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Pre-/Co-requisites: Biostatistics, Epidemiology Methods, or permission of the instructor.

Course credits: 3  
Class hours: Spring 2012 to be assigned.

The enrollment of the course is limited, with graduate students having priority over advanced professional students.

Course Description
Pharmacoepidemiology and the Science of Safety play an important role in drug safety, drug effectiveness, and outcome assessment and regulatory decision-making. Although randomized clinical trials are considered the recommended approach to testing drug efficacy, often, drug safety issues are addressed with observational study designs, including patient follow-up studies, case-control and cohort designs.

The advance of clinical databases facilitates the conduct of large-scale cohort studies and nested case-control studies. Because the economic impact of pharmacoepidemiology studies are significant, sound methodological approaches are needed.

The US FDA introduced the concept of Therapeutic Risk Management. Therapeutic Risk Management allows restricted marketing of designated drugs so that a positive benefit/risk balance is maintained.

Course Objectives
The Behavioral Outcome Objectives for the course are:
1.) At completion of the course the student will be able to recognize drug safety issues and develop appropriate strategies to optimize the benefit/risk ratio of the product involved.
2.) Is expected to be able to write a study protocol in a clear, simple, and parsimonious manner, responsive to the question at hand, and proposing a methodological sound design.

Course texts and readings
Recommended Texts:
Hartzema AG, Tilson HH and Chen A. *Pharmacoepidemiology and Therapeutic Risk Management*. Harvey Whitney Press, Inc. Cincinnati 2008 (Your instructor for this course, does not receive any royalty from the book.)


**Useful websites:**
Food and drug Administration(FDA) [www.fda.gov](http://www.fda.gov)
Pharmaceutical Research and Manufacturers Administration (PhRMA)[http://www.phrma.org/](http://www.phrma.org/)
Observational Medical Outcomes Partners (OMOP)[http://omop.fnih.org/?q=node/122](http://omop.fnih.org/?q=node/122)
National Institute for Clinical Excellence (NICE) - [www.nice.org.uk](http://www.nice.org.uk)
COCHRANE GROUP - [www.cochrane.org](http://www.cochrane.org)
Website Searches multiple websites for listing, trial results and trial news [http://searchclinicaltrials.org/](http://searchclinicaltrials.org/)
Assignments, exams, and grading system
Required for the course are:

*Group Discussions and Assignments*--- Current drug safety issue. Any alternate week a case study of an actual drug safety issue will be assigned. The purpose of the case studies is to help students relate materials taught in lectures and discussed in the problem-based learning group sessions to an important issue in drug safety. Each student is required to hand-in a one page summary of the major issues involving this case. (20 points)

*Midterm Exam* --- The midterm exam covers the course materials including the lectures, readings and group assignments covered prior to the exam. (20 points)

*Final Exam* --- The final exam covers the lecture materials and the readings as well as the group activities planned throughout the course. (30 points)

*Protocol*--- A one-page outline of the topics should be submitted in the second month of the course for approval, the format of the protocol should conform to the NIH guidelines for R-01 grants" as posted on the internet. It should include the sections: abstract; aims, background; preliminary studies; and methodology. The methodology should include variable definitions, level of measurement; power analysis, research design; and a data analysis plan. The length of protocol should not exceed 10 pages. This protocol is due end the end of finals week. (30 points)

*Late Assignment Policy*
Assignments are due at the beginning of the stated class period. The final manuscript is due at 5.00PM on the indicated date. Late papers will receive either: (1) the class mean if the actual score is the mean or higher or (2) the actual score if the score is lower than the class mean. Delays due to unforeseen and distressing events (serious illness, a death in the family, computer hardware/software failure, etc.) will be treated on a case-by-case basis by the course coordinator.

*Attendance*
Attendance is mandatory. Please observe the courtesy of emailing your instructor at least 24 hours in advance if you are unable to attend class due to extenuating circumstances. Make-up exams will be given at the instructor’s discretion.

