This course adheres to the items listed in the College of Pharmacy Central Syllabus: https://docs.google.com/a/umn.edu/document/d/1artQ5e1rbzxe8IETWo7BE8k8snZAEgMMZ_QcW8yJ-II/edit?pli=1

Meeting Times & Locations

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<tr>
<th>Day</th>
<th>Time</th>
<th>Duluth Room</th>
<th>Twin Cities Room</th>
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<td>Monday</td>
<td>3:30 – 5:30pm</td>
<td>LSci 205A</td>
<td>WDH-7-173</td>
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Course Website: http://canvas.umn.edu

Instructional Team

If you need assistance with the course, contact one of the Teaching Assistants.

Technology Help, Duluth: 218-726-8847 itsshelp@d.umn.edu
Technology Help, Twin Cities: 612-301-4357 help@umn.edu

Faculty Office Hours: by appointment

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Email: zhan1386@umn.edu
Course Description

Course content: Pharmacoepidemiology is the study of the uses and effects of drugs in patient populations. The science of pharmacoepidemiology borrows from pharmacology and epidemiology. This course will introduce students to the field of pharmacoepidemiology including study methodology, relevant statistics, data sources, measurement of treatments and outcomes, sources of bias and control of confounding, techniques to reduce bias and confounding, survival analysis and regression techniques, interpretation of results, and drug safety surveillance and risk management.

Course format: This course is mainly lecture-based. Students are expected to prepare for each class, as debate and discussion of various concepts presented in class will take place. Near the end of the course, students will be expected to use information gained throughout the course to compose a written critique of a pharmacoepidemiology study and then orally present their critique in class.

Prerequisites

- SAPh, ECP or SPH Graduate student or 2nd, 3rd or 4th year pharmacy student. First year students may enroll with permission of course directors. First year students will need to show that they have had previous relevant courses in epidemiology, or public health.

Requirements

Course Materials

Required


Optional (for additional perspective)

- Epidemiology, Fifth edition (Available online from Biomed Library)
- Medical Epidemiology 2005 (Available online from Biomed Library)

Computer / Technology Requirements

- The University of Minnesota computer requirements are listed here: [http://www1.umn.edu/moodle/start/technical.html](http://www1.umn.edu/moodle/start/technical.html)
Attendance Policy
Students are expected to attend every class for which they are registered. Students are expected to attend classes on the campus where they are enrolled. Instructors may choose to take attendance. When a student is unable to attend a class for health or family reasons, the instructor must be informed in advance.

Goals & Objectives

Course Goals
Main course concepts:

The aim of the course is to help students acquire a basic understanding of the concepts and practice of pharmacoepidemiology.

Learning Objectives

1. Discuss the concept of pharmacoepidemiology
2. Compare and contrast typical pharmacoepidemiologic study designs and explain their strengths and weaknesses
3. Discuss the roles that pharmacoepidemiology studies have had in the past regarding drug use and health outcomes and the future roles that pharmacoepidemiology can play in drug safety surveillance and comparative drug effectiveness and safety
4. Debate the threats to validity that are possible in pharmacoepidemiology studies and the variety of solutions available to avert or control for these threats
5. Understand the use of regression and matching techniques used in pharmacoepidemiologic research
6. Using the information provided by the text, lectures, and assigned readings, compose a written critique of a recently-published pharmacoepidemiology study and orally present this critique in class
Assessments and Grading

Assignments and learning activities

Graded Assessments

- Class participation/attendance (20%)
- Midterm exam – multiple choice, short answer/essay (40%)
- End-of-semester written critique of journal article (20%)
- End-of-semester oral presentation of journal article (same as above) [slides, 15-20 minutes] (20%)

The midterm exam, written critique, presentation and class participation/attendance will be graded by the course directors.

Thorough reading of assigned readings prior to class, attendance and class participation is expected. The student will take the midterm exam, select one study from recently-published pharmacoepidemiology studies, compose a written critique of the study and orally present this critique in class. You will be expected to have prepared for each class and completed any homework assignments prior to class. Class participation points will be assigned based on course director’s assessment of your preparedness for class which will be assessed through your class participation.

Course Letter Grades

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<th>B+</th>
<th>B</th>
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<td>70-72</td>
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Late paper or presentation material submission

Late papers or late presentation materials will be assessed a penalty. Your grade will be reduced by 5% for each day that your materials are late.

Re-grade Policy:

There will be no re-grades in this class.

