CME

Understanding of Blinding and its Reporting in Randomized Controlled Trials

*Sada Nand Dwivedi**

To generate reliable evidence regarding public health care/ clinical practice, a well-designed randomized controlled trial (RCT) is the ultimate answer for assessing the efficacy of a newly proposed intervention/ drug and/ or to identify more efficacious interventions/drugs regarding any of the health problems. In such RCTs, to avoid known as well as unknown biases, the role of random allocation (i.e., randomization) of considered patients in different intervention/ drug arms is already discussed in another continuing medical education (CME) published in the previous issue of this journal. In spite of avoiding allocation bias in every RCT, one may also avoid intentional/ unintentional bias through blinding to strengthen the credentials of observed findings further. To be more specific, if feasible, study participants and/ or researchers/ observers/ outcome assessors and/ or data analysts in an RCT need not be aware of the specific intervention/ drug being received by study participants in various arms and keeping in view of feasibility, one of the various types of blinding (e.g., single; double; triple) may be used. Further, recently reviews of reported RCTs have documented incomplete as well as inaccurate reporting of blinding in the articles. The present write-up therefore addresses important issues related to possible blinding under RCT, its type & method, and its reporting in the reports/ articles.

Access this article online

Website: www.cijmr.com

DOI: 10.58999/cijmr.v4i02.257

Keywords: Randomized Controlled Trial, Blinding, Single Blinding, Double Blinding, Triple Blinding

Introduction

Blinding can be used in various study designs, but for the purpose of the present write-up, the focus is on randomized controlled trial (RCT).[1-3] For assessing the efficacy of a newly proposed intervention/ drug and/ or identifying more efficacious interventions/drugs regarding any of the health problems, well-designed RCTs are necessary for establishing evidence-based decisions.[1-5] As such, the quality RCTs (i.e., phase III trials) provide reliable evidence regarding public health care/ clinical practice. To avoid allocation bias, randomized allocation of appropriately sampled patients in different intervention/ drug arms is followed. As emphasized earlier, an experimental study becomes an RCT only if random allocation of patients between intervention arms is ensured. In other words, random allocation is a basic principle of experimental design to avoid unexpected biases. To allocate patients in different intervention arms, it basically uses random numbers. It helps to secure unbiased comparisons between intervention arms through balancing almost all of the known as well as unknown factors likely to affect the outcome. It ultimately paves the way for statistical inference on the intervention effects.[6-8] Intuitively, after completion of an RCT, considered outcomes are compared between intervention and non-intervention groups to conclude one of the three possibilities:[3,9] (i) intervention is efficacious; or (ii) the difference in the outcome is exclusively due to chance; or (iii) there is systematic bias between the groups due to factors other than intervention. Like randomization, blinding (if feasible) also focuses on precluding the third possibility further. Reviews in the recent past have reported inappropriate and inaccurate documentation of used blinding in the articles.[10] This write-up is aimed at addressing a few of the important issues related to the possible use of blinding under RCT in subsequent sections. This may help the readers to be fully aware of possible blinding in an RCT; consideration of feasible types as well as approaches in this regard; and its proper reporting in related documents/articles.

International Centre for Health Research, RD Gardi Medical College, Ujjain, Madhya Pradesh, India.

Correspondence to: Sada Nand Dwivedi, International Centre for Health Research, RD Gardi Medical College, Ujjain, Madhya Pradesh, India.. E-mail: dwivedi7@hotmail.com

Submitted: 12/05/2025 Revision: 15/05/2025
Accepted: 20/05/2025 Published: 14/08/2025

How to cite this article: Dwivedi SN. Understanding of Blinding and its Reporting in Randomized Controlled Trials. Central India Journal of Medical Research. 2025;4(2):7-10.

