Journal of Clinical Epidemiology 112 (2019) 53−58

Journal of Clinical Epidemiology

ORIGINAL ARTICLE

Risk of bias assessments for selective reporting were inadequate in the majority of Cochrane reviews

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Accepted 16 April 2019; Published online 19 April 2019

Abstract

Objectives: The aim of the study was to analyze adequacy of risk of bias (RoB) judgments for selective reporting in Cochrane systematic reviews.

Study Design and Setting: We extracted RoB assessments, including judgment (low, high, or unclear risk) and supporting comment from Cochrane reviews of randomized controlled trials using computer parser. We analyzed sources of information mentioned in supporting comments. We compared judgments of Cochrane authors with guidance from the Cochrane Handbook for Systematic Reviews of Interventions (Cochrane Handbook) and categorized them into adequate or inadequate.

Results: At least 60% of judgments for risk of selective reporting bias of trials in analyzed Cochrane reviews were not in line with the Cochrane Handbook. Few Cochrane authors mentioned the trial protocol as a source of data for assessing selective reporting. Most of the inadequate judgments were made among trials that were judged with low risk of selective reporting bias; more than 90%. In 9% of analyzed RoB tables, Cochrane authors did not use this RoB domain at all.

Conclusion: Cochrane authors frequently make RoB judgments about selective reporting that are not in line with Cochrane Handbook and not mentioning trial protocol. Interventions aimed at helping Cochrane authors to make adequate RoB assessments in Cochrane reviews would be beneficial.

Keywords: Cochrane; Systematic reviews; Bias; Selective reporting; Reporting bias; Epidemiologic methods

1. Introduction

The validity of systematic reviews (SRs) can be negatively affected by selective reporting of outcomes. Comparison of outcomes reported in protocols of randomized controlled trials (RCTs) with information reported in methods and results of subsequent articles showed that 71% and 88% of RCTs, respectively, had at least one outcome unreported in article [1,2]. Outcome reporting bias has been proven in many RCTs since then [3]. This type of bias has an impact on the quantitative synthesis of data in SRs [4].

Therefore, it is important to report in SR whether there is evidence of selective reporting in included RCTs. Cochrane risk of bias (RoB) tool has seven domains for assessing the risk of different types of bias. One of the domains is "selective reporting bias" [5]. In the RoB tool, authors are expected to provide judgment whether the risk of a certain type of bias is high, unclear, and low. Then, the authors are expected to write an accompanying comment as support for judgment [6]. The Cochrane Handbook gives straightforward instructions to Cochrane authors about judging this domain of RoB. The authors are instructed that the risk of selective reporting bias is low if the study protocol is available and if all primary and secondary outcomes that were prespecified in the protocol, and are of interest in the review, were reported as prespecified. The Handbook also indicates that RoB for this domain may be low if the study protocol is not available, but it is clear from the study report that all expected prespecified outcomes were reported, although it is emphasized "convincing text of this nature may be uncommon" [6].

In our previous studies, we found that RoB assessments for various domains of Cochrane RoB tools are frequently inadequate, that is, not in line with instructions provided in the Cochrane Handbook [7−10]. The aim of this study was

Conflict of interest statement: None.

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https://doi.org/10.1016/j.jclinepi.2019.04.007
0895-4356/

What is new?

Key findings

- Cochrane authors frequently make risk of bias (RoB) judgments about selective reporting that are not in line with Cochrane Handbook and not mentioning trial protocol.

What this adds to what was known?

- It has been known already that RoB judgments in SRs are not necessarily dependable, but our study indicates that certain RoB domains, such as selective reporting bias, have very high prevalence of inadequate judgments.

What is the implication and what should change now?

- Interventions aimed at helping Cochrane authors to make adequate RoB assessments in Cochrane reviews would be beneficial.

to analyze whether judgments for risk of selective reporting bias in Cochrane SRs of RCTs about interventions are consistent with the Cochrane Handbook guidance.

