Critical reading of clinical study results

Introduction

Clinical study results comprise all the data, measures, and statistical analyses generated during a clinical study. They include a description of the study population, baseline data, measures capturing the effect of the treatment on participants, and adverse events experienced by the study participants. Clinical study results and analyses enter the public domain through various channels, especially through scientific meetings and in medical journals.

Readers should perform a critical reading of clinical study results, in particular to assess the levels of evidence present and to identify any possible sources of error in the publication. The reader must take into account relevant information from the best available sources. The reader may search the literature to identify relevant articles by using the available tools – for instance, PubMed. The reader could also consider texts published by reputable organisations (for example, the EMA, the FDA, or national or international umbrella patient organisations).

The following article covers questions that the critical reader may address in their review of clinical study results.

Is the study reliable?

- Consider whether the **objectives** and the precise nature of the hypothesis are clear.
- Can the results of the study be **generalised** to the broader population? The reader needs to consider to whom the results of the trial can be applied. The

characteristics of the recruited population sample need to be described.
- Are all **treatments used in the study clearly detailed**, and would the experimental treatment be relevant to the reader's question?
- What are the patient's likely **benefits and risks** from the therapy?
- Consider any **conflicts of interest** – whether the authenticity and objectivity of the research can be relied upon.

Is the study methodology appropriate to assess the stated hypothesis?

- Is the **reference treatment** a fair comparator that corresponds to current practice? Is it a placebo, available therapy, best supportive care, or a historical control group?
- The **study population should be clearly defined**. It should be clear whether the whole population or a subset has been studied, and whether there is any possible selection bias. Consider the relevance and reasons of any patients who have dropped out of the study.
- Assess whether the **control group** was well matched and whether any exclusion criteria were valid.
- Are the study **endpoints** well defined and meaningful?
- Is it clear how the study was **powered** for the primary endpoint?
- Was the study **long enough for the outcome measure to occur** and in order to capture enough events?

Are the results convincing?

- The results should be clearly and objectively presented

in **sufficient detail** – for instance, results broken down by disease stage, age, gender, and/or any possible confounder.
- Consider how convincing the results are, whether the **statistics are appropriate**, and whether there are any possible alternative explanations for the results.
- Identify the **rate of loss of follow-up** during the study and how **non-responders** have been dealt with – for instance, whether they have been considered as treatment failures or included separately in the analysis.
- Check for any **bias**. Assess whether the researchers controlled or reduced this risk.

Is the discussion section convincing?

- The discussion should include **all the results** of the study and not just those that have supported the initial hypothesis.
- The discussion should address whether the initial objectives have been met, and whether the **research question(s) has been answered**.
- Assess whether the authors have **ruled out possible bias** and acknowledged the possible limitations of the study.
- Check whether any generalisation is made by incorrectly applying the study results.
- Check whether it fits with **existing literature** (always look for other publications on the same topic).

Is the demonstrated effect clinically significant?

- Critically assess if the claimed effects are clinically relevant – **do they have a significant effect on the health of a patient?** For instance, a statistically

significant effect may be of such low magnitude that it is not clinically relevant for the patient. The larger the size of the trial, the smaller the magnitude of the effect that can be detected becomes. A statistically significant but non-clinically relevant effect could be the result of an oversized or overpowered clinical trial.

- On the other hand, the absence of evidence does not mean the absence of any effect. When a statistically significant difference is not found between the study arms, this does not mean that the compared treatments are equivalent. This is because statistical tests do not measure for evidence in support of the hypothesis, but rather set out to evaluate the evidence that supports the null hypothesis not being true (evidence that supports the null hypothesis). In other words, statistical tests attempt to validate the null hypothesis. Even if the efficacy of the treatments truly differ, a statistical test may be non-significant due to the play of chance (Type II Error) or because an insufficient amount of information is available (small study size, lack of power).

Are the conclusions valid?

- The conclusions provided by the author should be supported by the **available data**. Check that the conclusions relate to the stated aims and objectives of the study.

Attachments

- Presentation: Critical Reading of Clinical Study Results

  Size: 399,949 bytes, Format: .pptx

A presentation describing how to do a critical reading of clinical study results, which can be adapted for own use.

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