Blinding

Blinding in an RCT literally means that at least persons of one of the various categories (e.g., study participants, researchers/ observers/ outcome assessors, data analysts) involved in that RCT remain unaware of specific interventions given to study participants in various intervention arms. It basically precludes intentional/ unintentional biases like reducing performance bias through blinding of study participants and research personnel; minimizing detection bias through blinding of outcome assessors; and also increasing the validity of results by avoiding analyst bias through blinding of statistical analysts. By incorporating blinding, RCTs can provide more accurate and reliable estimates of intervention effects. Hence, depending on the considered RCT design, the possibility of using one of the various approaches of blinding may be explored. Further, there is a need to strengthen reporting of blinding appropriately while preparing reports/ articles related to RCT.[11]

Types of Blinding

Considering the status of blinding in an RCT, they may be of various types:

Open-Label

In spite of known merits of considering blinding in a RCT, because of feasibility issues, sometimes every person from various categories (e.g., study participants; researchers/ observers/ outcome assessors; data analysts) involved in the RCT has to be kept aware about specific interventions given to study participants in various intervention arms.[12] Such RCTs are conventionally known as open-label RCTs. For example, under a non-inferiority RCT on optimization of radioactive iodine dose (123I) to achieve remnant ablation among differentiated thyroid cancer patients after six months of its first-dose administration, only an open-label RCT could be feasible.[5] The results under such trials involving very specific doses and deriving objective outcomes may not be affected much due to the absence of blinding. Otherwise, because of expected biases at various levels (described briefly later), the validity of the observed findings, especially in the case of subjective outcomes under open-label RCT, may be questionable up to some extent.

Blind RCT

As indicated earlier, blinding[13-15] in an RCT literally means that at least persons of one of the various categories (e.g., study participants, researchers/ observers/ outcome assessors, data analysts) involved in that RCT remain unaware of specific interventions given to study participants in various intervention arms. In other words, they do not know about the intervention received by any study participant. The RCTs involving blinding are conventionally known as blind RCTs. They are often categorized further as follows:

Single-blind

Intuitively, under a single blind RCT, persons from any one of the various categories (e.g., study participants, researchers/ observers/ outcome assessors, data analysts) involved in the RCT may be kept unaware about specific interventions given to study participants in various intervention arms.[13] Hence, it is better to specify the blinded category in the report/ article instead of merely mentioning single-blind. Further, as such, conventionally single-blind refers to the blinding of study participants. If they are not blinded, they may change the behavior regarding participation/ continuation in the RCT and/ or manipulate the reported outcome (s) by them. For example, under RCTs involving placebo (i.e., no intervention), randomly allocated participants in placebo arm may decide to either drop from the study or report the outcome inaccurately. To be more specific, in case of vaccine trials related to coronavirus, unblinded participants in the placebo group might start frequent hand washing, sanitization, and keeping a distance from crowded places. It might ultimately narrow the gap between experienced positivity rate between intervention and non-intervention arms. In other words, it may indicate lesser effectiveness of the vaccine. In summary, if feasible, study participants need to be blinded to avoid such problems.

Double-Blind

Like in the case of single-blind, under double blind RCT[14], persons from any two of the various categories (e.g., study participants, researchers/ observers/ outcome assessors, data analysts) involved in the RCT may be kept unaware about specific interventions given to study participants in various intervention arms. Hence, it is better to specify the blinded categories in the reports/ articles instead of mentioning merely double-blind. As a matter of fact, conventionally double-blind refers to blinding of study participants as well as researchers/ observers/ outcome assessors. To be more specific, even if study participants are blinded, if researchers/ observers/ outcome assessors are not blinded, recording of outcome (s) might be influenced/ altered by them/ study participants. For instance, under corona RCTs involving placebo,

observers/ outcome assessors may sometimes share this information with randomly allocated participants in the placebo arm who may decide to either drop from the study or adopt more hygienic public health practices, which might impact the outcomes inappropriately. In case of involvement of observable outcomes, they themselves may record them inaccurately. In other words, it might result in to narrowing down the outcome experiences between vaccine and non-vaccine arms, showing lesser effectiveness of the vaccine. Hence, if feasible, study participants as well as researchers/ observers/ outcome assessors need to be blinded to overcome such problems.

