CHL5430 - FUNDAMENTALS OF GENETIC EPIDEMIOLOGY
SYLLABUS

When: Fall 2014, Wednesdays 16:00-18:30.

Note: It is expected that you will attend the first lecture having reviewed pre-requisite materials as needed (see below Block A “Additional reading materials”).

*** No class on October 22 ***

Where: 155 College St., HS 618

Course coordinator and lead instructor
France Gagnon
france.gagnon@utoronto.ca
http://www.dlsph.utoronto.ca/faculty-profile/france-gagnon
www.stage.utoronto.ca

Office hours: by appointment; office HSB Room 662

Invited lecturers:
Steven Narod (Women’s College Research Institute and DLSPH Div. of Epidemiology)
Lisa Strug & Melissa Miller (SickKids and DLSPH Div. of Biostatistics)
Mohammad R. Akbari (Women’s College and DLSPH Div. of Epidemiology)
Esteban Parra (Dept. of Anthropology)

Course description
This introductory course provides an overview of central concepts and topical issues in genetic epidemiology, providing an overall framework for investigating the role of genetic factors in the etiology of common complex disorders. This course integrates human genetics, biostatistics and epidemiology. The main course objective is to provide the common terminology and fundamental concepts underlying the design and conduct of genetic epidemiologic studies. Advanced genetic epidemiology study designs and methods will not generally be discussed in depth as this goes beyond the scope of the course. The students are expected to be active participants in their learning experience. Critical appraisal and presentation of selected scientific articles in the field will be a major component of the course, as well as in-class exercises.

Target audience & Prerequisites
Students with a strong interest in learning basic elements of genetic epidemiologic studies but with minimal or no formal training in the field. This is a required course for trainees of the CIHR STAGE (Strategic Training for Advanced Genetic Epidemiology) program. Aiming for a group size of 8 students. Prerequisites: Introduction to Epidemiology (CHL 5401), Biostatistics (CHL 5201), or equivalent. Students who have not taken these courses must discuss their eligibility with the course coordinator.
Specific goals
1. The students will have basic understanding of the fundamental principles and concepts underlying the main study designs and methods used in genetic epidemiologic research, and their specific objectives.

2. The students will have some level of critical appraisal skills for the interpretation of scientific articles in the field of genetic epidemiology.

Required readings: Articles listed for each blocks. Note that some weeks will require more reading than others - Be prepared. Additional and/or more advanced reading materials will be recommended based on the specific individual interests of each student based on assignment #1.

A few great – but not required – Textbooks and Review papers
- October 2012 Human Genetics Special Issue on “Study Designs and Methods Post-GWAS” with Guests Editors Andreas Ziegler, Yan V. Sun and France Gagnon.

Web resources:
- Website with a comprehensive list of pedagogical references in genetic epidemiology - M. Tevfik DORAK website: http://www.dorak.info/epi/genetepi.html

Learning opportunities outside the classroom:
- STAGE International Speaker Seminar Series (ISSS): http://www.stage.utoronto.ca/home/issss

For your curiosity:
1) CIHR STAGE (Strategic Training for Advanced Genetic Epidemiology) training program: http://www.stage.utoronto.ca/
2) International Genetic Epidemiology Society (IGES): http://geneticepi.org/content/about/what-iges
3) Careers and recruitment opportunities in genetic epidemiology: http://www.stage.utoronto.ca/about/jobs
DETAILED COURSE OUTLINE

Block A – Introduction and overview of study design types in genetic epidemiology
What are the main goals in genetic epidemiologic studies? What are the big questions? What are the main steps in genetic epidemiologic studies? What is the basic vocabulary used in genetic epidemiology?

September 10 (France Gagnon)

• Presentation of the course syllabus and dialogue re. learning outcomes, students & instructors’ expectations
• Fundamental genetic terminology/biology; Complex phenotypes/traits
• Introduction to genetic epidemiologic research objectives and tools

Required reading materials
1. Burton PR, Tobin MD, Hopper JL (2005) Key concepts in genetic epidemiology. Lancet 366: 941-951. (First article from a series of seven on Genetic Epidemiology; The whole series is a nice overview of fundamental concepts in the field of genetic epidemiology)


**Additional reading materials as needed**

1) A genetic textbook (or other reliable tools such as chapter 1 of Ziegler A and König IR (2010) to answer questions such as:
   a. Where is the genetic information located?
   b. What does the genetic information mean?
   c. How is the genetic information translated?
   d. How is genetic information transmitted from generation to generation?
   e. How do individuals differ with regard to their genetic information?
   f. How can individual differences be detected?

