University of Pittsburgh
School of Public Health
Department of Human Genetics

HuGen 2080
Statistical Genetics

Monday 1:00 - 2:25 PM
Wednesday 1:00 - 2:25 PM
312 Crabtree – Human Genetics Conference Room
Public Health Building
3 Credit Hours
Spring 2024

Faculty

Daniel E. Weeks, Ph.D.
3119 Public Health
412-624-5388
weeks@pitt.edu
Office Hours available upon request

John Shaffer, Ph.D.
3120 Public Health
412-624-3018
john.r.shaffer@pitt.edu
Office hours available upon request

Faculty Availability

We are available to meet with you upon request - please feel free to set up an appointment.

We welcome your questions at any time. For questions about the course content, we prefer that you submit your questions via the Canvas Discussion Board, so that other students, who may have similar questions, may also benefit from the discussion.

While the Discussion Board is preferred, e-mail is also an excellent way to reach us. However, since we get so many e-mails, please use an informative subject line, starting with "HuGen 2080:". And if we don't respond to your e-mail in a timely manner, please feel free to send a reminder e-mail.

Course Description

AN ADVANCED COURSE WHICH DISCUSSES THE PRINCIPLES AND PRACTICE OF STATISTICAL GENETICS IN THE AREA OF GENETIC EPIDEMIOLOGY OF HUMAN DISEASES AND TRAITS. THE COURSE WILL COVER STATISTICAL MODELING AND METHODOLOGY IN FAMILIAL AGGREGATION, LINKAGE ANALYSIS AND ASSOCIATION ANALYSIS; THE COURSE INCLUDES HANDS-ON EXPERIENCE WITH CURRENT COMPUTER PROGRAMS USED IN THESE RESEARCH AREAS.

The objective of this class is to introduce students to advanced topics in genetic epidemiology, specifically related to human diseases and traits, with an emphasis on statistics and the mathematics behind the statistics. As such, the course requires familiarity with basic probability theory and statistical principles, as well as population genetics. After finishing this course, the student should understand the assumptions, strengths, and weaknesses of the various statistical

tests, as well as be well prepared to undertake a statistical genetics analysis, including study design, phenotype definition and modeling, estimation of heritability, linkage analysis, and association analysis.

Learning Objectives
Upon completion of this course the student will be able to:

- Explain the assumptions, strengths, and weaknesses of the various statistical tests used in genetic epidemiology.
- Devise testable hypotheses in human genetics and identify appropriate study designs to test these hypotheses.
- Describe preferred methodological alternatives to commonly used statistical methods when assumptions are not met.
- Apply the statistical models presented in analyzing and interpreting real data sets.
- Apply genetic analysis programs and interpret the results.
- Read and evaluate current literature in statistical genetics.

Course Prerequisites
HUGEN 2022 · Human Population Genetics
BIOST 2041 · Introduction to Statistical Methods 1

or approval of the instructor

Required Textbooks
Andreas Ziegler, Inke R. König (2010) A Statistical Approach to Genetic Epidemiology: Concepts and Applications, Second Edition
Full text available online: https://ebookcentral.proquest.com/lib/pitt-ebooks/detail.action?docID=708055

E-learning platform:
https://application.wiley-vch.de/books/geneticepidemiology/IMS_LO/onCampusBook/65270/index.html

Supplemental Readings

Henry Stewart Talks: https://info.hsls.pitt.edu/updatereport/?p=4167

There are multiple methods for locating the Henry Stewart Talks:

1. All talks are catalogued in PITT*Cat*; search for **Henry Stewart Talks** under "Title Begins with" for an alphabetical list or to search by individual title.
2. Click on the "Videos" tab on the MolBio home page.
3. Visit Henry Stewart Talks: Online Seminars by Leading World Experts.

