Epidemiology for Clinical Research

U88 HCS 588 / M17 CLNV 588

Spring, 2009

Time: Wednesday, 4:30 to 7:00 p.m.

Location: Holden Auditorium, 1st Floor Farrell Learning and Teaching Ctr

Instructors: Mario Schootman, Ph.D. (course master)
Associate Professor of Medicine
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Email: mschootm@wustl.edu

Anjali Deshpande, Ph.D., M.P.H.
Assistant Professor of Medicine
Office: 286-0148
Email: adeshpan@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: Beth Beato (bbeato@wustl.edu)

Target audience: Clinicians (house officers, fellows, and junior faculty) interested in conducting clinical research, those enrolled in the Masters of Science in Clinical Investigation program, Health Care Services program, or Genetic Epidemiology Master of Science 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.

- 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 Instructor:

- 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 with us 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 us 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 that are not available online will be handed out during class or emailed. 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%), a short quiz (20%), and a 4-page study proposal (60%). 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 reviews that are not completed independently by the student will not be graded.

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

1. 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 Beth Beato (bbeato@wustl.edu).

The 4-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 (about ½ page), B) Background and Significance (about ½ page), C) Preliminary Studies (not required), and D) Research Design and Methods (about 3 pages). 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 Beth Beato (bbeato@wustl.edu) of:
- Specific Aims, Background and Significance (due 3/25/2009)
- Research Design and Methods section (due 4/15/2009)
The final written proposal of the Specific Aims, Background and Significance, and the Research Design and Methods sections, due 5/4/2009, will constitute 50% of the final grade (100 points). We will provide you with comments throughout the course 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. The student is encouraged to select a topic that relates to his or her area of interest. Late submissions will not be accepted, and proposals that are not completed independently by the student will not be graded.

The student's 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) for all students who complete the course.

**Grading scale**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Range</th>
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<tbody>
<tr>
<td>A</td>
<td>95 – 100%</td>
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<tr>
<td>A-</td>
<td>91 – 94.9%</td>
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<tr>
<td>B+</td>
<td>87 – 90.9%</td>
</tr>
<tr>
<td>B</td>
<td>84 – 86.9%</td>
</tr>
<tr>
<td>B-</td>
<td>80 – 83.9%</td>
</tr>
<tr>
<td>C+</td>
<td>76 – 79.9%</td>
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<tr>
<td>C</td>
<td>73 – 75.9%</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 (Schootman &amp; Deshpande)</th>
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</thead>
<tbody>
<tr>
<td>1/14</td>
<td>1</td>
<td>Course overview</td>
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<tr>
<td></td>
<td></td>
<td>Evidence-based medicine, clinical guidelines</td>
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<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: Assessing abnormality (Schootman)</th>
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<tbody>
<tr>
<td>1/21</td>
<td>2</td>
<td>Clinical measurement (types of data)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Performance of measurement: validity, reliability, kappa</td>
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<tr>
<td></td>
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<td>Statistical distributions of data</td>
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</tbody>
</table>

**Readings:** Chapter 2 – Abnormality  

<table>
<thead>
<tr>
<th>Date</th>
<th>Week</th>
<th>Topic: Measurement in epidemiology (Deshpande)</th>
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<tbody>
<tr>
<td>1/28</td>
<td>3</td>
<td>Variation</td>
</tr>
<tr>
<td></td>
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<td>Methods of data collection</td>
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<tr>
<td></td>
<td></td>
<td>Reducing measurement errors</td>
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</tbody>
</table>

**Readings:**  
Scheuren F. What is a survey. Chapter 6 - Designing a questionnaire, 2004. [link](#)

<table>
<thead>
<tr>
<th>Date</th>
<th>Week</th>
<th>Topic: Determining a diagnosis (Deshpande)</th>
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<tbody>
<tr>
<td>2/4</td>
<td>4</td>
<td>Sensitivity &amp; Specificity</td>
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<td></td>
<td></td>
<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>
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</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: Frequency of disease</th>
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<tbody>
<tr>
<td>2/11</td>
<td>5</td>
<td>Incidence &amp; prevalence</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Numerator issues: visits vs. patients</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Denominator issues: who is at risk</td>
</tr>
</tbody>
</table>

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

**Due:** Exercises about Diagnosis (2/4 class)
2/18

6

Topic: Risk of disease (Deshpande)
- Definition of risk factors
- Recognizing risk
- Uses of risk
- Comparing risk

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 (2/11 class)

2/25

7

Topic: Chance and statistical testing (Deshpande)
- Hypothesis testing (alpha, beta, power)
- Types of statistical tests
- Point estimates & confidence intervals
- Multivariable models

Readings: Chapter 10 – Chance

Due: Exercises about Risk (2/18 class)

3/4

8

Short Quiz about classes 5-7 (Schootman)

Topic: Cohort studies
- Continuation of Feb. 18 class


3/11

Spring break – no classes

3/18

9

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

Readings: Chapter 7 – Prognosis

3/25

10

Topic: Treatment (Deshpande)
- 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

Due: Draft of Specific Aims, Background & Significance sections of the study to Beth Beato: bbeato@wustl.edu
**4/1 11 Topic: Treatment (continued from 3/25) (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](#)


**4/8 12 Topic: Prevention (Deshpande)**
- Levels of prevention and screening (primary, secondary, tertiary)
- Screening & effectiveness: number of cases to be detected, number needed to be screened
- Sensitivity
- Biases

*Readings:* Chapter 9 – Prevention

**4/15 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 Beth Beato: bbeato@wustl.edu (also include Specific Aims, Background & Significance sections)

**4/22 14 Topic: To be determined**

**4/29 15 Topic: Cause & Summing up (Schootman)**
- Concepts of cause & establishing cause
- Weighing the evidence
- Judging studies
- Systematic review

*Readings:* Chapter 11 - Cause
Chapter 12 – Systematic reviews


*Due:* Exercises about Studying Cases (4/15)

**5/4 Due:** Final study proposal to Beth Beato: bbeato@wustl.edu