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**Department of Pharmaceutical Outcomes & Policy**  
**University of Florida College of Pharmacy**  
**PHA 7807: Advanced Pharmacoepidemiology (3 credit hours)**  
**Fall 2021**

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**(Last update: 6.11. 2021)**

**Lead instructors**

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**Course Prerequisite:**

Two graduate-level statistics courses – STAT 6166 and 6167 (or equivalent) and three graduate-level courses—PHA 6717, PHA 6805, and PHA 6268 (or equivalent) or instructor permission

**Course Description:**

PHA7807 is a graduate-level course that is structured as an interactive discussion of selected readings based on topics in contemporary pharmacoepidemiology and the application of advanced pharmacoepidemiology techniques. Students will be required to prepare the assigned readings for the topic of the week in addition to other pertinent background material to support the readings. For example, the student is expected to deduce from the assigned reading, the particular technique being examined for the week and may need to cover papers beyond the assigned reading to gain a better understanding of the topic of interest. We will review current papers on proposed methodological advances to enable students to critically evaluate papers involving these approaches. Hands-on analytic exercises allow students to learn the implementation of these advanced methods.

*Instructional Methods:* The course will meet once a week for 2-3 hours in length depending on the scope of the materials. Each in-class session includes two sections: 1-2 hours lecture and 1-hour discussion that may involve critical appraisal of assigned article(s) or SAS programming skills of specific pharmacoepidemiological analytical approaches. Classes are lecture- and discussion-based.

## Learning Objectives:

At the completion of the course, students should be able to:

- Identify research questions that require advanced pharmacoepidemiologic methods to mitigate bias
- Implement advanced analytical techniques to avert complex bias
- Critically appraise advanced epidemiologic studies for methodological strengths, limitations and the choice of analytical procedures and interpretation of findings

**Final grades** will be assessed based on the following course requirements:

- **Summary note assignments (30 points):** Students are required to read 10 assigned articles (each is worth 3 points). For each article, students need to submit 1 page summarizing the core learning objectives.
- **Two programming assignments (20 points):** There will be 2 assignments requiring programming. Students will be required to conduct pre-specified analyses and submit them for evaluation.
- **Research project (30 points):** Each student is required to have a research project in which background and rationale, research questions, and data sources are well developed. Students are required to give 1 presentation and 2 summaries during the course.
  - **Midterm (before spring break):**
    - **Presentation:** Each student will give a 20-minute presentation to introduce his/her project, identify potential biases, and proposed an advanced pharmacoepidemiological method (s) that addresses the biases.
    - **1-page summary:** Students need to submit 1-page summarizing background, rationale, significance, research questions, and data sources.
  - **Final report:**
    - **2-page summary:** Students will provide a 2-page summary of the same project proposed in the midterm. One page updates the summary of the background, rationale/significance/research questions/data sources. The second page provides details on methods, including study design, sample selection, key exposure and outcomes, potential confounders, and the chosen advanced pharmacoepidemiological methods and analytic plans. The student will also discuss the pros and cons of the methods selected.
- **Class participation/discussion (20 points)**

**Assignment rules.** You are required to comply with the following rules:

- Your assignment must be turned in no later than 11:59 pm on the day it is due.
- Late homework assignments will NOT be accepted and received no credit unless you have formal proof of the exception (e.g., a written doctor note, a police ticket, etc.).
- No handwritten assignment. All assignments need to be submitted electronically through the online system (will be clarified at the beginning of the course).
- DO NOT COPY OTHERS' HOMEWORK. There is zero tolerance. The one who copies the homework will receive 0 points, and the one who is copied will get only 50% of the points that he/she should have received.

- Page size and margins: Use paper size no larger than standard letter paper size (8 ½" x 11"). Provide at least one-half-inch margins (½") - top, bottom, left, and right - for all pages. No applicant-supplied information can appear in the margins.

### **Grading Scale**

A:	93-100
A-:	90-92
B+:	87-89
B:	80-86
C+:	77-79
C:	73-76
C-:	70-72
D:	65-69
E:	<65

**Late assignment policy:** Assignments are due at the eve of the stated class period. The final exam is due at 5:00 PM 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.

**Student responsibility and participation:** Students are responsible for preparing all assigned readings before the lecture. Readings should be brought to class on the day they will be discussed. Students are also 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 orientation 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 an accommodation.

