



Department of
Pharmacy Practice
Paul O. Gubbins, Pharm.D.
Professor, Chair

*Evidence-based Medicine, Biostatistics, and
Pharmacoeconomics*

FALL 2010

PHPR 5643

Co-Course Coordinators

Jill Johnson, Pharm.D., BCPS, and Bradley C Martin, Pharm.D., Ph.D.

UNIVERSITY OF ARKANSAS FOR MEDICAL SCIENCES
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Evidence-based Medicine, Biostatistics, and Pharmacoeconomics
Ph. Pract. 5643
Fall 2010 Syllabus
 CPH G225

Description: This 3 credit hour core course will teach the student to formulate a focused clinical question, to improve the student's literature critical appraisal skills, to determine the appropriateness of various biostatistical analyses, to interpret research outcomes, and to apply pharmacoeconomic techniques in order to inform drug product selections.

Credits: 3 hours

Time: Lecture Time 1:00-2:50pm Mondays
 1:00-1:50pm Wednesdays

Place: CPH G225

Course Coordinators:

Co-Course Coordinator: Jill T. Johnson, Pharm.D., BCPS Office: 6/132G

Phone: 686-7919

Email: johnsonjillt@uams.edu

Drop by or make an appointment. Appointments can be made with me via email, phone, or in person.

Co-Course Coordinator: Bradley C. Martin, Pharm.D., Ph.D. Office: 6251

Phone: 603-1992

Email: bmartin@uams.edu

Open door policy and by appointment: If my door is open please feel to drop in to discuss anything course related. Alternatively, you can schedule an appointment by email, phone or in person should I be unavailable when you come by.

Instructors:

Jill T. Johnson, Pharm.D., BCPS	johnsonjillt@uams.edu	686-7919
Bradley C. Martin, Pharm.D., Ph.D.	bmartin@uams.edu	603-1992
Kat Neill, Pharm.D.	neillkathryn@uams.edu	603-1515
Chenghui Li, Ph.D.	CLi@uams.edu	686-6298
Scott Warmack, Pharm.D., BCPS	warmackthomass@uams.edu	686-5579
Nalin Payakachat, Ph.D.	npayakachat@uams.edu	686-7701

Course Objectives:

1. To learn to create a focused clinical question.
2. To learn common statistical techniques and apply them to critique the medical literature
3. To identify the strengths and weaknesses in the primary literature.
4. To become aware of potential biases in the medical literature and to put them in their proper perspectives
5. To assess and interpret patients' health related quality of life.
6. To interpret and apply pharmacoeconomic information to inform drug product selections.

Overall Competencies:

1.1	Evaluate patient data and make an assessment: d. Assess patient quality of life.
1.3	Design and implement an individual patient-centered pharmacotherapy plan to maximize desired effects and minimize undesired effects: a. Conduct a focused evidence-based review of the necessary literature to determine the best evidence to support pharmacotherapy recommendations, applying pharmaceutical science principles, c. Evaluate patient factors that are relevant to selecting pharmacotherapy (e.g., sex, age, race, ethnicity, culture, and genetics)
1.5	d. Recognize and solve problems using creativity, analysis, and intuition
2.3	c. Provide medication information to patients and health care providers to promote rational drug therapy
3.1	c. Provide drug-therapy evaluation and monitor for medication safety.
3.2	Apply research processes to inform pharmaceutical policy: a. Demonstrate the ability to conduct drug literature evaluations, c. Apply evidence-based principles when making pharmaceutical policy recommendations, including drug benefit design recommendations, and d. Apply principles of pharmacoeconomics and outcome assessment.

Course Structure:

The course will utilize traditional lecture format and online course materials. Students will be assigned regular out-of-class assignments and there will be unannounced quizzes on required readings offered throughout the semester at beginning of course lecture. See Grading policy. Assigned readings are available in the course packet and students are expected to read the assigned reading PRIOR to class.

The statistics sections of the course will be primarily offered online using Blackboard. The online course material will be released according to the topic outline. Optional discussion sessions are available and will provide opportunities for students to ask questions, seek clarification, and see examples. Student mastery of the online content will be assessed using homework assignments and traditional exams.

