week 11: Race and Diversity and PM

- Sarah A Tishkoff & Kenneth K Kidd (2004) Implications of biogeography of human populations for 'race' and medicine. *Nature Genetics* volume 36, pages S21–S27.
- Popejoy AB1, Fullerton SM2. (2016) Genomics is failing on diversity. Nature. 2016 Oct 13;538(7624):161-164. doi: 10.1038/538161a.
- Cohn EG1,2, Henderson GE3, Appelbaum PS4. (2017) Distributive justice, diversity, and inclusion in precision medicine: what will success look like? Genet Med. 2017 Feb;19(2):157-159. doi: 10.1038/gim.2016.92. Epub 2016 Aug 4.

Week 12: Thanksgiving, no class

Week 13: Familial Hypercholesterolemia Screening

- Santos, RD ; Frauches, Ts ; Chacra, Apm. Cascade Screening in Familial Hypercholesterolemia: Advancing Forward. Journal Of Atherosclerosis And Thrombosis, 2015, Vol.22(9), pp.869-880
- Foody, Joanne M. Familial Hypercholesterolemia: An Under-recognized but Significant Concern in Cardiology Practice. Clinical Cardiology, Feb, 2014, Vol.37(2), p.119(7)

Week 14: Class Discussion/Work Time

- Will Precision Medicine Improve Public Health? NCI Webinars (June 27, 2016) YouTube: https://www.youtube.com/watch?v=3qjTfpCiT9o

COURSE OUTLINE/WEEKLY SCHEDULE

Week/Date	Lecture Topic	Instructor	Readings	Assessments
Week 1: 9/5	Introduction to Public Health Genomics and Precision Medicine (Genetics terminology slides to review on your own)	Demerath	Text, Chapter 1 Collins and Varmus, 2015 Khoury et al., 2011	
Week 2: 9/12	Genetic Epidemiology: Overview, Family History, and Heritability	Demerath	Text, Chapter 2 https://www.ncbi.nlm.nih.gov/books/NBK21866/ Walter et al., 2013 (Journal Club reading 1)	
Week 3: 9/19	Genetic Epidemiology: Genetic Association and Mendelian Randomization	Demerath	Text, Chapter 8 Benn et al., 2010 Lawlor, 2008	
Week 4: 9/26	Genetic Epidemiology: Genome-wide Association Study; Intro to Genetic Testing	Demerath	Text, Chapter 7 Manolio, 2010 Burke, 2014	Assignment 1: Weeks 1-3
Week 5: 10/3	CVD Genomics and Precision Hypertension Treatment	Tang	O'Donnell and Nabel, 2011 Swerdlow et al., 2012 Tang et al., 2013 Khera et al., 2016 (Journal Club reading 2)	
Week 6: 10/10	Childhood Cancer Genomics in the Era of Precision Medicine	Poynter	Yang et al., 2015 (Journal Club reading 3) Roberts et al., 2014	
Week 7: 10/17	Epigenomics and Health Disparities	Demerath	Text, Chapter 14 Relton et al., 2010 Olden et al., 2015 (Journal Club reading 4)	Assignment 2: Weeks 4-6
Week 8: 10/24	Public Health Genomics: Polygenic Testing for Complex Diseases and DTC genetic testing	Demerath	Chatterjee, 2016 Mihaescu et al, 2011 (Journal Club reading 5) Ostergren et al., 2015	
Week 9: 10/31	'Omics in Epidemiology and Medicine: Precision Medicine and Pharmacogenomics	Wen	Ritchie et al., 2012 Korngiebel et al., 2016 TBD (Journal Club Reading 6)	
Week `10: 11/7	Newborn Screening in Minnesota: Ethics and Controversies	Gaviglio	Carmichael, 2007 Bearder Decision TBD (Journal Club Reading 7)	Assignment 3: Weeks 7-9
Week 11: 11/14	The Science of Race and Ancestry: How is Precision Medicine Doing?	Demerath	Tishkoff and Kidd, 2004 Cohn et al., 2016 Popejoy and Fullerton, 2012 TBD (Journal Club Reading 8)	
Week 12: 11/21	Thanksgiving Break	NO CLASS	N/A	
Week 13: 11/28	Genetic Screening: The case of FH	Zierhut	Foody, 2014 Santos et al., 2015	
Week 14: 12/5	Will Precision Medicine Improve Public Health? and group work time	Video/Students	N/A	Assignment 4: Weeks 10-14
Week 15: 12/12	DTC Infographic Presentations	Students	N/A	Infographics Due

