

CLINICAL TRIALS COURSE

November 8, 2017 - February 7, 2018
MSB 2.103

November 3, 2017

Course Directors:

Andrew Barreto, MD, MS, Jon Tyson, MD, MPH

Assistant Directors:

Trey Miller, PhD, Joyce Samuel, MD, MS, Josh Samuels, MD, MS, Farhan Vahidy, MD, PhD, Ricardo Mosquera, MD, John Harvin, MD

Textbooks: Hulley SB et al. Designing Clinical Research, 4th edition. Lippincott, 2013

Before signing up, you should decide whether you wish to take course for Usual Credit or if you are highly committed and have the required time, for Honors Status. The requirements are noted below;

1. Usual Credit. Participation to obtain usual credit will require approximately 2 hours reading per week, attendance at class from 5-5:45 PM on Wednesdays and satisfactory completion the final examination which has generally been considered a difficult exam by participants

This material is designed to help you better understand and apply clinical research in patient care, particularly if you might want to serve as a co-investigator in clinical trials. All students should complete the assigned readings *before* class (excluding those marked with an asterisk which are required for honors students only). The lectures are intended to provide additional information and help you apply and integrate this information and that in the readings. Additional readings beside those noted below may be assigned, and may not be reflected on this schedule (notification will be made in class and by email.) You will also need to submit assignments by e-mail (Deborah.Garcia@uth.tmc.edu) on or before the dates below. Any material in the required readings or lectures may appear on the final exam. To pass the course you must attend at least 8 of the 11 sessions and attend or view the videotaped sessions of at least 10 of the sessions as well as pass the exam.

2. Honors. Participation for honors will require approximately 6 hours preparation per week, class attendance from 5-6:45 (with participation in small group sessions from 5:45-6:45), develop a detailed and well-conceived outline of an interventional study you would like to conduct, and learn the course material well enough to earn an honors on the final exam. Students who wish to take the course for honors should notify us at the e mail address above before the first class and attach their CV or Biosketch. We have a limited number of spots for honors students; please don't apply for honors if you can't realistically commit the time or effort required.

Provisional Plan: 4 honors groups, leaders (co-leaders): Baretto (Samuel), Miller (Mosquera), Samuels (Harvin), and Tyson (Vahidy)

Class Schedule and assignments (* indicates material required only for honors students).

Date/Topic	Speaker	Hulley Chapter	Other Reading	Other Assignment
<p>1. 11/8/2017- Clinical Trials: What Are They? When Are They Ethical and Necessary? When Are They Unethical or Unnecessary?</p> <p>Honors: Brief (10 minute) presentations of successful projects by 4 former course participants: Samuel, Harvin, Barreto, Mosquera</p>	Tyson	1,10	<p>Pound P et al. Is animal research sufficiently evidence based to be a cornerstone of biomedical research? BMJ. 2014 May 30; 348; g3387. (If you are a preclinical or translational investigator or you are clinician or clinical investigator concerned about the treatment recs. inferred from or based largely on animal studies, you may wish to also read Singh VP et al. Critical evaluation of challenges and future use of animals in experimentation for biomedical research. Int J Immunopathol Pharmacol. 2016;29:551-561).</p> <p>Glasziou P et al. When are randomized trials unnecessary? Picking signal from noise. BMJ 2007;334:349.</p>	*Honors:
<p>2. 11/15/2017 - What is the Study Question & Hypothesis? How Should the Treatment Effect Be Assessed and Interpreted?</p> <p>Honors: Small group sessions to discuss possible questions for study that group members hope to design.</p>	Barreto	2,3,4	Moher D et al. CONSORT 2010 Explanation and Elaboration: updated guidelines for reporting parallel group randomized trials. BMJ 2010;340:c869 .	*Honors: Before class, send to your group leader and to Deborah.Garcia@uth.tmc.edu and be prepared to discuss a treatment or management question in PICO format that 1) are important for your patients and of great interest to you; 2) have not been clearly answered in any well designed study; and 3) you may wish to evaluate in a systematic review or that your colleagues and you might assess in a pilot or definitive clinical trial funded with obtainable internal or external sources. (You can consider designs other than parallel group designs, including n of 1, stepped wedge designs, time series, or cluster designs).
11/22/2017 – THANKSGIVING Break				
<p>3. 11/29/2017 - How Should a Trial Be Designed to Maximize Validity, Precision, and Generalizability? Discussion of an Challenging and Influential Trial</p>	Tyson	5	<p>Guyatt G, et al. GRADE guidelines: 1. Introduction- GRADE evidence profiles and summary of findings tables. J Clin Epidemiol. 2011 Apr;64(4):383-9</p> <p>*Van den Berghe G et al. Intensive insulin therapy in the</p>	*Honors: Based partly on the discussions and readings to this point, e-mail to your small group leaders 2-3 page preliminary outline of interventional study