Thomas, Duncan C. Statistical Methods in Genetic Epidemiology. Oxford University Press, 2004.
Web access:
https://pitt.primo.exlibrisgroup.com/permalink/01PITT_INST/e8h8hp/alma9998566428306236

Laird NM, Lange C (2011) The Fundamentals of Modern Statistical Genetics. New York, Springer Science.
DOI: 10.1007/978-1-4419-7338-2
Web access:
https://pitt.primo.exlibrisgroup.com/permalink/01PITT_INST/e8h8hp/alma9998511583406236
https://link.springer.com/book/10.1007%2F978-1-4419-7338-2

Zheng G, Yang Y, Zhu X, Elston RC. Analysis of Genetic Association Studies. 1. Aufl. Netherlands: Springer US; 2012. DOI: https://doi.org/10.1007/978-1-4614-2245-7
Web access:
https://pitt.primo.exlibrisgroup.com/permalink/01PITT_INST/i25aoe/cdi_openaire_primary_doi_10a71f547c7a072bba1b6d526eef4d83

Statistical Human Genetics
Methods and Protocols
Editor: Robert C. Elston
New York: Humana Press; Springer, 2017.
Web access:
https://pitt.primo.exlibrisgroup.com/permalink/01PITT_INST/i25aoe/cdi_springer_books_10_1007_978_1_4939_7274_6
https://link.springer.com/book/10.1007/978-1-4939-7274-6

Handbook on Analyzing Human Genetic Data
Computational Approaches and Software
2010
Web access:
https://pitt.primo.exlibrisgroup.com/permalink/01PITT_INST/i25aoe/cdi_springer_books_10_1007_978_3_540_69264_5
https://link.springer.com/book/10.1007%2F978-3-540-69264-5

Current Protocols in Human Genetics. New York, John Wiley
DOI: 10.1002/0471142905
Web access:
https://pitt.primo.exlibrisgroup.com/permalink/01PITT_INST/1sjtb5p/alma9998843113206236
http://onlinelibrary.wiley.com/book/10.1002/0471142905
Genetic Mapping Section:
https://currentprotocols.onlinelibrary.wiley.com/doi/toc/10.1002/(ISSN)1934-8258.GeneticMapping

Stram, Daniel O (2014) Design, analysis, and interpretation of genome-wide association scans
Web access:
https://pitt.primo.exlibrisgroup.com/permalink/01PITT_INST/e8h8hp/alma9998552695806236
https://link.springer.com/book/10.1007%2F978-1-4614-9443-0

Electronic Supplementary Material:
http://www.springer.com/cda/content/document/cda_downloaddocument/Electronic+Supplementary+Material%2C+Ch.2-8.zip?SGWID=0-0-45-1430364-p176269527

Canvas and GitHub Classroom Instruction
This course will extensively use the University's Canvas site (canvas.pitt.edu). To login, you must have a Pitt account. Your login ID is the same as your login ID for your Pitt account and your password is the same as for your Pitt account. This will be augmented with GitHub Classroom.

We strongly recommend that you set up your notifications in Canvas so that any announcements will be sent to your preferred e-mail address.

Each lecture will be accompanied by supporting material and further reading, all of which will be made available around the time of the lecture. It is the student's responsibility to check for, and read, this material.

Discussion topics related to the course may also be posted on Canvas, and, for the purpose of determining a student's grade, participation in these discussions will be considered when evaluating the student's active participation in our course.

The instructors will use the Canvas site and GitHub Classroom as the primary means of communicating with the students, who are expected to check these sites on a regular basis throughout the semester.

Accessibility
Ensuring an accessible and pleasant experience to all users, regardless of disability, is a key focus of Canvas. The Canvas LMS platform was built using the most modern HTML and CSS technologies, and is committed to W3C's Web Accessibility Initiative and Section 508 guidelines. Specific details regarding individual feature compliance are documented and updated regularly.

GitHub Classroom's compliance with §508 guidelines can be found at government.github.com/accessibility/.

