PUBH 6381

Genetics in Public Health in the Era of Precision Medicine
Fall, 2019

COURSE & CONTACT INFORMATION

Credits: 2
Meeting Day(s): Wednesdays
Meeting Time: 11:15 am – 1:10 pm
Meeting Place: Bruininks Hall, Room 512B

Instructor: Ellen W Demerath
Email: ewd@umn.edu
Office Phone: 4-8231
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. 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 genetic risk for major health conditions (positive family history and specific genetic variants)
- 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 and health inequalities

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:

Additional Readings, by week:

Week 1: Introduction of PHG and PM
- Text, Chapter 1

Week 2: Fam Hx and Heritability
• Text, Chapter 2

Week 3: Genotyping, Sequencing, and Genetic Association
• Text, Chapter 8

Week 4: Genome Wide Association Studies
• Text, Chapter 7

Week 5: CVD Genomics

Week 6: Polygenic Risk Scores for Complex Diseases

Week 7: Direct to Consumer Genetic Testing for Disease Risk
• Tandy-Connor et al., (2018) False-positive results released by direct-to-consumer genetic tests highlight the importance of clinical confirmation testing for appropriate patient care. Genetics in Medicine 20 (12): 1515-1521

Week 8: Origins of Human Genetic Diversity and the Inequality of Precision Medicine


Week 9: Pharmacogenomics

• Abbasi J. Getting pharmacogenomics into the clinic. JAMA October 18, 2016 Volume 316, Number 15: 1533-5.

Week 10 Mendelian Randomization


Week 11 Epigenomics

• Text, Chapter 14
Week 12 Newborn Screening

Week 13: Thanksgiving, no class
Week 14: Discussion (No readings)
- Will Precision Medicine Improve Public Health? NCI Webinars (June 27, 2016) YouTube: https://www.youtube.com/watch?v=3qiTfpCiT9o

Week 15: Presentation of Group DTC Genetic Testing Infographic Projects
## COURSE OUTLINE/WEEKLY SCHEDULE

<table>
<thead>
<tr>
<th>Week/Date</th>
<th>Lecture Topic</th>
<th>Instructor</th>
<th>Resources and Readings</th>
<th>Assessments</th>
</tr>
</thead>
</table>
| Week 1: 9/4 | Introduction to Public Health Genomics and Precision Medicine | Demerath | Bkgrd Video 1: Human genome Intro: https://www.youtube.com/watch?v=EJp7B6u_dYB  
Bkgrd Video 2: The human genome sequence what and how: TED talk: https://www.youtube.com/watch?v=MvuYATh7Y74&t=11s  
Readings: Collins and Varmus, 2015  
Khoury et al., 2011 | |
| Week 2: 9/11 | Family History, and Heritability | Demerath | Bkgrd Video Heritability background lecture: https://www.youtube.com/watch?v=BoGHlgFl6Q&list=PLgh8WcYegg44s-NIxYPVHQsCa0-bCR7-G&index=4  
Heritability readings: https://www.ncbi.nlm.nih.gov/books/NBK21866/  
Text, Chapter 2  
Walter et al., 2013 (Journal Club reading 1) | |
| Week 3: 9/18 | Genotyping and Genomic Sequencing for Epidemiologic Research; Genetic Association | Thyagaragan | Bkgrd Video 1: Genetic variation in populations: https://www.youtube.com/watch?v=OvY1rsYUZD8  
Bkrd Video 2: SNP variants in populations https://www.youtube.com/watch?v= YorPzn2gpUH  
Bkgrd Video 3: How SNP typing works: https://www.youtube.com/watch?v=Naona1y_I2U  
Bkgrd Video 4: Genomic sequencing https://www.youtube.com/watch?v=1pHlaSsEvgw  
Readings:  
Text, Chapter 1  
Text, Chapter 8  
Benn et al., 2010 | |
| Week 4: 9/25 | Genetic Epidemiology; Genome-wide Association Study (GWAS) | Demerath | Bkgrd Video: GWAS: https://www.youtube.com/watch?v=--WrmAvL7i1Y&list=PLgh8WcYegg44s-NIxYPVHQsCa0-bCR7-G&index=5  
Bkgrd Video 2: Using GWAS for personalized health risk assessment https://www.youtube.com/watch?v=a---vfQt7-s  
Readings:  
Text, Chapter 7  
Manolio, 2010 | Assignment 1: Weeks 1-3 |
| Week 5: 10/2 | Genetic Epidemiology of CVD | Tang | O’Donnell and Nabel, 2011  
Swerdlow et al., 2012  
Tang et al., 2013  
Khera et al., 2016 (Journal Club reading 2) |
| Week 6: 10/9 | Polygenic Testing for Complex Diseases | Demerath | Bkgrd Video: ROC and AUC: [https://www.youtube.com/watch?v=4jRBRDbJem](https://www.youtube.com/watch?v=4jRBRDbJem)  
Muller et al, 2016  
Mavaddat et al, 2015  
Richardson et al., 2019 |
| Week 7: 10/16 | Direct to Consumer Genetic Testing for Disease Risk | Demerath | Multhaup et al., 2019  
Tucker, 2018  
Tandy-Connor et al., 2018  
Ostergren et al., 2015 (Journal Club Reading 3) |
| Assignment 2: Weeks 4-6 |
| Week 8: 10/23 | The Science of Human Ancestry and Genomic Health Disparities | Demerath | Tishkoff and Kidd, 2004  
Cohn et al., 2016  
Popejoy and Fullerton, 2012  
All of Us Investigators, 2019 (Journal Club Reading 4) |
| Week 9: 10/30 | Precision Medicine and Pharmacogenomics | Wen | Ritchie et al., 2012 (supplemental)  
Korniebel et al., 2016  
Abbasi, 2016  
Culhane-Pera et al., 2017 (Journal Club reading 5) |
| Week 10: 11/6 | Mendelian Randomization | Demerath | Emdin et al., 2017  
Davey-Smith and Ebrahim, 2003  
Emdin et al., 2017 (Journal Club reading 6) |
| Assignment 3: Weeks 7-9 |
| Week 11: 11/13 | Epigenomics: Biomarkers of Environmental Exposure, Age, and Disease Risk | Nguyen | Epigenetics Intro Video: [https://www.youtube.com/watch?v=iW3fqA8RDcU](https://www.youtube.com/watch?v=iW3fqA8RDcU)  
Text, Chapter 14  
Relton and Davey-Smith, 2010  
Horvath and Raj, 2018  
Smith et al., 2017 (Journal Club reading 7) |
| Week 12: 11/20 | Newborn Screening in Minnesota: Ethics and Controversies | Gaviglio | Carmichael 2007  
Fost et al., 2016  
Kelly et al., 2016  
Genetti et al., 2018 (Journal Club Reading 8) |
| Week 13: 11/27 | Thanksgiving Break | NO CLASS | N/A |
| Assignment 4: Weeks 10-12 |
| Week 14: 12/4 | Will Precision Medicine and Personal Genomics Improve Public Health? | Class Discussion | N/A |
| Week 15: 12/11 | DTC Infographic Presentations | Students | 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