Honors: small group sessions to discuss attached two articles			<p>medical ICU. N Engl J Med 2006;354:449-461</p> <p>*Baicker K et al. The Oregon experiment – effects of Medicaid on clinical outcomes. N Engl J Med 2013;368:1713-22.</p>	question you hope to address.
<p>4. 12/6/2017 - Alternatives in Trial Designs</p> <p>Honors – small group sessions to discuss assigned two studies considering Kemming, Vohra, Wheatley and Poldervaart articles</p>	Blackwell /Samuel	11	<p>*Kemming K, et al. The stepped wedge cluster randomized trial; rationale, design, analysis and reporting. BMJ 2015;350:h391</p> <p>*Vohra et al. CONSORT extension for reporting N-of-1 trials (CENT) 2015 Statement. BMJ. 2015 May 14;350:h1738. (You may also be interested in Lillie EO et al. The n-of-1 clinical trial: the ultimate strategy for individualizing medicine? Per Med. 2011; 8: 161-173.)</p> <p>*Wheatley E, Kennedy KA. Cross-over trial of treatment for bradycardia attributed to gastroesophageal reflux in preterm infants. J Pediatr. 2009; 155: 516-521.</p> <p>*Poldervaart JM .Effect of Using the HEART Score in Patients With Chest Pain in the Emergency Department: A Stepped-Wedge, Cluster Randomized Trial. Ann Intern Med. 2017;166:689-69</p>	
<p>5. 12/13/2017 – Sample Size, Power, and Subgroup Analyses</p> <p>Honors – Small group sessions to discuss assigned two studies</p>	Barreto	6: (pages 55-59, 71, & 82 only)	<p>Schulz K, Grimes D. Sample size calculations in randomized trials: mandatory & mystical. Lancet 2005;365:1348</p> <p>Sun X, Ioannidis JPA, Agoritsas T, Alba AC, Guyatt G. How to use a subgroup analysis. User's guide to the medical literature. JAMA 2014;311:405-11.</p> <p>*Kraemer HC, Frank E, Kupfer DJ. Moderators of treatment outcomes: clinical, research, and policy importance. JAMA. 2006; 296:1286-9</p> <p>* Nichol G Trial of continuous or interrupted chest compressions during CPR. <u>N Engl J Med.</u> 2015;373:2203-14.</p> <p>*Kimmel SE, et al. A pharmacogenetic vs. a clinical algorithm for warfarin dosing. N Engl J Med 2013;369:2283-93.</p>	<p>Honors: e mail <u>revised</u> outline of Interventional Study Design without Sample Size.</p> <p>*Deborah.Garcia@uth.tmc.edu</p>
<p>12/20/2017</p> <p>12/27/2017 HOLIDAY BREAK</p>				

<p>6. 1/03/2018. Bayesian design and analysis of clinical trials; Estimating treatment effects; Bayesian vs. frequentist approaches</p> <p>Honors: Small group sessions - Discussion of one article</p>	<p>Pedroza</p>	<p>Lilford R. Clinical trials and rare diseases: a way out of a conundrum. <i>BMJ</i> 1995;311:1621-5.</p> <p>Bayesian clinical trial designs: Another option for trauma trials? Jansen JO1, Pallmann P, MacLennan G, Campbell MK; UK-REBOA Trial Investigators. <i>J Trauma Acute Care Surg.</i> 2017 Oct;83(4):736-741</p> <p>*Wijeysundera DN, Austin PC, Hux JE, Beattie WS, Laupacis A. Bayesian statistical inference enhances the interpretation of contemporary randomized controlled trials. <i>J Clin Epidemiol.</i> 2009 Jan;62(1):13-21.e5.</p> <p>*Laptook A et al. Effect of Therapeutic Hypothermia Initiated after 6 Hours of Age on Death or Disability among Newborns with Hypoxic-Ischemic Encephalopathy: A Randomized Clinical Trial, in press, <i>JAMA</i></p>	
<p>7. 1/10/2018 – Learning Healthcare and Comparative Effectiveness and Quality Improvement Trials.</p> <p>Honors: Small group sessions - Discussion of two articles</p>	<p>Wootton/ Miller</p>	<p>Grumbach K, Lucey CR, Johnston SC. Transforming from centers of learning to learning health systems. The Challenge for academic health centers. <i>JAMA</i> 2014; 311:1109.</p> <p>Wootton S et al. Unproven therapies in clinical research and practice: The necessity to change the regulatory paradigm. <i>Pediatrics</i> 2013;132:599-601.</p> <p>Fan E et al. How to use an article about quality improvement. <i>JAMA.</i> 2010;304:2279-87</p> <p>Cho, MK et al. Attitudes toward risk and informed consent for research on medical practices: a cross sectional survey. <i>Ann Intern Med</i> 2015; 162: 690 (<i>you need read only the abstract</i>).</p> <p>*Noto MJ et al. Chlorhexidine bathing and health care-associated infections: a randomized clinical trial. <i>JAMA</i> 2015; 313:369-78,</p> <p>* Carlo WA, et al. Target ranges of oxygen saturation in extremely preterm infants. <i>N Engl J Med.</i> 2010 May 27;362(21):1959-69</p>	