Health and Safety
It is important that you abide by Pitt's Health Rules. These rules have been developed to protect the health and safety of all of us. If you do not comply, you will be asked to leave class. It is your responsibility have the required face covering when entering a university building or classroom if Pitt's rules require it.

If you are required to isolate or quarantine, become sick, or are unable to come to class, contact us as soon as possible to discuss arrangements. Do not come to class if you are sick, may be sick, or should isolate/quarantine.

Class Expectations/ Behavior and Ground Rules
Attendance and active participation are expected. If you need to 'attend' by Zoom due to illness or another issue, please obtain permission from your instructors to do so in advance.

Please be on time and silence your cell phone. While laptops may be used to complete computer exercises or to take notes, please do not use them during class time for non-class purposes. It is

expected that you will have read all the assigned readings prior to class. To facilitate our use of the readings, please bring an interesting discussion question from the readings to class with you. If you will miss a class, please let us know in advance.

Statement on Classroom Recording
To ensure the free and open discussion of ideas, students may not record classroom lectures, discussion and/or activities without the advance written permission of the instructor, and any such recording properly approved in advance can be used solely for the student's own private use.

Grading Scale

Grades scored between	will equal
97% and 100%	A+
94% and less than 97%	A
90% and less than 94%	A-
87% and less than 90%	B+
84% and less than 87%	B
80% and less than 84%	B-
77% and less than 80%	C+
74% and less than 77%	C
70% and less than 74%	C-
67% and less than 70%	D+
64% and less than 67%	D
60% and less than 64%	D-
0% and less than 60%	F

Student Performance Evaluation (Assessments and Weights)
Evaluation will be based on the following components:

Attendance and Participation
Attendance and active participation are expected. If you need to 'attend' by Zoom due to illness or another issue, please obtain permission from your instructors to do so in advance.

Homework (50% of final grade)
The homework assignments will comprise problems that extend the in-class activities and complement the lectures.

Students will read the weekly assigned scientific paper and summarize their understanding of the main points of the assigned paper.

Paper Presentation (10% of final grade)
All students will give a 30 minute presentation on an assigned paper in statistical genetics.

Mid-term exam (20% of final grade)
A written in-class mid-term exam will be given.

Final exam (20% of final grade)
A written in-class final exam will be given.

Schedule of Sessions and Assignments
The detailed schedule is provided at the end of this document.

Email communication
Each student is issued a University e-mail address (username@pitt.edu) upon admittance. This e-mail address may be used by the University for official communication with students. Students are expected to read e-mail sent to this account on a regular basis. Failure to read and react to University communications in a timely manner does not absolve the student from knowing and complying with the content of the communications. The University provides an e-mail forwarding service that allows students to read their e-mail via other service providers (e.g., Hotmail, AOL, Yahoo). Students that choose to forward their e-mail from their pitt.edu address to another address do so at their own risk. If e-mail is lost as a result of forwarding, it does not absolve the student from responding to official communications sent to their University e-mail address.

Accommodation for Students with Disabilities
If you have a disability for which you are or may be requesting an accommodation, you are encouraged to contact both your instructor and Disability Resources and Services (DRS), 140 William Pitt Union, (412) 648-7890, drsrecep@pitt.edu, (412) 228-5347 for P3 ASL users, as early as possible in the term. DRS will verify your disability and determine reasonable accommodations for this course.

Academic Integrity Statement
Students in this course will be expected to comply with the University of Pittsburgh's Policy on Academic Integrity. Any student suspected of violating this obligation for any reason during the semester will be required to participate in the procedural process, initiated at the instructor level, as outlined in the University Guidelines on Academic Integrity. This may include, but is not limited to, the confiscation of the examination of any individual suspected of violating University Policy. Furthermore, no student may bring any unauthorized materials to an exam, including dictionaries and programmable calculators.

To learn more about Academic Integrity, visit the Academic Integrity Guide for an overview of the topic. For hands-on practice, complete the Understanding and Avoiding Plagiarism tutorial.

