PHA 6935

ADVANCED PHARMACOEPIDEMIOLOGY

Course Description:

PHA6935 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 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 will afford students the opportunity to learn the implementation of these advanced methods.

Total Course Credit: 3

Course Prerequisite:

Student taking this course would be required to have taken the 2 graduate level statistics courses – STAT 6166 and 6167, PHA 6717: Measurement in Pharmaceutical Outcomes and Policy Research and PHA 6805: Applied Data Analysis, Interpretation and Reporting of Findings in Pharmacy

Learning Objectives:

At 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

Methods of Student Evaluation:

Each week, resources will be posted, along with an overview of the learning objectives, required readings and reference materials. A student will be selected to present the core learning content for the week as it relates to the learning objective for the week. The student would be required to lead discussions, pose questions identified and be prepared to answer the questions of the other students. The other students will also be expected to contribute during these discussions, providing individual perspectives as they studied the materials.

Students are encouraged to bring supplemental materials to enhance understanding of the topic.

The class is discussion-oriented and self-directed; therefore, each student is expected to have read the assigned readings and be prepared to discuss them. Students will be required to prepare and submit 1-2 pages summarizing the learning objective on the evening before the class discussion. Classes will be held every Thursday at 1pm and will be 2-3 hours in length depending on the scope of the materials. No slide presentation will be allowed. There will 2 assignments requiring programming. Students will be required to conduct pre-specified analyses and submit for evaluation.
Final grades will be assessed on the basis of the following course requirements:

Assigned Class Discussion: 35 points
Class Participation/Summary notes1: 15 points
Statistical Analysis: 20 points
Final Exam: 30 points

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 prior to 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 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.

Tentative lecture schedule:

Week	Date	Topic	Readings
1	9/2	Review of Epidemiological Principles: Review of various components of epidemiological research design and discuss sources of bias when conducting epidemiologic studies	Kramer MS. Epidemiologic research design: an overview Kramer MS. Analytic Bias
2	9/12	Bias in Defining exposure	Lévesque Linda E, Hanley James A, Kezouh Abbas, Suissa Samy. Problem of immortal time bias in cohort studies: example using statins for preventing progression of diabetes BMJ 2010; 340 :b5087 Suissa S. Immeasurable time bias in observational studies of drug effects on mortality. Am J Epidemiol 2008;168:329-35. Jurek AM, Greenland S, Maldonado G. How far from non-differential does exposure or disease misclassification have to be to bias measures of association away from the null? Int J Epidemiol. 2008;37(2):382-5. Dosemeci M. Does non-differential misclassification of exposure always bias a true effect toward the null value? Am J -Epidemiol. 1990 132 (4): 746-748
3	09/19	Time-varying Exposure in Pharmacoepidemiology	Stricker BH, Stijnen T. Analysis of individual drug use as a time-varying determinant of exposure in prospective population-based cohort studies. *European journal of epidemiology.* Apr 2010;25(4):245-251. Suissa S. Effectiveness of Inhaled Corticosteroids in Chronic Obstructive Pulmonary Disease. *American Journal of Respiratory and Critical Care Medicine.* 2003/07/01 2003;168(1):49-53.
4/5	09/26 & 10/3	Analyzing a stratified Cox-proportional hazards model Analyzing survival data with time-varying variables Non-proportional hazards: Cox model with interaction term with time	Software: SAS *Programming assignment I: using proc phreg, conduct analysis of a time-dependent variable

