

**Genetic Epidemiology**  
**Population Health Sciences 904 Section 002**  
**Fall 2010, 11/01/10 – 12/15/10**

**Instructor:** Corinne Engelman, MSPH, PhD  
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**Office Hours:** 20 minutes before class in HSLC 1222  
**Lecture Time:** Monday and Wednesday, 9:55-11:15  
**Location:** HSLC 1222  
**Discussion Time:** Friday, 9:55-10:55  
**Location:** HSLC 1220 (note that this is the room next door to the lecture room)

**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 haplotype tests of association in the context of candidate gene, candidate region, 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). 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 ~20 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 – Genetic epidemiology of a disease/trait 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.

Each student should read the paper in Nature, Vol 447 (7) 655-660 by the NCI-NHGRI Working Group, “Replicating genotype-phenotype associations”, before reading their first journal article and use Boxes 1-3 as a guide in reviewing the original research articles, as well as relating 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, 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.

### **Exam**

For the final 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 (OMIM can also be used for this). Selection of these two papers can begin at any time, but it is highly recommended that it be done before the exam is distributed. Once you have selected the two papers, you will email them to the instructor. On Wednesday, December 15<sup>th</sup>, the final exam will be distributed in class. 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. You will have the option of meeting with the instructor for 30 minutes during finals week to help you with any questions you may have (e.g., using a public database, study design, conceptual clarifications). Think of this as a meeting with your thesis advisor where you would ask conceptual questions that would help you write your thesis or thesis proposal, but you would not ask your advisor to write a paragraph for you. Since you will only have 30 minutes, it would be to your advantage to have attempted to complete the entire exam and come with your questions organized because I will cut you off after 30 minutes in fairness to other students. The motivation behind this type of exam (including the meeting with the instructor) is that I want this to complete your learning experience, and not merely test you on what you know.

## Required readings:

The field of genetic epidemiology is evolving rapidly so the few text books that are written quickly become out of date and no one text book adequately covers the material that will be presented in this class. Therefore, we will use selected chapters from the text books below and original research and review articles as supplements to the lecture notes. These will be available at Learn@UW.

Although the required readings from the text books below will be available at Learn@UW, purchasing one or both of these text books is highly recommended for anyone who plans to be involved in a genetic study in the future. These books can be purchased from <http://www.addall.com/> (this website searches for the best price) or other textbook sources and they are also on reserve at Ebling Library.

Jonathan L. Haines and Margaret A. Pericak-Vance

Genetic Analysis of Complex Disease

John Wiley and Sons Inc 05 May 2006

ISBN: 0471-08952-4

List price is \$112.95, but you can find it for as low as \$76.04 at <http://www.addall.com/>.



## Genetic Analysis of Complex Disease

by [Jonathan L. Haines, Margaret A. Pericak-Vance](#)

**About this title:** Second Edition features the latest tools for uncovering the genetic basis of human disease

The "Second Edition" of this landmark publication brings together a team of leading experts in the field to thoroughly update the publication. Readers will discover the tremendous advances made in human genetics in the seven years that have elapsed since the "First Edition." Once again, the editors have assembled a comprehensive introduction to the strategies, designs, and methods of analysis for the discovery of genes in common and genetically complex traits. The growing social, legal, and ethical issues surrounding the field are thoroughly examined as well.

Rather than focusing on technical details or particular methodologies, the editors take a broader approach that emphasizes concepts and experimental design. Readers familiar with the "First Edition" will find new and cutting-edge material incorporated into the text: Updated presentations of bioinformatics, multiple comparisons, sample size requirements, parametric linkage analysis, case-control and family-based approaches, and genomic screening; New methods for analysis of gene-gene and gene-environment interactions; A completely rewritten and updated chapter on determining genetic components of disease; New chapters covering molecular genomic approaches such as microarray and SAGE analyses using single nucleotide polymorphism (SNP) and cDNA expression data, as well as quantitative trait loci (QTL) mapping.

The editors, two of the world's leading genetic epidemiologists, have ensured that each chapter adheres to a consistent and high standard. Each one includes all-new discussion questions and practical examples. Chapter summaries highlight key points, and a list of references for each chapter opens the door to further investigation of specific topics.

Molecular biologists, human geneticists, genetic epidemiologists, and clinical and pharmaceutical researchers will find the "Second Edition" a helpful guide to understanding the genetic basis of human disease, with its new tools for detecting risk factors and discovering treatment strategies.

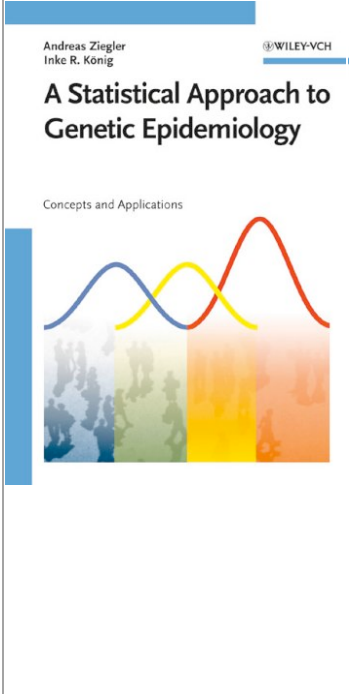
Andreas Ziegler and Inke R. König

A Statistical Approach to Genetic Epidemiology: Concepts and Applications

John Wiley and Sons Inc 31 Mar 2006

ISBN: 3527-31252-8

List price is \$115.00, but you can find it for as low as \$74.75 at <http://www.addall.com/>.