Plagiarism
Integrity of the academic process requires that credit be given where credit is due. Accordingly, it is unethical to present as one's own work the ideas, representations, words of another, or to permit another to present one's own work without customary and proper acknowledgement of sources.

A student has an obligation to exhibit honesty and to respect the ethical standards of the profession in carrying out his or her academic assignments. Without limiting the application of this principle, a student may be found to have violated this obligation if he or she:

1. Presents as one's own, for academic evaluation, the ideas, representations, or words of another person or persons without customary and proper acknowledgment of sources.

2. Submits the work of another person in a manner which represents the work to be one's own.

See: http://www.bc.pitt.edu/policies/policy/02/02-03-02.html

To avoid plagiarism, you must give "customary and proper acknowledgment of sources" by appropriately and clearly identifying which thoughts are yours and which are others, and appropriately citing your sources.

Sophisticated plagiarism detection software will be used in this course. If plagiarism is detected, you will automatically receive a grade of zero for that assignment and the incident will be reported, as required, to your Dean.

Use of Artificial Intelligence Tools
Large language models (LLMs) like ChatGPT can help answer questions and solve problems, but they are not a substitute for learning the concepts and solving the problems yourself, especially since LLMs can and do easily generate convincing incorrect or overly complicated answers with fabricated references. That said, you are permitted to use LLMs in your work (*with citation*), but you are of course responsible for any and all of their errors. Note that you must acknowledge/cite usage of these tools when used.

The use of such tools is not permitted during in-class exams.

Sexual Misconduct, Required Reporting and Title IX Statement
If you are experiencing sexual assault, sexual harassment, domestic violence, and stalking, please report it to me and I will connect you to University resources to support you.

University faculty and staff members are required to report all instances of sexual misconduct, including harassment and sexual violence to the Office of Civil Rights and Title IX. When a report is made, individuals can expect to be contacted by the Title IX Office with information about support resources and options related to safety, accommodations, process, and policy. I encourage you to use the services and resources that may be most helpful to you.

As your professor, I am required to report any incidents of sexual misconduct that are directly reported to me. You can also report directly to Office of Civil Rights and Title IX: 412-648-7860 (M-F; 8:30am-5:00pm) or via the Pitt Concern Connection at: Make A Report

An important exception to the reporting requirement exists for academic work. Disclosures about sexual misconduct that are shared as a relevant part of an academic project, classroom discussion, or course assignment, are not required to be disclosed to the University's Title IX office.

If you wish to make a confidential report, Pitt encourages you to reach out to these resources:

- The University Counseling Center: 412-648-7930 (8:30 A.M. TO 5 P.M. M-F) and 412-648-7856 (AFTER BUSINESS HOURS)
- Pittsburgh Action Against Rape (community resource): 1-866-363-7273 (24/7)

If you have an immediate safety concern, please contact the University of Pittsburgh Police, 412-624-2121

Any form of sexual harassment or violence will not be excused or tolerated at the University of Pittsburgh.

Diversity Statement
The University of Pittsburgh does not tolerate any form of discrimination, harassment, or retaliation based on disability, race, color, religion, national origin, ancestry, genetic information, marital status, familial status, sex, age, sexual orientation, veteran status or gender identity or other factors as stated in the University's Title IX policy. The University is committed to taking prompt action to end a hostile environment that interferes with the University's mission. For more information about policies, procedures, and practices, visit the Civil Rights & Title IX Compliance web page.

I ask that everyone in the class strive to help ensure that other members of this class can learn in a supportive and respectful environment. If there are instances of the aforementioned issues, please contact the Title IX Coordinator, by calling 412-648-7860, or e-mailing titleixcoordinator@pitt.edu. Reports can also be filed online. You may also choose to report this to a faculty/staff member; they are required to communicate this to the University's Office of Diversity and Inclusion. If you wish to maintain complete confidentiality, you may also contact the University Counseling Center (412-648-7930).

