Genetic Epidemiology
(course #: 810-849; formerly 904-102)
Fall 2015, 09/03/15 – 12/15/15

Instructor: Corinne Engelman, MSPH, PhD
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Office Hours: 20 minutes before class in HSLC Room 3330
Time: Tuesday and Thursday, 9:30-10:45
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 loose this room!)**
Prerequisites: The student must be in a graduate or health care professional program, or have permission from the instructor.

Course description:

This course will provide an introduction to genetic 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, selection of genetic markers, determination of the type of biologic sample to be collected for extraction of the DNA, data collection and management, and choice of analytic methods. We will briefly discuss some of the original study designs (e.g., linkage analysis) and will then focus on current study designs (e.g., association analysis) for the remainder of the class. We will cover analysis methods for case-control and family data, single marker and □aplotype tests of association in the context of candidate gene and genome-wide association studies. Throughout, we will demonstrate the application of these methods 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 sequence data and analysis, structural variation, gene expression studies, epigenomics, proteomics, comparative genomics, bioinformatics, systems biology, nutrigenomics, pharmacogenomics, public health genomics, and ethical, legal, and social issues (ELSI).

Course objectives:

At the completion of this course students will be able to critically review and discuss genetic epidemiologic literature, provide input on the design of genetic epidemiologic studies, identify and apply appropriate tests of association between genetic markers and both qualitative and quantitative outcomes using either unrelated individuals or families, and summarize and interpret the results of these tests of association.

Lecture:

The reading(s) and a short homework assignment will need to be completed before each lecture class time. The completed 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.

Discussion:
The objective of the discussion class time is to critically review current literature in genetic epidemiology and discuss study design, data collection, statistical analysis and interpretation, and other issues with your peers and to make a connection between topics we have discussed in class and the journal article being reviewed.

The discussion class time will be spent discussing published journal articles. Each journal discussion will be led by one or more students. The student(s) leading the topic will search 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 instructor.) If you would like help selecting an article, please ask the instructor. The student(s) leading the discussion should email the instructor with the article chosen at least one week prior to the discussion for verification of article appropriateness. The instructor 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 10-15 minutes presenting the paper (please stick to this timeframe so we can have plenty of time for discussion). The rest of the time (45-50 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 instructor 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). Also, for the latter paper, you may need to go back to the pre-GWAS era (before 2007) to find a review that focuses on the genetic component versus a summary of GWAS findings. Selection of these two papers can begin at any time, but you must email the papers to the instructor by Sunday, 10/11. The instructor 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 epidemiologic study design) from the original research paper you selected.

Final project

You will form analysis/writing groups with 2-3 students, having combined expertise in epidemiology, 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 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 instructor. Additional time outside of class will be necessary to conduct data analysis and writing.

Required readings:

Readings will include the required textbook listed below, as well as selected textbook chapters and original research and review articles available at Learn@UW.

Andreas Ziegler and Inke R. König
A Statistical Approach to Genetic Epidemiology: Concepts and Applications
Wiley-Blackwell Mar 2010
ISBN: 3527323899

Evaluation:

Mid-term exam	40%
Final project	20%
Assignments	20%
Journal article presentation and participation	20%

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

Academic integrity:

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.

Accommodations for disabilities:

If you need accommodations due to a disability please see me as soon as possible.

