# The ABCs of randomized controlled trials

# Course organizers

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# Presentations

Presenters and presentations may change.

| **Time**  | **Topic** | **Speaker**  |
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| 1-1:10pm | Welcome and introduction | Tianjing Li, MD, MHS, PhD andPenny Asbell, MD, FACS, MBA, FARVO |
| 1:10-1:45pm | Why do a RCT: Identifying your research question, key steps for developing a RCT | Penny Asbell, MD, FACS, MBA, FARVODepartment of Ophthalmology, University of Tennessee Health Science Center |
| Overview of types of clinical trials and the pyramid of research design that reflects the quality of evidence will be described. History and attributes of randomized clinical trials (RCT) that are now considered the “gold standard” of evidence are outlined. Steps to get started in developing a RCT beginning with a clear, straightforward question(s) or hypothesis and how the RCT will address the question and what metrics will be used as outcome measures. Key steps to develop your one-page summary of the planned RCT, including background, what work has been done to date, specific aims to be addressed and value of planned study to public health and future research. Overview of key planning steps and the most important considerations for a successful RCT reviewed. Links to further information provided.  |
| 1:45-2:30pm | How to minimize bias?  | Mae Gordon, PhD, Washington University, St. Louis  |
| Bias corrupts data. Statistical adjustments cannot usually restore data integrity. The magnitude of common sources of bias will be described, such as bias from clinician /patient expectation and differential recruitment, retention or treatment. Will describe how to mitigate these biases by proactive monitoring, randomization, masking of clinicians and participants, and participant retention strategies.  |
| 2:30-3:10 | What are different trial designs? | Jimmy T. Le, ScD, MAProgram Director for Collaborative Clinical ResearchNational Eye Institute, National Institutes of Health |
| Clinical trial design refers to the structure and sequence of activities that clinical trialists (investigators) follow to answer a specific research question. The most common clinical trial design is the parallel group, two-arm, randomized trial. Investigators randomly assign participants to two groups (arms). Depending on the research question, both groups may receive different interventions (e.g., treatment arm vs active comparator arm) or one group may receive the intervention and the other serves as control (e.g., treatment arm vs placebo). Investigators observe (follow-up) participants for the outcome of interest, and they compare differences in outcomes to determine the effect of the intervention.Choice of clinical trial design depends on the trial objectives and factors such as availability of resources and ethical considerations. For example, it is possible for investigators to alter the allocation ratio reflecting the intended relative number of participants randomized to each group (e.g., 2:1 or 3:1). Investigators may also adopt a parallel group design that includes three or more arms (e.g., treatment A vs treatment B vs placebo). Adding more groups in a parallel group design, however, means that investigators will need to recruit more participants to maintain power, i.e., the probability of detecting a difference in outcomes between study groups, if a true difference does exist. Instead, investigators may want to consider other designs such as:* (i) Crossover – a design where participants receive both intervention and comparator but at different time points, effectively allowing each participant to serve as their own control.
* (ii) Factorial – a design where two or more sets of interventions/comparators are tested simultaneously, allowing investigators to study how multiple interventions affect outcomes independently and together.
* (iii) Cluster-randomized – a design where groups (clusters) of participants are allocated to different arms, rather than individual participants.

In this session, we aim to outline different clinical trial designs and their purposes. Investigators should be able to justify their choice of clinical trial design and recognize how this decision may influence study methods, conduct, analysis plan, length of follow-up, and interpretation of results. We will also briefly discuss considerations for sample size and power calculations and how they may change depending on the clinical trial design. |
| 3:10-3:30 | Break (20 minutes)  |  |
| 3:30-4:10pm | Key components of a clinical trial’s protocol, manual of operations, and monitoring plan. | David Musch, PhD, MPH, FARVO, Department of Ophthalmology and Visual Sciences, Department of Epidemiology, Kellogg Eye Center, University of Michigan  |
| The protocol of a clinical trial specifies the trial’s design, objectives, eligibility criteria, sample size, unit of randomization, visit schedule, primary and secondary outcome variables, masking requirements, and a summary of the statistical analysis plan. An example will be provided from a protocol of an ongoing ophthalmic clinical trial. The background of the trial, all protocol elements, detail on methods used to obtain outcome measures, data entry and forms to be used, are fleshed out in the trial’s manual of operations, which provides those who enroll and examine trial participants all they need to know to properly address the trial’s requirements. An example of a manual of operations from a multicenter trial will be provided. As clinical trials expose participants to devices or drugs that may have safety implications, need to be conducted efficiently, and yield results that are credible, data monitoring committees (DMCs) are assigned to oversee the safety of trial participants as well as the conduct and integrity of the trial. An overview of when DMCs are needed, their responsibilities. composition, typical meeting format, and legal considerations will be provided. |
| 4:10-4:30pm | Approvals and regulations needed in randomized controlled trials | Tianjing Li, MD, MHS, PhDDepartment of Ophthalmology, University of Colorado Anschutz Medical Campus |
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| 4:30-5pm | Panel and Q&A | All speakers |
| Open panel discussion about the role of the PI, the organization and resources needed to conduct a multi-center RCT in eye and vision (e.g., coordinating centers, reading centers, and enrollment centers). |
| 5pm | Adjourn |  |