Copyright Notice
These materials may be protected by copyright. United States copyright law, 17 USC section 101, et seq., in addition to University policy and procedures, prohibit unauthorized duplication or retransmission of course materials.

See Library of Congress Copyright Office and the University Copyright Policy.

Religious Observances
The observance of religious holidays (activities observed by a religious group of which a student is a member) and cultural practices are an important reflection of diversity. As your instructor, I am committed to providing equivalent educational opportunities to students of all belief systems. At the beginning of the semester, you should review the course requirements to identify foreseeable conflicts with assignments, exams, or other required attendance. If at all possible, please contact me (your course coordinator/s) within the first two weeks of the first class meeting to allow time for us to discuss and make fair and reasonable adjustments to the schedule and/or tasks.

Your Well-being Matters
College/Graduate school can be an exciting and challenging time for students. Taking time to maintain your well-being and seek appropriate support can help you achieve your goals and lead a fulfilling life. It can be helpful to remember that we all benefit from assistance and guidance at times, and there are many resources available to support your well-being while you are at Pitt. You are encouraged to visit Thrive@Pitt to learn more about well-being and the many campus resources available to help you thrive.

If you or anyone you know experiences overwhelming academic stress, persistent difficult feelings and/or challenging life events, you are strongly encouraged to seek support. In addition to reaching out to friends and loved ones, consider connecting with a faculty member you trust for assistance connecting to helpful resources.

The University Counseling Center is also here for you. You can call 412-648-7930 at any time to connect with a clinician. If you or someone you know is feeling suicidal, please call the University Counseling Center at any time at 412-648-7930. You can also contact Resolve Crisis Network at 888-796-8226. If the situation is life threatening, call Pitt Police at 412-624-2121 or dial 911.

Tentative Schedule of Sessions and Assignments
Note: This schedule is subject to change and will be updated as we proceed through the course.

Required Reading:
Background reading:
Ziegler and König - Chapter 1: Molecular Genetics
Ziegler and König - Chapter 2: Formal Genetics

Henry Stewart Talk:
Genotyping algorithms for genome wide association studies/ Dr. Vincent Plagnol

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1/8/2024 - Lecture 01: **Models, Maps, and Markers**
Lecturer: Dan Weeks

Required Reading:
Ziegler and König - Chapter 3: Genetic Markers
Ziegler and König - Chapter 5: Genetic Map Distances

Henry Stewart Talk:
Introductory genetics for statisticians/ Robert C. Elston.

Supplementary reading:
Elston RC (2000) Introduction and overview. Statistical methods in genetic epidemiology. Stat Methods Med Res 9:527-541

Chapters 1, 2, and 3: Laird NM, Lange C (2011) The Fundamentals of Modern Statistical Genetics. Springer.

Learning objectives:
To review basic genetic models
To learn about genetic markers

1/10/2024 - Lecture 02: **Study Design Overview**
Lecturer: Dan Weeks
Active Learning: Intro to Unix & PLINK

Henry Stewart Talk:
Designing a genome-wide association study/ Dr. Chris Spencer

Learning objectives:

To learn the basic principles of study design for genetic studies
To understand the vital importance of phenotype definition
To understand the best sample selection strategies

1/15/2024: **No class - Martin Luther King Day**

1/17/2024 - Lecture 03: **Familial Aggregation: Recurrence Risk Ratios, Heritability**
Lecturer: Dan Weeks
Active Learning: Student Presentation

Required Reading:
Ziegler and König - Chapter 6: Familiality, Heritability, and Segregation Analysis

Henry Stewart Talk:
Heritability and its uses/ Doug Speed.

Inferring relatedness/ Prof. Emmanuelle Génin

Supplementary reading:
Chapter 4: Laird NM, Lange C (2011) The Fundamentals of Modern Statistical Genetics. Springer.

