University of Wisconsin-Madison

Genetic Epidemiology
(POP HLTH, AN SCI, GENETICS 849)
Fall 2022
(September 8 – November 22)

Instructor: Corinne Engelman, MSPH, PhD
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Meeting time: Tuesday and Thursday, 11-12:30

Meeting location: HSLC 3330 **(Please note that this room is inside the library so we need to keep the noise level very low when coming and going through the Ebling library or we may lose this room!)**

Instructional mode: Face-to-face

Course website: https://canvas.wisc.edu/courses/325566

Credits: 3 credits

Credit hours: This class meets two 90-minute class periods each week for the **first 11 weeks of the fall semester** (class will not meet in the 12th week, as this is reserved for a final assessment, which this class will not have) and carries the expectation that students will work on course learning activities for about 3 hours out of the classroom for every class period. The syllabus includes more information about meeting times and expectations for student work.

Instructor availability: 20 minutes before class and immediately after class in the classroom or by appointment

Course description:
This course will provide an introduction to genetic/genomic epidemiology. Topics will include a general overview of genetics and Mendelian and complex inheritance. We will discuss the various elements of study design, including definition of study population, participant ascertainment, phenotype definition, determination of the type of biologic sample to be collected for extraction of the DNA, genotyping and sequencing, data collection and quality control, and choice of analytic methods. We will briefly discuss some of the original study designs (e.g., heritability and linkage analysis) and will then focus on current study designs (e.g., association analysis of genome-wide chip and sequencing data, and polygenic risk scores) for the remainder of the class. We will cover analysis methods for case-control and family data. Throughout, the application of these methods will be demonstrated both by hand calculation and by using available statistical software. We will use real data examples and examples from the literature. Additional current topics will be briefly touched upon in the last week of class.

Course learning outcomes:
1. Evaluate and discuss genetic/genomic epidemiologic literature.
2. Design simple genetic/genomic epidemiologic studies.
3. Identify and apply appropriate tests of association between genetic variants and both qualitative and quantitative outcomes using either unrelated individuals or families.
4. Summarize and interpret the results of genetic/genomic tests of association.

Lecture, readings, and homework:
The reading(s) and a short homework assignment will need to be completed before each lecture class period. Readings will include selected textbook chapters and original research and review articles available through

Canvas. A paper copy of the homework will be turned in at the start of class; full credit will be given for work that is completed in full, partial credit will be given for partially completed homework, and no credit will be given for homework not turned in or turned in late. (Please talk to the instructor if you would prefer to submit your homework electronically.) The homework turned in at the previous class will be distributed at the beginning of each lecture class and the first ~15 minutes of class will be spent reviewing/discussing the homework answers, especially any problems that a number of students had difficulty with. This will be followed by a ~60-minute lecture and, usually, a 15-minute group activity at the middle or end of the lecture.

Journal article discussion:

The objectives of the discussion class periods are to critically review current literature in genetic/genomic epidemiology; discuss study design, data collection, statistical analysis and interpretation, and other issues with your peers; and make a connection between topics we have discussed in class and the journal article being reviewed. Each journal discussion will be led by one or more students. The professor will select the article for discussion and post it on the Canvas website at least one week before the discussion so all students can access it. Students should try to relate concepts discussed in the lectures to the article. The student(s) leading the discussion should spend 10 minutes presenting the paper (please stick to this timeframe so we can have plenty of time for discussion) so that 50 minutes can be spent in discussion as questions arise through each section of the paper. After this discussion, I will take the remaining 30 minutes to talk about why the studies were designed the way they were and any alternate study designs that would have worked. This will help prepare the students for the mid-term paper.

For those leading the discussion: While everyone should have read the paper, don't assume that everyone will remember everything, let alone understand it. Give an overview of the paper and follow with specifics, including going through what you think might be the hardest parts to understand. If you don't understand everything, present what you do understand and pose questions to the other students regarding what you don't understand. Develop a set of questions to facilitate discussion. Try to connect the Methods and Results sections with concepts presented in lecture. You will be evaluated on the clarity of your presentation and your efforts to facilitate discussion. In an effort to provide an informal environment and encourage active discussion, you may NOT use PowerPoint slides for your presentation. When you are leading the discussion, you do not need to submit anything via Canvas or turn anything in to the instructor.

