EPI 507: Principles of Genetic Epidemiology

Fall 2 2025

Meeting Time: Monday/Wednesday 09:45 - 11:15 AM
Location: FXB G12 (HSPH)
Credits: 2.5 credits
Website: https://canvas.harvard.edu/courses/159480

Instructor Information

Faculty

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Teaching Fellows

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Course Description

Genetic epidemiology is the study of genetic influences on human traits and disease in populations with direct clinical and public health applications. Genetic epidemiology also contributes to a deeper understanding of disease mechanisms, such as disease biology, etiology, and pathophysiology, all potentially informing development of new therapeutics. This course introduces the goals and methods of genetic epidemiology. After a review of the history of genetic epidemiology and basic molecular genetics, the course will cover study designs, data resources, and analytic approaches for related but distinct goals, including: genome-wide association studies (GWAS) and gene discovery; clinical and public health applications of genetics; and understanding the joint contributions of inherited genetics, social factors, and environmental exposures to disease etiology and the distribution of disease in populations. The course will also review empirical findings on the contribution of genetics to the understanding of human traits diseases with some applications in healthcare.

The target audience includes doctoral and masters' students looking for a non-specialist introduction to genetic epidemiology. This course is required for epidemiology Ph.D. students and fulfills a core requirement for

Computational Biology and Quantitative Genomics M.Sc. students. Pre-Requisites: [EPI 201 and (EPI 202 or BST 210)] or PHS 2000A or BST 213.

Learning Objectives

Upon successful completion of this course, students will be able to:

- Describe how molecular, Mendelian, and population genetics relate to epidemiology
- Use publicly available resources describing genetic variation in human populations and its association with diseases and traits
- Relate concepts from genetic epidemiology to general epidemiologic concepts (e.g. population stratification bias is an example of confounding)
- Evaluate and develop appropriate and well-powered study designs and analytic approaches for understanding the relationship between genetic variation and variation in human traits
- Critically evaluate genetic association studies as well as claims regarding the importance of genetic variation in different contexts (basic research, clinical epidemiology, public health)
- Distinguish concepts of race/ethnicity from genetic ancestry and understand how to appropriately incorporate race/ethnicity/ancestry in genetic studies

Competencies

This course covers the following Program/Field of Study Competencies:

SM 80 CBQG

1. Examine the basics of techniques modern population genetics such as genome wide association study methodology

Course Structure

This course will consist of lectures, in-class interactive exercises and discussions (including small group activities), individual homeworks, asynchronous recorded vignettes, online exercises (Canvas quizzes), and a final group project (see below). The lectures will not be offered via Zoom. Lectures will be recorded but made available only for exceptional circumstances.

The Canvas site is an important learning tool for this course where students will access required articles and recordings, submit course assignments, and share other resources with the class. Students will be expected to check the Canvas site on a weekly basis for course announcements.

During the first two weeks (until the drop date), students will assemble into small groups, targeting 4 students per group, for the final project and interactive activities throughout the course. Students are expected to participate in discussions and exercises in class and are encouraged, but not required, to do so within their group.

Course Readings and Pre-recorded Vignettes

There is no required textbook for this class. Readings will consist of book chapters, journal articles, recorded didactic video vignettes available through PDFs and URL links supplied via the Canvas site. Required readings for each week are listed on the Canvas site. The vignettes were prepared during the COVID-19 pandemic to convey the foundational concepts of genetic epidemiology and complement the readings. Lecture material, readings, and the vignettes form the basis of quizzes, homeworks, and in-class discussions.

Grading, Progress, and Assessment

The final grade for this course will be based on:

- Canvas Quizzes (10%)
- Team-learning exercises (15%)
- Homework (40%)

- Final project (35%)

Canvas Quizzes (10%)

The canvas quizzes will be graded on a participation basis**.** That is, full credit for timely completion, regardless of whether answers are correct. Note that the quiz questions are designed to be helpful for checking understanding of the course material and for completing homework.

Team-learning exercises (15%)

In-class exercises will be graded on a participation basis and completed, preferably and most efficiently within groups, although working within groups is not required**.** These exercises will cover hands-on skills in genetic data resources and analytic approaches relevant to the 1) UCSC Genome Browser, 2) LD link, 3) GWAS Catalog, and 4) gnomAD. The materials for in-class exercises will be available on the Canvas site. There will be 4 in-class exercises throughout the semester on the following dates.

Exercises #1: Wednesday, November 5th (UCSC browser)
Exercises #2: Monday, November 10th (LD link)
Exercises #3: Monday, November 17th (GWAS catalog)
Exercises #4: Monday, December 8th (gnomAD)

Homework (40%)

There will be a total of six graded homeworks throughout the course**.** The homeworks will elaborate on concepts presented in lectures, vignettes, and in-class discussions and provide opportunities to learn and use some of the online resources and software tools introduced in lectures and exercises. It is allowed to discuss the homework assignments with other students, but students must submit their own answers. See also guidance about academic integrity below.

