

General Information							
Course Title:	Clinical Trials: Design and Analysis	Course Designation:	PHS 580		Credits: 3		
Semester:	Fall	Year:	2008				
Department:	Public Health Sciences						
Director:	Vernon M. Chinchilli, PhD	Phone #	4262	Email:	vchinch@psu.edu	Office Rm #	
						A2200	
Time :	07:30 AM to 10:00 AM	Days:	Friday (8/29/08 - 12/19./08)			Location:	C1847A

Course Information

Description and/or Overview:

This introductory course stresses the concepts of statistical design and analysis in biomedical research, with special emphasis on the clinical trial. The following topics will be covered:

- Introduction to clinical trials and research
- Ethical considerations
- Clinical trials as experimental designs
 - Parallel vs. crossover designs
 - Cross-sectional vs. longitudinal designs
 - Factorial designs
 - Phase 1, Phase II, Phase III, and Phase IV trials
- Bias and random error
 - Clinical bias
 - Statistical bias
 - Design features to minimize bias
- Objectives, endpoints, and surrogate measures
- Sample size and power
- Active-controlled trials and equivalence
- The study cohort
- Treatment allocation and randomization
- Interim analyses and data-dependent stopping
- Multi-center clinical trials
- Counting patients and events
- Intent-to-treat philosophy
- Estimating clinical events
- Prognostic factor analyses
- Reporting
- Factorial designs
- Crossover designs
- Overviews and meta-analyses
- Diagnostic testing

Goals and/or Objectives:

The student will become acquainted with the principles underlying the design and conduct of clinical trials, including estimation of sample size requirement, analytic methods, ethical considerations, and reporting.

Pre-requisites:

Principles of Biostatistics (PHS 520)

Requirements; course-specific policies and expectations:

Students should have access to a PC with SAS for Windows and SAS Enterprise. Students also should have email access and read email regularly. ANGEL, the Penn State course management system, will be used to post pdf files, PowerPoint files, SAS programs, etc. with all course materials.

Required Texts and Resources:

Clinical Trials: A Methodologic Perspective Second Edition by [Steven Piantadosi](#)

Publisher: Wiley-Interscience; 2nd edition (August 1, 2005)

ISBN-10: 0471727814

Electronic Links:

Attendance Policy:

Students are expected to attend class when they are in town. If a student expects to miss more than one lecture, then the students should discuss the situation with the Instructor.

Examination Policy:

There will not be any examinations, but there will be take-home assignments.

Grading Criteria:

There will be a minimum of four take-home assignments. The total points from these assignments will comprise the final grade for the course. Students are expected to do their own work and not collaborate with others.

Academic Integrity

Academic Integrity at Penn State is defined by Faculty Senate Policy 49-20 as “the pursuit of scholarly activity in an open, honest and responsible manner”. The University's Code of Conduct states that “all students should act with personal integrity, respect other students' dignity, rights and property, and help create and maintain an environment in which all can succeed through the fruits of their efforts.

Academic integrity includes a commitment not to engage in or tolerate acts of falsification, misrepresentation or deception. Such acts of dishonesty violate the fundamental ethical principles of the University community and compromise the worth of work completed by others”. Academic dishonesty (including, but not limited to cheating, plagiarism, or falsification of information) will not be tolerated and can result in academic or disciplinary sanctions such as a failing (F) grade in the course.

Plagiarism

[For more information, see: <http://tlt.its.psu.edu/suggestions/cyberplag/cyberplagstudent.html>]

Statement on Remediation

The basis for grades, as stated in [Senate Policy 47-20](#), is "...the instructor's judgment of the student's scholastic achievement..." Occasionally, a disagreement arises in the assignment of a grade. A student who wishes to question or challenge the grade assigned in a course must first discuss grading practices and assignments with the instructor. It is expected that the student and instructor will try to eliminate any misunderstandings and will attempt to work out any disagreements over grades.

On the rare occasion that a student and instructor fail to resolve the grade dispute through informal means, the student may request that the head of the academic program offering the course act as a mediator. If this mediation does not resolve the dispute, the student who is a graduate student may request further mediation from the associate dean for graduate studies.

[For more information, see: <http://www.psu.edu/dept/oue/aappm/G-10.html>]

Educator's Code of Conduct

The Penn State Milton S. Hershey Medical Center and Penn State College of Medicine are dedicated to developing and maintaining a strong commitment to ethical teaching practices at all levels of the education process.

