# Chapter 1

# Clinical Trial Design

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## Aim

The purpose of this chapter is to provide students with a comprehensive overview for the critical aspects of designing a RCT using the SPIRIT guidelines.

## Summary

Randomised trials are conducted to provide evidence to support better and more informed decisions about medicine and other healthcare initiatives. Trials support these decisions through the results generated by collecting data guided by a research question and appropriate trial design to answer this research question. Trials are designed to minimise bias as far as possible. Typical methods to reduce bias are, for example, the use of a control group, randomisation etc. The purpose of the randomised trial is assessment of efficacy, safety, or risk benefit ratio and the goal may be to show treatment superiority, non-inferiority, or equivalence when compared to placebo or standard therapy. Clinical trials are usually described based on their phase: Phase 1, 2, 3 and 4. These may include trials of therapeutic agents, prophylactic agents, diagnostic agents, surgical procedures, or health service strategies. Who is involved in the design of the trial is usually at the discretion of the principal investigator, but we would like to see a full trial design team, including, statisticians, methodologists, patients and the public representatives, research nurses, trial managers, data scientists and quality and regulatory affairs representatives. The Randomised Controlled Trial design is crucial to ensure the trial is effectively designed to collect the trial outcomes and answer the research question with high quality data.

## Methods

E-learning materials (study materials, links to publications), quiz questions, discussion boards.

## Learning Outcomes

Students will

1. Apply the SPIRIT guidelines to trial design.
2. Apply what was learned to correctly develop a clinical trial protocol when given a specific study question.
3. Compare and contrast trial designs aimed at establishing superiority vs. equivalence and non-inferiority.
4. Discuss equipoise and how it relates to developing the research question.
5. Explain the importance of allocation concealment for the integrity of a trial, and evaluate commonly used methods for achieving it.
6. Discuss the use of cluster-randomized trials.
7. Apply randomisation principles to discuss the difference between cluster randomisation and individual randomisation and when to apply one of the two.

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8. Apply the PRECIS 2 tool to design an explanatory or pragmatic trial.

**Complementarity to CONSCIOUS I Materials**

While CONSCIOUS I is focused on introductory epidemiological principles and discussed the basics of trial design in terms of phases, parallel trials, superiority/equivalence/non-inferiority, it was taught at the level for undergraduate students. We will now discuss in depth specific and more advanced designs: cluster randomised trial, adaptive designs. The concept of pilot and feasibility studies will be discussed and their role in the clinical trial lifecycle. Students will become skilled in protocol design and learn to utilise the SPIRIT (Standard Protocol Items: Recommendations for Interventional Trials) guidelines, widely endorsed as an international standard for trial protocols. The module will be addressing each of the SPIRIT items (https://www.spirit-statement.org/) to design a clinical trial and write a trial protocol. This was not covered in CONSCIOUS I.

**Content**

1 Introduction to the chapter
2 Review of Superiority, Non-Inferiority and Equivalence Trials
3 Trial Phases
4 Cluster Randomised Trials
5 Adaptive Trial Design; Explanatory and Pragmatic Trials
6 The SPIRIT 2013 Statement
7 PICO, Equipoise and the Research Question
8 Eligibility Criteria and Outcome Data
9 Sample Size, Randomisation
10 Blinding
11 Conclusion

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