

Clinical trials — discussing your findings

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Abstract

Discussing findings of a clinical trial gives an opportunity to the investigator to elaborate the meaning of the findings of the trial. It should consist of the major findings, interpretation of the results in light of the available literature, theory and practice, limitations, generalizability of the findings and its implication, and way forwards for future research. One should avoid repetition of results in the discussion and give critical appraisal of the findings in such a way as to give a true picture of the internal and external validity of the clinical trial.

Keywords: Discussion, CONSORT, Interpretation, limitation, Generalizability.

Introduction

Clinical trial, as defined by world health organization (WHO), is a prospective clinical research that assigns human participants or group of human participants to a health intervention (including but not restricted to drugs, biological products, surgical procedures, radiological processes, behavioral treatment, preventive care etc) and measures its effect on health related outcome.¹ Phases of clinical trial include:²

- ◆ Phase-1: It aims at investigating the metabolic and pharmacological effects and side effects of the biological agent in humans including its safety and safe dose ranges. It usually involves 20 to 80 healthy participants or patients.
- ◆ Phase-2: It investigates the efficacy of the new drug or treatment in 100 to 300 patients and also assesses its relative safety.
- ◆ Phase-3: These clinical trials are large randomized trial to measure the effectiveness and relative safety of the intervention. Sample size usually range from 1000 to 3000 or more participants.
- ◆ Phase-4: These studies are usually referred as 'post-

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marketing surveillance study' as it studies the side effects of the drug once brought in use by the general public.

Intervention can be allocated to the participants randomly, meaning that each participant has an equal chance of receiving the intervention (new treatment) and control (placebo or standard treatment). In this case it is called 'randomized controlled trial'. Reporting of the clinical trial should be done step by step using the checklist provided by the revised CONSORT (Consolidated Standards of Reporting Trials) statement 2010.³ Discussing the findings of clinical trial is as important as reporting the rationale, objectives, hypothesis, planning and conduct of the trial in the 'Introduction' and 'Methodology' section of the manuscript and reporting findings in the 'Results' section. This review will embark upon the importance of the 'Discussion' section, its intellectual content and how to write it in an effective way.

Importance of Discussing the Clinical Findings

Though discussion section is considered the last segment of writing a research paper or dissertation/thesis, it is the heart of the research paper. It is considered pivotal to the research as the meaning of the results in the light of the research question and explaining them to the readers is the task one seeks to achieve in the discussion section.⁴ It is not simply the summary of results or findings of the research, but a critical appraisal of the findings of the trial.

Content of the 'Discussion' of the Clinical Trial

'Discussion' is the segment that appears after 'Results' in reporting of the clinical trial. According to the revised CONSORT (Consolidated Standards of Reporting Trials) statement 2010, it appears as item number '20-22', namely limitations, generalizability and interpretation on the checklist.³ These CONSORT statement items of discussion must be covered, irrespective of the sequence they appear in. The following logical flow of the discussion section should be followed:

1- Major Findings

State the major findings of the trial clearly in the first paragraph of the discussion section. Remember that this does not mean repetition of the results.

Example: Samaha FF et al in their clinical trial on obesity,⁵

states as the first line of discussion: "We found that severely obese subjects with a high prevalence of diabetes and the metabolic syndrome lost more weight in a six-month period on a carbohydrate-restricted diet than on a fat- and calorie-restricted diet"

2- Interpretation

After elaborating on the major findings, interpret these findings according to the available literature. Findings from other clinical trials may support or refute the findings of your clinical trial — explain in both cases, as to what may have lead to such findings. Systematic review of other such trials should be referred to whenever possible, as it gives a whole picture to the audience as to how the current trial was similar or different from the rest with regards to the study population, study settings and others which have led to the findings reported.³

Example: Friendenreich CM states in their randomized controlled trial of physical activity in post menopausal women:⁶ "Our study differed from previous randomized trials exercise interventions among postmenopausal women that were at least 6 months duration and examined adiposity outcomes. It had a large sample size, used quantitative imaging techniques that are preferable for measuring adiposity, had a low drop-out rate, excellent adherence and used a supervised, high volume of exercise. Of these trials, only two studies carried out by Irwin et al. in the United States and Velthuis et al. in the Netherlands were sufficiently comparable with ours with respect to study design, exercise volume and outcome measures."

