Risk Calculation for Genetic Counseling
Human Genetics 2039
Graduate School of Public Health
University of Pittsburgh
Spring 2016
1 credit

Wednesdays 3:30 – 4:20, room A115 or A312 (TBD)
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Course Description
Provides training in calculating risk of disease, or carrier status, in a variety of genetic counseling situations by learning to identify the sources of risk in the counselee’s personal and family history and to analyze and synthesis a single overall risk of disease from these competing risks.

This course provides hands-on training in calculating risk of disease or carrier status in a variety of typical genetic counseling situations, as well as discussion of the limitations of those calculation methods. Seven topics are included:

• Pedigree-based risk calculation for dominant diseases
• Pedigree-based risk calculation for recessive diseases
• Pedigree-based risk calculation for X-linked diseases
• Pedigree-based risk calculation using linked markers
• Risk prediction based on population screening
• Epidemiological models for risk calculation (e.g. for breast cancer)
• Risk prediction/discussion based on whole-exome or whole-genome sequence

Detailed learning objectives are listed at the end of the syllabus.

Course Format
For each calculation topic, there will be one or two lectures to demonstrate the calculation methods, a homework set to practice solving problems, and an exam consisting of problems very similar to those on the homework. The course is “competency-based,” which means that students may re-take exams on each topic as many times as desired to achieve competency. Only the final grade on each exam will count toward the course grade. Homeworks must be turned in, but will not be graded for correctness, only completion. Solutions will be posted on courseweb and discussed in class.
Textbook and Course Materials
The recommended text is *Risk Calculation in Genetic Counseling* by Ian Young, 3rd edition (purple cover). All other course materials will be posted on courseweb.

Grading
The final grade will be based on 20% for class participation (including homework completeness) and 20% for the final grade achieved on each of the four exams. There is no predefined numerical grading scale for this course.

Academic Integrity
Homework can and should be done collaboratively, but most students learn better if they try the problems themselves first, then consult with others, then create their own final write-up.

Exams will be in class and should be entirely your own work. A one-page “cheat sheet” will be allowed for each exam.

*All students are expected to adhere to the school’s standards of academic honesty. Any work submitted by a student for evaluation must represent his/her own intellectual contribution and efforts. The Graduate School of Public Health’s policy on academic integrity, approved by EPCC on 10/14/08, which is based on the University policy, is available online in the Pitt Public Health Academic Handbook ([www.publichealth.pitt.edu/home/academics/academic-requirements](http://www.publichealth.pitt.edu/home/academics/academic-requirements)). The policy includes obligations for faculty and students, procedures for adjudicating violations, and other critical information. Please take the time to read this policy.*

*Students committing acts of academic dishonesty, including plagiarism, unauthorized collaboration on assignments, cheating on exams, misrepresentation of data, and facilitating dishonesty by others, will receive sanctions appropriate to the violation(s) committed. Sanctions include, but are not limited to, reduction of a grade for an assignment or a course, failure of a course, and dismissal from the school.*

*All student violations of academic integrity must be documented by the appropriate faculty member; this documentation will be kept in a confidential student file maintained by the Office of Student Affairs. If a sanction for a violation is agreed upon by the student and instructor, the record of this agreement will be expunged from the student file upon the student’s graduation. If the case is referred to the Pitt Public Health Academic Integrity Hearing Board, a record will remain in the student’s permanent file.*
**Accommodation for Students with Disabilities**

If you have any disability for which you may require accommodation, you are encouraged to notify both me and the Office of Disability Resources and Services, 140 William Pitt Union (Voice or TTD 412-648-7890) as early as possible in the term.

**Schedule**

<table>
<thead>
<tr>
<th>Date</th>
<th>Topic</th>
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<tbody>
<tr>
<td>January 6</td>
<td>Intro lecture</td>
</tr>
<tr>
<td>January 13</td>
<td>Dominant lecture</td>
</tr>
<tr>
<td>January 20</td>
<td>Recessive lecture; Dominant homework due</td>
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<tr>
<td>January 27</td>
<td><strong>No class</strong>; Recessive homework due</td>
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<tr>
<td>February 3</td>
<td>Discuss dominant and recessive homeworks</td>
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<tr>
<td>February 10</td>
<td>Dominant test</td>
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<tr>
<td>February 17</td>
<td>Recessive test</td>
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<tr>
<td>February 24</td>
<td>X-linked lecture</td>
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<tr>
<td>March 2</td>
<td>Screening and Epi models; X-linked homework due (discuss)</td>
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<td>March 9</td>
<td><strong>Spring break</strong></td>
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<tr>
<td>March 16</td>
<td>X-linked test (John Shaffer)</td>
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<tr>
<td>March 23</td>
<td><strong>No class</strong></td>
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<td>March 30</td>
<td>Linked marker lecture</td>
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<tr>
<td>April 6</td>
<td>Linked marker lecture</td>
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<tr>
<td>April 13</td>
<td>WES and WGS; linked marker homework due (discuss)</td>
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<tr>
<td>April 20</td>
<td>Linked marker test</td>
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<tr>
<td>April 27</td>
<td>Extra day for repeat tests</td>
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Detailed Learning Objectives

**Dominant inheritance**
Be able to infer Mendelian inheritance patterns and obligate carrier status and calculate risks in a pedigree, considering the following factors.
- various affected and unaffected pedigree members
- reduced and age-dependent penetrance
- genetic test results
- negligible or high mutation rate

**Recessive inheritance**
Be able to infer carrier status and calculate Mendelian risks in a pedigree, considering the following factors in addition to those listed for dominant inheritance.
- consanguinity
- relatively common disorders with multiple mutations

**X-linked inheritance**
Know and/or be able to calculate risks for common pedigree situations such as mother of an isolated case, mother of two cases, sister of an isolated case, etc., and be able to calculate Mendelian risks in a pedigree, considering the following factors in addition to those listed for dominant inheritance.
- various configurations of affected and unaffected relatives in the generation of the consultand, the generation above, and the generation below

**Calculations using linked markers**
Be able to calculate risks based on linked markers for the following situations.
- dominant disease with phase known
- dominant disease with phase unknown
- recessive disease
- x-linked recessive disease

**Non-calculation topics**
Risk prediction based on screening tests and tools
- Be able to explain what is meant by a “screening” test
- Be able to explain why most positive results may be false positives
- Calculate posterior risk of disease
Epidemiological models for risk prediction (Gail, Klaus, etc.)
- Be able to discuss what they are, how they work, strengths, weaknesses
Risk prediction from sequencing data
- Be able to discuss what it is, how it works, strengths, weaknesses