Homeworks will be assigned on Wednesdays and due the following **Wednesday before class (before 9:45 AM Boston time**) except for homework #4 that is given an extra week and due after the Thanksgiving break. Note, the project draft is due on the Monday before Thanksgiving (next section). Homeworks should be uploaded to Canvas. The schedule below summarizes the exact due dates for the homeworks.

#	Topic	Assign	Due
1	DNA Sequence, Genetic Variation	W. Oct. 29th	W. Nov 5th
2	Population Genetics, Genotype/Allele Frequencies and Hardy-Weinberg Equilibrium, UCSC Genome Browser	W. Nov 5th	W. Nov 12th
3	Linkage disequilibrium	W. Nov 12th	W. Nov 19th
4	GWAS basics, GWAS Catalog, Association analysis	W. Nov 19th	W. Dec 3rd
5	Polygenic Risk Scores, Mendelian Randomization, Gene-environment interaction effects	W. Dec 3rd	W. Dec 10th
6	Sequencing, Rare variation, and gnomAD,	W. Dec 10th	W. Dec 17th

Final project (35%: 5% for draft version, 30% for final version)

Each group will submit a final project. The final project will consist of a short (up to four pages) **proposal** for analysis using available (i.e. public or by application) data sources (e.g. the UK Biobank, TOPMed, dbGaP, All of Us, publicly available GWAS summary statistics, etc.) and a short (<5 mins) “elevator pitch” (in PowerPoint or PDF) presentation describing the proposal. This project will allow students to identify specific hypotheses that they can investigate using genetic epidemiology and choose designs and analyses appropriate for those hypotheses. The project is restricted to publicly available data sets to conform to real-world limitations on technology and budgets and to give students familiarity with available resources. The proposal will consist of the following four sections:

1. Background & Significance
2. Design
3. Analytic Approach

4. Strengths and Limitations

The final project is a group project; most groups will have four (4) members. It is intended that each group member will be primarily responsible for drafting one of the four sections as decided within the group and that the group will work together to harmonize the separate sections. The project will be graded in two phases: the **draft** version, due November 25, 2025 (11:59 PM), and the **final** version, due December 17, 2025 (9:45 AM). All students in a group will receive the 5% credit for submitting the initial draft and meeting with instructors to review comments (below) and the same grade for the final version of the project according to the rubric for the remaining 30% credit. **N.B. Due to time, budget, and computing restraints, the final project is solely an analysis proposal. Students should not actually perform their proposed analyses.**

The instructors will return feedback comments on the draft by December 3th. Between Wednesday December 3rd and Friday December 12th, the teaching staff will schedule meetings with each group in person or on zoom to review the preparation of the final project. To receive the full 5% participation credit for the draft, all students from a group are expected to attend, unless specifically excused. The final class (December 17th) will be dedicated to brief, i.e. <5 minutes, oral group presentations from each group of their final project with slides (think elevator pitch, e.g. ~1 slide for each section). From the experience of past editions of the course, it cannot be stressed enough that the more developed the ideas in the draft proposal, the better the final project. Students are strongly encouraged to start discussing the project within their groups at the beginning of the term and to reach out to the instructors during office hours for feedback as they develop proposals. Having a clear sense of the aims and analytic approach for the project proposal as early in the term as possible will make the proposal more coherent and also easier to prepare.

Class Attendance

Attendance in-person is expected. The lectures will not be offered for remote learning via Zoom. However, the course staff and HSPH recognize that some absences may be unavoidable. If you cannot attend class for an unavoidable reason, please contact the teaching staff as soon as you anticipate being absent so we can make alternate arrangements.

Late completion of assignments

Late assignments will be graded but will not receive full credit. Excepting unavoidable lateness, deductions of credit will depend on how long after the deadline assignments are submitted, imposing 10% deduction for each day late.

Harvard Chan Policies and Expectations

Inclusivity Statement

Diversity and inclusiveness are fundamental to public health education and practice. Students are encouraged to have an open mind and respect differences of all kinds. The EPI507 teaching team shares responsibility with you for creating a learning climate that is hospitable to all perspectives and cultures; please feel free to contact us if you have any concerns or suggestions.

Bias Related Incident Reporting

The Harvard T.H. Chan School of Public Health believes all members of our community should be able to study and work in an environment where they feel safe and respected. As a mechanism to promote an inclusive community, we have created an anonymous bias-related incident reporting system. If you have experienced bias, please submit a report here so that the administration can track and address concerns as they arise and to better support members of the Harvard Chan community.

Title IX

The following policy applies to all Harvard University students, faculty, staff, appointees, or third parties: Harvard University Sexual and Gender-Based Harassment Policy. Procedures For Complaints Against a Faculty Member

Procedures For Complaints Against Non-Faculty Academic Appointees

Academic Integrity

Each student in this course is expected to abide by the Harvard University and the Harvard T.H. Chan School of Public Health School's standards of Academic Integrity. All work submitted to meet course requirements is expected to reflect each student's effort as prescribed in the assignment. For example, students must submit their own answers to quizzes and homeworks but answers may be influenced by discussions with other students. Similarly, all students within a group are expected to contribute equally to the entire group project, including drafting, finalizing, and presenting. In the preparation of work submitted to meet course requirements, students should always take great care to distinguish their own ideas and knowledge from information derived from sources.