3- Limitations

The limitations of the study and methods implied to minimize them should be discussed in detail. This is done to prove the internal validity of the clinical trial. 'Internal validity' refers to the conduct of the trial in such a way as to minimize the potential biases in the study to eliminate the likelihood of obtaining the results of the clinical trial by chance. Precision or imprecision in the conduct of the study as well as the reporting of the results should be mentioned.³ One may also attempt to do a subgroup analysis in order to discuss the limitation and overcoming of the limitation of the trial under study. Confidence interval (CI) gives more information than the p-value; narrow CI not only points towards the precision of the results, but the non-overlapping of CI also indicate the statistical difference of the intervention arms in the clinical trial and vice versa.

Example: Galmiche JP et al in the discussion of LOTUS trial,⁷ states that "...14% of participants randomized to

receive surgery were not operated on for various reasons. Despite our efforts, we were unable to follow up this patient cohort, who did not differ from participants at baseline but who declined surgery. For this reason, we performed a sensitivity analysis with best and worst-case scenarios as summing that all participants not completing the study after randomization either had treatment response or treatment failure. The results of this were similar to our overall findings."

4- Generalizability

'Generalizability' or 'External Validity' of the study means the extent to which the results of the current study/clinical trial can be generalized to those similar in characteristics to the study population. Internal validity is a pre-requisite for the external validity.³

Example: Richardson AJ et al in the DOLAB study,⁸ mentions about generalizability of their clinical trial: "Generalizability to all children aged 7-9 years attending mainstream UK schools is clearly limited, as our sample was pre-selected for underperformance in reading. In terms of socioeconomic status, the children in this study were fairly representative of the general population of England, as the percentage receiving free school meals was comparable to national figures (20.2% vs. 18.6%)."

5- Implication of the clinical trial and way forwards

Health policy implication of the finding should be discussed as patient benefit and practice of evidence based medicine is the aim of all the clinical trials.⁴ This should be discussed in the concluding paragraph. Future research based on current findings should also be suggested to fill in the research gap on the topic under study.

Example: Hollis BW et al in their trial on Vitamin D supplementation in pregnant females,⁹ writes: "...owing to safety concerns that surrounded the use of 4000-IU of vitamin D supplementation during pregnancy, the study was designed to begin supplementation starting at the twelfth week of gestation, beyond the period of early organogenesis... Additional studies will be necessary to ascertain safety of 4000-IU/d of vitamin D supplementation before the twelfth week of gestation ... These findings suggest that the current vitamin D EAR and RDA for pregnant women issued in 2010 by the IOM should be raised to 4000-IU of vitamin D per day so that all women, regardless of race, can attain optimal nutritional and hormonal vitamin D status throughout pregnancy"

Dos and Don'ts of Discussion

Certain Dos and Don'ts should be adhered to, to make the

discussion more effective:

Dos:

- ◆ Be concise, brief and clear
- ◆ Use the same tense throughout i.e. past or present-tense
- ◆ Flow of discussion should be from specific to general: findings of the study and its relation to literature, theory and practice
- ◆ Use simple words and phrases
- ◆ Place the research findings in a greater scientific context
- ◆ Cite the most important and the most recent
- ◆ Be consistent in the use of words and medical terminologies

Don'ts:

- ◆ Avoid repetition of information given in introduction and results in discussion
- ◆ Don't over exaggerate the findings
- ◆ Avoid complicated long sentences
- ◆ Unwarranted speculations
- ◆ Avoid your own biases, just give the facts
- ◆ Don't use too many citations/ references

Conclusion

'Discussion' gives a fair, unbiased interpretation of the research findings and throws light on the evidence that supports these findings. The acronym MILGI (Figure) can be used to memorize the intellectual content of the discussion. Dos and Don'ts can be used to discuss findings of the clinical trial more effectively.

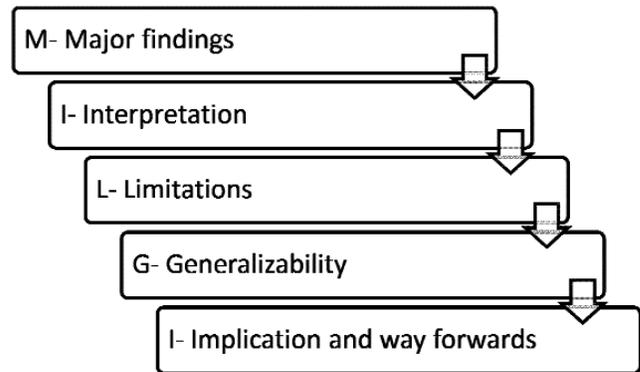


Figure: Contents of discussion section.

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