<p>8. 1/17/2018 - Systematic Reviews</p> <p>Honors: Small group sessions - Discussion of 2 articles</p>	<p>Samuels/ Kao</p>	<p>Shamseer L. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. <i>BMJ</i>. 2015 Jan 2;349:g7647</p> <p>How to read a systematic review and meta-analysis and apply the results to patient care: users' guides to the medical literature. Murad MH et al. <i>JAMA</i>. (2014)</p> <p>* Effect of dietary sodium restriction on arterial stiffness: systematic review and meta-analysis of the randomized controlled trials. D'Elia L, Galletti F, La Fata E, Sabino P, Strazzullo P. <i>J Hypertens</i>. 2017 Oct 27.</p> <p>* Effects of bariatric surgery on glycemic and lipid metabolism, surgical complication and quality of life in adolescents with obesity: a systematic review and meta-analysis. Qi L, Guo Y, Liu CQ, Huang ZP, Sheng Y, Zou DJ. <i>Surg Obes Relat Dis</i>. 2017 Sep 19. pii: S1550-7289(17)30924-3. doi: 10.1016/j.soard.2017.09.516.</p>	
<p>9. 1/24/2018 – Dissemination, Implementation, and De-Implementation Research</p>	<p>Wootton/ Kao</p>	<p>Rabin BA, Brownson RC, Haire-Joshu D et al. A glossary for dissemination and implementation research in health. <i>Journal of Public Health Management and Practice</i> 2008; 14(2): 117-123.</p> <p>*Glasgow R, Magid DJ, Beck A et al. Practical clinical trials for translating research to practice: design and measurement recommendations. <i>Med Care</i> 2005; 43: 551-557.</p> <p>Prasad V, Ioannidis JP. Evidence-based de-implementation for contradicted, unproven, and aspiring healthcare practices. <i>Implement Sci</i>. 2014; 9: 1. PMC3892018.</p> <p>* Extended Consort with RE-AIM figure (e mailed to you)</p> <p>*Rycroft-Malone J, Seers K, Crichton N et al. A pragmatic cluster randomised trial evaluating three implementation interventions. <i>Implement Sci</i> 2012 Aug 30; 7: 80.</p> <p>* Tija J, Field T, Mazor K et al. Dissemination of</p>	<p>*E-mail Final study outline with Sample Size to: grp leaders & Deborah.Garcia@uth.tmc.edu</p> <p>Receive <u>Final Exam</u>.</p>

Honors: Small group sessions Discussion of two articles			evidence-based antipsychotic prescribing guidelines to nursing homes: a cluster randomized trial. <i>J Am Geriatr Soc</i> 2015 Jul; 63(7): 1289-98.	
10. 1/31/2018 - Cost Effectiveness, Cost Utility, and Cost Benefit Analyses in Clinical Research Honors – small group sessions review of one study	Swint		Husereau D, Drummond M, Petrou S, et al. Consolidated Health Economic Evaluation Reporting Standards (CHEERS) statement. <i>J Med Econ.</i> 2013;16(6):713-9. *Luce BR, Drummond M, Johnsson B, Neumann PJ, Schwartz JS, Siebert U, Sullivan SD. EBM, HTA, and CER: Clearing the Confusion. <i>Milbank Memorial Fund Quarterly</i> , Vol. 88, No. 2, 2010 (pp. 256–276) *Mosquera R et al. Effect of an enhanced medical home on serious illness and cost of care among high-risk children with chronic illness: a randomized clinical trial. <i>JAMA</i> 2014;312:2640-8. (40 minutes)	E-mail Final Exam by 5 PM to Deborah.Garcia@uth.tmc.edu
11. 2/7/2018 - Review of Exam Honors- small group sessions- case presentations	Barreto		Review notes for any questions that you were uncertain about .*Small group sessions: presentation and critique of 3 of best study designs (20 minutes each [concise 5 min presentation; 15 min discussion])	