Minimum Passing Level: C-
## Schedule

| Week 1 | Monday  
| Sept 9 |
| --- | --- |
| **What is Pharmacoepidemiology? Wendy St. Peter** | - Distinction between pharmacoepidemiology, epidemiology, and clinical pharmacology  
- Historical Background  
- Potential Contributions |
| **Required Reading** |  
**Textbook of Pharmacoepidemiology** | - Chapter 1 (pages 3-16)  
- Chapter 4 (pages 40-41) |
| **Basic Principles of Statistics and Application to Pharmacoepidemiology studies Wendy St. Peter** | - Causality, associations and strength of evidence  
- Hypothesis testing |
| **Required Reading (note: find a reading below that you can understand for each topic above)** |  
**Textbook of Pharmacoepidemiology** | - Chapter 2 (pages 17-18, 20-21-Causality, associations, strength of evidence)  
- Chapter 3 (pages 30-33, Sample size, Type 1 and 2 errors, power)  
- Chapter 5 (pages 57-58, Hypothesis testing) |
| **Essentials of Clinical Research (ECR)** | - Chapter 16 (pages 357-359-Causality)  
- Chapter 2 (pages 11-21, Hypothesis testing, Type 1 and 2 errors, strength of evidence)  
- Chapter 15 (pages 327-344; Hypothesis testing, statistical power, sample size, Type 1 and 2 errors)  
- Chapter 18: pages 373-383, Hypothesis testing |

| Week 2 | Monday  
| Sept 16 |
| --- | --- |
| **Pharmacoepidemiologic Study Designs Wendy St. Peter** | - Basic features, strengths and weaknesses of pharmacoepidemiology study designs  
  - Case reports and case series  
  - Ecological studies  
  - Cross-sectional studies  
  - Case-control studies  
  - Nested-case control studies |
Homework

1) Describe basic differences between cross-sectional study, case-control study and cohort study, with 1 strength and 1 weakness for each of these 3 study designs.

2) Which of the study designs above, if any, could be used to determine the causal association between a drug and an outcome (such as mortality)?

Required Reading:

Pharmacoepidemiology Text
- Chapter 2 (pages 22-29)

Essentials of Clinical Research (ECR)
- Chapter 2 (pages 21--Strength of Relationships to page 31)

Other Required Readings
- Etminan M & Samii A. Pharmacoepidemiology I: A review of pharmacoepidemologic study designs. Pharmacotherapy 2004;24:964. Read pages 964-966 (don’t read section on case-crossover studies) and 968 (confounding bias only).
- Etminan M. Pharmacoepidemiology II: the nested case-control study-a novel approach in pharmacoepidemiologic research. Pharmacotherapy 2004;1105-1109.

Bring a hardcopy to class or be able to access electronically in class for an exercise
- Block GA. Cinacalcet hydrochloride treatment significantly improves all-cause and cardiovascular survival in a large cohort of hemodialysis patients. Kidney International 2010;78:578-89.

Week 3

Sources of Data and Data Extraction

Cathy Starner and Pat Gleason
- Administrative datasets (Medicare, commercial)
- Medical records (Structured data, Unstructured Data)
- Critical assessment of data sources
- Limitation of data sources

Required Reading: Pharmacoepidemiology Text
- Chapter 8 (Pages 118-122)
- Chapter 9 (pages 123-143 & 152-177) with a focus on the strengths and weaknesses sections.

Measurement of treatments and outcomes
Cathy Starner and Pat Gleason
- Baseline disease status
## Required Reading: Textbook of Pharmacoepidemiology

- Chapter 6 (Pages 65-67)
- Chapter 20 (Pages 314-322)
- PQA Adherence Measure Specifications on Proportion of Days Covered (PDC) (see class folder)
- PDC Measure Calculation (see class folder)

### Homework:
Use pharmacy claims data extract for sample members (see ‘Sample members for PDC calculation’ excel spreadsheet in class folder) to calculate adherence using proportions of days covered (PDC) calculation for statins for members 1 and 5. Feel free to try calculations for other members as well for extra practice.

### Week 4

#### Monday

**Sept 30**

**Bias, Confounding and Control of confounding, Validity**

**Holly Epperly Budlong**

- **Validity**
  - Face validity
  - Internal validity
  - External validity

- **Types of bias**
  - Selection bias
  - Indication bias
  - Measurement bias
  - Information bias
  - Misclassification (disease or exposure)
  - Mortality bias
  - Lead time bias

### Homework:
Choose 1 type of bias described in the required reading (Delgado-Rodriguez article) that is most interesting to you and use available class or online resources to further describe the type of bias and implications to study results.

*Write up your answer to the homework and please email your answer to Dr. Budlong by 12 midnight on Saturday September 28th.*

### Required Reading:


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<tr>
<th>3. Drug effectiveness versus efficacy</th>
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<td>o Treatment effect heterogeneity</td>
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<td>4. Drug exposure</td>
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<td>o Intent-to-treat versus as-treated</td>
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<td>o First fill, days’ supply, adherence, persistence</td>
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<td>5. Outcomes</td>
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<td>o Clinical outcomes</td>
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Monday Oct 7

**Introduction to Statistics, and Regression Techniques used in Pharmacoepidemiology**

**Eric Weinhandl**

- Statistical power and sample size, Type 1 and 2 errors, p-values
- Means (SD), medians (25th-75th percentiles) and standardized differences
  - Example: Assessing patient characteristic tables
- Regression Modeling Techniques
  - Logistic regression
  - Linear regression
  - Gamma regression (briefly introduce)
  - Poisson regression (briefly introduce)
  - Cox regression (briefly introduce)

- Difference between OR and RR and calculations for OR and RR
- What is HR and how it is different than RR
- What is the difference between relative risk, risk ratio, and rate ratio
- Interpretation of results (RR, HR, absolute risk reduction, numbers needed to treat)

**Required reading:** TBA

**Homework:** TBA

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**Week 6**

Monday Oct 14

**Analytic Approaches for Improved Confounding Control**

**Eric Weinhandl**

- Difference in difference approach for confounding control
- Propensity scores
- Instrumental variables (brief introduction)

**Homework:** Read required readings below and answer the following questions

1. What types of variables should and should not be included in propensity score models?

2. Explain why p-values should not be used to diagnose the quality of matching, and describe what methodology should instead be used.