Learning objectives:

To learn aggregation analysis
To learn how to estimate recurrence risk ratios
To review the concept of heritability

1/22/2024 - Lecture 04: **Familial Aggregation: Segregation Analysis, Ascertainment**
Lecturer: Dan Weeks

Active Learning: SOLAR heritability computer lab

Required Reading:
Ziegler and König - Chapter 6: Familiality, Heritability, and Segregation Analysis

Learning objectives:

To learn about segregation analysis
To understand how to take ascertainment into account in the segregation models
To formulate testable hypotheses about genetic models

1/24/2024 - Lecture 05: **LOD scores: Model-based Linkage Analysis**
Lecturer: Dan Weeks
Active Learning: Student Presentation

Required Reading:
Ziegler and König - Chapter 7: Model-based Linkage Analysis

Henry Stewart Talk:
Linkage and sequence analysis in families/ Christopher Amos.

Supplementary reading:
Chapters 5 and 6: Laird NM, Lange C (2011) The Fundamentals of Modern Statistical Genetics. Springer.

Learning objectives:
To learn how to compute LOD scores
To learn about different map functions, and the distinction between genetic and physical maps
To formulate testable hypotheses about linkage

1/29/2024 - Lecture 06: **Non-parametric methods**
Lecturer: Dan Weeks
Active Learning: Merlin computer lab

Required Reading:
Ziegler and König - Chapter 8: Model-free Linkage Analysis for Dichotomous Traits

Supplementary reading:
Shih MC, Whittemore AS (2001) Allele-sharing among affected relatives: non-parametric methods for identifying genes. Stat Methods Med Res 10:27-55

Learning objectives:
To learn how to carry out non-parametric linkage analyses
To understand the motivation behind non-parametric linkage analysis approaches

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1/31/2024 - Lecture 07: **Association: Case/Control & Quantitative Traits**
Lecturer: Dan Weeks
Active Learning: Student Presentation

Required Reading:
Ziegler and König - Chapter 10: Fundamental Concepts of Association Analysis
Ziegler and König - Chapter 11: Association Analysis with Unrelated Individuals

Henry Stewart Talk:
Introduction to genetic association analysis/ Jenny Barrett.

Statistical tests for association/ Dr. Andrew Morris

Supplementary reading:
Chapter 7: Laird NM, Lange C (2011) The Fundamentals of Modern Statistical Genetics. Springer.

Cardon LR, Bell JI (2001) Association study designs for complex diseases. Nat Rev Genet 2:91-99.

Balding DJ (2006) A tutorial on statistical methods for population association studies. Nat Rev Genet 7:781-791

Learning objectives:

To formulate testable hypotheses about association
To understand and apply various case/control association tests
To understand allele-based and genotype-based association tests, and trend tests.

2/5/2024 - Lecture 08: **Association: Family-based and Haplotype-based**
Lecturer: Dan Weeks
Active Learning: PLINK computer lab

Required Reading:
Ziegler and König - Chapter 12: Association Analysis in Families

Supplementary reading:
Chapter 9 & Chapter 10, Section 2: Laird NM, Lange C (2011) The Fundamentals of Modern Statistical Genetics. Springer.

Ott J, Kamatani Y, Lathrop M (2011) Family-based designs for genome-wide association studies. Nat Rev Genet 12:465-474

Learning objectives:

To learn how to analyze family data for association
To learn how to test haplotypes for association
To understand sparsity issues involved in haplotyped-based tests

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2/7/2024 - Lecture 09: **Multiple testing**
Lecturer: Dan Weeks
Active Learning: Student Presentation

Required Reading:
Ziegler and König - Chapter 14, Section 14.4: Multiple Testing

Henry Stewart Talk:
Assessing significance in genome-wide studies/ Dr. David Evans

Supplementary reading:
Chapter 10, Section 1: Laird NM, Lange C (2011) The Fundamentals of Modern Statistical Genetics. Springer.