The foundation for this Educator's Code of Conduct is provided by the Penn State University Graduate School Statement on Teaching Ethics (1). The development of this Graduate School statement was based on a special issue of the journal, *New Directions for Teaching and Learning*. In this special issue, entitled *Ethical Dimensions of College and University Teaching: Understanding and Honoring the Special Relationship between Teachers and Students* (2), several authors provided theoretical and practical guidelines for honing ethical college teaching skills. Some of the authors' recommendations have been used to formulate the Educator's Code of Conduct provided herein. Some of these recommendations were modified to specifically fit the needs of both educators and students at the Hershey Medical Center and the Penn State College of Medicine. Both the Unified Campus Commitment to Excellence of the Hershey Medical Center and Penn State College of Medicine (3) and the Code of Ethical Behavior of the Hershey Medical Center, Policy A-20 HAM (4) were also consulted in preparing this Educator's Code of Conduct.

Four Norms to Govern Teaching

Honesty

Honesty and integrity must be practiced during all aspects of the education process.

Promise-Keeping

Promise keeping requires the educator to fulfill the "promises" made at the beginning of the semester or any other learning activity. Syllabi, assignments, grading principles, and class and office hour schedules each involve promises that are made to students and that must be adhered to under normal circumstances.

Respect for Persons

The educator must approach the learner with personal respect. In addition, the educator ought to encourage mutual respect among students. In particular, respect for race, religion, sexual orientation, disability gender, age, marital status, cultural differences, and political conviction should be supported and encouraged in all aspects of the educational process. Additionally, educators ought to show respect and common courtesy for students both during interpersonal interactions and in responding promptly to students' need for guidance and feedback. An environment free from harassment and discrimination, verbal abuse, physical violence, and intimidation in any form must also be provided for all learning activities.

Fairness

Recognizing the inherent subjectivity involved in grading, an educator ought to ensure that their grading practices are as objective as possible by creating and adhering to unambiguous criteria.

Principles of Ethical College and University Teaching

Content Competence

An educator maintains a high level of subject matter knowledge and ensures that the content of the educational experience is current, accurate, representative, and appropriate to the position of the learning experience within the students' program of study. The educator must be capable of approaching each learner with a commitment to meeting his or her educational needs.

Pedagogical Competence

A pedagogically competent educator communicates the objectives of the educational experience to students, is aware of alternative instructional methods or strategies, and selects methods of instruction that are effective in helping students to achieve the course objectives.

Dealing with Sensitive Topics

Topics that students are likely to find sensitive or discomfiting are dealt with in an open, honest, and positive way.

Student Development

The overriding responsibility of the educator is to contribute to the intellectual development of the student, at least in the context of the educator's own area of expertise, and to avoid actions such as exploitation and discrimination that detract from student development.

Dual Relationship with Students

To avoid conflict of interest, an educator does not enter into dual-role relationships with students that are likely to detract from student development or lead to actual or perceived favoritism on the part of the educator. The establishment of a romantic/sexual relationship between an educator and a student should be reported to the immediate supervisor of the educator. Such relationships should be dealt with consistent with Penn State Administrative Policy AD41 — Sexual Harassment (5).

Student Confidentiality

Student grades, letters of evaluation, attendance records, and private communications are treated as confidential materials and are released only with student consent, for legitimate academic purposes, or if there are reasonable grounds for believing that releasing such information will be beneficial to the student or will prevent harm to the student or to others.

Patient Privacy and Confidentiality

Educators who utilize patient information as part of any educational experience must follow patient privacy and confidentiality guidelines as outlined by the Health Insurance Portability and Accountability Act of 1996 (HIPAA).

Respect for Colleagues

An educator respects the dignity of his or her colleagues and works cooperatively with colleagues in the interest of fostering student development.

Valid Assessment of Students

An educator is responsible for taking adequate steps to ensure that the assessment of a student's performance is valid, open, fair, and congruent with the course/educational experience objectives. An educator must be aware that such assessments are important in students' lives and in the development of their careers.

Respect for Institution and Profession

In the interest of student development, an educator is aware of and respects the educational goals, policies, and standards of the institution in which he or she teaches and the profession which he or she represents.