Required Texts, Manuals, readings, and technology access

- ❖ EBM, Biostatistics, and Pharmacoeconomics course manual which includes the course syllabus, lecture notes, and assigned readings.
- ❖ Access to Blackboard
- ❖ Regular access to PubMed or OVID will be required in order to access required readings in the case they are not otherwise provided

- ❖ Biostatistics Text: Beth Dawson and Robert G. Trapp. Basic & Clinical Biostatistics, 4th Edition. Lange Medical Books/McGraw-Hill Companies Inc. (available online through UAMS library Clinical Resource Access Medicine). Please be advised that the College of Pharmacy prohibits the printing of required textbook content in the computer lab. If you have any questions, please direct questions to the Dean's office (Drs. DeHart or Stowe).

Recommended Texts (not required)

- ❖ Users' Guides to the Medical Literature, JAMA

Grading:

<u>Exam/Quiz</u>	<u>percent of final grade</u>	<u>Points</u>
Regular Exam-1	25%	250
Regular Exam-2	25%	250
Final Exam	25%	250
Homework	10%	100
Quizzes	<u>15%</u>	<u>150</u>
Total:	100%	1000 pts

No fewer than 6 un-announced quizzes will be given at the beginning of selected class periods based on the assigned readings for the day. Your lowest quiz grade will be dropped and will not be used in determining your quiz average for the course. A significant portion of this course will utilize examples derived from the literature and pre-reading the material will be important to appropriately grasp the concepts discussed in class. There will be no make ups for missed quizzes.

Quizzes will be administered by paper, Turning Point, or Blackboard. You will be responsible for bringing your Turning Point clicker to class each day and time the class meets. Failure to bring your clicker on a day of a pop quiz will result in a zero for that quiz. Students found with more than one clicker will be given a zero for his/her quiz as will the absent owner(s) of the clickers and all students involved will be subject to the Honor Code for academic dishonesty.

Grades will be assigned in the following manner:

Standard Scale:	89.5-100% (895-1000 pts)-A	79.5-89.4%(795-894pts)-B
	69.5-79.4%(695-794 pts)-C	69.4% or less (694 or fewer pts)-F

NOTES:

As your instructors and as a student in this class, it is our shared responsibility to develop and maintain a positive learning environment for everyone. As your instructors, we take this responsibility seriously and will inform members of the class if their behavior makes it difficult to carry out this task. As a fellow learner, you are asked to respect the learning needs of your classmates and assist your instructor to achieve this critical goal.

As your instructors, it is our responsibility to present learning opportunities through the course syllabus, lectures, and in and out of class assignments. It is your responsibility to do the learning by completing the readings, by attending class, and participating in class discussions and assessment exercises.

This course will conduct student assessments that you can use to determine how successful you are at achieving the course learning outcomes. If you find you are not mastering the material and skills, you are encouraged to reflect on how you study and prepare for each class. We welcome a dialogue on what you discover and may be able to assist you in finding resources on campus that will improve your performance.

POLICIES:

Make Up Examinations

If a student misses an examination, a grade of **0 (zero)** will be awarded unless a valid reason for missing the exam is documented. If a student does not notify a course coordinator **PRIOR TO** the beginning of the exam, **THERE WILL BE NO MAKE-UP ALLOWED**. The course coordinators will have the final authority determining whether a reason is valid to allow a make-up exam. Any special circumstances which a student feels may affect his/her test performance in this course must be brought to the attention of the course coordinator in writing within the first week of the course or within 24 hours of an exam. Make-up exams may consist of an oral examination. Make-up exams will be given as soon as possible following the missed examination, however they must occur within 7 days of the original exam, or a zero will be awarded. There will be no makeups allowed for missed quizzes.

The dates of the exams are listed in the syllabus; exam locations are listed in the lecture schedule. During the regular exams, **NO BOOKS OR NOTEBOOKS, CELL PHONES, OR OTHER ELECTRONIC DEVICES, with the exception of calculators (non programmable)** will be allowed. Cell phones must be turned off and stowed in a backpack/bag. Any form of academic dishonesty (i.e. unauthorized assistance during an exam or quiz, etc.) will warrant a grade of zero on the exam/quiz. (Please also refer to page 63-67 in the Student Handbook.)