For those not leading the discussion: All students not leading the discussion will prepare a type written short paragraph summarizing the paper (1-2 sentences each for purpose, general approach, and conclusions) along with 3-4 questions/comments for discussion, including questions that relate the paper to concepts presented in lecture and anything you don't understand, which will be submitted via Canvas prior to the start of class. You will be evaluated on your preparation (handing in your summary and discussion questions) and participation.

Mid-term exam

For the mid-term exam, each student will select a disease or trait and find one or two papers reviewing the genetic epidemiology of the disease or trait. Selection of these papers should begin **several weeks before the mid-term exam is due.** For the exam, you will be asked to write a research proposal (3-page limit) for a genome-wide association study or polygenic risk score study. If you need guidance, please ask me, but **do not discuss the mid-term exam with other students**. Further instructions will be provided when the exam is distributed.

Evaluation:

Homework	25%
Journal article presentation and participation	25%
Mid-term exam	50%

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The grading scale will be: 93-100 = A, 88-92 = AB, 83-87 = B, 78-82 = BC, 70-77 = C, 60-69 = D. Final grades are not curved.

Academic integrity and attendance:
Students may discuss and/or work together on homework assignments. However, please realize that the homework assignments serve as preparation for the mid-term exam so it is to your benefit to solve as many of the homework problems as you possibly can on your own. Students may NOT work together on or discuss the mid-term exam.

Attendance in person is expected at all class periods unless you have received prior approval to miss a class (e.g., due to attendance at a conference, a family emergency, or other extenuating circumstance) or are sick. Please notify me as soon as possible if you will have to miss class. All assignments will still need to be turned in on time, so please plan ahead.

By enrolling in this course, each student agrees to uphold the high academic standards of the University of Wisconsin-Madison; academic misconduct is behavior that negatively impacts the integrity of the institution. Cheating, fabrication, plagiarism, unauthorized collaboration, and helping others commit these previously listed acts are examples of misconduct which may result in disciplinary action. Examples of disciplinary sanctions include but are not limited to, failure on the assignment/course, written reprimand, disciplinary probation, suspension, or expulsion.

Accommodations for students with disabilities:
The University of Wisconsin-Madison supports the right of all enrolled students to a full and equal educational opportunity. The Americans with Disabilities Act (ADA), Wisconsin State Statute (36.12), and UW-Madison policy (UW-855) require the university to provide reasonable accommodations to students with disabilities to access and participate in its academic programs and educational services. Faculty and students share responsibility in the accommodation process. Students are expected to inform faculty of their need for instructional accommodations during the beginning of the semester, or as soon as possible after being approved for accommodations. Faculty will work either directly with the student or in coordination with the McBurney Center to provide reasonable instructional and course-related accommodations. Disability information, including instructional accommodations as part of a student's educational record, is confidential and protected under FERPA. (See: McBurney Disability Resource Center)

Diversity and inclusion:
Diversity is a source of strength, creativity, and innovation for UW-Madison. We value the contributions of each person and respect the profound ways their identity, culture, background, experience, status, abilities, and opinion enrich the university community. We commit ourselves to the pursuit of excellence in teaching, research, outreach, and diversity as inextricably linked goals. The University of Wisconsin-Madison fulfills its public mission by creating a welcoming and inclusive community for people from every background – people who as students, faculty, and staff serve Wisconsin and the world.

Use of course materials:
Lecture materials and recordings for this course are protected intellectual property at UW-Madison. Students in courses may use the materials and recordings for their personal use related to participation in class. Students may also take notes solely for their personal use. If a lecture is not already recorded, students are not authorized to record lectures without permission unless they are considered by the university to be a qualified student with a disability who has an approved accommodation that includes recording. [Regent Policy Document 4-1] Students may not copy or have lecture materials and recordings outside of class, including posting on internet sites or selling to commercial entities, with the exception of sharing copies of personal notes as a notetaker through the McBurney Disability Resource Center. Students are otherwise prohibited from providing or selling

their personal notes to anyone else or being paid for taking notes by any person or commercial firm without the instructor's express written permission. Unauthorized use of these copyrighted lecture materials and recordings constitutes copyright infringement and may be addressed under the university's policies, UWS Chapters 14 and 17, governing student academic and non-academic misconduct.