		Analyzing survival data with Recurrent events Analyzing survival data with competing risks	
6	10/10	Confounding in observational studies	Confounding In the Causal inference book. Hernan and Robbins Miettinen O. Confounding and effect-modification. Am J Epidemiol. 1974 nov;100(5):350-3.
		Channeling Bias	MacDonald TM, Morant SV, Goldstein JL, Burke TA, Pettitt D. Channelling bias and the incidence of gastrointestinal haemorrhage in users of meloxicam, coxibs, and older, non-specific non-steroidal anti-inflammatory drugs. *Gut.* Sep 2003;52(9):1265-1270. Blais L, Ernst P, Suissa S. Confounding by indication and channeling over time: the risks of beta 2-agonists.Am J Epidemiol. 1996 Dec 15;144(12):1161-9.
7	10/17	Mitigating confounding: Design approach	Eworuke E, Shaya F, Graham DJ, et al. Strategies addressing inadequate information on health factors in pharmacoepidemiology studies relying on healthcare databases: commentary from a public workshop. *Pharmacoepidemiol Drug Saf.* Jul 7 2016. Psaty BM, Siscovick DS. Minimizing bias due to confounding by indication in comparative effectiveness research: the importance of restriction. JAMA. 2010 Aug 25;304(8):897-8.
8	10/24	Mitigating confounding: Propensity Scores and High dimensional propensity scores	Brookhart MA, Schneeweiss S, Rothman KJ,.Glynn RJ, Avorn J, Stürmer T. Variable selection for propensity score models. Am J Epidemiol 2006;163:1149-1156. Rubin DB. Estimating causal effects from large data sets using propensity scores. Ann Intern Med. 1997;127:757-63. Schneeweiss S, Rassen JA, Glynn RJ, Avorn J, Mogun H, Brookhart MA. High-dimensional propensity score adjustment in studies of treatment effects using health care claims data. Epidemiology. 2009 Jul;20(4):512-22.

		Propensity score methods in Distributed data	Gagne JJ et al. A modular, prospective, semi-automated drug safety monitoring system for use in a distributed data environment. Pharmacoepidemiol Drug Saf 2014;23:619-27. Gagne JJ et al. Successful comparison of US Food and Drug Administration Sentinel analysis tools to traditional approaches in quantifying a known drug-adverse event association. Clin Pharmacol Ther 2016 Jul 14 [Epub ahead of print]
9/10	10/31, 11/7	Propensity score development: Analyzing the data • Propensity score matching • Propensity score stratification: ATE • Propensity score weighting	Software SAS *Programming assignment II: create a propensity score using proc logistic and use one of the techniques to adjust for confounding
11	11/14	Mitigating time-varying confounding: Marginal structural models, Standardized mortality ratio	IP Weighting and marginal structural models IN the causal inference book Hernan M. Estimating the causal effect of zidovudine on CD4 count with a marginal structural model for repeated measures. Stat Med. 2002 21. 1689-1709 Kurth T, Walker AM, Glynn RJ, Chan KA, Gaziano JM, Berger K, Robins JM. Results of multivariable logistic regression, propensity matching, propensity adjustment, and propensity-based weighting under conditions of nonuniform effect. Am J Epidemiol 2006;163:262-70.
12	11/21	Understanding the SAS programming behind conducting marginal structural models.	
13	11/28	Mitigating confounding: Instrumental Variables	Brookhart MA, Wang PS, Solomon DH, Schneeweiss S. Evaluating short-term drug effects using a physician-specific prescribing preference as an instrumental variable. Epidemiology 2006;17:268–75. Hernán MA, Robins JM. Instruments for causal inference: an epidemiologist's dream? Epidemiology. 2006 Jul;17(4):360-72. Basu A. Estimating Decision-Relevant Comparative Effects Using Instrumental Variables. Stat Biosci. 2011;3(1):6-27.

14	12/5	Special Biases and design approaches: ✓ Confounding by Healthy user effect ✓ Confounding by frailty ✓ Confounding by functional/cognitive status ✓ Sick Stopper bias ✓ Healthy adherer effect (compliance bias) ✓ Prevalent user bias	Robert J. Glynn, Eric L. Knight, Raisa Levin, Jerry Avorn. Paradoxical relations of drug treatment with mortality in older persons. Epidemiology 2001;12:682-9. Brookhart MA, Patrick AR, Dormuth C, Avorn J, Shrank W, Cadarette SM, Solomon DH. Adherence to lipid-lowering therapy and the use of preventive health services: an investigation of the healthy user effect. Am J Epidemiol 2007;166:348-54. 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 Simpson SH, Eurich DT, Majumdar SR, Padwal RS, Tsuyuki RT, Varney J, Johnson JA. A meta-analysis of the association between adherence to drug therapy and mortality. BMJ 2006;333:15. 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.