Learning objectives:
To understand how to adjust for multiple testing

2/12/2024 - Lecture 10: **Power to detect Association: Linkage vs. Association**
Lecturer: Dan Weeks
Active Learning: Student Presentation

Supplementary reading:
Clerget-Darpoux F, Elston RC (2007) Are linkage analysis and the collection of family data dead? Prospects for family studies in the age of genome-wide association. Hum Hered 64:91-96

Learning objectives:
To learn how to compute power for detecting association
To compare and contrast linkage and association
To understand the relative strengths and weaknesses of linkage and association tests

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2/14/2024 - Lecture 11: **Rare variants**
Lecturer: Dan Weeks
Active Learning: Student Presentation

Supplementary reading:
Asimit J, Zeggini E (2010) Rare variant association analysis methods for complex traits. Annu Rev Genet 44:293-308

Bansal V, Libiger O, Torkamani A, Schork NJ (2010) Statistical analysis strategies for association studies involving rare variants. Nat Rev Genet 11:773-785

Learning objectives:
To learn how to test rare variants for association
To learn about burden tests, collapsing or grouping tests, weighted sum tests, and variable threshold tests.

2/19/2024 - Lecture 12: **Methods for correlated data: LME, GEE, Score**
Lecturer: Dan Weeks
Active Learning: Student Presentation

Required Reading:
Sul JH, Martin LS, Eskin E. Population structure in genetic studies: Confounding factors and mixed models. PLoS Genet. 2018; 14(12):e1007309. doi:10.1371/journal.pgen.1007309

Learning objectives:

To learn about linear mixed effects models, generalized estimating equations, and score tests

To learn how to properly model relatedness while testing genetic hypotheses

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2/21/2024 - Lecture 13: **Bayesian Methods in Human Genetics**

Lecturer: Dan Weeks

Active Learning: Student Presentation

Required Reading:

Stephens M, Balding DJ. Bayesian statistical methods for genetic association studies. Nat Rev Genet. 2009 Oct;10(10):681-90. doi: 10.1038/nrg2615. Review. PubMed PMID: 19763151.

Supplementary reading:

Wakefield J. Bayes factors for Genome-wide association studies: Comparison with P-values. Genetic Epidemiology. 2009;33(1):79–86. DOI: https://doi.org/10.1002/gepi.20359

Learning objectives:

To learn about Bayesian methods in human genetics

To understand Bayesian principles

2/26/2024 - Lecture 14: **Review for Mid-term exam**

2/28/2024 - Lecture 15: **Mid-term exam**

3/4/2024 - Lecture 16: **Gene x Gene interaction, vQTLs**

Lecturer: John Shaffer

Required Reading:

Cordell HJ (2009) Detecting gene-gene interactions that underlie human diseases. Nat Rev Genet 10:392-404

Supplementary reading:

Gilbert-Diamond D, Moore JH (2011) Analysis of gene-gene interactions. Curr Protoc Hum Genet Chapter 1:Unit1 14

Learning objectives:

To learn how to test for gene x gene interaction

To formulate testable hypotheses about gene x gene interaction

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3/6/2024 - Lecture 17: **Gene x Environment interaction**

Lecturer: John Shaffer

Active Learning: Student Presentation

Required Reading:
Thomas D (2010) Gene--environment-wide association studies: emerging approaches. Nat Rev Genet 11:259-272

Henry Stewart Talk:
Statistical issues in epidemiologic studies of gene-environment interaction/ Peter Kraft, Donna Spiegelman.

GxE interactions in genome-wide association studies/ David V. Conti.

Supplementary reading:
Chapter 10, Section 3: Laird NM, Lange C (2011) The Fundamentals of Modern Statistical Genetics. Springer.

