Epidemiology for Clinical Research

M88-588

Spring, 2014

Time:       Wednesday, 4:30 to 7:00 p.m.
Location:   Occupational Therapy auditorium
            1st floor, 4444 Forest Park Avenue
Instructors: Mario Schootman, Ph.D. (coursemaster)
             Professor of Epidemiology, Health Services Research, Medicine
             Office: 977-8133
             Email: schootm@slu.edu
             Department of Epidemiology
             College for Public Health and Social Justice
             Saint Louis University
             schootm@slu.edu

             Anjali Deshpande, Ph.D., M.P.H.
             Research Assistant Professor of Medicine
             Office: 286-0148
             Email: adeshpan@dom.wustl.edu
             Division of Health Behavior Research
             Department of Medicine
             4444 Forest Park Ave., Suite 6700, Box 8504
             Fax: 286-1919

Office Hours: By Appointment (Assistant: Barb Stabler bstadler@dom.wustl.edu)

Target audience: Clinicians (house officers, fellows, and junior faculty)
                 interested in conducting clinical research, including those
                 enrolled in the Masters of Science in Clinical Investigation
                 program and Applied Health Behavior Research program.
                 Prior clinical research experience is helpful but not required.

Credits:       3
Course Overview

Introduction: This course introduces principles of epidemiology as they apply to clinical research. The course provides basic tools used in descriptive and analytical epidemiology, which are crucial for making informed decisions in the care of patients. Critical thinking and scientific/analytic competencies are emphasized throughout the course.

Purpose: This course will focus on common applications of epidemiologic principles and tools in clinical research, in clinical issues, and in understanding the medical literature concerning these issues. This will be accomplished via different venues that will enhance the critical thinking and scientific/analytic competencies for the students who complete the course.

Course Description

Course Format: The course format will include lectures, class discussion of exercises, supplementary reading material, critiquing a research study, and writing a small study proposal.

Course Elements and Requirements for Students:
- It is very important that students attend all classes. The information needed to master the course objectives will be presented and discussed in class. Students who miss three or more classes may be asked to withdraw from the course and to re-take the course at a later time. Arrangements for quizzes or assignments that will be missed due to travel/conferences, etc. must be made ahead of the expected missed class.

- Students are expected to complete the assigned readings before each lecture. The readings have been selected to complement the lectures, and will provide additional examples for applying basic epidemiologic methods and tools in clinical research.

- Students should be prepared to discuss the exercises and any assigned readings at the start of each class and to participate in class discussion.

- Students are required to complete a written review of a research study. Students are also required to develop a small study proposal as described in more detail in the “grading determination and policy” section.

Course Elements and Requirements for the Instructors:
- We will usually be available during normal business hours to answer any questions that you may have about the course. If your schedule precludes you from meeting during normal business hours, we will make every effort to meet with you at times that may be more convenient for you. Please feel free to contact either instructor by telephone or via email to discuss any issues concerning the course.
• We retain the right to change the order of the lectures and the content of the class to meet the needs of the students who are enrolled in the course.

Readings:

Assigned weekly readings: Articles can be obtained from the Internet using the pdf-file of this syllabus. Articles or book chapters that are not available online will be emailed or posted on Blackboard. These articles are intended to supplement the text and are required to be read by all students.

Grading Determination and Policy: Each student will complete a 3-page written critique of a study (30%), 2 short quizzes (20%), and a 3-page study proposal (50%). The instructor will assign each student to critique a specific study. Grading will be based on the written critique. Late submissions will not be accepted, and critiques that are not completed independently by the student will not be graded.

The critique of the published study (30%) will be based on the following criteria. Please use the following separate headings in your critique.

1) Study objective, setting and participants (5 points).
2) Description of the study design (5 points).
3) Brief description of the study results and its implications (5 points).
4) Strengths and weaknesses of the study identified by you and by the authors (5 points).
5) How these weaknesses of the study affected the findings (15 points).
6) How the authors addressed the weaknesses of the study (10 points).
7) How the study could be improved (15 points)

For items 4-7, focus your critique on the issues of selection bias, measurement bias, confounding, and any other methodological issues pertaining to the type of study design used in the study that were discussed during class. Please use narrative to write your critique and email it to Barb Stabler (bstadler@dom.wustl.edu).

