I. Course description:
This 1 credit course explores the special challenges inherent in the design, implementation and evaluation of intervention studies in older adults. Common challenges faced by investigators working with older adults include population heterogeneity, reduced tolerance to demand, family protectiveness, and competing events. Sessions will examine the theoretical and practical issues confronting the investigator who must tailor the study population, setting, intervention, comparison arm, duration of follow-up, and outcome measures to fit together to achieve internally valid results while maintaining feasibility and generalizability. Students are expected to demonstrate integration of information provided over the course of the semester by critiquing a set of published clinical trials on an aging related topic of their choice. This course is required for completion of the aging concentration in the Clinical Research Training Program.

II. Course objectives:
Specific objectives are to:
1. Describe the aspects of standard clinical trials design that must be considered when developing intervention trials for older adults.
2. Be familiar with the types of interventions that are relevant to the health of older adults.
3. Describe tradeoffs in the design of trials for older adults related to eligibility and exclusions, settings, adherence, intervention protocols and reproducibility and outcome determination.
4. Become familiar with the modifications to operations of clinical trials for older adults including adaptations to the manual of procedures, treatment protocols, staff training, data tracking, and safety monitoring.
5. Understand how the phases of trial development and adaptive designs might aid in adapting to the special challenges of trials in older adults.

III. Course requirements:
Prerequisites: Introduction to Patient Oriented Research in Aging, a prior course in clinical trials design and implementation is preferred but maybe waived by application to the instructor.

IV. Location:
Parkvale 305-A-B
V. Course credits and contact hours:
1 credit; 16 contact hours; 1 session/week for 5 weeks (2.5 hours per session, plus 3.5 hours for site visiting)

VI. Grading:
Letter grade, based on assignments:
Class participation 20%
Clinical trials critique 30%
Study Site Visit report 30%
Oral Presentation 20%

VII. Readings:
1. Familiarity with the fundamentals of clinical trials design and operations is assumed. The following are classic texts on clinical trials that may be used for reference in this course.

or
Piantadosi S Clinical Trials A Methodological Perspective 1997 John Wiley and sons New York

You should at minimum have completed the clinical trials section of CLRES 2010 or read the chapters on clinical trials in Hulley Designing Clinical Research Lippincott (available from me as handout if you need it)

2. The following are overviews of issues in clinical trials with older adults. We will refer to these papers throughout the course.


Studenski S Ferrucci L Resnick N Clinical Research in Older Adults in Robertson and Williams eds Clinical and Translational Science Academic Press 2008

Cherubini A Del Signore S Ouslander J et al Fighting Against Age Discrimination in Clinical Trials JAGS 58:1791-1796 2010

3. The following is a standard reference regarding the reporting of clinical trials


VIII. Teaching methodology:
Lectures and classroom discussions will be supplemented with readings discussing special issues in clinical trials involving older adults. Researchers who are currently conducting clinical trials with older adults will present their work for discussion. Students will observe and report on at least one ongoing trial involving older adults and will review the design and operation of published clinical trials in a topic relevant to their own work.

IX. Major Assignments
1. Written critique of a published clinical trial on a topic of interest to you using the attached format. This review should be at least 3 double spaced typed pages. It is due for class 5, March 29, 2011.
2. Oral presentation describing your findings from the written critique. This is a 20 minute presentation and discussion of your findings and recommendations. Presentations will be made at class 5, March 29, 2011.
3. A Site Visit Report, based on the attached structured format will be due at any time at or prior to the last class, March 29, 2011. You will visit one of the listed ongoing trials (or an alternative approved by the instructor) where you will review study design and plans, operations, protocols, materials and participants.

Session 1 Introduction, orientation to assignments, overview of trials in the older adult, ethical issues in trials for older adults

Date 3/1/2011

Topics:
1. Clinical Trials: Brief review of key issues
2. What is different about trials in older adults—overview
3. Types of interventions that are relevant to aging
4. Consent to participate and influential others
5. Clinical equipoise

Session Objectives:
1. Review key issues in clinical trial design and interpretation
2. Identify the effects of age related clinical heterogeneity, low tolerance to burden and intervening events on clinical trials design and execution.
3. Describe types of interventions used in older adults
4. Discuss who influences the decision to participate in a trial for older adults
5. Consider the effect of the goal of clinical equipoise on trial design for older adults

Class Discussion:
1. Discuss ways in which the characteristics and needs of older adults conflict with classical RCT concepts
2. Consider patient, family and provider perspectives on trials participation for older adults

Readings:
Required


Optional

Marsden J, Bradburn J; Consumers' Advisory Group for Clinical Trials; Lynda Jackson Macmillan Patient and clinician collaboration in the design of a national randomized breast cancer trial. Health Expect. 2004 Mar;7(1):6-17


**Assignment**

1. Precourse Survey
2. Consider topics you would like to explore through your analysis of an RCT due class 5. Identify a trial on your topic and submit a single page with your name, preferred topic and the primary reference to the instructor by class 3
3. Review options for your site visit to an ongoing clinical trial involving older adults using attached list.