Grading system
A total of 100 points are possible in this course. Weights will be assigned to the required assignments in the following manner:

<table>
<thead>
<tr>
<th>Assignment Type</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group/Class Participation/Contribution</td>
<td>20% (or 20 points)</td>
</tr>
<tr>
<td>Midterm</td>
<td>20% (or 20 points)</td>
</tr>
<tr>
<td>Final exam</td>
<td>30% (or 30 points)</td>
</tr>
</tbody>
</table>
Protocol --- 30% (or 30 points)

Your scores from each of the assignments will be combined to calculate your total score. Final grades will be assigned according to the following scheme:

95-100 = A
90-94 = A-
86-89 = B+
83-85 = B
80-82 = B-
76-79 = C+
73-75 = C
70-72 = C-
66-69 = D+
63-68 = D
60-62 = D-
<60 = E

Student responsibility and participation
Students are responsible for preparing all assigned readings in advance of the lecture period. Readings should be brought to class on the day they will be discussed. Students also are encouraged to bring to the attention of the instructor and other class members relevant items of interest.

Academic Dishonesty. Familiarize yourself with the University's policy regarding academic dishonesty. See the Statements regarding the Student Conduct Code in the 2008-2009 Graduate Catalog. This policy will be strictly enforced. The University's conduct regulations are available on the Internet at http://oss.ufl.edu/stg/. Please note that the course instructors will closely examine your paper submissions for plagiarism. Please review your notes from our orientations session about academic dishonesty and make sure that you understand the steps needed to avoid plagiarism.

Accommodations for Students with Disabilities. Students requesting classroom accommodation must first register with the dean of Students Office. The Dean of Students Office will provide documentation to the student who must then provide this documentation to the Instructor when requesting accommodation.

COURSE SCHEDULE

Lecture 1
Course overview; introduction of terminology; review of major methodologies.
Readings:
1) AG Hartzema, HH Tilson, KA Chan. The Contribution of Pharmacoepidemiology to the Study of Drug Uses and Effects, and Risk Management.
2) Robert F. Reynolds Epidemiology in Drug Development


January 16
Reflection: Maarten Luther King Day

Lecture 2
Drug approval process; PDUFA; NDA; BLA: ANDA; branded versus generics; biological


PDUFA IV
http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/default.htm

Lecture 3
MedWatch; EMEA; Pharmacovigilance; Spontaneous Reporting Systems;
Ahmad SR, Quellet_Hellstrom, McClosky CA. Pharmacovigilance. In same
Shakir SAW. Prescription Event Monitoring in the United Kingdom. In same

Assignment: Please write a 1-2 page summary of your responses to the questions posed in the Sitaxsentan withdrawal case for hand-in in the class; be also prepared to participate in the class discussion.

Lecture 4
Data Mining
Bate A., Edwards IR. Data Mining Techniques in Pharmacovigilance. In same

Lecture 5
Drug Utilization studies
Wettermark B. Drug Utilization research. Chapter 7. In same
Haaijer-Ruskamp FM Prescribing Quality Indicators. Chapter 8. In same.

Lecture 6
Safety Trials / Cohort Studies


See readings in course content.

**Lecture 7**  
Case-control, nested case-control studies; cross-over designs studies and matching in pharmacoepidemiology


**SPRING BREAK**

**Lecture 8**  
Misclassification / Biases


**Lecture 9**  
Midterm Exam

**Lecture 10**  
Confounding and Propensity scores

Schneeweiss S. Confounding. Chapter 11. In same.

**Lecture 11**  
Large Data Base Research  
Student discussion of data source selection


**Lecture 12**  
*Patient Registries*


**Lecture 13 (last day of classes)**
Therapeutic Risk Management Strategies
Evaluation of Therapeutic Risk Management Strategies/ Good Pharmacoepidemiology Practices


Final Exams: April 28, 30, May 1-4

Protocols are due at Last day of class 2012 at 5.00PM in an electronic format to Hartzema@ufl.edu. Use as filename (insert your last name)protocol, example hartzemaprotocol.doc. No pdf files as they cannot be marked up that easily.