<table>
<thead>
<tr>
<th>Assignment</th>
<th>Points</th>
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<tbody>
<tr>
<td>Assignment 1</td>
<td>50</td>
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<tr>
<td>Assignment 2</td>
<td>50</td>
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<tr>
<td>% In Class</td>
<td>Grade</td>
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<tr>
<td>93 - 100%</td>
<td>A</td>
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<tr>
<td>90 - 92%</td>
<td>A-</td>
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<tr>
<td>87 - 89%</td>
<td>B+</td>
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<tr>
<td>83 - 86%</td>
<td>B</td>
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<tr>
<td>80 - 82%</td>
<td>B-</td>
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<tr>
<td>77 - 79%</td>
<td>C+</td>
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<tr>
<td>73 - 76%</td>
<td>C</td>
</tr>
<tr>
<td>70 - 72%</td>
<td>C-</td>
</tr>
<tr>
<td>67 - 69%</td>
<td>D+</td>
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<tr>
<td>63 - 66%</td>
<td>D</td>
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<tr>
<td>&lt; 62%</td>
<td>F</td>
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- 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).
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](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](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](http://z.umn.edu/iuplagiarism)).

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<tr>
<th>Late Assignments</th>
<th>Points are deducted for late assignments (10% reduced each day they are late)</th>
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<tbody>
<tr>
<td>Attendance Requirements</td>
<td>Attendance at all lectures is required; Absences require permission of the unit instructor</td>
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<td>Extra Credit</td>
<td>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.</td>
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**CEPH Competencies**

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<tr>
<th>Competency</th>
<th>Learning Objectives</th>
<th>Assessment Strategies</th>
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<tbody>
<tr>
<td>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</td>
<td>Conduct a family history assessment for a major disease</td>
<td>In-class Activity Week 2</td>
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<td>Correctly identify types of genomic risk factors (genetic, epigenetic, genomic) and their role in major diseases</td>
<td>Assignments 1-3</td>
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<td>Apply epidemiologic concepts and methods, including confounding, causal inference, sensitivity, specificity, validity, and risk estimation, to the special case of genetic epidemiology</td>
<td>Assignment 2-3</td>
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| 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, Journal Club  
Infographic Project, Journal Club  
Infographic Project |
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<tr>
<td>Epi: Summarize and interpret the results of an epidemiologic study in both tabular and figure formats</td>
<td>Use genomic vocabulary and terms correctly to summarize and interpret tables and figures describing results of genetic epidemiology studies</td>
<td>Assignment 1-2</td>
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<td>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</td>
<td>Advocate for attention to ethical and social implications of genomics and Precision Medicine, including structural bias</td>
<td>Assignment 4</td>
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| Foundational F9: Design a population-based policy, program, project, or intervention.  
Foundational F19: Communicate audience-appropriate public health content, both in writing and through oral presentation | Apply epidemiologic concepts to select approaches for population-based testing and screening  
Research and create public health genomics educational materials and present orally in class | Class Activity Week 13  
Infographic Project |