2) Biostatistics and epidemiology textbooks to review the following concepts:
   a. Population and sample
   b. Parameters and statistics
   c. Descriptive statistics
   d. Measurement scale
   e. Random variables
   f. Probability distribution
   g. Hypothesis testing
   h. Type I error
   i. Power
   j. Estimation of a population parameter
   k. Modeling
   l. Case-control & cohort designs
   m. Risk factors/determinants of health
   n. Measure of disease frequency and association
   o. Bias
   p. Confounders
   q. Effect modifier/interaction
Block B – Segregation studies

September 17 (Steven Narod) & 24 (France Gagnon)

Segregation studies: What is the nature of the genetic determinants involved in the disease/trait?
- Simple segregation analysis (Narod)
- Complex segregation analysis & Family ascertainment (Gagnon)
- Weekly critical appraisal of an article (Journal Club format – presentation & discussion/critical appraisal led by a team of two students): Segregation analysis studies

Required reading materials


Additional & Advanced reading materials

Block C – Linkage studies

October 1 (Melissa Miller) & 8 (France Gagnon)

Linkage studies: Where are these genetic determinants located on the genome?
- Model-based (Parametric) linkage analysis (Miller)
- Model-free (Non-parametric) linkage analysis (Gagnon)
- Weekly critical appraisal of an article (Journal Club format – presentation & discussion/critical appraisal led by a team of two students): Linkage analysis studies

Required reading materials

Additional & Advanced reading materials
Block D – Genetic Association studies

October 15 (Lisa Strug) & No class on October 22 & 29 (France Gagnon)

What are the causal variants?

- Association studies in unrelated individuals, including GWAS (Strug)
- Family-based association studies (Gagnon)
- Weekly critical appraisal of two articles (Journal Club format – each presentation & discussion led by a team of two students): Association studies

Required reading materials

October 15:

4. Gordon D and Finch SJ (2005) Factors affecting statistical power in the detection of genetic association. JCI 115: 1408-1418. (Nice and easy review paper on statistical power; also includes a glossary of terms used in genetic epidemiology and statistical genetics)

October 29:

Additional and Advanced reading materials

October 15:
1. Morton NE (2005) Linkage disequilibrium maps and association mapping. JCI 115: 1425-1430. (‘Friendly-user’ review paper on statistical aspects of LD mapping; also with a glossary)

October 29:
Block E – Clinical and Public Health Genomics

November 5 (Steven Narod)
• Clinical and public health genomics (Narod)

Required reading materials


Additional and Advance reading materials


Block F – Emerging and Advanced topics

November 12 (Mohammad Akbari) & 19 (Esteban Parra) & 26 (France Gagnon)
- Next generation sequencing applications in genetic epidemiology (Akbari)
- Human genetic variation and Admixture mapping (Parra)
- Epigenetic epidemiology (Gagnon) & Course evaluation

Required reading materials

November 12:

November 19:

November 26:
Additional and advanced reading materials

November 12:


November 19:


November 26:


Evaluations

1. **Assignment 1: (500-1000 words paper)**
   20%
   Due September 24 at 9:00 AM.
   Marks will be deducted at the rate of 15%/day (-5% before noon; -10% before 18:00; -15% after 18:00; including weekend days) to a maximum of 100%.

2. **Assignment 2: (two journal club presentations and discussion)**
   30% (15% + 15%)
   Presentation dates and assignment of papers will be done on September 10.
   Each student from the team will be individually marked i.e., based on their response to questions, etc.

3. **Assignment 3: (take-home exam)**
   40%
   You will receive the assignment on November 12. Due November 19 at 9:00 AM.
   Marks will be deducted at the rate of 15%/day (-5% before noon; -10% before 18:00; -15% after 18:00; including weekend days) to a maximum of 100%.

4. **Assignment 4: (600 words max. paper)**
   10%
   Due December 3 at 9:00 AM.
   Marks will be deducted at the rate of 15%/day (-5% before noon; -10% before 18:00; -15% after 18:00; including weekend days) to a maximum of 100%.
Assignment 1

Assignment 1 is to develop your personal learning outcomes and major goal for the course, and propose ways of how you plan to achieve it. This is an individual assignment. It should be electronically submitted as a Word document (other formats will not be accepted), and typed single-spaced, 1" margins, 12 pt. Times New Roman. The length should be of 500-1500 words, including the table but excluding title page and references if any. Please: Be precise! Be concise!

Your assignment should follow the guidelines below.