Electronic Devices:

Students are encouraged to use calculators for solving problems and may use one of the following when taking exams: Casio fx-300ES or TI-30XS. No other calculators will be allowed during exams. Any student using an unapproved calculator during an exam will receive a zero for that exam. **BE ADVISED:** the use of PDAs, cell phones, computers, etc. will not be allowed during exams. The use of such devices will result in a zero for that exam.

Challenges to Examinations/Quizzes

Any individual who wishes to challenge an exam/quiz question must submit the challenge in writing, with documentation *no later than one week* after the return of the exam/quiz. Challenges will be acted on by the Course Coordinators and faculty member involved. Upon an exam/quiz challenge, instructors may reassess the exam/quiz in its entirety. Points will be adjusted accordingly. All challenges will be resolved and all grades finalized within one week of the challenge deadline. Once all grades are finalized for any examination or quiz, no challenges will be accepted or grades altered for that examination or quiz.

Any concerns, questions, or procedural matters related to this course should be addressed in the following order of progress in: the Instructor or Course Coordinator, Department Chair, and finally the Dean's office.

The course syllabus is a general plan for the course; the syllabus may be modified at any point during the semester and deviations communicated to the class by the Course Coordinators via email, verbal announcement, or by replacement page for the syllabus.

Dress Code: Please refer to the Student Handbook regarding professionalism and dress.

Printing: Please be advised that the College of Pharmacy prohibits the printing of required textbook content in the computer lab. If you have any questions, please direct questions to the Dean's office (Drs. DeHart or Stowe).

Special Test Taking Accommodations: Please refer to the Student Handbook.

- **Class Attendance:** Students are required to be diligent in their studies and regular in their attendance at classes. They will be held responsible for making satisfactory arrangements with their instructors regarding absences. Students will not be permitted to be absent from a class in excess of the semester hours of credit for that course. Repeated absences will be reported to the office of the Dean. Absences should be reported to the Dean's office. Absences must be phoned in, not e-mailed, to the Dean's office on the day classes will be missed.

Academic Dishonesty: all students must act ethically and professionally. Behavior must concur with the UAMS COP Pledge of Professionalism. Please refer to the "Pledge of Professionalism" in the current Student Handbook. Please see the student handbook. Please also see the UAMS COP Honor Code (http://www.uams.edu/cop/current_students/pdfs/honor_code.pdf).

Topic/Calendar Outline:

