**EPI 507: Principles of Genetic Epidemiology**

Fall 2 2024

**Meeting Time:** Monday/Wednesday 09:45 - 11:15 AM

**Location:** Kresge G1 (HSPH)

**Credits**: 2.5 credits

**Website:** https://canvas.harvard.edu/courses/146313

**Instructor Information**

**Faculty**

Dan Chasman, PhD

Associate Professor, Medicine, Harvard Medical School

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Office hours: Tuesday, TBD (1-2 or 4-5 PM) by [Zoom](https://harvard.zoom.us/j/92430795468?pwd=S1R4MC9NTzA0NjZXaU5obldKbVVndz09) (Password: 974057), or by appointment

Jie (Jack) Hu, MD, PhD

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Office hours: Thursday, TBD (1-2 or 4-5 PM) by [Zoom](https://harvard.zoom.us/j/5133737854), or by appointment

**Teaching Fellows**

Buu Truong, MD

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Office hours: Monday, 11:30 AM -12:30, FXB G03, or by appointment

**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 biology, potentially leading to 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

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| 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 team-learning exercises (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 required to check the Canvas site on a weekly basis for course announcements.

During the first week, students will be assigned to small discussion groups, typically 4 students in each group, for the group activities throughout the course and for the final project. Students are expected to participate in discussions and group exercises in class.

**Course Readings**

There is no required textbook for this class. Readings will consist of book chapters and journal articles available through PDFs supplied via the Canvas site, links to publicly available articles, and through Countway Library. Required readings for each week are listed on the Canvas site. Lecture material and readings will 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, team-learning exercises will be graded on a participation basis and completed within assigned groups. These exercises** will cover hands-on skills in genetic data resources and analytic approaches relevant to the UCSC Genome Browser, LD link, GWAS Catalog, and gnomAD. The materials for the labs will be available on the course website. There will be 4 team-learning exercises throughout the semester on the following dates.

Exercises #1: Wednesday, November 6st (UCSC browser)

Exercises #2: Monday, November 11th (LD link)

Exercises #3: Monday, November 18th (GWAS catalog)

Exercises #4: Monday, December 2nd (gnomAD)

**Homework (40%)**

**There will be a total of six graded homeworks throughout the course.** The homeworks will elaborate onconcepts presented in lectures and discussions and provide opportunities to learn and use some of the online resources and software tools introduced in lectures and exercises. You are allowed to discuss the homework assignments with other students, but you must submit your 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.

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| **#** | **Topic** | **Assign** | **Due** |
| 1 | DNA Sequence, Genetic Variation | W. Oct. 30th | W. Nov 6th |
| 2 | Population Genetics, Genotype/Allele Frequencies and Hardy-Weinberg Equilibrium, UCSC Genome Browser | W. Nov 6th | W. Nov 13th |
| 3 | Linkage disequilibrium | W. Nov 13th | W. Nov 20th |
| 4 | GWAS basics, GWAS Catalog, Association analysis | W. Nov 20th | W. Dec 4th |
| 5 | gnomAD, Sequencing and Rare variation | W. Dec 4th | W. Dec 11th |
| 6 | Polygenic Risk Scores, Mendelian Randomization, Gene-environment interaction effects | W. Dec 11th | W. Dec 18th |

**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) analysis proposal using available (i.e. public or by application) data sources (e.g. the UK Biobank, TOPMed, dbGaP, publicly available GWAS summary statistics, etc.) and a short (< 5 mins) “elevator pitch” (PowerPoint or pdf format) 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 members. It is intended that each group member will be primarily responsible for drafting one of the four sections as decided withing the group. The project will be graded in two phases: the draft version and the final version. Students will receive individual grades for submitting his/her section for the draft version on a participation basis, i.e. 5% credit for submitting, 0% for not submitting. All students in a group will receive the same grade for the final version of the project according to the [rubric](https://canvas.harvard.edu/files/21133147/download?download_frd=1) for the remaining 30% credit. **Due to time, budget and computing restraints, students should not actually perform their proposed analyses.**

For full credit on the final project, draft text for all sections must be provided (due by 9:45 AM. November 25th) so feedback can be returned by December 4th. The final projects will be due by 9:45 AM December 18th. The final class (December 18th) 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 and TFs during office hours for feedback as they develop proposal. 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, please contact the 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. Deductions of credit will depend on how long after the deadline assignments are submitted.**