ASSIGNMENTS / EXAMINATIONS

1) Assignments (50% of grade) There will be 4 open-book, take-home assignments, submitted on the Moodle site. Each assignment will assess understanding of core concepts and demonstration of competencies highlighted in the course objectives for a set of 3 lessons / weeks, and will include problem solving, short-response, and essay questions. All questions come from the lectures and assigned readings.

2) Journal Club and Participation in Class Discussion (25% of grade) Most weeks of the course (see weekly schedule, above) there will be a 30-minute discussion of one of the assigned readings from the literature, in which students (between 1 and 3) will be the journal club leader/s. Journal club leaders are responsible for thoroughly understanding the reading to the point that they can provide a 10 minute overview of the purpose, methods, and findings, explain to the other students key tables, figures or concepts, and generate 2-3 discussion questions for the class. Students will sign up to lead the discussion for a specific week of class during the first class meeting. A rubric for grading journal club and participation will be provided the first week of class.

3) In-Class Presentation of Infographic: Direct to Consumer Genetic Testing (25% of grade) Students will be assigned to a working group to produce an infographic to educate the general public on the benefits and risks of direct to consumer genetic testing products and services now being marketed to assess health and disease risks. In these groups, you will assign tasks to each group member related to searching the literature, documenting evidence, writing the text, formatting and producing the infographic, etcetera. A limited search of the recent literature on PubMed, as well as internet-based research and blogs will provide you with plenty of interesting and helpful ideas and information. Each individual working on the infographic must list the elements that they were primarily responsible for, so that individual grades can be assigned. A rubric for grading of this assignment will be provided at least four weeks prior to the final deadline.

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

Evaluation

Assignment 1:	50 points

Assignment 2:	50 points
Assignment 3:	50 points
Assignment 4	50 points
Journal Club/Participation	100 points
Infographic and Presentation	100 points
TOTAL:	400 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	Points are deducted for late assignments (10% reduced each day they are late)
Attendance Requirements	Attendance at all lectures is required; Absences require permission of the unit instructor
Extra Credit	Students have the opportunity to attend a Precision Medicine seminar during the semester and write a summary and critique of the content for extra credit points. A list of seminars will be provided in the first class meeting.

CEPH COMPETENCIES

Competency	Learning Objectives	Assessment Strategies
Epi: Demonstrate a basic understanding of the distribution, by person, place and time, and the risk factors for the major public health challenges now facing humans	Conduct a family history assessment for a major disease Correctly identify types of genomic risk factors (genetic, epigenetic, genomic) and their role in major diseases Apply epidemiologic concepts and methods, including confounding, causal inference, sensitivity, specificity, validity, and risk estimation, to the special case of genetic epidemiology	In-class Activity Week 2 Assignments 1-4 Assignment 2-3
Epi: Conduct a literature search and critically evaluate the published epidemiologic research with regard to internal and external validity as well as public health importance	Identify sources of information on public health genomics Gain practice reading the public health genomics literature to assess the evidence for the role of genomic variants (genetic, epigenetic, microbial genomic) in the etiology of major diseases Research and create public health genomics educational materials and present orally in class	Infographic Project Infographic Project, Journal Club Infographic Project
Epi: Summarize and interpret the results of an epidemiologic study in both tabular and figure formats	Use genomic vocabulary and terms correctly to summarize and interpret tables and figures describing results of genetic epidemiology studies	Assignment 1-2
Foundational F6: Discuss the means by which structural bias, social inequities and racism undermine health and create challenges to achieving health equity at organizational, community and societal levels	Advocate for attention to ethical and social implications of genomics and Precision Medicine, including structural bias	Assignment 4
Foundational F9: Design a population-based policy, program, project, or intervention.	Apply epidemiologic concepts to select approaches for population-based testing and screening	Class Activity Week 13

Foundational F19: Communicate audience-appropriate public health content, both in writing and through oral presentation	Research and create public health genomics educational materials and present orally in class	Infographic Project