Date	Hours	Lecture Title	Faculty
M	8/16 1-2:50p	2 Introduction to EBM	Johnson
Define Clinical Question			
W	8/18 1-1:50p	1 The EBM Framework: Assess, Ask, Acquire, Appraise, Apply	Johnson
Retrieve Pertinent Information			
M	8/23 1-1:50p	1 Review Searching the Literature/ EBM Resources	Susan Steelman, Library
Evaluate Literature			
Study Design			
M	8/23 2-2:50p	1 Validity: Populations, External validity, exclusion/inclusion criteria <ul style="list-style-type: none"> ○ <u>Required Readings:</u> ○ MEDENOX. Sanama MM, Cohen AT, Darmon JY, Desjardin L, et al. A comparison of enoxaparin with placebo for the prevention of venous thromboembolism in acutely ill medical patients. <i>N Engl J Med</i> 1999;341: 793-800. ○ PROWESS. Bernard GR, Vincent JL, Laterre PF, LaRosa SP, et al. Efficacy and safety of recombinant human activated protein C for severe sepsis. <i>N Engl J Med</i> 2001;344:699-709. ○ Warfarin/ASA/Both post MI. Hurlen M, Abdelnoor M, Smith P, Erikssen, et al. Warfarin, aspirin, or both after myocardial infarction. <i>N Engl J Med</i> 2002;347:969-74.) 	Johnson
W	8/25 1-1:50p	1 Validity: Study Design: Controlled Trials, Randomization, Allocation Concealment, Blinding, LTFU <ul style="list-style-type: none"> ○ <u>Required Readings:</u> ○ AFFIRM Investigators. A COMPARISON OF RATE CONTROL AND RHYTHM CONTROL IN PATIENTS WITH ATRIAL FIBRILLATION. <i>N Engl J Med</i> 2002;347:1825-33.) ○ RACE. Van Gelder IC, Hagens VE, Bosker HA, Kingma JH, et al. A comparison of rate control and rhythm control in patients with recurrent persistent atrial fibrillation. <i>N Engl J Med.</i> 2002;347:1834-40. 	Johnson
M	8/30 1-1:50p	1 Results...ITT vs PP analysis, baseline characteristics <ul style="list-style-type: none"> ○ <u>Required Reading:</u> ○ Moher D, Schulz KF, Altman DG, et al. The CONSORT Statement: Revised Recommendations for improving the quality of reports of parallel-group randomized trials. <i>Ann Intern Med.</i> 2001;134:657-662. 	Johnson
M	8/30 2-2:50p	1 Other factors: Composite endpoints, Run-in's, Differences in baseline characteristics, Flawed assumptions, MATCH trial <u>Required Reading:</u> <ul style="list-style-type: none"> ○ Diener HC, Bogousslavsky J, Brass LM, Cimminiello C, et al. Aspirin and clopidogrel compared with clopidogrel alone after recent ischaemic stroke or transient ischaemic attack in high-risk patients (MATCH): randomized, double-blind, placebo-controlled trial. <i>Lancet.</i> 2004;364:331-37. 	Johnson/Neill

W	9/1 1-1:50p	1	***PICO Exercise***	Johnson
			Biostatistics	
M	9/6		LABOR DAY HOLIDAY	
W	9/8 1-1:50p	1	(Class meets) Introduction and Descriptive Statistics- Organizing, displaying and summarizing data Required Reading: <ul style="list-style-type: none"> • Dawson and Trapp (2004), Chapter 3. • Castilla-Puentes R (2007). Effects of psychotropics on glycosylated hemoglobin (HbA1c) in a cohort of bipolar patients. 	Li (released 8/30 and discussed on 9/8)
M	9/13 1-2:50p	2	(3)(Class meets) Probability, distribution and normal distribution & Sampling distribution of sample means and estimation Required Reading: <ul style="list-style-type: none"> • Dawson and Trapp (2004), Chapter 4, page 61-72; Page 76-90. 	Li (released on 9/6 and discussed on, 9/13)
W	9/15	1	(2)(Class NOT Meeting) Hypothesis Testing and Statistical Inferences	Li (released on 9/13 and discussed on 9/20)
M	9/20 1-2:50p	2	(2)(Class Meets) Hypothesis Testing and Statistical Inferences Required Reading: <ul style="list-style-type: none"> • Dawson and Trapp(2004), Chapter 5 Page 93-110. 	Li
W	9/22	1	Exam 1 (15 lecture hours)	
M	9/27 1-1:50p	1	Validity: Results...Power, Beta error	Neill
M	9/27 2-2:50p	1	Non-inferiority trials Required Reading: <ul style="list-style-type: none"> ○ ONTARGET: Telmisartan, Ramipril, or Both in Patients at High Risk for Vascular Events. <i>N Engl J Med</i> 2008;358:1547-59. 	Johnson
W	9/29 1-1:50p	1	Results—RR, NNT, NNH, HR, OR, 95% CI <ul style="list-style-type: none"> ○ Required Readings: ○ CURE Trial Investigators. Effects of clopidogrel in addition to aspirin in patients with acute coronary syndromes without ST-segment elevation. <i>N Engl J Med</i>. 2001;345: 494-502. ○ Bhat VM, Cole JW, Sorkin JD, Wozniak MA, et al. Dose-response relationship between cigarette smoking and risk of ischemic stroke in young women. <i>Stroke</i>. 2008;39:2439-2443. 	Johnson
M	10/4 1-2:50p	2	(2)(Class meets) t – tests Required Reading: <ul style="list-style-type: none"> • Dawson and Trapp (2004). Chapter 5, page 115-118; Chapter 6, page 134-143. 	Li (released on 9/20 and discussed on 10/4)
W	10/6	1	(Class not meeting)-work on Non-parametric Inferential Statistics and Other Common test statistics (e.g. ANOVA?)	Li
M	10/11 1-2:50p	2	Non-parametric Inferential Statistics and Other Common test statistics (e.g. ANOVA) Required Reading:	Li (released on 10/4 and discussed on 10/11)

