Clinical Trials Formative

Raul Unnithan

Durham University

February 3, 2025

Contents

Chapter 1 Questions

1.1 Question 1 (10 marks)

Suppose a trial is designed to have an 80% power to detect a difference of τ_M, with a significance level of $\alpha = 0.05$. The trial is run with the required number of participants. When the data is analysed, the P-value is greater than α.

(a) **Can we conclude that there is no difference between the treatment and control?**

Since the p-value is greater than the significance level ($\alpha = 0.05$), we fail to reject the null hypothesis, i.e. there is no difference between the treatment and the control. Therefore, there is insufficient evidence to suggest a significant difference between the treatment and control groups based on this test at a 5% level.

(b) **Can we conclude that there is no clinically significant difference between the treatment and control?**

The p-value is greater than 0.05, so we do not have statistical evidence to support a difference. However, whether there is no clinically significant difference cannot be concluded depending on the context and the size of the difference, even if it's not statistically significant.

(c) **Assume the true treatment effect is $k\tau_M$, where $0 < k < 1$. What is the trial's probability of detecting this difference? You can assume that the variance σ^2 was specified when calculating the sample size accurately, and you can use R (or similar).**

The trial was originally designed with 80% power to detect a treatment effect of τ_M at a significance level of $\alpha = 0.05$. However, if the true treatment effect is $k\tau_M$, where $0 < k < 1$, the power to detect this smaller effect decreases.

The table below shows how power changes with different values of k. The table's results indicate that as the true treatment effect becomes smaller (i.e., as k decreases), the probability of detecting this effect also decreases. For example, if the true treatment effect is only 10% of τ_M ($k = 0.1$), the trial has only about a 5.9% chance of detecting this difference. Conversely, if the true effect is closer to the hypothesised effect ($k = 0.9$), the power increases to approximately 71.3%.

k	Power
0.1	5.9%
0.2	8.7%
0.3	13.4%
0.4	20.2%
0.5	28.9%
0.6	39.0%
0.7	50.1%
0.8	61.1%
0.9	71.3%

1.2 Question 2 (10 marks)

Listen to the 'JAMAevidence: JAMA Guide to Statistics and Methods' podcast episode on Randomisation. The episode contains a discussion about relying on observational data from the wider population rather than randomised controlled trials. Explain some of the main arguments for and against this approach (at least one point in each direction).

One of the main advantages of relying on observational data rather than randomised controlled trials (RCTs) is its availability. The podcast notes that patient populations in RCTs tend to be idealised and may not generalise to the average patient. And that observational data should be relied upon because it is a lot more available, and we can see how treatments play out in actual clinical practice.

However, there are arguments against using observational data rather than RCTs, such as a high subject to bias because of unrecognised confounding. There are many factors that determine what treatments patients are recommended or take or successfully complete in routine clinical care, and it is highly unusual for the data sets that are available administratively to truly allow us to adjust for those patient characteristics that may affect the choice of therapy or compliance.

1.3 Question 3 (10 marks)

Read the article 'Designing a research project randomised controlled trials and their principles' Kendall (2003). Identify three issues relating to design/planning that we haven't covered in the course (so far!), and briefly discuss their impact on the trial.

One issue is the importance of pilot studies in trial design. Pilot studies will guide decisions about designing approaches to recruitment and outcome measurement. A limited

pilot study is essential to gauge the recruitment rate and address in advance any practical issues that may arise once data collection in the definitive study is underway.

Another is the need for blinding. Blinding is an essential part of RCTs to reduce bias, but it is not always feasible. For example, surgical trials make it difficult to blind participants, and some treatments may have distinct side effects that reveal group allocation. Kendall (2003) discusses that if blinding is ineffective, investigator bias or participant expectations could influence outcomes. In some cases, systematic testing of blinding effectiveness is recommended to assess its impact on the results.

Another issue is confounding. Confounding occurs when factors related to both the intervention and the outcome distort the true effect of treatment. Kendall (2003) notes that while Randomisation helps balance these factors, it does not always guarantee equal distribution, especially in small trials.