The 3-page study proposal is based on the format from the National Institutes of Health. It will only include the technical part of the proposal (budgets, biosketches, etc. are not required). The main subject headings for a study proposal are: A) Specific Aims (no more than ½ page), B) Significance (no more than ¼ page), C) Innovation (no more than ¼ page) and D) Research Design and Methods (about 2 pages). Preliminary Studies and Power and Sample Size sections are not required. Please complete the Bias Form that describes how bias may play a role in your proposed study. Please use 0.5 inch margins throughout and Arial 11 font size. An evidence-based guide to writing study proposals for clinical research can be found here: link. Each student will be required to do each of the following items:

Submit drafts by email to Barb Stabler (bstadler@dom.wustl.edu) of:
• Specific Aims, Significance, and Innovation (due 3/19/2012)
• Research Design and Methods section (due 4/9/2012)
The final written proposal of the Specific Aims, Significance, Innovation, and the Research Design/Methods sections, due 4/30/2014, will constitute 50% of the final grade (100 points). I will provide you with comments on each section of the proposal up to two times prior to final submission for grading and return them to you in a timely manner to enable you to revise your proposal. Please also describe how you addressed each of the comments throughout your revisions using Track Changes and the “comment” facility in Microsoft Word. You are encouraged to select a topic that relates to your current or proposed area of interest. Late submissions will not be accepted, and proposals that are not completed independently by the student will not be graded.

The final grade will be based on the class distribution of 200 points from the written critique of a study (60 points), written study proposal (100 points), and 2 short quizzes (20 points each).

**Grading scale**

<table>
<thead>
<tr>
<th>Grades/sub-grades</th>
<th>% Range</th>
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<tbody>
<tr>
<td>A+</td>
<td>98% to 100%</td>
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<tr>
<td>A</td>
<td>93% to 97%</td>
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<tr>
<td>A-</td>
<td>90% to 92%</td>
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<tr>
<td>B+</td>
<td>88% to 89%</td>
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<tr>
<td>B</td>
<td>83% to 87%</td>
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<tr>
<td>B-</td>
<td>80% to 82%</td>
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<tr>
<td>C+</td>
<td>77% to 79%</td>
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<tr>
<td>C</td>
<td>73% to 77%</td>
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<tr>
<td>C-</td>
<td>70% to 72%</td>
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Total points available: 200

**Academic Integrity Policy**

Students are expected to abide by and uphold the Academic Integrity Policy for Graduate Students from the Graduate School of Arts & Sciences. All students should have received this policy. Please contact the Office of the Dean of the School of Arts & Sciences to obtain copies of this document.

**Pagers and cellular phones**

Although clinicians may be expected to be available by pager or cellular phone, please limit their use as much as possible during class.

**Students with disabilities**

Washington University is committed to providing accommodations and/or services to students with documented disabilities. Students who are seeking support for a disability or a suspected disability should contact the Disability Resource Center (DRC) at 5-4062 on the lower level of the Women’s Building (drc@dosa.wustl.edu). The DRC is responsible for approving and arranging all accommodations for University students.
<table>
<thead>
<tr>
<th>Date</th>
<th>Week</th>
<th>Topic: Introduction (Deshpande)</th>
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<tbody>
<tr>
<td>1/15</td>
<td>1</td>
<td>Course overview</td>
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<tr>
<td></td>
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<td>Evidence-based medicine, clinical guidelines, comparative effectiveness</td>
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<td></td>
<td></td>
<td>Course overview &amp; format</td>
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<td>Expectation of the students</td>
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*Readings*: Chapter 1 – Introduction

<table>
<thead>
<tr>
<th>Date</th>
<th>Week</th>
<th>Topic: Determining a diagnosis (Deshpande)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/22</td>
<td>2</td>
<td>Sensitivity &amp; Specificity</td>
</tr>
<tr>
<td></td>
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<td>ROC curves</td>
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<td>Predictive values</td>
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<td>Parallel or multiple tests</td>
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<tr>
<td></td>
<td></td>
<td>Test interpretation</td>
</tr>
</tbody>
</table>

*Readings*: Chapter 3 – Diagnosis
Feinstein AR. Misguided efforts and future challenges for research on diagnostic tests. J Epidemiol Community Health 56, 330-332, 2002. [link](#)

<table>
<thead>
<tr>
<th>Date</th>
<th>Week</th>
<th>Topic: Measurement in epidemiology (Deshpande)</th>
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<tbody>
<tr>
<td>1/29</td>
<td>3</td>
<td>Variation</td>
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<tr>
<td></td>
<td></td>
<td>Methods of data collection</td>
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<tr>
<td></td>
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<td>Reducing measurement errors</td>
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Scheuren F. What is a survey. Chapter 6 - Designing a questionnaire, 2004. [link](#)

*Due*: Exercises about Diagnosis (1/22 class)

<table>
<thead>
<tr>
<th>Date</th>
<th>Week</th>
<th>Topic: Frequency of disease (Deshpande)</th>
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</thead>
<tbody>
<tr>
<td>2/05</td>
<td>4</td>
<td>Incidence &amp; prevalence</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Numerator issues: visits vs. patients</td>
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<tr>
<td></td>
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<td>Denominator issues: who is at risk</td>
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</tbody>
</table>

*Readings*: Chapter 4 – Frequency
Gordis L. Chapter 3 - Measuring the occurrence of disease.