Date	Topic	Required Readings and Homework
09/03/15 (Thurs)	Course overview, intro to genetic epidemiology and basic concepts in genetics	Ziegler chapter 1.1 – 1.3.1 Optional: Online genetics tutorial: Biological Basis of Heredity (topics 1, 2, 3, and 5)
09/08/15 (Tues)	Inheritance and the genetic component of diseases/traits	Ziegler chapters 2 – 2.2.2 and 6 – 6.5 (do not need to read statistical sections in chapter 6 in detail) Optional: Online genetics tutorial: Basic Principles of Genetics (topics 1 and 2) and Ziegler chapter 2.4
09/10/15 (Thurs)	Journal article discussion: Genetic component of diseases/traits (e.g., heritability from a twin study)	Journal Discussion 1 reading on Learn@UW
09/15/15 (Tues)	Complex inheritance	Ziegler chapter 2.3 Optional: Online genetics tutorial: Basic Principles of Genetics (topic 3)
09/17/15 (Thurs)	Journal article discussion: Complex inheritance	Journal Discussion 2 reading on Learn@UW
09/22/15 (Tues)	Study design, DNA collection and genotyping	Haines chapter 3 pages 92-99 Optional : Haines chapter 5 HW1 due
09/24/15 (Thurs)	Linkage disequilibrium	Haines chapter 12 pages 330-333 HW2 due
09/29/15 (Tues)	SNP selection and public databases (**HSLC Room 2121, Computer Lab**)	HW3 due
10/01/15 (Thurs)	Data collection, management and analysis	Ziegler chapter 4 – 4.3.1 HW4 due
10/06-08	NO CLASS	**Select papers for mid-term exam and email to instructor by Sunday, 10/11**
10/13/15 (Tues)	Unrelated case-control association analysis	Ziegler chapters 10 – 10.1.2 and 11 – 11.2.2 (skip Algorithm 11.1) HW5 due
10/15/15 (Thurs)	Population stratification	Ziegler chapter 11.4 – 11.4.5 HW6 due
10/20/15 (Tues)	Journal article discussion: Case-control association analysis and population stratification	Journal Discussion 3 reading on Learn@UW
10/22/15 (Thurs)	Family-based association analysis	Ziegler chapter 12 – 12.2 (do not need to read statistical sections in detail), 12.7.3 (DSP = discordant sib-pair), and 12.8 HW7 due
10/27/15 (Tues)	Journal article discussion: Family-based association analysis	Journal Discussion 4 reading on Learn@UW
10/29/15 (Thurs)	Genome-wide association studies (GWAS) (genetic counseling students joining us)	Ziegler chapters 14 (skip 14.4.1-3 and 14.5.3.1-2) and 4.4 HW8 due
11/03/15 (Tues)	Journal article discussion: GWAS	Journal Discussion 5 reading on Learn@UW
11/05/15 (Thurs)	Special topics 1: Beyond GWAS	Ziegler chapters 13 – 13.2 (skip 13.2.1-2) and 11.5 HW9 due
11/10/15 (Tues)	Journal article discussion: Beyond GWAS	Journal Discussion 6 reading on Learn@UW
11/12/15 (Thurs)	Special topics 2: "Omics" and related fields	View 13 minute PBS NOVA video on Epigenomics HW10 due

11/17/15 (Tues)	Special topics 3: Public health genomics	**Mid-term exam distributed; turn in to instructor Tuesday, 11/24, at start of class**
11/19/15 (Thurs)	Introduction of dataset for final project (**HSLC Room 2121, Computer Lab**)	
11/24/15 (Tues)	Group work on descriptive analysis (**HSLC Room 2121, Computer Lab**)	Work on final project
11/26/15 (Thurs)	NO CLASS – THANKSGIVING HOLIDAY	
12/01/15 (Tues)	Group work on genetic analysis (**HSLC Room 2121, Computer Lab**)	Work on final project
12/03/15 (Thurs)	Group work on genetic analysis or writing up results (**HSLC Room 2121, Computer Lab**)	Work on final project
12/08/15 (Tues)	Group work on genetic analysis or writing up results (**HSLC Room 2121, Computer Lab**)	**Rough draft of final project due by the end of the day**
12/10/15 (Thurs)	Group work on writing up results (**HSLC Room 2121, Computer Lab**)	Receive comments on rough draft at beginning of class
12/15/15 (Tues)	Group presentations of final project	**Final project due Thursday, 12/17, by the end of the day**