			<ul style="list-style-type: none"> • Dawson and Trapp (2004): Chapter 5, page 121-122; Chapter 6, page 143-146. <p>Supplemental Reading (examples of nonparametric tests):</p> <ul style="list-style-type: none"> ○ Batterham RL, Cohen MA, Ellis SM, Le Roux CW, et al. Inhibition of food intake in obese subjects by Peptide YY3-36. N Engl J Med. 2003 ;349 :941-8. ○ Martinez E, Arnaiz JA, Podzamczar D, Dalmau D, et al. Substitution of nevirapine, efavirenz, or abacavir for protease inhibitors in patients with HIV infection. N Engl J Med. 2003;349:1036-46. ○ Subak LL, Wing R, West DS, Franklin F, et al. Weight loss to treat urinary incontinence in overweight and obese women. N Eng J Med. 2009;360:481-90. 	
W	10/13	1	(Class not meeting)-work on Categorical Data Analysis: OR, RR, Chi-Square	Li(released on 10/11 and discussed on 10/18)
M	10/18 1-2:50p	2	(Class meets to discuss) Categorical Data Analysis: OR, RR, Chi-Square Required Reading: <ul style="list-style-type: none"> • Dawson and Trapp (2004): Chapter 5, page 119-121; Chapter 6 Page 149-154. 	Li
W	10/20 1-1:50p	1	Levels of Evidence & Guidelines	Johnson
M	10/25		Exam 2 (12 lecture hours)	
W	10/27	1	(Class Not Meeting) Work on Statistical Adjustment	
M	11/1 1-2:50p	2	Statistical Adjustment: OLS, Logistic Regression and Survival Analysis Required Reading: <ul style="list-style-type: none"> • Dawson and Trapp (2004) Chapter 8, page 202-214; Chapter 9, Chapter 10, page 247-267 • Nash D, Magder L, Lustberg, et al. Blood lead, blood pressure, and hypertension in perimenopausal and postmenopausal women. JAMA. 2003;289(12):1523-32. <p>Supplemental Reading (examples of survival analyses):</p> <ul style="list-style-type: none"> ○ Knoop KTB, de Groot LCPGM, Kromhout D, et al. Mediterranean diet, lifestyle factors, and 10-year-mortality in elderly European men and women : the HALE project. JAMA. 2004;292(12):1433-1439. ○ Kadan-Lottick NS, Ness KK, Bhatia S. Survival variability by race and ethnicity in childhood acute lymphoblastic leukemia. JAMA. 2003;290(15):2008-2014. ○ Grady D, Herrington D, Bittner V, et al. Cardiovascular disease outcomes during 6.8 years of hormone therapy: Heart and estrogen/progestin replacement study follow up (HERS II). JAMA. 2002;288(1):49-57. ○ AFFIRM Investigators. A COMPARISON OF RATE CONTROL AND RHYTHM CONTROL IN PATIENTS WITH ATRIAL FIBRILLATION. N Engl J Med 2002;347:1825-33.) 	Li(released on 10/18 and discussed on 11/1)
W	11/3 1-1:50p	1	Study interpretation: Observational Studies--various	Warmack