**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 contact us if you have any concerns or suggestions.

**Bias Related Incident Reporting**

The Harvard Chan School 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](https://reportinghotline.harvard.edu/) 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.](http://hwpi.harvard.edu/files/title-ix/files/harvard_sexual_harassment_policy.pdf) Procedures [For Complaints Against a Faculty Member](http://hwpi.harvard.edu/title-ix/complaints-against-faculty-member-hsph)

Procedures[For Complaints Against Non-Faculty Academic Appointees](http://hwpi.harvard.edu/title-ix/complaints-against-non-faculty-academic-appointees-hsph)

**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, each student will be responsible for a section of the group project although the project, conceptually and as final text, will come from the group. 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 collaboration in the completion of assignments is prohibited unless explicitly specified, e.g. for the 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](https://www.hsph.harvard.edu/student-handbook/academic-support/academic-integrity/) 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](mailto: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](https://www.hsph.harvard.edu/student-handbook/student-life-policies/religious-holidays/) 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**

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|  | **Lecture** | |  |  |
| **Week** | **Monday** | **Wednesday** | **In-class exercise/class discussion** | **Assignment(s) due** |
| **1** | Oct 28th (DC)   * Introduction * Scope of genetic epidemiology | Oct 30th (DC/JH)   * Review basic molecular genetics * Groups/project discussion |  | Oct 29th 9:00 AM (pre-class) Enrollment questionnaire  Oct 30th 9:45AM Quiz #1-3 |
| **2** | Nov 4th (JH)   * Mendelian genetics, familial aggregation, heritability | Nov 6th (JH/DC)   * Population genetics | Nov 6st (exercise 1, JZ)  UCSC Genome Browser | Nov 4th 9:45AM Quiz #4-5  Nov 6th 9:45AM Quiz #6-8  Nov 6th 9:45AM HW #1 |
| **3** | Nov 11th (DC)   * Linkage Disequilibrium | Nov 13th (DC)   * Genetic Association Studies and GWAS (Part 1) | Nov 11th (exercise 2, BT)  Linkage Disequilibrium | Nov 11th 9:45AM Quiz #9  Nov 13th 9:45AM Quiz #10-11  Nov 13th 9:45AM HW #2 |
| **4** | Nov 18th (JH)   * Genetic Association Studies and GWAS (Part 2) | Nov 20th (DC)   * Power Calculations * Population Stratification | Nov 18th (exercise 3, JZ)  GWAS Catalog | Nov 18th 9:45AM Quiz #12  Nov 20th 9:45AM HW #3 |
| **5** | Nov 25th (DC & Guest lecturer Anna Lewis, PhD)   * Ethical use of ancestry in genetic studies * Class discussion (ancestry) | Nov 27nd (No class)   * Thanksgiving Break | Nov 25th (class discussion)  Ancestry readings | Nov 25th 9:45AM Review readings and study guide for class discussion  Nov 25th 9:45AM Group project draft |
| **6** | Dec 2th (DC)   * “Rare variants I: discovery, population genetics, analysis” | Dec 4th (DC)   * Rare variants II: examples * Class discussion (sequencing) | Dec 2nd (exercise 4, BT)  gnomAD Database  Dec 4th (class discussion)  sequencing readings | Dec 4th 9:45AM HW #4  Dec 4th 9:45AM Review readings and study guide for class discussion  Dec 4th Staff returns comments on project drafts |
| **7** | Dec 9th (DC)   * Mendelian Randomization (MR) * Class discussion (MR) | Dec 11th (Guest lecturer Hugo Aschard, PhD)   * PRS (w/ causal variant/fine mapping * Gene-environment interactions | Dec 9th (class discussion)  MR readings | Dec 9th 9:45AM Review readings and study guide for class discussion  Dec 11th 9:45AM HW #5 |
| **8** | Dec 16th Guest lecturers   * Chrissy Austin-Tse, PhD Genetic diagnosis in the clinic; * Jordan Smoller, MD All of Us project: Fostering diversity, inclusion, and equity in genetic studies | Dec 18th (Instructors/class)   * Project Presentations |  | Dec 18th 9:45AM Group project final (proposal as \*.docx or \*.pdf; slides for presentation as \*.ppt or \*.pdf)  Dec 18th 9:45AM HW #6 |