RESEARCH ARTICLE

# The Risk of Bias in Randomized Controlled Trials

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**ABSTRACT**

Randomized controlled trials (RCTs) are vulnerable to internal and external bias, particularly when examining complex health behavioural interventions. The effects of postnatal education interventions on parent's knowledge of caring for their newborn in low-and middle-income countries (LMICs) is a growing area of study. Therefore, the aim of this review was to assess the risk of bias (RoB) in such studies. MedLine, CINAHL, and SCOPUS were searched from January 2000 - October 2017 using key words such as RCT, parent-targeted, postnatal, education, interventions, and LMICs. Two reviewers screened title and abstracts and full text of eligible studies. Outcomes of interest were RoB measured using the Cochrane RoB tool, as well as intervention fidelity and contamination bias. Data were descriptively analyzed with 29 RCTs included. Highest risk of bias was in participant (55%) and personnel (76%) blinding with the lowest risk of bias in random sequence generation (76%), and attrition bias (72%). Overall, 89.7% of studies on postnatal parent-targeted education interventions in LMICs had a high RoB score in at least one domain. While difficult to avoid such biases, opportunities can be sought to minimize these during the design and conduct of future studies in this area.

## INTRODUCTION

The goal of evaluating health behavioural interventions is to offer strong evidence that changes in the desired outcome are attributable to the intervention, holding other factors constant [1]. While randomized controlled trials (RCTs) hold promise and rigor in evaluating interventions [2,3], they are vulnerable to bias. Systematic errors occur due to a flaw in the RCT design, conduct, or analysis, resulting in either an over- or under-estimation of the effect size [4]. Given social and gendered norms, available resources and capacity, or nuanced confounding factors that may influence the implementation and effectiveness of interventions, there can be a potential risk of bias (RoB) when conducting global health intervention trials in low- and middle- income countries (LMICs).

Recently, there has been an increase in the number of parent-targeted postnatal educational interventions in LMICs, with the goal of enhancing parents', particularly mothers', knowledge and ability to care for their newborn at home [5]. Parent-targeted postnatal educational interventions are "structured interventions where parents are provided with education or information related to caring for their newborn that is meant to change behaviour and improve newborn outcomes" (p.61-62) [5,6]. For the purpose of this study, parent-targeted postnatal educational interventions must have been related to improving one or more essential newborn care behaviours (e.g., breastfeeding, skin-to-skin contact) that began after

birth and before six weeks postnatally [5].

Despite the increasing use of these interventions, the quality of RCTs is yet to be examined. Therefore, the objective of this review was to examine the RoB in RCTs of parent-targeted postnatal educational interventions in LMICs using the Cochrane Collaboration RoB tool.

## METHODOLOGY

This analysis is based on RCTs identified through a scoping review [5]. Full details of the search, inclusion and exclusion criteria, and data extraction procedure are available in the original study [5]. The Cochrane Collaboration RoB standardized tool was used [7]. When considering the risks in parent-targeted postnatal intervention and global health research more broadly, and following other studies evaluating RCTs in LMICs [9,10] and on behavioural interventions [11,12], two additional bias domains were added: contamination bias [7] and intervention fidelity bias [8].

## RESULTS

The original search identified 77 studies and after non-RCTs (n=45) and secondary analyses (n=3) were excluded, 29 RCTs remained. The number of publications increased over time: 2 between 2000 and 2004, and eleven between 2015 and 2017. Most of the studies were randomized at the individual level (n=24, 82.8%) with five cluster RCTs (17.2%).

Figure 1 illustrates the RoB for each of the studies and Figure 2 illustrates the RoB graph as percentages across included studies. Among all the studies, 26 (89.7%) had a high RoB score in at least one domain with an average of 2.3 domains with a high risk of bias (range: 0 - 6).

Most studies had a low RoB for random sequence generation (72.4%) but only 51.7% had low RoB for allocation concealment. Biases occurred due to poor concealment, sequence generated by odd/even number, or the use of non-sequentially numbered or opaque envelopes.

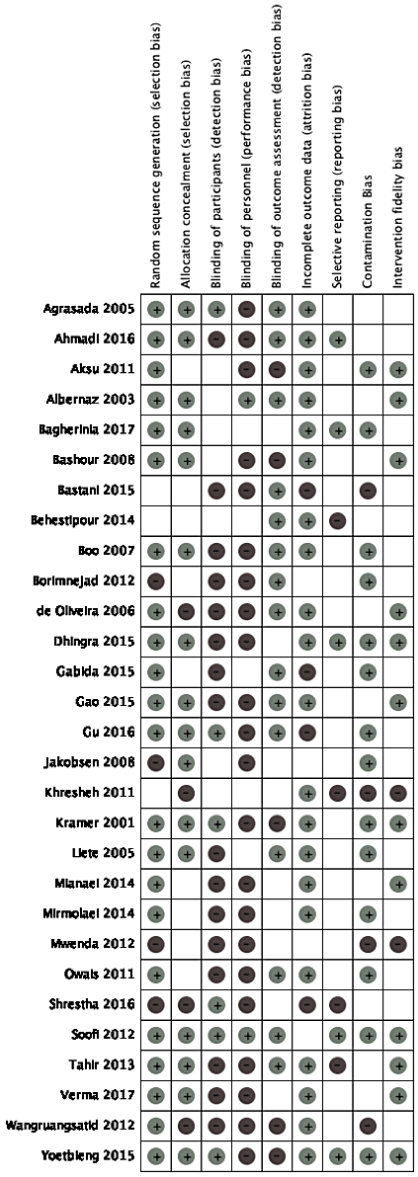


**Figure 1.** Risk of bias summary: Authors' judgements about each risk of bias item for each study.

Over half had high RoB for lack of blinding participants (55.2%) and personnel (75.9%). For detection bias, only 51.7% had a low RoB. Due to the nature of postnatal education as structured, interactive interventions, double-blind trials are not always possible as mothers are aware of whether they received education or not. Many of the studies used a single-blind RCT design which meant participants were unblinded to their group allocation.