3. What is the definition of an instrumental variable? (That is, what are the conditions that define an instrumental variable?)

**Required Reading:**

- Glynn RJ et al. Indications for propensity scores and review of their use in pharmacoepidemiology. Basic and Clinical Pharmacology and Toxicology 2006;98:253-259
- Persson F et al. Dapagliflozin compared to DPP-4 inhibitors is associated with lower risk for CV events and all-cause mortality in type 2 DM patients (CVD-REAL Nordic): a multinational observational study. (in press) and Appendices S1 and S2.
| Monday Oct 21 | **Selected Pharmacoepidemiology Applications: Drug Utilization, Comparative Effectiveness and New User Design**  
Wendy St. Peter |
|---|---|
| | o Review expectations for article review and presentation (course directors)  
| | o Drug utilization studies  
| | o Comparative effectiveness and safety research (observational studies)  
| | o Active comparator new user design |

**Homework TBD:**

1. Review the 'Pharmacoepidemiology Article Review and Presentation Evaluation Form' and come to class with questions for course directors  
2. Read Coding Systems by Optum, RxNorm Overview, Generic Product Identifier  
   Q1: Why are hierarchical numerical coding systems used to categorize drugs within databases?  
   Q2: What are the similarities and differences between NDC, GPI and RXNorm drug coding?  
   Q1: In what direction does confounding by indication bias (selection bias) change the effect estimate? (i.e. exaggerate positive drug effects or exaggerate safety effects?)  
   Q2: How does an active comparator new user design reduce selection bias?  
   Q3: In which direction does 'healthy initiator effect' or 'healthy user effect' change the effect estimate? (i.e. exaggerate positive drug effects or exaggerate safety effects?)  
   Q4: How does an active comparator new user design reduce healthy user (initiator) effect?  

**Bring or have access to these articles for in-class use (see class folder)**

   b. Yusuf AA. CE of calcium acetate and sevelamer on clinical outcomes in elderly HD patients enrolled in Medicare Part D. AJKD 2014.
<table>
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<th>Week 8</th>
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<td><strong>Monday Oct 28</strong></td>
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**Write up your answer to the homework and please email your answer to Dr. Budlong by 12 midnight on Saturday October 26th.**

**Required Reading:** Textbook of Pharmacoepidemiology

- Chapter 22 (pages 370-378, 384-392)

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**Homework:** Read the Kadra A article and VassarStats tutorial (below) and answer the questions.

- Q1: Why do we need Kaplan-Meier estimate?
- Q2: Use the tool from the VassarStats website to calculate the example in Figure 1 in the Kadra A. article.

**Required Reading:**

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| **Monday Nov 18** | **Selected Pharmacoepidemiology Applications—Systematic Review and Meta-analysis**  
**Arun Kumar**  
**Homework:** TBD |

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<th>Week 12</th>
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| **Monday Nov 25** | **Miscellaneous topics**  
**Eric Weinhandl and Wendy St. Peter**  
Topics may include some or all of the following  
12. Sensitivity analyses  
13. Update on FDA  
   a. Patient preferences  
   b. Patient-reported outcomes  
   c. Using claims data analyses to imitate clinical trials  
**Homework TBD:**  
1) Using required reading and other information learned in class, critique patient characteristic tables from Yusuf A. Comparative Effectiveness...Am J Kidney Dis 2014;64:95-103, Block GA. Cinacalcet hydrochloride..Kidney Int 2010;78:578-589, and Arnold ME. Impact of pharmacist intervention...Am J Health-Syst Pharm 2015;72(suppl 1);S36-42.  
   a. Should p-values be used to compare intervention and control groups?  
   b. When should mean +/- SD be used, when should median and IQR (25th-75th percentile) be used to represent central patient characteristics?  
   c. Explain value of using standardized differences to evaluate differences in patient characteristics.  
2) Using required reading, describe the advantage of using a "new user" study design over analysis of current or existing phosphate binder users in the article Yusuf A. Am J Kidney Dis 2014;64:95-103.  
3) Explain how difference-in-difference analyses resolve the problem inherent in before-after studies using Chertow GM. Epoetin alfa and outcomes in dialysis amid regulatory reform. JASN 2016;27.  
**Required Reading:**  
- Austin PC. Using the standardized difference to compare the prevalence of a binary variable between two groups in observational research. Communications in Statistics-Simulation and Computation, 2009;38:1228-34.  
- Textbook of Pharmacoepidemiology  
  - Page 325: New Users  
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<tr>
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<td>Oral Presentations and Course Evaluation</td>
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