

Identifying and handling potentially untrustworthy trials – Trustworthiness Screening Tool (TST) developed by the Cochrane Pregnancy and Childbirth Group

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Background

Cochrane’s mission is to promote evidence-informed health decision-making by producing high-quality, relevant, and accessible systematic reviews. We are increasingly being made aware of the publication of untrustworthy and potentially fraudulent trials in a number of obstetrics and gynaecology journals. Including such trials in our Cochrane Reviews has serious implications – not only for the reputation of Cochrane and our review authors, but also for the impact on pregnant women and their babies as a result of healthcare decisions informed by our Cochrane Review evidence.

We acknowledge the guidance available to date in the Cochrane Handbook¹ and the Committee on Publication Ethics (COPE) guidelines regarding a journal’s responsibilities for retracting fraudulent reports.² Cochrane have also recently introduced a new policy, with implementation guidance, for managing potentially problematic studies in systematic reviews – and implementation guidance.

The Cochrane Pregnancy and Childbirth Group (which closed 31 March 2023) developed a process for identifying and handling untrustworthy (potentially fraudulent) trials in the group’s Cochrane Reviews which we have described in this document.

Retracted studies

If an already-included study has been retracted since the publication of the Cochrane review, the editorial office will contact the review team and ask them to move the study from included to excluded, edit all sections of the review accordingly, then resubmit the amended review. Authors are asked to summarise the changes that they have made to the review and the impact that removing the study has had on the review’s results/conclusions.

In this scenario, there should be a statement in the main sections of the review to explain what was done in this amended version of the review, and why. An example statement is provided below in Figure 1.

Since publication of this updated review in Issue X, 2018, the Smith 2019 study has now been retracted by the Journal of Impossible Science due to implausible data (link to retraction notice). We have moved this study from included to excluded studies and updated our results and text accordingly.

Figure 1 – example of a statement added to a Cochrane Review after removal of a retracted study.

High-risk studies in terms of scientific integrity (trustworthiness)

Currently, the onus is on peer reviewers, journal editors, publishers, systematic review authors, and institutions where the research was done and/or the authors work, to prove that a study is fraudulent. We believe that the time has come for the onus to be on the authors of primary research to prove that a study is trustworthy and have acted accordingly. We are aware of one recently published tool to assist us in this endeavour but felt that its implementation may not be feasible, given the limited resources at our disposal.³ Another suggested approach might be to include a study only if the study protocol has been prospectively registered. While this is

undoubtedly a step in the right direction, an expectation of prospective trial registration is not only relatively recent, but also no guarantee of scientific integrity.

1. Cochrane Pregnancy and Childbirth Trustworthiness Screening Tool (TST)

We have produced a list of questions that could help us flag potentially untrustworthy trials. Criteria that need to be considered when assessing trustworthiness include:

- Domain 1 - Research governance
 - Are there any retraction notices or expressions of concern listed on the [Retraction Watch Database](#) relating to this study?
 - Was the study prospectively registered (for those studies published after 2010)? If not, have the authors provided a plausible reason?
 - When requested, did the trial authors provide/share the protocol and/or ethics approval letter?
 - Did the trial authors engage in communication with Cochrane Pregnancy and Childbirth within the agreed timelines?
 - Did the trial authors provide IPD data upon request? If not, was there a plausible reason?
- Domain 2 - Baseline characteristics
 - Is the study free from characteristics of the study participants that appear too similar (e.g. distribution of the mean (SD) excessively narrow or excessively wide, as noted by Carlisle⁴)?
- Domain 3 - Feasibility
 - Is the study free from characteristics that could be implausible (e.g. large numbers of women with a rare condition recruited from a single centre within 12 months)?
 - In cases with (close to) zero losses to follow-up, is there a plausible explanation?

We learned during the early implementation phase that Domain 4, *Results*, was being criticized by peer reviewers because of possible biased, post-hoc exclusions; therefore, any issues related to the implausible data (e.g. equal number of randomized participants when ‘no blocking was used’, or if the authors say they used ‘blocks of 4’ but the final numbers differ by 6) should be included in Domain 3.

2. Handling of studies with one or more TST domain failures

When a study does not meet one or more of the above criteria it is classified as ‘screen positive’, and the primary study authors should be contacted to address any possible lack of information/concerns. In cases where it is not possible to obtain contact details for the study authors, or where adequate information has not been provided, the study should remain in ‘awaiting classification’, with the reasons and communications with the author (or lack of) described in detail. See **Appendix 1** for details of how to apply the TST.

3. When a study is under investigation by a journal

The information regarding possible investigation of a published fraudulent trial may come from various sources. However, this information should be shared in the Cochrane Review only if there is a written confirmation for this to be true. In this scenario, the Editor-in-Chief of the relevant journal (with copies to the journal publisher) should be approached to seek clarification regarding the status of investigation and whether any action is currently being taken. If the journal editor confirms that a formal investigation is underway, the study should be moved from included to studies awaiting assessment with all sections of the review edited accordingly. Review authors will be asked to summarise the changes that they have made to their review and the impact that removing the study has on the review’s results/conclusions. If, after a reminder, no reply is received from the relevant journal, this information should be included in the amended version.

4. When there are serious concerns relating to a study included in a Cochrane review, but for legal reasons the details cannot be shared with the review team in the short term

In this instance, the editorial office should contact the review team informing them that there are potentially serious issues, but the information is not sufficient to act on it. At this stage, the Cochrane Review is not edited until more information is available. The editorial office maintains lines of communication between whistleblower, the editorial office and the Cochrane Review authors. Any decisions/amended versions should be approved by the sign-off editor.

5. Abstracts

Data from abstracts should be included if, in addition to the trustworthiness assessment, the study authors have confirmed in writing that the data to be included in the review have come from the final analysis and will not change. If such information is not available/provided, the study will remain in 'awaiting classification' (as above).

6. Which sections of a review need to be edited when we identify a problematic included study?

Removing an included study from the review is likely to require edits to all sections of the review and may have implications for the overall conclusions of the review. The authors will need to re-assess the relevant trial as 'excluded' or as a study 'awaiting classification'. Data will need to be removed from the data and analysis tables and the GRADE assessments re-done if those analyses were affected by edits to data tables. The results will need to be reconsidered and re-reported in all sections of the review, considering any changes to the GRADE certainty reassessments. For the examples see reviews by Sotiriadis et al.⁵ and McGoldrick et al.⁶ In our experience, even removing one study from a relatively small review will take about one day. When resubmitted, the edited review will need to undergo full checks in the editorial base (including editing the study flow diagram) to ensure that the amended review is correct and internally consistent.

Notifying stakeholders that the Cochrane review has been amended

A large number of our reviews have been used to inform the clinical care of pregnant women and their babies via national or international guidelines, or policy documents. We have, therefore, a duty of care to inform our key stakeholders that an amended review has been published, especially when removing fraudulent, or potentially fraudulent trial affected the review's conclusions/and or direction of effect estimates for priority outcomes underpinning corresponding guidelines or policies.

References

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Appendix 1 – Applying the TST