**Lecture schedule:**

Week	Date	Topic (Instructor)	Readings ( <b>assigned reading and assignment due</b> )
1	Aug 25, 2021	ICPE Virtual Annual Meeting (no class)	
2	Sep 1, 2021	<p>Overview epidemiological research and discuss sources of bias in defining exposures and outcomes (<b>Wei</b>)</p> <p>Survival analysis I (<b>Wei</b>)</p> <ul style="list-style-type: none"> <li>• Introduction</li> </ul>	<p>Kramer MS. Epidemiologic research design: an overview</p> <p>Kramer MS. Analytic Bias</p> <p>Dowd B and Town R. Does X really cause Y? Academy Health, 2002.</p>
3	Sep 8, 2021	<p>Survival analysis II (<b>Wei</b>)</p> <ul style="list-style-type: none"> <li>• Estimating and comparing survival curves</li> <li>• Estimating Cox- proportional hazards model</li> </ul> <p>* Programming assignment I</p>	<p>Ray WA, Chung CP, Murray KT, et al. Prescription of long-acting opioids and mortality in patients with chronic noncancer Pain. JAMA. 2016;315(22):2415- 2423 (<b>assigned 1 due on Sep 8, 2021</b>)</p>
4	Sep 15, 2021	<p>Survival analysis III (<b>Wei</b>)</p> <ul style="list-style-type: none"> <li>• Estimating non-proportional hazards: Cox model with an interaction term with time</li> <li>• Estimating survival data with time-varying variables</li> </ul>	<p>John B. Holcomb, Deborah J. del Junco, Erin E. Fox, et al. The Prospective, Observational, Multicenter, Major Trauma Transfusion (PROMMTT) Study: Comparative Effectiveness of a Time-Varying Treatment With Competing Risks. JAMA Surg. 2013;148(2):127-136. (<b>assigned 2 due on Sep 15, 2021</b>)</p> <p><b>*Programming assignment I due on Sep 15, 2021</b></p>
5	Sep 22, 2021	<p>Mitigating confounding: Survival Analysis IV (<b>Wei</b>)</p> <ul style="list-style-type: none"> <li>• Estimating survival data with competing risks</li> <li>• Estimating survival data with recurrent events</li> </ul>	<p>Edwards JK, Hester LL, Gokhale , Lesko CR. Methodologic Issues When Estimating Risks in Pharmacoepidemiology. Curr Epidemiol Rep. 2016 Dec;3(4):285-296. doi: 10.1007/s40471-016-0089-1. Epub 2016 Sep 13 (<b>assigned 3 due on Sep 22, 2021</b>)</p>
6	Sep 29, 2021	<p>Mitigating confounding: Propensity Score (PS) matching I (<b>Wei</b>)</p> <ul style="list-style-type: none"> <li>• Introduction</li> <li>• Estimating PS score</li> <li>• Forming PS matching sets</li> <li>• Assessing balance in characteristics</li> </ul>	<p>Brookhart MA, Schneeweiss S, Rothman KJ, et al. Variable selection for propensity score models. Am J Epidemiol 2006;163:1149-1156. (<b>assigned 4 due on Sep 29, 2021</b>)</p>
7	Oct 6, 2021	<p>Mitigating confounding: Propensity Score (PS) matching II (<b>Wei</b>)</p> <ul style="list-style-type: none"> <li>• Estimating treatment effect</li> <li>• PS methods: matching, stratification, weighting, and covariate adjustment using PS</li> </ul>	<p>Stukel TA, Fisher ES, Wennberg DE, et al. Analysis of observational studies in the presence of treatment selection bias: effects of invasive cardiac management on AMI survival using propensity score and instrumental variable methods. JAMA. 2007 Jan 17;297(3):278-85. (<b>assigned 5 due on Oct 6, 2021</b>)</p>