Triple- Blind

Under triple-blind RCT,[15] if feasible, persons from all three categories (e.g., study participants, researchers/ observers/ outcome assessors, and data analysts) involved in the RCT may be kept unaware about specific interventions given to study participants in various intervention arms. It is always better to specify details of the blinded categories in the reports/ articles instead of merely mentioning triple-blind. To be more specific, even if study participants as well as researchers/ observers/ outcome assessors are blinded, analytical results might be influenced/ altered by an unblinded data analyst/ biostatistician, more so if they are part of the RCT. For instance, under corona vaccine RCTs involving a placebo, the data may be manipulated to show the vaccine ineffective, or vice versa. Hence, if feasible, study participants, researchers/ observers/ outcome assessors, as well as data analysts, need to be blinded to overcome above above-described biases as well as manipulations.

Methods of Blinding

In an RCT, as a commonest approach for blinding, apparently similar interventions (e.g., one active intervention capsule; one placebo intervention capsule) may be used. Since they are substantially similar, it becomes impossible for everyone (i.e., study participants/ researchers/ observers/ outcome assessors/ data analysts) to know the identity of the active intervention capsule. As such, this approach ensures vigorous blinding. Sometimes, due to oversight, there is a risk of bias. For example, in spite of similar capsules, an active intervention capsule might involve some clues, like specific smell. In summary, considering not only feasibility (like in surgical RCTs) but also all pros and cons, blinding[13-15] needs to be planned to strengthen the scientific strength of RCTs, providing more reliable and valid results related to the efficacy of an intervention.

Summary

If feasible, blinding in an RCT makes the study participants and/ or researchers/ observers/ outcome assessors and/ or data analysts unaware of specific interventions given to study participants in various intervention arms, to further reduce bias. It makes a study a blind RCT. A blind RCT may further be conventionally categorized as a single-blind RCT, double blind RCT, and triple blind RCT. Conventionally, single-blind refers to blinding of study participants, which may mainly ensure their unchanged behavior regarding participation/ continuation in the ongoing RCT and/ or non-manipulation in reported outcome (s), mainly when outcomes are subjective (e.g., quality of health). Like in the case of single blind, conventionally under double blind, study participants as well as researchers/ observers/ outcome assessors are blinded. Even if study participants are blinded, blinding of researchers/ observers/ outcome assessors also helps further in avoiding biases, especially in the recording of outcome (s) by them/ study participants. Under a triple-blind RCT, if feasible, specific interventions given to study participants in various intervention arms may not be known to persons from all three categories (e.g., study participants, researchers/ observers/ outcome assessors, and data analysts) involved in the RCT. To be more specific, even if study participants as well as researchers/ observers/ outcome assessors are blinded, unblinded data-analyst/ biostatistician may influence/ alter analytical results, more so if they are part of the RCT. As such, if there is no feasibility of blinding at all, the study remains an open RCT. As indicated earlier, the reports and articles on every RCT need to provide detail information about the used method and types of blinding, not merely stating that no blinding, single blinding, double-blinding, and triple blinding was used. In other words, it needs to be elaborated on which method of blinding was used, and persons from which of the groups were blinded. In view of a specific type of RCT, the write-up about used blinding needs to follow the concerned CONSORT guidelines.11

To conclude, if feasible, blind randomized controlled trials (RCTs) supersede open RCTs as the methodological standard of excellence in public health/ clinical research. Because of blinding, they minimize the bias further and establish a more reliable causal relationship between the considered intervention and the outcome. While conducting an RCT, proper blinding can be achieved by the medical researchers with careful planning and execution. As a result, by prioritizing scientific accuracy,

they can ensure the credibility and integrity of their findings further. They need to execute a planned approach of blinding appropriately to ensure unawareness about the given specific interventions in different arms and clearly document the used approaches to enhance the credibility of their findings further.

