Genetic Epidemiology
(AN SCI, GENETICS, POP HLTH 849)
Fall 2019

Instructor: Corinne Engelman, MSPH, PhD
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Meeting time: Tuesday and Thursday, 9:30-10:45
Meeting location: HSLC 3330 (Please note that this room is inside the library so we need to keep the noise level very low when leaving this room until we exit the library or we may lose this room!)

Instructional mode: Face-to-face

Credits: 3 credits (https://canvas.wisc.edu/courses/94077)

Hours: This class meets two 75-minute class period each week over the fall semester 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) 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 topics will be briefly touched upon, including epigenomics, transcriptomics, metabolomics, proteomics, bioinformatics, pharmacogenomics, public health genomics, and ethical, legal, and social issues (ELSI).

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 time. Full credit will be given for homework 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. 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
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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.

**Journal article discussion:**
The objectives of the discussion class time 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. This class time will be spent discussing published journal articles. Each journal discussion will be led by one or more students. The professor can select the article for discussion or the student(s) leading the topic may select the article by searching the literature to find a recent (within the last year) original research (not review, commentary, etc) article related to the topic. (Note: for some topics – complex inheritance in particular – a review article may be appropriate; please consult the professor.) Please notify the professor at least two weeks before your journal discussion date if you would like to select the article; in this case, the article should be emailed to the professor at least one week prior to the discussion for verification of article appropriateness. The professor will then put the article up on the Learn@UW website one week before the discussion so all students can access it.

For genetic association articles, each student should read the paper in Nature, Vol 447 (7) 655-660 by the NCI-NHGRI Working Group, “Replicating genotype-phenotype associations” and use Boxes 1-3 as a guide in reviewing the original research articles. For all articles, 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). The rest of the time (50 minutes) should be spent in discussion as questions arise through each section of the 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 a projector with PowerPoint slides for your presentation. You may, however, provide a 1-page handout for the other students.

**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 for discussion (including, but not limited to items from Boxes 1-3 of the Nature paper above (if applicable), questions that relate the paper to concepts presented in lecture, and anything you don’t understand), which will be handed in to the professor at the end of the discussion. 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 a recent (within the last year) original research paper and a paper reviewing the genetic epidemiology of the disease or trait (for this paper, it will be better to find a review paper instead of an original research paper by setting a “Limit” of “Review” for type of article). Selection of these two papers can begin at any time, but you must email the papers to the professor by Sunday, 10/20. The professor will then verify that the articles are appropriate or suggest that other articles be found. For the exam, you will be asked to write a research proposal (3 page limit) for a study that takes the next logical research step (using a genetic/genomic epidemiologic study design and existing databases from dbGaP or other existing data sources [if at all possible]) from the original research paper you selected.
Final project
You will form analysis/writing groups with 2-3 students, preferably having combined expertise in epidemiology/population health, genetics (human or animal), biostatistics, and/or computational sciences. Each group will formulate a hypothesis regarding the data provided, test the hypothesis, and write up the results in a shortened research paper format (approximately 3 single spaced pages including the aim/hypothesis, methods (limited to the quality control and statistical analysis of the genetic/genomic data), results, a short discussion (interpretation of findings), and tables and figures). Class meetings will be utilized to work on the data analysis and writing under the guidance of the professor. Additional time outside of class will be necessary to conduct data analysis and writing.

Required readings:
Readings will include the required textbook listed below (available for free online through the UW-Madison Libraries), as well as selected textbook chapters and original research and review articles available through Canvas.

Andreas Ziegler and Inke R. König
A Statistical Approach to Genetic Epidemiology: Concepts and Applications
Wiley-Blackwell Mar 2010
ISBN: 3527323899
Free online access through the UW-Madison Libraries:  

Evaluation:
Homework 20%
Journal article presentation and participation 20%
Mid-term exam 35%
Final project 25%

The grading scale will be: 93-100 = A, 88-92 = AB, 83-87 = B, 78-82 = BC, 70-77 = C, 60-69 = D.

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. Students are expected to be in class unless extreme circumstances arise. Please let me know before class whenever possible if you will be unable to attend due to such circumstances.

By enrolling in this course, each student assumes the responsibilities of an active participant in UW-Madison’s community of scholars in which everyone’s academic work and behavior are held to the highest academic integrity standards. Academic misconduct compromises the integrity of the university. Cheating, fabrication, plagiarism, unauthorized collaboration, and helping others commit these acts are examples of academic misconduct, which can result in disciplinary action. This includes but is not limited to failure on the assignment/course, disciplinary probation, or suspension. Substantial or repeated cases of misconduct will be forwarded to the Office of Student Conduct & Community Standards for additional review. For more information, refer to studentconduct.wiscweb.wisc.edu/academic-integrity/.

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
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policy (Faculty Document 1071) require that students with disabilities be reasonably accommodated in instruction and campus life. Reasonable accommodations for students with disabilities is a shared faculty and student responsibility. Students are expected to inform faculty of their need for instructional accommodations by the end of the third week of the semester, or as soon as possible after a disability has been incurred or recognized. Faculty will work either directly with the student or in coordination with the McBurney Center to identify and provide reasonable instructional accommodations. Disability information, including instructional accommodations as part of a student's educational record, is confidential and protected under FERPA.