		<ul style="list-style-type: none"> <li>Stabilized IPTW and Standardized mortality ratio</li> </ul> <p>*Programming assignment II</p>	
8	Oct 13, 2021	<p>Mitigating confounding: Propensity Score (PS) matching III (<b>Wei</b>)</p> <ul style="list-style-type: none"> <li>Sensitivity analysis</li> <li>PS scoring with missing values</li> <li>High-dimensional PS matching</li> </ul>	<p>Schneeweiss S, Rassen JA, Glynn RJ, et al. High-dimensional propensity score adjustment in studies of treatment effects using health care claims data. <i>Epidemiology</i>. 2009 Jul;20(4):512-22.</p> <p><b>*Programming assignment II due on Oct 13, 2021</b> <b>1-Page summary of research project due on Oct 19, 2021</b></p>
9	Oct 20, 2021	<p>Mitigating time-varying confounding (<b>Eworuke</b>)</p> <ul style="list-style-type: none"> <li>Marginal structural models</li> </ul>	<p>IP Weighting and marginal structural models in the causal inference book part 2</p> <p>Kurth T, Walker AM, Glynn RJ, et al. Results of multivariable logistic regression, propensity matching, propensity adjustment, and propensity-based weighting under conditions of nonuniform effect. <i>Am J Epidemiol</i> 2006;163:262-70.</p> <p>Williamson T, Ravani P. Marginal structural models in clinical research: when and how to use them? <i>Nephrol Dial transplant</i> 2017: Apr 1; 32 (<b>assigned 6 due on Oct 20, 2021</b>)</p>
10	Oct 27, 2021	<p>Understanding the SAS programming behind conducting marginal structural models (<b>Eworuke</b>)</p>	<p>Cole &amp; Hernan M. Constructing inverse probability weights for marginal structural models. <i>Am J Epidemiol</i>. 2008 Sep 15;168(6):656-64. doi: 10.1093/aje/kwn164 (<b>assigned 7 due on Oct 27, 2021</b>)</p>
11	Nov 3, 2021	<p>Mitigating confounding: Instrumental Variables (<b>Eworuke</b>)</p>	<p>Brookhart MA, Wang PS, Solomon DH, Schneeweiss S. Evaluating short-term drug effects using a physician-specific prescribing preference as an instrumental variable. <i>Epidemiology</i> 2006;17:268–75.</p> <p>Hernán MA, Robins JM. Instruments for causal inference: an epidemiologist's dream? <i>Epidemiology</i>. 2006 Jul;17(4):360-72.</p> <p>Basu A. Estimating Decision-Relevant Comparative Effects Using Instrumental Variables. <i>Stat Biosci</i>. 2011;3(1):6-27. (<b>assigned 8 due on Nov 3, 2021</b>)</p>
12	Nov 10, 2021	<p>Special biases and design approaches I (<b>Eworuke</b>)</p> <ul style="list-style-type: none"> <li>Confounding by Healthy user/ adherer effect (compliance bias)</li> <li>Confounding by frailty</li> </ul>	<p>Brookhart MA, Patrick AR, Dormuth C, et al. Adherence to lipid-lowering therapy and the use of preventive health services: an investigation of the healthy user effect. <i>Am J Epidemiol</i> 2007;166:348-54.</p>

		<ul style="list-style-type: none"> <li>• Confounding by functional/cognitive status</li> <li>• Prevalent user bias</li> </ul>	<p>Jackson LA, Nelson JC, Benson P, Nuxil. Functional status is a confounder of the association of influenza vaccine and risk of all- cause mortality in seniors. <a href="#">Int J Epidemiol.</a> 2006 Apr;35(2):345-52</p> <p>Hampp C, Greene P, Pinheiro SP. Use of Prescription Drug Samples in the USA: A Descriptive Study with Considerations for Pharmacoepidemiology. Mar 2016;39(3):261-270. (assigned 9 due on Nov 10, 2021)</p>
13	Nov 17, 2021	Special topic: Quantitative Bias Analysis in the setting of unmeasured confounding (Eworuke)	Lash et al, Good practices for quantitative bias analysis. <a href="https://academic.oup.com/ije/article/43/6/1969/705764">https://academic.oup.com/ije/article/43/6/1969/705764</a> (assigned 10 due on Nov 17, 2021)
14	Nov, 24 2021	Thanksgiving holiday (no class)	
15	Dec 1, 2021	Case-only designs (a double- edged sword) (Eworuke)	Presentation only
16	Dec 8, 2021	Student preparation for final research project (No class)	<b>Final research project due on Dec 8, 2021</b> (Eworuke & Wei)