1-day Agenda for Designing Randomized Controlled Trials

1. Importance of randomized controlled trials in clinical research (9:00 – 9:20)

- Levels of evidence in clinical research
- Difference between RCTs and observational studies
- Relevant limitations

This module provides the foundation for the day by establishing the importance of RCTs as the gold standard in evaluating the efficacy of an intervention. We discuss the various types of study designs used in clinical research and compare experimental (RCTs) and observational studies. We also highlight some of the important limitations of RCTs that researchers should be aware of before they begin.

2. Ethical guidelines and trial registration (09:20 – 10:15)

- Working with human participants
- Ethical approval and clinical trial oversight
- Conflicts of interests
- Importance of trial registration

This section covers numerous ethical issues that researchers need to be aware of when conducting RCTs. We first discuss the Declaration of Helsinki and working with human participants. We then review ethical approval of the study before it begins as well as reviewing the integrity of the trial during the study. As pharmaceutical companies are frequently involved in RCTs, we then discuss potential conflicts of interests and how they should be handled. Lastly, we discuss the importance of prospective registration of RCTs in WHO-approved trial registries and how to do this properly.

Break (10:15 – 10:30)

3. Randomized clinical trial designs (10:30 – 12:00)

- Rationale for different phases and types of RCTs
- Parallel designs
- Cross-over designs
- Adaptive designs

This module introduces the different designs associated with RCTs. We first discuss the various phases (phase I through IV) and their goals, as well as when to conduct superiority, non-inferiority, and equivalence trials. We then discuss parallel designs, which are the most common RCT design, but highlight some of its limitations as well. We then review two other commonly used designs to overcome these limitations, such as cross-over and adaptive designs.

Lunch (12:00 – 13:00)

4. Ensuring you enroll the right participants (13:00 – 14:10)

- Avoiding underpowered studies
- Inclusion and exclusion criteria

This section focuses on how to ensure your RCT has improved generalizability and external validity. We begin by discussing how to determine the appropriate number of participants, such as power calculations and estimating attrition. We then review how to define appropriate inclusion and exclusion criteria to minimize selection bias in the RCT.

Break (14:10 – 14:20)

5. Sampling and randomization (14:20 – 15:30)

- Sampling strategies
- Randomization strategies

This section first reviews the importance of probability sampling followed by a discussion of stratification and clustering to improve generalizability. We then discuss various randomization strategies to strengthen the design and improve the reliability of the results.

Break (15:30 – 15:40)

6. Trial monitoring and interpreting results (15:40 – 16:50)

- Interim analyses
- Evaluating efficacy and safety
- Subgroup and sensitivity analyses
- Selective reporting and publication biases

This final module focuses on evaluating data obtained during the trial. We first review the advantages and disadvantages of interim analyses and then discuss properly evaluating efficacy and safety of the intervention. Next, we review how to properly conduct subgroup and sensitivity analyses along with their limitations. Lastly, we highlight the importance of transparency when reporting RCTs by avoiding selective reporting and publication biases once the study is completed.

Final Q&A (16:45 – 17:00)