1. A title page that includes:
   - Project Title
   - Your name and U of T student number
   - Course name and number
   - Date

2. Personal learning outcomes/objectives: Guidelines for developing learning outcomes have been developed by the University of Toronto Office of Teaching Advancement (OTA) and are summarized by the acronym “SMART(TT)”. The acronym "SMART(TT)" characterizes the qualities of good learning outcomes. This acronym has been borrowed from goal-setting strategies from the management literature and has been adapted for teaching purposes. Here, I slightly revised SMART(TTT) to become a self-assessment tool not only for me, the instructor, but also for each of my students. I re-labeled the student version of the instrument “SMART 4 YOU”. Your main goal will guide the development of your learning outcomes.

   When writing your learning outcomes, keep in mind that they should be SMART 4 YOU:

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<tbody>
<tr>
<td>Speak to you:</td>
<td>Learning outcomes should address what you will know or be able to do at the completion of the course or assignment. §/2</td>
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<td>Measurable:</td>
<td>Learning outcomes must indicate how learning will be assessed. §/1</td>
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<td>Applicable:</td>
<td>Learning outcomes should emphasize ways in which you are likely to use the knowledge or skills gained. §/2</td>
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<td>Realistic:</td>
<td>Successfully completing this course/activity, you should be able to demonstrate the knowledge or skills addressed in the outcome. §/2</td>
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<td>Time-bound:</td>
<td>*The learning outcomes should set a deadline by which the knowledge or skills should be acquired. Should be achievable within the course timeline. §/1</td>
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<td>Training (Transparent):</td>
<td>*Should be appropriate to your level of training and experience. §/1</td>
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<td>Transferable:</td>
<td>At least some outcomes should address knowledge and skills that you will use in a wide variety of contexts. §/2</td>
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<td>Tonic:</td>
<td>*Should challenge you. §/2</td>
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<td>Yo!:</td>
<td>*It’s calling for your attention and excitement! §/1</td>
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<td>Open:</td>
<td>*Should open your mind and creativity. §/2</td>
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<td>Unique:</td>
<td>*Should be specific to your own needs and interests. §/4</td>
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   *Refers to new elements specific to SMART 4 YOU; § max. marks allocated; The clarity, the organization and the precision of the language used will be taken into account in the marking scheme.

The assignment is free format and will be evaluated based on the above criteria. To help you writing your learning outcomes, you may prepare a table such as the one below. I expect 3-6 learning outcomes, depending on how challenging each is. Learning outcomes/goals from the syllabus are not allowed! Original units of instruction are most welcome!
<table>
<thead>
<tr>
<th>Unit of instruction</th>
<th>Objective</th>
<th>Outcome</th>
<th>How do you know?</th>
<th>Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>e.g. literature review, exercise, additional activity outside the class (provide a specific example)</td>
<td>e.g. What specific content or skills in this unit of instruction?</td>
<td>What should you know or be able to do as a result of this unit of instruction?</td>
<td>How will you be able to tell that you have achieved this outcome?</td>
<td>What kind of work can you produce to demonstrate this?</td>
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<tr>
<td>The row below shows an example that the teacher uses to translate her instruction goals; you need to adapt for your own goals as a learner.</td>
<td>Computation of HWE</td>
<td>At the exam, students will be able to compute and interpret results of an HWE test.</td>
<td>Students will accurately compute and interpret the results of an HWE test based on the data provided.</td>
<td>Based on the data provided, compute an HWE test and provide your interpretation of the results.</td>
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</table>

In the preparation of this assignment, I recommended that you read the document entitled “Developing learning outcomes” prepared by the OTA (I will send you the pdf on request). When reading the document, simply replace the words “the students” by “you”. When writing your learning objectives, replace “the students” by “I”. There are several examples in the document, as well as useful appendices.

With respect to the “units of instruction”, use some of the tools that I proposed in the context of the course (e.g. oral presentation, written critical appraisal, regular or specific journal clubs) - but more importantly, develop other original ideas. If you feel adventurous, you are welcome to propose an exercise to be done in the context of one of our regular classes.

**Hoping that “SMART 4 YOU” will become an exercise that you can use for personal development in future courses and endeavors!**
Assignment 2

For assignment 2, you and a fellow student will lead two journal club sessions in the field of genetic epidemiology i.e., critical appraisal of a scientific article. For each, you will be responsible for preparing a **20-25 minutes presentation** on a pre-determined scientific article, and leading the **discussion for the remaining 35-40 minutes**. It is expected that you will prepare questions for your audience about the study design choices, as well as challenges you encountered while reading the paper. Please, electronically send your Power Point presentation to France before or right after your presentation. Each presentation is worth 15% (total of 30% for both presentations). Each student is marked separately based on their level of preparedness and quality of their answers to questions.

Your assignment should follow the guidelines below.

1. Brief introduction of the topic – including some biological background, hypothesis, justification and objectives. Why is this study important? What gap in the literature does it fill?