**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 opinions enrich the university community. We commit ourselves to the pursuit of excellence in teaching, research, outreach, and diversity as inextricably linked goals. The UW-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.

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<th>Date</th>
<th>Topic</th>
<th>Required Readings and Homework</th>
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| 09/05/19 (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) |
| 09/10/19 (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 |
| 09/12/19 (Thurs) | Journal article discussion: Genetic component of diseases/traits (e.g., heritability) | Journal Discussion 1 reading on Canvas |
| 09/17/19 (Tues) | Complex inheritance | Ziegler chapter 2.3  
Optional: Online genetics tutorial: Basic Principles of Genetics (topic 3) |
| 09/19/19 (Thurs) | Journal article discussion: Complex inheritance (e.g., gene-environment interaction) | Journal Discussion 2 reading on Canvas |
| 09/24/19 (Tues) | Study design, DNA collection and genotyping | Haines chapter 3 pages 92-99  
Optional: Haines chapter 5  
HW1 due |
| 09/26/19 (Thurs) | Linkage disequilibrium | Haines chapter 12 pages 330-333  
HW2 due |
| 10/01/19 (Tues) | Data collection, quality control, and analysis | Ziegler chapter 4 – 4.3.1  
Optional: Ellingson and Fardo 2016, Turner…Ritchie 2011  
HW3 due |
| 10/03/19 (Thurs) | Unrelated case-control association analysis | Ziegler chapters 10 – 10.1.2 and 11 – 11.2.2 (skip Algorithm 11.1)  
HW4 due |
| 10/08/19 (Tues) | Population stratification | Ziegler chapter 11.4 – 11.4.5  
HW5 due |
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<th>Activity</th>
<th>Reading/Assignment</th>
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<tr>
<td>10/10/19 (Thurs)</td>
<td>Genome-wide association studies (GWAS) (genetic counseling students joining us)</td>
<td>Ziegler chapters 14 (skip 14.4.1-3 and 14.5.3.1-2) and 4.4 &lt;br&gt; OR Coleman 2016 HW6 due</td>
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<td>10/15-17/19</td>
<td>NO CLASS</td>
<td>Select papers for mid-term exam and email to professor by Sunday, 10/20</td>
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<td>10/22/19 (Tues)</td>
<td>Journal article discussion: GWAS</td>
<td>Journal Discussion 3 reading on Canvas</td>
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<td>10/24/19 (Thurs)</td>
<td>Genomic sequencing in unrelated individuals</td>
<td>Austin chapters 3.6 – 3.8 and 5.8 – 5.9 HW7</td>
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<td>10/29/19 (Tues)</td>
<td>Journal article discussion: Genomic sequencing in unrelated individuals</td>
<td>Journal Discussion 4 reading on Canvas</td>
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<td>10/31/19 (Thurs)</td>
<td>Family studies (linkage, association, and rare variant prioritization algorithms)</td>
<td>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</td>
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<td>11/05/19 (Tues)</td>
<td>Journal article discussion: Family studies</td>
<td>Journal Discussion 5 reading on Canvas</td>
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<td>11/07/19 (Thurs)</td>
<td>Beyond GWAS: Polygenic scores and ‘omics (lecture by Danny Panyard)</td>
<td>Reading TBD</td>
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<td>11/12/19 (Tues)</td>
<td>Utilizing genomic databases (lecture by Eva Vasiljevic)</td>
<td>dbGaP reading</td>
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<td>11/14/19 (Thurs)</td>
<td>Journal article discussion: Polygenic scores</td>
<td>Journal Discussion 6 reading on Canvas</td>
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<td>11/19/19 (Tues)</td>
<td>Introduction of dataset for final project and begin group work on quality control (Computer Lab?)</td>
<td>Email mid-term to professor by Wednesday, 11/20, 11:59 pm</td>
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<td>11/21/19 (Thurs)</td>
<td>Group work on quality control (Computer Lab?)</td>
<td>Write up final project and prepare presentation</td>
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<td>11/26/19 (Tues)</td>
<td>Group work on quality control (Computer Lab?)</td>
<td>Write up final project and prepare presentation</td>
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<td>11/28/19 (Thurs)</td>
<td>NO CLASS – THANKSGIVING HOLIDAY</td>
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<td>12/03/19 (Tues)</td>
<td>Group work on genetic analysis (Computer Lab?)</td>
<td>Write up final project and prepare presentation</td>
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<tr>
<td>12/05/19 (Thurs)</td>
<td>Group work on genetic analysis (Computer Lab?)</td>
<td>Rough draft of final project due by the end of the day (you will receive comments from me the next day and should incorporate these into your presentation and final paper)</td>
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<td>12/10/19 (Tues)</td>
<td>Group presentations of final project</td>
<td>Final project due Wednesday, 12/18, 11:59 pm</td>
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