2. Methods

2.1. Study design

We conducted a methodological study of published Cochrane reviews.

2.2. Inclusion and exclusion criteria

We included Cochrane reviews of RCTs of interventions published from July 2015 to June 2016 ($N = 955$). We searched The Cochrane Library via Advanced search, using date restrictions. Exclusion criteria were diagnostic reviews, overviews of SRs, empty reviews that did not include a single RCT after searching the literature, and withdrawn reviews. In Cochrane reviews that have included both RCTs and nonrandomized studies, we analyzed only RoB table of included RCTs.

2.3. Screening for study eligibility

One study author screened reviews against inclusion criteria. The second author verified all assessments of the first author. There were no disagreements between the authors.

2.4. Data extraction

We used automated data extraction in a stepwise manner in Microsoft Excel 2010 (Microsoft, Redmond, WA, USA) using macrocommands written in Visual Basic for Applications (VBA, Microsoft, Inc., Redmond, WA, USA) by author O.B. We did data scraping by automated copying of the targeted content from the Web page of The Cochrane Library for every eligible review to a separate spreadsheet in Microsoft Excel. Information included in RoB tables was extracted from raw data for every study included in a review. Precise automatic data extraction was possible because each Cochrane review has the section ‘‘Characteristics of included studies,’’ with the following uniform data organization: for each included study, first, a unique identifier (usually name of the first author and year of publication) is indicated, followed by a table with characteristics of a study, and then an RoB table titled ‘‘Risk of bias.’’

To achieve such data extraction, we used programming and testing for every step to avoid errors or missing data. Coded algorithms we used (presented in Supplementary Files 1 and 2) were applicable for this purpose only and cannot be reused to extract other data without reprogramming. Initial testing of the data extraction presented us with several challenges. First, we noticed that some of the seven predefined RoB domains from the Cochrane RoB tool were sometimes missing, and Cochrane authors sometimes inserted new domains in the RoB table. For this reason, we extracted entire RoB tables as they were published in a review. Missing domains were logged by error handling subs and additionally checked manually. In addition, we noticed that, on rare occasions, Cochrane authors did not create RoB table for each included study. Therefore, we extracted also the number of included studies from the text to double-check the number of RoB tables that were supposed to be present in the Cochrane review.

2.5. Assessing judgments and comments

We compared each full RoB assessment of selective reporting (i.e., assessment including both judgment and a supporting comment) with instructions from the Cochrane Handbook available in the ‘‘Table 8.5.d: Criteria for judging risk of bias in the ‘Risk of bias’ assessment tool,’’ and assessed whether the comment was, maybe was, or was not in line with the Cochrane Handbook. When Cochrane authors judged RoB for selective reporting as high or unclear, we used more lenient approach, with the ‘‘maybe adequate’’ category because although instructions from Cochrane Handbook mostly base their recommendations on whether outcomes and outcome measures were prespecified, the instructions also give some flexibility to authors with the following instructions for judgment of high risk of selective reporting, without mentioning prespecification of outcomes: *One or more outcomes of interest in the review are reported incompletely so that they cannot be entered in a meta-analysis*; *The study report fails to include results for a key outcome that would be expected to have been reported for such a study* [6]. Because knowing what a key outcome is and whether missing information was

supposed to be used in a meta-analysis would require familiarity with the content of each review, we decided to rate as "maybe adequate" judgments related to missing data that were judged as either high or unclear RoB. After calibration exercise, categorization of data and assessment for adequacy were done by one author (F.S.), and all categories and assessments were then verified by another author (L.P.) to ensure consistency.

2.6. Statistics

Results were presented using descriptive statistics, using frequencies and percentages. Results were analyzed using Microsoft Excel.

