Overview

In this seminar course, students will review published papers and other methodological aspects of randomized controlled trials that are relevant to oral epidemiology. Each student who has enrolled for credit will select one paper from the published literature describing findings from a randomized controlled trial, conduct a critical review of it, and present their review at one session towards the end of the semester. The semester assignment is a review of a randomized controlled trial that has been submitted to a journal for publication.

Policies

The class will meet in a seminar setting for one or two hours per week. Students are expected to attend and participate in each session. Class materials will be circulated by email in the week before each session.

Meeting times and location

The class will meet weekly on Tuesdays at 1-2 pm in room 4615, Koury Oral Health Sciences Building, UNC School of Dentistry. Additional times for student presentations will be determined during the first few weeks of class.

Assignments to be completed by students enrolled for credit

1. In-class presentation of a paper selected by the student

During the first few weeks of class, each students enrolled for credit will identify a published paper of a randomized controlled trial and verify its suitability with Dr. Slade. Students will critically review the paper and present it at a class meeting later in the semester, at a date to be determined. Students will be graded on three aspects of their presentation.

   a) A slide presentation that summarizes key aspects of the selected study, focusing on methodological issues that are important for epidemiologic interpretation.

   b) Up to half a dozen questions relating to the study. Questions should be circulated one week before class.

   c) During the class, students will lead a focused discussion among all attendees to address the previously-circulated questions and other topics that arise during the class.
2. Written review of a paper submitted for publication

During the first week, Dr. Slade will provide students with a paper from a randomized controlled trial that has been submitted for publication in a journal. Students will prepare a written critique, as though they were acting as a peer reviewer for the journal. The written critique should have three sections:

a) One paragraph summarizing the paper’s key findings from an epidemiologic perspective – do not simply repeat the abstract
b) Up to one paragraph summarizing your principal reason(s) for your praise, criticism (or both) of the paper
c) Itemized critique of aspects of the paper that are weak or that require clarification, including your justification for each critique

Reviews must be guided by three CONSORT documents, which can be downloaded from http://www.consort-statement.org/home/:

- CONSORT Statement
- Consort checklist and flow diagram
- CONSORT “Explanation and Elaboration” document

Students must respect the intellectual property of the paper’s authors. Specifically, students should not circulate the paper to others and they should not discuss the papers’ findings with people who are participating in the class.

Grading

H  Attendance at all classes, with active participation in at least some aspects of the discussion at each class. Thorough and critical appraisal of the student’s selected paper, as evidenced by thought-provoking questions, engaging slides and probing discussion during class. Detailed written critique of the submitted paper, showing evidence of advanced knowledge of each of the paper’s epidemiologic strengths and weaknesses.

P  Attendance at most classes with some contributions to discussion. Competent review of the student’s selected paper, and adequate leadership of discussion in class. Sufficient written critique of the submitted paper that reflects some of the study’s epidemiologic strengths and weaknesses.

F  Unexcused absence from three or more classes. Incomplete and/or uncritical review of the student’s selected paper and/or submitted paper.

Students enrolled for credit should work independently on their two semester assignments.
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**Reading materials**

1. **Overview of clinical trials. Slade**
   
   
   1. Do you think we should use the term “randomized clinical trial” or “randomized controlled trial”? Why?
   2. What features distinguish between Phase I, II, III and IV trials?
   3. What are the advantages and disadvantages of specifying a composite outcome?
   4. What are the advantages and disadvantages of specifying a surrogate endpoint?
   5. According to the authors, what are the main reasons for undertaking a pilot study?
   6. According to evidence hierarchies, randomized trials provided the best evidence about disease causation. What problems occur in clinical trials that can hamper causal inference?

2. **Trials of superiority and equivalence. Slade**
   
   
   1. Distinguish between statistical significance and clinical significance
   2. What metric does the author use to quantify clinical significance? What thresholds of the metric are used to make qualitative judgments about clinical significance?
   3. What conclusions about treatment superiority would you draw in an "active-control equivalence study" (ACES) where the ratio (90% confidence limits) of the treatment effects was 0.93 (0.88, 0.98), what conclusions would you draw about superiority using the three rules described by the author: SSR, CSR and TCR?
   4. And based on the same data, what conclusions would you draw about the experimental treatment being: a) equivalent; b) at least as good as the comparison treatment?
   5. Identify the data point in Figure 5 that supports the authors finding at page 354 that “On the other hand, the percentage of false positives (nonsuperior products concluded as superior) for the SSR is too large for the symmetric population (σ=0.38)”
   6. The author states that careful screening of patients to increase homogeneity of treatment groups will reduce the standard deviation, thereby making it easier to make the required inference. What steps can be taken in a clinical trial to reduce standard deviation?

3. **Split mouth study designs. Divaris**
   
   
   1. Philippe Hujoel (1992) discusses carry-across effects as one of the most important threats to the validity of split-mouth studies. What are some examples of carry-across effects?
   2. Of those carry-across effects, which are likely to be important ones?
   3. What are the differences between a carry-across effect and ‘no treatment’ effect or placebo?
   4. The author quotes a book chapter from Kleinbaum’s textbook claiming that “imprecise valid estimates are better than precise invalid estimates”. What are your thoughts? (consider that we’re typically interested in estimating probability densities rather than single point estimates)

4. **Intention-to-treat. Tchivileva**

   Spring break - no classes.

   AADR meeting - no classes.

5. **Group randomized study designs. Slade**

6. **Student presentation + discussion. Student**
7. Crossover study designs. Tchivileva

8. Student presentation + discussion. Student

9. IRB requirements for clinical trials. Sanders

10. Student presentation + discussion. Student

11. Data coordinating centers in clinical trials. Arbes

12. Student presentation + discussion. Student

13. TBD. TBD