M	11/8 1-1:50p	1	Pharmacoeconomics: Intro to Pharmacoeconomics <ul style="list-style-type: none"> ○ Supplemental Reading: ○ Motheral BR, Cox ER, Daniesl CE. Pharmacoeconomics and outcomes research: evaluating the studies. JMCP. 2000;6(1):4-15 supplement. Freely available on internet. 	Martin
M	11/8 2-2:50p	1	Pharmacoeconomics: Intro to PE-II-Interpreting Cost Studies	Martin
W	11/10 1-1:50p	1	Pharmacoeconomics: Satisfaction and Quality Measure	Payakachat
M	11/15 1-2:50p	2	Pharmacoeconomics: Interpreting Cost-effectiveness Studies and Data Sources for Cost Effectiveness Studies <ul style="list-style-type: none"> ○ <u>Required Reading:</u> ○ CDC Diabetes Cost-effectiveness Group. Cost-effectiveness of intensive glycemic control, intensified hypertension control, and serum cholesterol level reduction for type 2 diabetes. JAMA. 2002;287:2542-2551. 	Martin
W	11/17 1-1:50p	1	Pharmacoeconomics: QOL and Utility assessment Required Reading: <ul style="list-style-type: none"> ● Picchianti-Diamanti A, Germano V, Ferlito C, Migliore A, et al. Health-related QOL and disability in patients with rheumatoid, early rheumatoid and early psoriatic arthritis treated with etanercept. Qual Life Res (2010) 19:821–826 	Payakachat
M	11/22 1-1:50p	1	(continued) Pharmacoeconomics: QOL and Utility assessment	Payakachat
M	11/22 2-2:50p	1	Narrative Reviews, Systematic Reviews, & Meta-analysis <ul style="list-style-type: none"> ○ <u>Required Reading:</u> ○ Reichenbach S, Sterchi R, Scherer M, Trelle S, Bürgi E, Bürgi U, Dieppe PA, Jüni P. Meta-analysis: chondroitin for osteoarthritis of the knee or hip. Ann Intern Med. 2007 Apr 17;146(8):580-90. 	Martin
W	11/24	1	Review/Catch up	Any
M	11/29 1-1:50p	1	Study interpretation: Statistical vs clinical significance <ul style="list-style-type: none"> ○ <u>Required Reading:</u> ○ CAPRIE. A randomized, blinded, trial of clopidogrel vs aspirin in patients at risk of ischaemic events. Lancet. 1996;348:1329-39. ○ CAST. Echt DS, Liebson PR, Mitchell LB, Peters RW, et al. Mortality and morbidity in patients receiving encainide, flecainide, or placebo. N Engl J Med. 1991;324:781-8. 	Johnson/ Neill
M	11/29 2-2:50p	1	Using evidence to influence formulary decisions	Martin
W	12/1 1-1:50p		Review	All
F	12/3	3	Final Exam 1-3:50p, 8 th flr comp. labs (15 lecture hours)	All

A Worksheet for Articles about Treatment

Determine *Relevance*

Is this article worth taking the time to read? If the answer to any of these questions is No, it may be better to read other articles first.

Based on the conclusion of the abstract:

A. Did the authors study an outcome that patients would *care* about? (Be careful to avoid results that require extrapolation to an outcome that truly matters to patients)

Yes (go on) No (**stop**)

B. Is the problem studied one that is *common* to your practice and the intervention feasible?

Yes (go on) No (**stop**)

C. Will this information, if true, require you to *change* your current practice?

Yes (go on) No (**stop**)

Determine *Validity*:

If the answers to all three questions above are Yes, then continued assessment of the article is mandatory.

D. Population

1. Are the studied patients similar enough to your patients that you can apply the results in your practice?	Yes	No (Stop)
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E. Study design

1. Was it a controlled trial?	Yes	No (Stop)
2. Were the subjects randomly assigned?	Yes	No (Stop)
3. Were steps taken to conceal the treatment assignment from study personnel entering patients into the study?	Yes	No
4. Were patients and study personnel “blind” to treatment?	Yes	No

F. Study conduct

1. Were all patients who entered the trial properly accounted for at its conclusion?	Yes	No
2. Was follow-up complete?	Yes	No
3. Were patients analyzed in the groups to which they were randomized (“intention-to-treat” analysis)?	Yes	No
4. Were the intervention and control groups similar? (Table 1)	Yes	No

G. Study results

1. What were the results? _____

2. Are the results clinically as well as statistically significant?	Yes	No
3. If a negative trial, was the power of the study adequate?	Yes	No
4. Were there other factors that might have affected the outcome?	Yes	No
5. How will it change your practice?		