Academic calendar and religious observances:
Academic Calendar & Religious Observances

Schedule:

Date	Topic	Required Readings and Homework
09/08/22 (Thurs)	Course overview, intro to genetic epidemiology and basic concepts in genetics	Basic Genetics online lecture Genetic Variation online lecture Ziegler chapters 1.1 – 1.3.1 and 2 – 2.2.2 *Optional: Online genetics tutorial: 3. Basic Principles of Genetics (topics 1 and 2) and 4. Biological Basis of Heredity (topics 1, 2, 3, and 5)*
09/13/22 (Tues)	Inheritance and the genetic component of diseases/traits	Ziegler chapter 6 – 6.5 (do not need to read statistical sections in chapter 6 in detail) *Optional: Ziegler chapter 2.4*
09/15/22 (Thurs)	Complex inheritance	Ziegler chapter 2.3 *Optional: Online genetics tutorial: Basic Principles of Genetics (topic 3)*
09/20/22 (Tues)	Study design, DNA collection and genotyping	Haines chapter 3 pages 92-99 *Optional: Haines chapter 5* HW1 due
09/22/22 (Thurs)	Linkage disequilibrium	Haines chapter 12 pages 330-333 HW2 due
09/27/22 (Tues)	Data collection, quality control, and analysis	Ziegler chapter 4 – 4.3.1 *Optional: Ellingson and Fardo 2016, Turner…Ritchie 2011* HW3 due
09/29/22 (Thurs)	Unrelated case-control association analysis	Ziegler chapters 10 – 10.1.2 and 11 – 11.2.2 (skip Algorithm 11.1) HW4 due
10/04/22 (Tues)	Population stratification	Ziegler chapter 11.4 – 11.4.5 HW5 due
10/06/22 (Thurs)	Genome-wide association studies (GWAS)	Ziegler chapters 14 (skip 14.4.1-3 and 14.5.3.1-2) and 4.4 **OR** Coleman 2016 HW6 due **Mid-term exam distributed**
10/11/22 (Tues)	Journal article discussion: Population stratification	Journal Discussion 1 reading on Canvas
10/13/22 (Thurs)	Journal article discussion: GWAS	Journal Discussion 2 reading on Canvas
10/18/22 (Tues)	Beyond GWAS: Polygenic scores	NIH NHGRI short video on PRS PRS Primer Wray…Visscher 2020 *Optional: Guide to performing PRS 2020* HW7 due
10/20/22 (Thurs)	Journal article discussion: Polygenic scores	Journal Discussion 3 reading on Canvas

10/25/22 (Tues)	NO CLASS	Work on mid-term
10/27/22 (Thurs)	NO CLASS	Work on mid-term
11/01/22 (Tues)	Journal article discussion: Polygenic scores and complex inheritance (gene-environment interaction)	Journal Discussion 4 reading on Canvas
11/03/22 (Thurs)	Lab to get started on homework 8: Linux commands and using PLINK	**Mid-term due Thursday, 11/03, 11 am**
11/08/22 (Tues)	Genomic sequencing in unrelated individuals	Austin chapters 3.6 – 3.8 and 5.8 – 5.9 *Optional: Human Genome Sequencing Primer* No homework due
11/10/22 (Thurs)	Journal article discussion: Genomic sequencing in unrelated individuals	Journal Discussion 5 reading on Canvas
11/15/22 (Tues)	Family studies (linkage, association, and rare variant prioritization algorithms)	Ziegler chapter 12 – 12.2 (do not need to read statistical sections in detail), 12.7.3 (DSP = discordant sib-pair), and 12.8 HW8 due
11/17/22 (Thurs)	Journal article discussion: Family studies	Journal Discussion 6 reading on Canvas
11/22/22 (Tues)	'Omics	HW9 due