Citing Sources of Educational Material

An educator acknowledges and documents, as appropriate, the sources of information and other materials used for teaching.

Violations of the Educator's Code of Conduct

Should a learner experience conduct that is inconsistent with the Educator's Code of Conduct, he/she is encouraged to first address the issue with either the educator responsible for the inconsistency or the director of the course in which the educator teaches. Should this attempt to resolve the problem fail, or if the nature of the inconsistency is such that the learner does not feel comfortable addressing the issue with either the educator or the course director, the student may consult other individuals. These individuals may include but are not limited to: faculty advisor, student ombudsman, departmental chair, the Vice Dean for Educational Affairs, and the Vice Dean for Faculty and Administrative Affairs. The decision of who to contact may be dependent on the educational program of the learner and/or type of violation that was encountered.

References:

- (1) <http://www.gradsch.psu.edu/research/ethics.html#teaching>)
- (2) <http://cte.uncwil.edu/et/br030697.htm>
- (3) Unified Campus Commitment to Excellence of the Penn State Milton S. Hershey Medical Center and College of Medicine; 05/11/01
- (4) Code of Ethical Behavior of the Hershey Medical Center, Policy A-20 HAM; Effective Date October, 2001
- (5) <http://guru.psu.edu/POLICIES/Ad41.html>

Developed by the Unified Campus Academic Team Endorsed by Teams Council — May 21, 2003

Course Schedule

Course Title:		Clinical Trials: Design and Analysis	Course Designation:	PHS 580	
Course Director:		Vernon M. Chinchilli, PhD			
Time :	07:30 AM to 10:00 AM	Days:	Friday	Location:	C1847A
Date	Lecture #	Instructor Last, first	Instruction Type (Lecture or lab)	Projected Lecture Topic - This list is an approximate guide to lecture topics. Titles and content are subject to change	
08/29/08	01	Chinchilli, VM	Lecture	Preliminaries	
	02	Chinchilli, VM	Lecture	Clinical Trials as Research	
	03	Chinchilli, VM	Lecture	Why Clinical Trials Are Ethical	
	04	Chinchilli, VM	Lecture	Contexts for Clinical Trials	
09/05/08	05	Chinchilli, VM	Lecture	Statistical Perspectives	
	06	Chinchilli, VM	Lecture	Clinical Trials As Experimental Designs	
	07	Chinchilli, VM	Lecture	Random Error and Bias	
	08	Chinchilli, VM	Lecture	Objectives and Outcomes	
09/12/08	09	Chinchilli, VM	Lecture	Translational Clinical Trials	
	10	Chinchilli, VM	Lecture	Dose-Finding Designs	
	11	Chinchilli, VM	Lecture	Sample Size and Power	
09/19/08	11	Chinchilli, VM	Lecture	Sample Size and Power	
09/26/08	12	Chinchilli, VM	Lecture	The Study Cohort	
	13	Chinchilli, VM	Lecture	Treatment Allocation	
10/03/08	14	Chinchilli, VM	Lecture	Treatment Effects Monitoring	
10/10/08	15	Chinchilli, VM	Lecture	Counting Subjects and Events	
10/17/08	16	Chinchilli, VM	Lecture	Estimating Clinical Effects	
10/24/08	17	Chinchilli, VM	Lecture	Prognostic Factor Analyses	
10/31/08	18	Chinchilli, VM	Lecture	Reporting and Authorship	
11/07/08	19	Chinchilli, VM	Lecture	Factorial Designs	
11/14/08	20	Chinchilli, VM	Lecture	Crossover Designs	
11/21/08	21	Chinchilli, VM	Lecture	Meta-Analyses	
11/28/08	THANKSGIVING BREAK - NO CLASSES				
12/05/08	22	Chinchilli, VM	Lecture	Misconduct and Fraud in Clinical Research	
12/12/08	23	Chinchilli, VM	Lecture	Medical Diagnostic Testing	
	24	Chinchilli, VM	Lecture	Correlation and Agreement	
12/19/08	FINALS WEEK				

Contact Information

Faculty / Title	Department	Phone #	EMAIL	Office Room #	Mail Code
Vernon M. Chinchilli, PhD	PHS	4262	vchinch@psu.edu	A2200	A210
Mardi Sawyer	PHS	1286	mds21@psu.edu	A2200	A210