**Session 2 participants, measures, preparation for a clinical trial**

Date 3/8/11

**Topics:**

1. Defining the target population: effect of responsiveness, expected event rate and heterogeneity
2. Tracking the source, target, recruited, randomized and completing sample
3. Selection and implementation of recruitment strategies
4. Study materials: manual of procedure, intervention protocols, data collection protocols, equipment and materials, staff training
5. Primary and secondary outcomes, composite outcomes
6. Estimating event rates for power
7. Alternative methods for collecting data on primary outcome
8. Blinding
9. Methods of outcome monitoring and attribution
10. Design and implementation of the analysis plan: intention to treat, missing data, change effects
11. Plan for site visit to ongoing clinical trial involving older adults

Session Objectives:
1. Identify tradeoffs and challenges in obtaining an appropriate sample of older adults for a clinical trial
2. Understand how to optimize and track study recruitment
3. Be familiar with reporting expectations and study procedures related to recruitment
4. Understand the use and design of study materials for clinical trials
5. Be able to identify strengths and limitations of various choices of outcome measures
6. Describe the effects of lack of blinding on outcomes

Panel members: Greenspan, Karp

Class discussion for panel members:
1. What is your study design?
2. How did you define and find your target population?
3. How did you protocolize your intervention?
4. What is your comparison group?
5. What have you learned from your experience with RCTs in older adults? What is working well and what would you differently?

Readings:
Required

Bonk J A road map for the recruitment and retention of older adult participants for longitudinal studies. JAGS 2010 Oct;58 Suppl 2:S303-7


Assignment

Contact PI of your chosen trial to arrange at least one site visit. You may need to visit the trial more than once to acquire the information you need for your site visit report.

Session 3  Interventions

Date 3/15/11

Topics:
   1. single and combined interventions
   2. trial design, comparison groups, number of arms
   3. intervention and outcome target alignment
   4. randomization
   5. intervention reproducibility
   6. staffing
   7. respondent burden

Objectives
   1. Describe targets of interventions used for older adults (patient, provider, caregiver)
2. Identify the pros and cons of single versus multiple interventions
3. Describe the tradeoffs in randomization by individual versus cluster
4. Describe options for the comparison arm- placebo, usual care, delayed care, alternative trial intervention

Panel members: Glynn, Studenski, Reynolds

Class discussion for panel members:
1. What is your study design?
2. How did you define and find your target population?
3. How did you protocolize your intervention?
4. What is your comparison group?
5. What have you learned from your experience with RCTs in older adults? What is working well and what would you differently?

Readings:


Gomberg-Maitland M Frison L Halperin JL Active-control clinical trials to establish equivalence or noninferiority AM Heart J 2003 146:398-403


Optional

Optional
none

Assignment:
Continue work on critiques and site visit

Session 4 Pilot Studies
Date 3/22/11

Topics:
1. pilot studies and options for alternative designs (Moore)

Session Objectives:
1. Be able to determine the key aspects of trial development that can be addressed with various early phase trial designs

Panel members: Albert, Weiner, Goodpaster

Class Discussion with panel:
1. What is your study design?
2. How did you define and find your target population?
3. How did you protocolize your intervention?
4. What is your comparison group?
5. What have you learned from your experience with RCTs in older adults? What is working well and what would you differently

6. Readings:
Required

Optional


Assignment:
Continue work on critiques and site visit

Session 5 Safety monitoring, adverse events, student reports

Date 3/29/11

Topics:
1. Safety monitoring plan and team members
2. Adverse event monitoring, tracking and reporting
3. Stopping rules
4. Staff training for safety

Session Objectives:
1. Describe methods for monitoring trial safety
2. Describe options for managing intervention protocols throughout intercurrent illnesses and events

Class discussion:
1. What are the challenges of managing safety in trials with older adults?
2. What protocols and training have you used to promote safety in these trials?
**Readings:**
Cherubini A Del Signore S Ouslander J et al Fighting Against Age Discrimination in Clinical Trials JAGS 58:1791-1796 2010


LIFE MOP safety chapter

**Hour 2: Student reports from critical review of published clinical trial**

**Student Presentations**

Post course survey