Ottman R (1990) An epidemiologic approach to gene-environment interaction. Genet Epidemiol 7:177-185

Learning objectives:
To learn how to test for gene x environment interaction
To formulate testable hypotheses about gene x environment interaction

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3/11/2024: **Spring Recess**

3/13/2024: **Spring Recess**

3/18/2024 - Lecture 18: **Special Topic Lecture by Chris McKennan**
Lecturer: Chris McKennan

3/20/2024 - Lecture 19: **Fine mapping**
Lecturer: Dan Weeks
Active Learning: Student Presentation

Required Reading:
Schaid DJ, Chen W, Larson NB. From genome-wide associations to candidate causal variants by statistical fine-mapping. Nature Reviews Genetics. Nature Publishing Group; 2018 Aug 29;19(8):491–504. DOI: https://doi.org/10.1038/s41576-018-0016-z

Supplementary reading:
Cano-Gamez E, Trynka G. From GWAS to Function: Using Functional Genomics to Identify the Mechanisms Underlying Complex Diseases. Front Genet. 2020;11:424. PMID: 32477401 PMCID: PMC7237642 DOI: https://doi.org/10.3389/fgene.2020.00424

Learning objectives:
To learn how to carry out fine mapping
To understand and apply conditional tests of association

3/25/2024 - Lecture 20: **Meta analysis**
Lecturer: John Shaffer

Required Reading:
Ziegler and König - Chapter 14, Section 14.5: Accumulating Data from Genome-wide Association Studies

Henry Stewart Talk:
Winner's curse, replication and meta-analysis/ Frank Dudbridge.

Meta-analysis in genome-wide association studies: application to type 2 diabetes/ Dr. Eleftheria Zeggini

Learning objectives:
To learn about the different types of meta analysis.
To understand the assumptions made by meta analysis.

3/27/2024 - Lecture 21: **Methods for multivariate phenotypes**
Lecturer: John Shaffer
Active Learning: Student Presentation

Learning objectives:
To learn about methods for analyzing multivariate phenotypes
To learn how to properly account for correlation among phenotypes

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4/1/2024 - Lecture 22: **Heritability from GWAS**
Lecturer: John Shaffer
Active Learning: Student Presentation
Henry Stewart Talk:
Heritability and its uses/ Doug Speed.
Learning objectives:
To learn how to estimate heritability using unrelated samples.
To understand polygenicity.

4/3/2024 - Lecture 23: **LDscore regression**
Lecturer: John Shaffer
Active Learning: Student Presentation

Learning objectives:
To understand the principles of LDscore regression
To understand polygenicity.

4/8/2024 - Lecture 24: **Mendelian Randomization**
Lecturer: John Shaffer
Active Learning: Student Presentation
Henry Stewart Talk:

Causal inference in genetic epidemiology: Mendelian randomization and beyond / Krista Fischer.

Learning objectives:

To understand the basic principles of Mendelian Randomization.

To formulate testable hypotheses about causation using Mendelian Randomization approaches.

4/10/2024 - Lecture 25: **Genetic Risk Scores & Polygenic Risk Scores & Genomic Prediction**

Lecturer: John Shaffer

Active Learning: Student Presentation

Learning objectives:

To understand how to construct and use genetic risk scores.

To understand the limits of genomic predication.

4/15/2024 - Lecture 26: **Special Topic Lecture by Lacey Heinsberg**

Lecturer: Lacey Heinsberg

Required Reading:

Heinze G, Wallisch C, Dunkler D. Variable selection – A review and recommendations for the practicing statistician. Biometrical Journal. 2018;60(3):431–449. DOI: https://doi.org/10.1002/bimj.201700067

4/17/2024 - Lecture 27: **Special Topic Lecture by Jenna Carlson**

Lecturer: Jenna Carlson

4/22/2024 - Lecture 28: **Review for final exam**

4/24/2024 - Lecture 29: **Final exam**

4/27/2024: **Spring Term ends.**

5/1/2024: **Grades due by 11:59 PM**