	<p><b>Table of Contents:</b></p> <ul style="list-style-type: none"><li>• <b>INTRODUCTORY GENETICS</b><ul style="list-style-type: none"><li>○ Molecular Genetics</li><li>○ Formal Genetics</li><li>○ Genetic Markers</li><li>○ Data Quality</li></ul></li><li>• <b>LINKAGE ANALYSIS</b><ul style="list-style-type: none"><li>○ Genetic Map Distances</li><li>○ Model-based Linkage Analysis</li><li>○ Model-free Linkage Analysis for Dichotomous Traits</li><li>○ Model-free Linkage Analysis for Quantitative Traits</li></ul></li><li>• <b>ASSOCIATION ANALYSIS</b><ul style="list-style-type: none"><li>○ Fundamental Concepts</li><li>○ Association Analysis in Unrelated Individuals</li><li>○ Association Analysis in Families</li><li>○ Haplotypes in Association Analyses</li></ul></li><li>• <b>Appendix: Algorithms Used in Linkage Analyses</b></li></ul>
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Covering the latest developments, this advanced textbook focuses on introducing the relevant statistical methods applied in this field. Written by the prize-winning scientist Andreas Ziegler, President of the German Region of the International Biometric Society, and Inke R. König, who contributes more than five years of teaching experience, this is ideal for epidemiologists, geneticists, statistics specialists, biomathematicians, graduate and undergraduate students.

After providing a concise introduction to genetic fundamentals, the authors explain both linkage analysis and association analysis in detail. This includes novel techniques such as haplotype tagging or linkage disequilibrium maps. The textbook features more than 100 problems and solutions.

**Evaluation:**

Exam	50%
Assignments	25%
Journal article presentation and participation	25%

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 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 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.

<b>Date</b>	<b>Topic</b>	<b>Required Readings and Homework</b>
11/01/10	Course overview, intro to genetic epidemiology and basic concepts in genetics	Ziegler chapter 1 (skip 1.3.2) Online genetic tutorial: Biological Basis of Heredity (topics 1, 2, 3, and 5)
11/03/10	Inheritance and the genetic component of diseases/traits	Ziegler chapter 2-2.2.2 Online genetic tutorial: Basic Principles of Genetics (topics 1 and 2) and Modern Theories of Evolution (topic 2) Haines chapter 3 pgs 91-92 and 100-110
11/05/10	Journal article discussion: Genetic epidemiology of a disease/trait (Ryan Joerres, Julia Thorsen, and Cassie Thiel)	Journal Discussion 1 reading on Learn@UW
11/08/10	Complex inheritance	Ziegler chapter 2.3 Online genetic tutorial: Basic Principles of Genetics (topic 3)
11/10/10	Study design, DNA collection and genotyping	Haines chapter 3 pgs 92-99 HW1 due
11/12/10	Journal article discussion: Complex inheritance (Justin Kohl, Kristin Litzelman, and Maria Nikodemova)	Journal Discussion 2 reading on Learn@UW
11/15/10	Linkage disequilibrium	Haines chapter 12 pgs 330-333 HW2 due
11/17/10 <b>HSLC 2121</b>	SNP selection and public databases <b>(HSLC Computer Lab, room 2121)</b>	HW3 due
11/19/10	Data collection, management and analysis	Ziegler chapter 4-4.3.1 HW4 due
11/22/10	Unrelated case-control association analysis	Lunetta 2008 HW5 due
11/24/10	Population stratification	Ziegler chapter 10.4-10.4.4 HW6 due
11/26/10	No class – Thanksgiving recess	
11/29/10	Journal article discussion: Case-control association analysis and population stratification (Brooke Schmeichel, Yalda Zare, and Suzanna Grooms)	Journal Discussion 3 reading on Learn@UW
12/01/10	Family-based association analysis	Haines chapter 12 pgs 340-344 HW7 due
12/03/10	Journal article discussion: Family-based association analysis (Navnit Sekhon, Anne Atkins, and Nicole Brusky)	Journal Discussion 4 reading on Learn@UW
12/06/10	Guest lecture by Kristin Meyers: Genome-wide association studies (GWAS)	Pearson and Manolio 2008 HW8 due
12/08/10	Special topics 1: Beyond GWAS	Ziegler chapter 12-12.2 (skip 12.2.1-12.2.2) Hardy and Singleton 2009 HW9 due
12/10/10	Journal article discussion: GWAS (Yashar Kenarangui, Andy Thurman, Quoc Tran)	Journal Discussion 5 reading on Learn@UW
12/13/10	Special topics 2: “Omics” and related fields	View 13 minute <a href="#">PBS NOVA video on Epigenomics</a> HW10 due
12/15/10	Special topics 3: Public health genomics	<b>Exam distributed</b>
12/17/10	No class – Finals week	
12/20/10	No class – Finals week	