Advanced Population and Medical Genetics
EPI511, Spring semester, 2019
Tue/Thu 2:00-3:30pm, FXB G03

Instructor
Alkes Price, Professor (aprice@hsph.harvard.edu). Office Hours:
Thu 3:30-4:30pm, Building 2, Room 211 (Jan 31 - May 16, excluding Mar 21)

Teaching Assistant
Margaux Hujoel, Doctoral student (hujoel@g.harvard.edu). Office Hours:
Mon 11:15am-12:15pm + Fri 2-3pm, Building 2, Room 200 (Feb 1 - May 3, excluding Mar 18,22)

Prerequisites
• EdX course in Python or PERL, or equivalent programming experience in Python or PERL
  (see e.g. https://www.edx.org/course/subject/computer-science/python)
• BIO227 or EPI507 or EPI293, or equivalent experience in genetics

Course Description
This course will cover quantitative topics in human population genetics and applications to
general genetics, including the HapMap project, linkage disequilibrium, population structure and
admixture, population stratification, fine-mapping, heritability, genetic risk prediction, and mixed
model association. The course is aimed at Epidemiology and Biostatistics students with a
strong interest in statistical genetics, and is included in the Biostatistics Advanced Doctoral Core
and Biostatistics Master's core. The course will emphasize hands-on analysis of large empirical
data sets, thus requiring prior experience with a general-purpose high-level programming
language such as Python or PERL. After taking this course, each student will have the
experience and skills to develop and apply statistical methods to population genetic data.

Course Objectives
After taking this course, the student will be able to:
• Critically analyze large empirical data sets using a high-level programming language such as
  Python or PERL.
• Apply fundamental concepts in population and medical genetics such as linkage disequilibrium,
  population structure and admixture, population stratification, fine-mapping, and heritability.
• Develop and apply statistical methods to population genetic data.

Texts and Reading Materials
Lecture notes and links to relevant scientific papers will be provided on the course website.

Outcome Measures and Grading
Substantial and informed student participation in class discussions is expected of all students;
this includes reading the required advance reading and asking/answering questions in class.
The final grade for this course will be based on Experiences 1-6 (60%) + Research Paper (40%).

Experiences:
At the heart of this course are 6 Experiences: biweekly take-home projects in which students
apply fundamental concepts from the reading, lecture and discussion parts of the course to
analyze empirical data sets. The Experiences will determine 60% of the grade for this course.
Computer code written in Python (iPython notebook format preferred) or PERL, and its output,
are to be submitted via the Experiences dropbox on the course www site.

Research Paper:
In addition, each student will write a short research paper (1,000-1,500 words) describing their
scientific results on a project of their choice. A list of suggested project topics will be provided.
The short research paper will determine 40% of the grade for this course.
Harvard Chan Policies and Expectations:

Inclusivity Statement

Diversity and inclusiveness are fundamental to public health education and practice. It is a requirement that you have an open mind and respect differences of all kinds. I share responsibility with you for creating a learning climate that is hospitable to all perspectives and cultures; please contact me if you have any concerns or suggestions.

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 Codes of Academic Integrity. All work submitted to meet course requirements is expected to be a student’s own work. 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. 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. 

For this course, collaboration is allowed in the following instances:

• Experiences 1-6: OK to discuss Experiences with your colleagues, but each piece of code you write should be your own.
• Research Paper: OK to discuss Research Paper with your colleagues, but each piece of code you write should be your own and each piece of text you write should be your own.

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 the OSA (studentaffairs@hsph.harvard.edu) in all cases, including temporary disabilities.

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 Schedule

<table>
<thead>
<tr>
<th>Week</th>
<th>Dates</th>
<th>Topic</th>
<th>Recommended advance reading (Optional advance reading in parentheses)</th>
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<tr>
<td>Week 1:</td>
<td>Jan 29,31</td>
<td>Introduction + HapMap / 1000 Genomes projects</td>
<td>International HapMap3 Consortium 2010 Nature¹ (Visscher et al. 2017 Am J Hum Genet²)</td>
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<td>Week 2:</td>
<td>Feb 5,7</td>
<td>Linkage disequilibrium</td>
<td>Conrad et al. 2006 Nat Genet³ (Slatkin 2008 Nat Rev Genet⁴)</td>
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<td>Week 5:</td>
<td>Feb 26,28</td>
<td>Population stratification</td>
<td>Price et al. 2006 Nat Genet⁹ (Kang et al. 2010 Nat Genet¹⁰)</td>
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<td>Week 7:</td>
<td>Mar 12,14</td>
<td>Natural selection</td>
<td>Galinsky et al. 2016a Am J Hum Genet¹³ (Sabeti et al. 2006 Science¹⁴)</td>
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<td>Week 8:</td>
<td>Mar 26,28</td>
<td>Heritability</td>
<td>Yang et al. 2010 Nat Genet¹⁵ (Lee et al. 2012 Nat Genet¹⁶)</td>
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<td>Week 9:</td>
<td>Apr 2,4</td>
<td>Genetic risk prediction</td>
<td>Purcell et al. 2009 Nature¹⁷ (Khera et al. 2018 Nat Genet¹⁸)</td>
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<td>Week 10:</td>
<td>Apr 9,11</td>
<td>Mixed model association</td>
<td>Yang et al. 2014 Nat Genet¹⁹ (Loh et al. 2015a Nat Genet²⁰)</td>
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<td>Week 11:</td>
<td>Apr 16,18</td>
<td>Rare variant analysis</td>
<td>Do et al. 2015 Nature²¹ (Lee et al. 2014 Am J Hum Genet²²)</td>
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<td>Week 13:</td>
<td>Apr 30</td>
<td>Transcriptome-wide association studies*</td>
<td>Gusev et al. 2016 Nat Genet²⁵ (Gusev et al. 2018 Nat Genet²⁶)</td>
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*guest lecture by Alexander (Sasha) Gusev, Assistant Professor, DFCI/Harvard Medical School

**Experiences (due by 8:00am each Tue, via Experiences dropbox on course www site.)**
- Experience 1: due Tue Feb 12
- Experience 2: due Tue Feb 26
- Experience 3: due Tue Mar 12
- Experience 4: due Tue Apr 2
- Experience 5: due Tue Apr 16
- Experience 6: due Tue Apr 30

**Research Paper (due by 5:00pm Fri May 17. Please send by email to Alkes Price.)**
Each student should choose one topic for the short research paper. Possible topics will be suggested each week, and an aggregate list of suggested topics will be provided on Apr 30. Each student should schedule a 15-minute appointment with the instructor during the week of May 6-10, and should choose and begin work on their topic prior to this meeting. The short research paper will be due on Fri May 17. The paper should be 1,000-1,500 words long, and should include an abstract, plus one figure and one table and at least 10 references. Additional subdivision into Introduction, Results, Discussion and Methods sections is optional. For an example of a short research paper, see Lindstrom et al. 2011 Nat Genet²⁷.
Bibliography