<table>
<thead>
<tr>
<th>Date</th>
<th>Week</th>
<th>Topic: Risk of disease (Deshpande)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2/12</td>
<td>5</td>
<td>Definition of risk factors</td>
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<tr>
<td></td>
<td></td>
<td>Recognizing risk</td>
</tr>
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<td>Uses of risk</td>
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<tr>
<td></td>
<td></td>
<td>Comparing risk</td>
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</tbody>
</table>

*Readings*: Chapter 5 – Risk: Looking forward
Katz DL. Clinical epidemiology and evidence-based medicine, Chapter 5 – Measuring and conveying risk.

*Due*: Exercises about Frequency of Disease (2/05 class)
Short Quiz about classes 1-5

Topic: Cohort studies (Deshpande)
- Continuation of Feb. 15 class


Topic: Prognosis of disease (Deshpande)
- Prognostic factors
- Describing prognosis survival curves
- Bias in cohort studies & methods to reduce bias
- Prognostic models

Readings: Chapter 7 – Prognosis

Topic: Quasi-experimental design (Deshpande)
- Designs with and without control groups
- Interrupted Time Series
- Regression Discontinuity designs
- Other designs

Readings: Handley MA, Schillinger D, Shiboski S. Quasi-Experimental Designs in Practice-based Research Settings: Design and Implementation Considerations. J Am Board Fam Med 2011; 24:589-596. (Link or copy of article will be provided)
Sango A, McCarter YS, Johnson D, Ferreira J, Guzman N, Jankowski CA. Stewardship approach for optimizing antimicrobial therapy through use of a rapid microarray assay on blood cultures positive for enterococcus species. J Clin Microbiol 2013; 51:4008-4011. (Link or copy of article will be provided)

Spring Break – No Class

Topic: Treatment I (Schootman)
- Studies of treatment effects
- Randomized Clinical Trials: designs, randomization, blinding, intention-to-treat, strengths and limitations, phase I-IV trials, number-needed-to-treat, CONSORT guidelines

Readings: Chapter 8 – Treatment
Details of CONSORT guidelines from [www.consort-statement.org](http://www.consort-statement.org)
Due: Draft of Specific Aims, Significance, and Innovation sections to Barb Stabler bstadler@dom.wustl.edu

Topic: Treatment II (Schootman)
- Studies of treatment effects
- Randomized Clinical Trials: designs, randomization, blinding, intention-to-treat, strengths and limitations, phase I-IV trials, number-needed-to-treat, CONSORT guidelines

Black HR, Crocitto MT. Number needed to treat: Solid science or a path to pernicious rationing? Am J Hypertens 11, 128S-134S, 1998. [link]
4/2 12 Short Quiz about classes 6-8, 10-11

**Topic: Treatment III (Liu)**
- Drop outs, compliance, stopping rules, interim analysis, data safety monitoring

**Readings:**

4/9 13 Topic: Studying cases (Schootman)
- Case series
- Case-control studies: methodology, biases, analysis

**Readings:**
- Chapter 6 – Risk: Looking backward

**Due:** Draft of Design and Methods sections of the study proposal to Barb Stabler bstadler@dom.wustl.edu (also include Specific Aims, Significance, Innovation sections)

4/16 14 Statistical methods in epidemiology (Schootman)
- Measures of disease occurrence, association, risk
- Calculating 95% confidence intervals
- Confounding, biological and statistical interaction, effect modification
- Multivariable analysis, adjustment, model building

**Readings:** Grobbee DE & Hoes AW: Chapter 12 - Clinical epidemiological data analysis. [link on Google books](#)

4/23 15 Topic: Bias Analysis (Schootman)
- Overview of bias analysis
- Examination of selection bias
- Unmeasured confounding
- Misclassification bias

**Readings:** Lash chapters 2-3 (uploaded onto Blackboard)

4/30 16 Due: Final study proposal to Barb Stabler bstadler@dom.wustl.edu