Students must assume that collaborations, i.e., submitting responses collectively, in the completion of course assignments are prohibited, with exceptions for in-class exercises and the final group project. Students must acknowledge any collaboration and its extent in all submitted work. This requirement applies to collaboration on editing as well as collaboration on substance. Accordingly, submission of homework answers, text for the project, and/or material for the final oral presentations created by generative artificial intelligence (GAI) is not permitted. However, GAI may be used for help with brainstorming the project. Students who have questions about the use of GAI for assignments or would like to propose a use not addressed here should contact the instructors to discuss permission in advance of such uses.

Should academic misconduct occur, the student(s) may be subject to disciplinary action as outlined in the Student Handbook. See the Student Handbook for additional policies related to academic integrity and disciplinary actions.

Accommodations for Students with Disabilities

Harvard University provides academic accommodations to students with disabilities. Any requests for academic accommodations should ideally be made before the first week of the semester, except for unusual circumstances, so arrangements can be made. Students must register with the Local Disability Coordinator in the Office for Student Affairs to verify their eligibility for appropriate accommodations. Contact Colleen Cronin ccronin@hsph.harvard.edu in all cases, including temporary disabilities.

Religious Holidays, Absence Due to

According to Chapter 151c, Section 2B, of the General Laws of Massachusetts, any student in an educational or vocational training institution, other than a religious or denominational training institution, who is unable, because of his or her religious beliefs, to attend classes or to participate in any examination, study, or work requirement on a particular day shall be excused from any such examination or requirement which he or she may have missed because of such absence on any particular day, provided that such makeup examination or work shall not create an unreasonable burden upon the School. See the student handbook for more information.

Course Evaluations

Constructive feedback from students is a valuable resource for improving teaching. The feedback should be specific, focused and respectful. It should also address aspects of the course and teaching that are positive as well as those which need improvement.

Completion of the evaluation is a requirement for each course. Your grade will not be available until you submit the evaluation. In addition, registration for future terms will be blocked until you have completed evaluations for courses in prior terms.

Course Overview

Week	Lecture		In-class exercise/discussion	Assignment(s) due
	Monday	Wednesday		
1	Oct 27th (DC) - Introduction - Scope of genetic epidemiology	Oct 29th (DC/JH) - Review basic molecular genetics - Groups/project discussion		Oct 29th 9:00 AM (pre-class) Enrollment questionnaire Oct 29th 9:45AM Quiz #1-3
2	Nov 3rd (JH) - Mendelian genetics, familial aggregation, heritability	Nov 5th (JH) - Population genetics	Nov 5th (in-class exercise 1, SL) UCSC Genome Browser	Nov 3rd 9:45AM Quiz #4-5 Nov 5th 9:45AM Quiz #6-8 Nov 5th 9:45AM HW #1
3	Nov 10th (DC) - Linkage Disequilibrium - Introduction to GWAS	Nov 12th (DC) - GWAS	Nov 10th (in-class exercise 2, BT) LD link	Nov 10th 9:45AM Quiz #9-11 Nov 12th 9:45AM Quiz #12 Nov 12th 9:45AM HW #2
4	Nov 17th (DC) - Population stratification	Nov 19th (JH/DC) - DAG exercise - Power Calculations - Introduction to post-GWAS and application to genetic epidemiology	Nov 17th (in-class exercise 3, BT) GWAS Catalog	Nov 19th 9:45AM HW #3
5	Nov 24th (DC/JH) - Race/ancestry/ethnicity in genetic studies - Ethics consideration in genetic studies (video)	Nov 26th (No class) - Thanksgiving Break	Nov 24th (in-class discussion 1) Ethics consideration in genetic studies Project discussion	Nov 24th 9:45AM Review readings for class discussion Nov 25th 9:45AM Group project draft
6	Dec 1st (Guest lecture) - Hugues Aschard, PhD Fine mapping; Polygenic risk score; Gene-environment interaction	Dec 3rd (Guest lecture/DC) - Hugues Aschard: GxE continued - Mendelian Randomization (MR) - MR power calculation	Dec 3rd (in-class discussion 2) MR reading – Alcohol, BP, stroke paper	Dec 3rd 9:45AM HW #4 Dec 3rd Staff returns comments on project drafts
7	Dec 8th (DC) - MR power (if needed) - Rare variants: discovery, population genetics, analysis	Dec 10th (DC/Guest lecture) - Rare variants, applications - Monica Wojcik, MD, MPH Genetic diagnosis in the clinic	Dec 8th (in-class exercise 4, SL) gnomAD Database	Dec 10th 9:45AM HW #5
8	Dec 15th (Guest lecturer) - Jordan Smoller, MD All of Us project: Fostering diversity, inclusion, and equity in genetic studies	Dec 17th (Instructors/class) - Project Presentations	Dec 15th (In-class discussion 3) WGS in biobanks; pan-ancestry PRS; EHR-based datasets vs. longitudinal cohorts	Dec 17th 9:45AM Group project final (proposal as *.docx or *.pdf; slides for presentation as *.ppt or *.pdf) Dec 17th 9:45AM HW #6