3. Results

We included 729 Cochrane reviews (listed in Supplementary File 3) with 10,527 RCTs. For 970 (9%) trials, the Cochrane authors did not include selective reporting bias domain in the RoB table, and for further 15 trials, Cochrane authors did not create RoB table at all. In the remaining 9,542 trials, there were 4,901 (51%) trials judged by Cochrane authors as having low risk, 1,236 (13%) with high risk, and 3,405 (36%) with the unclear risk of selective reporting bias. Random examples of our assessment of the adequacy of those judgments are provided in Supplementary File 4.

3.1. Trials judged with low risk of selective reporting bias

Among the 4,901 trials judged by Cochrane authors with low risk for selective reporting bias, 418 (8.5%) were sufficiently informative to conclude that the Cochrane authors made a judgment in line with instructions from the Cochrane Handbook. For those RCTs, Cochrane authors indicated that a trial protocol was available, and all outcomes prespecified in a protocol were reported in an article. Information source for judging selection bias in all those 418 RCTs were trial protocols.

In the remaining 4,483 (91.5%) trials judged with low risk of selective reporting bias, Cochrane authors did not provide convincing information that the supporting comment indeed justifies a judgment for low RoB, and therefore, we considered them not in line with the Cochrane Handbook. Table 1 tabulates sources of information mentioned by Cochrane authors as support for these 4,483 judgments.

For 75% of those trials, Cochrane authors did not mention any source of data to support their judgment that the RoB for this domain was low. An example of such comment is "*All expected outcomes reported*." In 15% of trials, the comment indicated that Cochrane authors compared methods section of an article with results, and all outcomes mentioned in the methods were reported in results. In 7.5% of trials, Cochrane authors explicitly wrote that the RCT protocol was not available, but they still judged the risk of selective reporting bias as low. Examples of such comments are "*No protocol. However, systematic data collection and reporting of all outcomes*.", "*The study protocol was not available, but it was clear that the published report included all expected outcomes*.", "*Although we were unable to retrieve the trial protocol, there was no evidence of selective reporting*."

Table 1. Source of information mentioned by Cochrane authors in a supporting comment for judging the low risk of selection bias in trials for which comments were not in line with Cochrane Handbook

Source of information	*N* (%)
Not reported	3,341 (75)
Methods section	635 (15)
Lack of protocol	380 (7.5)
Protocol	72 (1.6)
Article	42 (0.9)
Abstract, methods, and results	7 (0.16)
Retrospectively registered protocol	5 (0.11)
Introductory section	1 (0.02)
Total	4,483

Comments for 1.6% of trials indicated that the protocol was available, but the comments did not match judgment of low risk because the Cochrane authors indicated in a comment simply that a protocol was available without any note on selection bias ($N = 35$), that they found discrepancies between protocol and article ($N = 34$) or a comment referred only to primary outcomes ($N = 2$).

For five trials, Cochrane authors wrote that the protocol was retrospectively registered, but they still judged the trial as low risk of selection bias. The remaining trials mentioned article as a source of information that was used to determine that there was no selective reporting. Most of those trials indicated that outcomes presented in methods were reported in results, whereas comment for one trial was: "*Results presented according to objectives stated in the introductory section*."

Overall, among 4,483 trials judged as having low risk, but with comments that do not imply low risk, the majority would be judged at least as unclear by following the Cochrane Handbook, and unclear or high RoB for 34 trials where discrepancies between protocol and publication were found.

3.2. Trials judged with a high risk of selective reporting bias

Among 1,236 trials judged as having a high RoB for selective reporting, for one trial, Cochrane authors did not provide a comment so we could not assess it. For the remaining 1,235 trials, we considered that 1,114 (90%)

judgments were or maybe were in line with the Cochrane Handbook. In comments of those trials, Cochrane authors mostly described that some outcomes or information were missing ($N = 1046$).

