

# Research in Pharmacoepidemiology & Drug Safety

Course No.: 25-PADM-672

Graduate-Level Course

Fall Quarter 2005

**Pre-requisite:** PharmD students and MS/PhD graduate students

**Credits:** 3 Quarter Hours

**Time meeting:** Tuesday 12pm – 1:30pm;  
Thursday 12pm – 1:30pm

**Classroom:** Classroom 231.

**Course Coordinator:**

**Jeff J. Guo, BPharm, PhD**

Assistant Professor of Pharmacoeconomics and Pharmacoepidemiology

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Other Instructors:

Pamela Heaton, RPh, PhD

Assistant Professor of Pharmacy Practice

Invited Speakers (to be named)

**Textbooks:**

Hartzema AG, Porta MS, Tilson HH. Introduction to Pharmaco-Epidemiology. Harvey Whitney Books.

Strom BL. Edited. Pharmacoepidemiology. Wiley Publisher.

Elizabeth Andrew (edited), Pharmacovigilance and Drug Safety. 2003.

Chris J. Boxtel, Budiono Santoso, Ralph Edwards. Drug Benefits and Risks. International Textbook of Clinical Pharmacology. 2003

**Course Brief Description:**

Research applications for post-marketing drug safety surveillance. Focus will be on pharmacoepidemiologic research protocol development, description of health care databases used for research, and pharmacoepidemiology contribution to pharmacy practices.

**Course Mission**

The goal of the course is to introduce pharmacoepidemiology and drug safety and research application for post-marketing drug safety surveillance. The course will describe how to develop a

research protocol and conduct a research, describe various health care data sources used for research, and discuss how pharmacoepidemiology contribute to pharmacy practice, such as, drug utilization review, assessment of drug therapy, and adverse drug reaction monitoring. A series of case studies from thalidomide to cisapride to cerivastatin will be also discussed in class. Students can have a better understanding of Pharmacoepidemiologic research, drug safety regulatory, pregnancy registry, and risk management.

### **Educational Outcomes**

This course contributes to the achievement of the following outcomes of the Center for the Advancement of Pharmaceutical Education (CAPE): Provide Pharmaceutical Care, Manage Medication Use Systems, Promote Public Health, Provide Drug Information and Education, Thinking, and Communication.

### **Course Objectives**

The objectives of this course consist of three components: Knowledge, Skill, and Values/Attitude.

#### Knowledge

Upon completion of this course, the successful graduate students or Doctoral of Pharmacy Candidate will be able to:

1. Understand basic concepts of pharmacoepidemiology:  
(Cognitive: calculation and comprehension)
  - Prevalence rate,
  - Incidence rate,
  - Relative risk and odds ratio, and
  - Index date of diagnosis and drug therapy.
  
2. Distinguish and interpret Pharmacoepidemiologic research methods:  
(Cognitive: comprehension and evaluation)
  - Observational database study vs. experimental clinical trials,
  - Case report,
  - Case-control,
  - Cohort study, and
  - Meta-analysis.
  
3. Explain development of research protocol and conduct a research:  
(Cognitive: comprehension)
  - Phase IV clinical trials and related drug safety surveillance
  - Phase IV clinical study design and operational strategies
  - Characteristics of health care databases (observational health care databases),
  
4. Discuss drug safety regulatory and monitoring system:  
(Cognitive: comprehension)
  - Overview of post-marketing drug surveillance and drug safety,
  - FDA and EMEA Risk Management Guidance,
  - Drug safety regulatory and monitoring system,
  - Drug utilization review (OBRA'90),
  - Pregnancy registry,
  - Off-label use of medications

- Vaccine safety, etc.
5. Discuss Pharmacovigilance in drug development
- Overview new drug application filing/approval process related to drug safety assessment
  - Explain packaging and labeling related to drug safety figures
  - Describe serious adverse event reporting requirements and guidelines (ICH), Good Clinical Practice, and regulatory reporting requirements.
  - Demonstrate FDA Severe Adverse Event (SAE) reporting forms- MedWatch and CIOMS, and SAE reporting process & challenges
  - Introduction to MedDRA (definition, structure, coding system, and term selection),
  - Describe medical monitoring for industry, and ADR signal detection in Pharmacovigilance.
6. Evaluate drug safety case studies and policy implications based on the medical and pharmacy literature.  
(Cognitive: evaluation)
- Thalidomide
  - Rotavirus vaccine
  - Troglitazone (Rezulin®) (*Drug-induced hepatotoxicity*),
  - “Fen-phen”
  - estrogen replacement therapy
  - cerivastatin (Baycol®)
  - cisapride (*Contraindicated medication use*)
  - alosetron, etc.
7. **How to develop a research protocol and conduct a research [for advanced level only].**
- **Review the major contents of a research proposal, including:**
  - **background,**
  - **research hypothesis,**
  - **specific aim (purpose of study),**
  - **methodology**
  - **data analysis**
  - **Draft a research protocol as a project for practice.**

#### Skills

At the end of this course, the student will be able to:

- Apply the foregoing epidemiology methods and concepts in analyzing and determining drug-related problem and drug safety surveillance.
- Apply the knowledge of drug therapy and epidemiology in Pharmacoepidemiologic research and pharmacy practice.
- Interpret and understand the medical and pharmaceutical literature related to adverse drug reaction, drug safety, and pharmacovigilance.