References

1. Pocock Stuart J. Clinical Trials: A Practical Approach. John Wiley & Sons Ltd. 2013 July. Online ISBN: 9781118793916.
2. Dwivedi SN. Understanding of Study Designs in Clinical Research: Major Prompting Points. Central India Journal of Medical Research. 2024; 3(3):3-11.
3. Peto R, Pike MC, Armitage P, et al. Design and analysis of randomized clinical trials requiring prolonged observation of each patient, I: introduction and design. Br J Cancer. 1976; 34:585-612.
4. Dwivedi SN. What are the major research methodology steps under a clinical study? Central India Journal of Medical Research. 2023; 2(2):4-9.
5. Bal C, Chandra P, Kumar A, Dwivedi SN. A randomized equivalence trial to determine the optimum dose of iodine131for remnant ablation in differentiated thyroid cancer. Nuclear Medicine Communications. 2012; 33(10): 1039-1047.
6. Dwivedi SN. Understanding of Randomization and its reporting in Randomized Controlled Trials. Central India Journal of Medical Research. 2025; 4(1):7-12.
7. Schultz KF, Grimes DA. Generation of allocation sequences in randomized trials: chance, not choice. Lancet. 2002; 359:515-19.
8. Dwivedi SN. Biases including confounding and effect size modification in clinical research and their mitigations. Central India Journal of Medical Research. 2024; 3(2):6-12.
9. Sundaram KR, Dwivedi SN, Sreenivas V. Medical Statistics: Principles and Methods. Wolters and Kluwer (Health). New Delhi. 2015 (Second Edition).
10. Penić A, Begić D, Balajić K, et al. Definitions of blinding in randomised controlled trials of interventions published in high-impact anaesthesiology journals: a methodological study and survey of authors. BMJ Open 2020;10:e035168. doi:10.1136/bmjopen-2019-035168.
11. Schulz KF, Altman DG, Moher D, for the CONSORT Group. CONSORT 2010 Statement: updated guidelines for reporting parallel group randomised trials. BMJ 2010;340:c332.
12. Saluja A, Vibha D, Pandit AK, Shukla G, Srivastava AK, Tripathi M, Srivastava MVP, Prasad K, Dwivedi SN. Comparison of dexamethasone regimens in tubercular meningitis (TBM): a randomized open label clinical trial. J Infect Dev Ctries. 2023 Dec 31;17(12):1769-1774. doi: 10.3855/jidc.17563. PMID: 38252729.
13. Zhou J, Liu B, Xu JF, Wang FB, Ye H, Duan JP, Cui XW. Home-based strength and balance exercises for fall prevention among older individuals of advanced age: a randomized controlled single-blind study. Ann Med. 2025 Dec;57(1):2459818. doi: 10.1080/07853890.2025.2459818. Epub 2025 Feb 7. PMID: 39918027; PMCID: PMC11809163.
14. Nakayama T, Iwanami M, Sakakibara S, Mukasa R, Ota A, Furihata K, Honda Y, Ishii KJ. Immunogenicity, safety, and tolerability of a β-glucan-CpG-adjuvanted respiratory syncytial virus vaccine in Japanese healthy participants aged 60 to 80 years: A phase 2, randomized, double-blind, dose-finding study. Hum Vaccin Immunother. 2025 Dec;21(1):2489900. doi: 10.1080/21645515.2025.2489900. Epub 2025 Apr 21. PMID: 40257186; PMCID: PMC12013440.
15. Aghajani R, Dehghani E, Khonji MS, Naghdi S, Nakhostin Ansari N, Dommerholt J, Nakhostin-Ansari A. Effect of dry needling on quadriceps muscles fatigue in taekwondo players: A protocol for a triple-blinded randomized controlled trial. Contemp Clin Trials Commun. 2025 Mar 28;45:101476. doi: 10.1016/j.conctc.2025.101476. PMID: 40235623; PMCID: PMC11997412.