2. Present, discuss and critique the study design and analytic strategies.

3. What are the most important results?

4. Significance – What is the impact of the study? What’s next?

5. Leading the class discussion: Be prepared with questions for your audience – even some for which you do not have answers!

6. Pay attention to presentation skills and the quality of your slides. Here, I do not refer to “how pretty” these can be but rather how "readable" they are, e.g. not too much information per slide, font that can be read by the audience. Make sure that each slide has a purpose. The text on the slide should be concise i.e., present the most relevant information but be ready to discuss the details during the discussion if necessary. The presentation should not last more than 25 minutes (excluding interruption time for questions); 15-20 slides should be sufficient.

Tip: consult any book about scientific presentations (e.g. Martha Davis, Scientific papers and presentations, 2nd edition, Elsevier Academic press)

A journal club presentation is a bit like a critical appraisal with the exception that you are not expected to be an expert on the topic that you are presenting. This means that you are not only allowed to ask questions to your audience about what you did not understand, but you are encourage to do so!

The STREGA checklist is a tool for critical appraisal of a genetic association study of any observational study designs. There are a number of “review” and “guidelines” articles on “How” to conduct and report genetic studies; some have been listed in your reading materials. These can be useful as well. With respect to linkage studies, the Teare and Barrett’s paper should be helpful.

*Now, have fun preparing it!*
ASSIGNMENT 2 - STUDENT PRESENTATIONS

SCHEDULE FALL 2014

1. Sept. 17 - Familial aggregation/Peretz 2007: ______________________________________
2. Sept. 24 - CSA/Plancoulaine 2000: ______________________________________________
4. Oct. 8 - Model-free linkage/Mira 2003: ___________________________________________
7. Nov. 5 - Clinical genomics/Eisen 2008: __________________________________________
8. Nov. 12 - Exome sequencing in epidemiology/Ng 2010: _____________________________
Assignment 2 - Marking scheme

1. Brief introduction of the topic – including some biological background, hypothesis, justification and objectives. Why is this study important? What gap in the literature does it fill?
   /2

2. Present, discuss and critique the study design and analytic strategies.
   /4

3. What are the most important results – and why?
   /2

4. Significance – What is the impact of the study? What’s next?
   /1

5. Leading the class discussion; questions for the audience.
   /4

6. Pay attention to the quality of your slides and presentation skills.
   /2
Assignment 3 (Take home exam)

Assignment 3 is a take home exam. This is an individual assignment. It should be electronically submitted as a Word document, and typed single-spaced, 1" margins, 12 pt. Times New Roman. Again, “Be precise! Be concise! – Points may be taken off for verbosity”.

Your assignment should follow the guidelines below.

1. A title page that includes:
   • Project Title
   • Your name and U of T student number
   • Course name and number
   • Date

2. Short answers to the take home exam questions. The take home exam will include a material that covers the entire term, including the last lecture and the proposed reading material. Some questions will go beyond the basic material presented in class.

We are now toward the end of the course and we expect that you will be more of an expert than you were at the beginning of the course!
Assignment 4

Assignment 4 is for you to critically evaluate if you have reached your personal learning outcomes and course goals, and summarize your auto-evaluation in 600 words max. The assignment should be handed in electronically. It should be a Word document, typed single-spaced with 1” margins, 12 pt. (10 pt. in the table) Times New Roman. The length should be of 600 words max., including tables if any, but excluding title page and references if any. Again, “Be precise! Be concise!”

Your assignment should follow the guidelines below.

1. A title page that includes:
   - Project Title
   - Your name and U of T student number
   - Course name and number
   - Date

2. Auto-evaluation: Evaluate your progress during this course against the set of personal outcomes that you developed for yourself in the context of assignment 1. Marks will be distributed as follows:

<table>
<thead>
<tr>
<th>Items to cover</th>
<th>Marks allocated</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Overall assessment (~ 1 paragraph)</td>
<td>/2</td>
</tr>
<tr>
<td>2. Based on the learning outcomes that you previously set for yourself, what did you learn? (be specific; you can use point form as the example below)</td>
<td>/2</td>
</tr>
<tr>
<td>e.g. I can distinguish the main goal of common study design types in genetic epidemiologic studies</td>
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<tr>
<td>3. Based on the learning outcomes that you previously set for yourself, what remains to be learned? (be specific; you can use point form as the example below)</td>
<td>/2</td>
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<tr>
<td>e.g. To interpret the results of gene-gene interaction studies</td>
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<tr>
<td>4. Aspects that contributed to achieving your learning outcomes</td>
<td>/2</td>
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<tr>
<td>5. Aspects that held you back from achieving your learning outcomes</td>
<td>/2</td>
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