#### Values and Attitudes

At the end of this course, the student will tend to:

- Accept the value of pharmacoepidemiologic research, critical thinking applied to pharmacy practice.
- Regard observational database analyses and drug regulatory implications as fundamentals to understand and improve pharmacy management and practice.

### **Educational Methods**

Course material is presented in interactive lectures with various demonstrations, examples, and discussions.

Each topic will have assigned reading from the text. Students are expected to prepare by reading the chapter or material prior to the class. Faculty may assign additional readings such as text book chapters and journal articles.

### **Educational Assessments**

The professional and general educational outcomes that will be evaluated in this course include:

- 1) Evaluate and interpret Pharmacoepidemiologic research analyses to improve pharmacy management and practices;
- 2) Assess critical thinking skills on drug regulatory and policy issues using case studies.
- 3) Students will complete one project individually on topic of Pharmacoepidemiology research, product specific case study, or drug safety regulatory issues based on published literature, then, present it in class. Faculty will evaluate their project papers and presentations.

### **Examinations and Grades:**

1. Ethical standards: The University Student Code of Conduct and the code of Ethics of the American Pharmaceutical Association will be in effect for this course. A candidate found in violation of this section will receive a score of zero (0%) for the work in question and will be reported to the Dean's office.
2. Disability: Any candidate with a disability that may potentially interfere with his/her performance in this course should contact the instructor during the first week of class.
3. Course Withdrawal: The University policy on withdrawal from this course will be followed.
4. Missed exams or assignments: Any examination or assignment can only be made up with the prior approval of the instructor.
5. Incomplete grades: Incomplete grades will only be given with the prior approval of the instructor.
6. Criteria for letter grades: Final grades will be assigned in compliance with the grading policies published by the Office of the Registrar, Student Records. No incomplete grade will be given without the course coordinator's approval.

<u>Percentage</u>	<u>Letter Grade</u>
90 – 100	A
86 – 89	B+
80 – 85	B
76 – 79	C+
70 – 75	C
≤ 69	F

Written final exam: 40%  
 Class attending and discussion: 20%  
 Quarter project (case study): 40% (with presentation).

### Tentative Course Schedule

<b>Week</b>	<b>Date</b>	<b>Topics</b>
1	Sept 22 (Thursday)	<b>Course Objectives, Syllabus</b> Introduction to pharmacoepidemiology Research in Pharmacoepidemiology  PBS frontline show “Dangerous prescription drugs”
2	Oct wk(1)	Pharmacoepidemiology: Prevalence, incidence, odd ratios Research Designs (case-control, nested case-control, cohort study, etc.)
3	Oct wk(2)	Drug utilization (denominator) Drug utilization review for Pharmacy Practice Physician prescribing behavior & Pharmacist dispensing behavior Characteristics for observational databases Use of health databases for research in pharmacoepidemiology and/or Pharmacovigilance.
4	Oct wk(3)	Drug safety consideration in drug development: New Drug Application filing/approval process related to drug safety assessment; Packaging and labeling related to drug safety figures; Phase IV clinical trials and related drug safety surveillance;  <b>Project assignment (out)</b>
5	Oct wk(4) Dr. Heaton	Hepatotoxic events associated with medication use and research applications, FDA/PhRMA White Paper of drug-induced hepatotoxicity (Hepatotoxic drug study, such as, Rezulin/glitazones case study)
6	Nov (1) (invited)	International Conference on Harmonization (ICH); Eudravigilance and EMEA Guidelines for Risk Management

	speaker)	Systems. FDA Severe Adverse Event (SAE) reporting forms- MedWatch and CIOMS <b>Drug safety and outcome research: Industry-perspective</b>
7	Nov (2)	FDA Risk Management & Post-marketing Surveillance European Risk Management Guideline (example: cisapride, isotretinoin, Lotronex case study)
8	Nov (3)	FDA Guideline for Industry to establish pregnancy exposure and registries Pregnancy registry and birth defects. (example: Child-bearing-age women medication use)
9	Nov (4)	Off-label use of medication: FDA regulation and industry practices (example: atypical antipsychotic medication & others) <b>Student presentation (1)</b>
10	Dec (1)	Development of research protocol and conduct a research, Case studies: Pancreatitis in HIV patients, Diabetes in bipolar patients <b>Student presentation (2)</b> <b>Written final exam (out)</b>
11	Dec (2)	written final exam (Due)