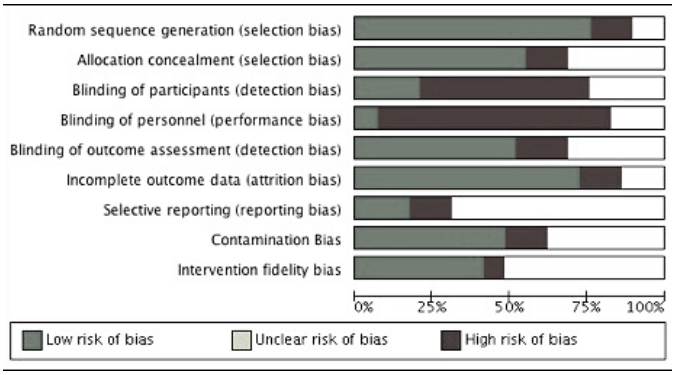


**Figure 2.** Risk of bias graph: Authors' judgements about each risk of bias item presented as percentages across all included studies.

Regarding attrition bias, over two-thirds were low RoB (72.4%) due to good reported follow-up rates, balanced withdrawals across groups for similar reasons not related to treatment or use of intention-to-treat analysis. However, a challenge was that attrition resulted in loss of power during analysis and inability to draw strong conclusions. Nearly all studies (n=26, 89.7%) stated their power calculations for their sample sizes but only 18 (69.2%) maintained this sample size at the final data collection point. For reporting bias, only four studies (13.8%) were considered low RoB as most trials were not registered or were retrospectively registered after data collection began.

While almost half of the studies had low risk of contamination bias (48.3%), 37.8% had an unclear risk. Low risk of contamination bias occurred where interventions did not have an in-hospital component or used cluster RCTs to reduce the likelihood of one group becoming aware of information available to the other group.For the studies that did have an in-hospital component, measures were taken to reduce contamination such as the use of private rooms for training. However, this was not always clearly stated.

For intervention fidelity, 48.3% had an unclear risk due to unclear reporting on maintaining the same intervention across participants. 41.4% had low RoB as they provided statements that training for implementers was provided.

## DISCUSSION

The variation in RoB for RCTs on parent-targeted postnatal education interventions in LMIC is not new [13–15]. Previous studies suggest that RCTs on non-communicable diseases using pharmacological and non-pharmacological treatments published in middle income countries were more likely to have a higher RoB and be of lower quality compared to those published in high income countries [15]. In Sub-Saharan Africa, 76% of RCTs on pharmacological and non-pharmacological treatments had at least one domain at high RoB [14].

The areas of greatest concern were in blinding of participants and personnel. The strength of RCTs lies in the successful randomization of participants which allows for the groups to be as similar as possible at the beginning to determine the effects of the intervention at the end [4]. It is challenging to conduct a double-blind trial for a postnatal educational intervention as the personnel working on the study may be required to provide the intervention based on the allocation and thus will be aware which participant is receiving which intervention. While double blinding for this type of intervention is a challenge, it is important and possible to blind outcome assessors and those doing the analyses.

It is important to consider ways to reduce risk of contamination bias, particularly in global health RCTs in LMICs where overcrowding in hospitals increases the possibility of cross-contamination and can threaten the validity of the control group [1]. Ideally, the intervention would be delivered uniformly to all participants without cross-contamination, yet this may not happen due to the interactive nature of postnatal educational interventions [11].

Challenges exist in conducting RCTs in resource/infrastructure limited LMIC settings and there may be a need for additional resources (such as training, funding, infrastructure) to help achieve the expected level of rigor. It also raises the question

that if these elements of rigor are not possible, what alternatives should be considered? Guidelines such as the Medical Research Council's management of global health trials provide important recommendations for the conduct of RCTs specifically occurring in LMICs [16]. Consideration is needed in relation to the availability of research infrastructure where additional training for personnel involved in the RCT may be required [17]. Also, there is a need to recognize the healthcare workforce challenges faced in many LMICs where healthcare providers might not have time to dedicate to research [17].

Beyond specific design measures that can be used to reduce RoB, minimizing risks can also occur through collaboration and partnership between researchers from high income countries experienced in RCTs and LMIC researchers. Capacity development of personnel in LMICs is needed to strengthen the workforce, minimize RoB, reduce risk of exploitation of participants, ensure ethical standards are met, build the project towards sustainability, ensure cultural awareness, and meet local needs [18,19]. Collaboration can help overcome some of the barriers to conducting RCTs in LMICs, including the capacity of healthcare providers to engage in research in addition to their clinical care; finance, resource, and personal constraints; as well as identifying and collaborating with gatekeepers, all of which may impact bias.

## CONCLUSION

Overall, 89.7% studies on postnatal parent-targeted education interventions in LMICs had a high RoB score in at least one domain. While difficult to avoid such biases, opportunities can be sought to minimize these during the design and conduct of future studies in this area.

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