BIOST 516/EPI 516/PHG 519:
Statistical Methods in Genetic Epidemiology
Autumn Quarter, 2010

Instructor:

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Office Hours: By Appointment

Time and Place:

Mondays and Wednesdays, Fishery Sciences 109, 1:30-2:50PM

Website:

http://courses.washington.edu/b516

Course Description:

This course focuses on the theory and application of statistical methodology used in genetic epidemiology. It includes discussions of linkage analysis and segregation analysis, as well as methods for genome-wide association studies. Examples are stressed with reference to assumptions and limitations.

Learning Objectives: By the end of this course, a student should be able to:

1. know the assumptions of the Hardy-Weinberg equilibrium model and how to test for violations of it
2. understand the theory and applications of both parametric and non-parameter linkage analysis
3. use family-based and case-control association testing methods
4. have an understanding of basic population structure theory and measures
5. estimate relationships with various statistical methods
6. appropriately apply statistical methodology to correct for cryptic population structure
7. understand the admixture mapping approach for identification of genetic variants
8. use both statistical and genetic software for the analysis of genetic data

Prerequisites: One year graduate sequence in biostatistics (e.g. BIOST 511-513, BIOST514-515 or BIOST 517-518) and a beginning course in genetic epidemiology (e.g. PHG 511). Otherwise, permission of instructor.

Grading: Participation in Class 10%
Homework 25%
Midterm 25%
Final Exam/Project 40%

Participation in class will be determined by lecture summaries and participation in class discussions and problem-solving exercises. Summaries will be given by a pre-selected student and are to be informal five-minute reviews of the previous lecture. Homework will be given approximately weekly.

Class Format: Most class presentations will use overhead slides or the chalkboard. Students will also work through problems as in-class exercises. Regular class attendance and participation is expected.

Textbook: There is no official textbook for this course. Course material will be a combination of lecture notes, journal articles, and handouts.

Students may find the following books helpful. These five books are on reserve in the Health Sciences Library for students' reference.

- Khoury M, Beaty TH, Cohen BH (1993) Fundamentals of genetic epidemiology. Oxford University Press.
- Ott J (1999) Analysis of Human Genetic Linkage. John Hopkins University Press
- Sham P (1998). Statistics in Human Genetics. Arnold.
- Vogel F, Motulsky AG (1997) Human Genetics: Problems and Approaches. Springer.
- Weir BS (1996). Genetic Data Analysis II. Sinauer.

Class Web Page: The class web page (http://courses.washington.edu/b516/) will serve as an archive of homework, handouts, lecture notes, and datasets. It will also be the place to find announcements concerning course logistics. Students should check the web page regularly for information.

Software   There is no official software for this course. Software packages for the analysis of genetic data will be introduced.

Acknowledgment: Some course material was developed by Dr. Stephanie Monks and Dr. Katie Kerr, both of whom previously taught this course.

Course Topics

	Introduction to genetic models Hardy-Weinberg equilibrium: assumptions and testing
	Parametric linkage analysis: 2-point and multi-point linkage analysis, LOD scores Non-parametric linkage analysis
	Linkage disequilibrium: pairwise measures Haplotype-phase inference with pedigrees and population data
	Allele/genotype/haplotype frequency estimation Family-based association: transmission/disequilibrium test (TDT) and related approaches
	Case-control association: Pearson's classical test, Fisher's Exact Test, Armitage Trend Test Odds ratios: estimates, confidence intervals, interpretation
	Pedigrees and relationships: gene identity by descent, 9 condensed identity states, kinship coefficients
	Estimating relatedness: Hidden Markov methods, EM algorithm, empirical kinship Implementation of methods in software
	Population structure: theory, Wright's F statistics Association methods for cryptic structure: Genomic Control, STRUCTURE, EIGENSTRAT
	Admixture mapping