For the 114 trials, where we considered that the comment did not justify the judgment of high risk of selection bias, Cochrane authors used supporting comments that should have been judged with either unclear or low risk. Most commonly such comments were that results were available only in the form of abstract ($N = 55$; 4.5%), there was no access to the protocol ($N = 28$; 2.3%), and there was no intention-to-treat analysis ($N = 24$; 2%). For 12 trials, Cochrane authors only indicated that results were reported only in figures or only in tables or that results could not be used for meta-analysis, without further information. For four trials comment indicated it was unclear whether there was selective reporting.

In 904 (73%) of the 1,236 trials judged with a high risk of selective reporting bias, the source of information was not reported. In the remaining trials with high-risk judgment for selective reporting bias, Cochrane authors indicated that protocol was not available for 103 (8%) trials and for the rest the following sources of information were mentioned: article ($N = 95$; 8%), study protocol ($N = 82$; 7%), or abstract ($N = 52$; 16%).

3.3. Trials judged with the unclear risk of selective reporting bias

Among 3,405 RCTs that were judged by Cochrane authors as having an unclear risk of selective reporting, we could not assess 10 in detail because there was no supporting comment for the judgment. For the remaining 3,395 RCTs, we considered that for 2,253 (66%) RCTs judgment of Cochrane authors was or maybe was adequate, whereas it was inadequate for 1,142 (34%) trials.

For the 2,253 trials where we considered that comment was or maybe was adequate to support judgment of unclear risk of selective reporting, the most common reasons were no access to protocol (65%), some outcomes or information were not reported (28%), study was published only as an abstract (2.3%), there was a language barrier due to publication in different language (1.1%), and discrepancies between protocol and publication (1%; Table 2).

For the remaining 1,142 trials, which we did not consider adequately judged, Cochrane authors most commonly used comments that were not thoroughly informative (69%), such as "*Insufficient information*," "*Not able to judge from available information*," "*Not reported*," "*Not mentioned*," and "*Not described*." Other inadequate comments indicated merely N/A, explained in the list of acronyms as "Not available" (7.5%), Cochrane authors did not seek protocol (6.8%), outcomes specified in methods were reported in results (5.5%), or indicated that prespecified outcomes were reported, but it was not reported where were they prespecified (4.3%).

Table 2. Comments that supported the judgment of unclear risk of selective reporting, considered adequate or maybe adequate

Category of a supporting comment	*N* (%)
No access to the protocol	1,468 (65)
Some outcomes or information not reported	625 (28)
Abstract	51 (2.3)
Language barrier	24 (1.1)
Discrepancies between protocol and publication	21 (1)
Obtained additional data from authors	21 (1)
A trial performed before mandatory trial registration	13 (0.6)
Retrospective protocol registration	11 (0.5)
Discrepancies between multiple reports	9 (0.4)
Unpublished data	6 (0.3)
Other	4 (0.2)
Total	2,253

3.4. The overall proportion of inadequate assessments

Among 9,542 trials with full RoB assessment for risk of selective reporting bias, at least 5,739 (60%) were not in line with Cochrane Handbook; 4,483 (91.5%) from 4,901 trials judged with low risk, 114 (9%) from 1,236 trials judged with high risk, and 1,142 (34%) from 3,405 trials judged with unclear risk.

4. Discussion

We found that at least 60% of judgments for risk of selective reporting bias in Cochrane reviews were not in line with Cochrane Handbook. Most of the inadequate judgments were made among trials that were judged with low risk of selective reporting bias. These assessments are considered inadequate because Cochrane authors mostly did not clearly specify the source of information provided in the comment or used meaningless comments. Cochrane Handbook instructs authors that assessment of selective reporting requires consultation with a trial protocol or availability of another convincing text. Cochrane authors rarely mentioned trial protocol in the analyzed RoB domain.

In our earlier studies, we conducted similar analyses for other Cochrane RoB domains, including allocation concealment, random sequence generation, other bias, and attrition bias, where we also found a high prevalence of inadequate assessments [7–10]. RoB domain for selective reporting bias showed by far the worst results compared with analyses of other domains [7–10].

It has been reported before that reasons provided for high risk of selective reporting bias were generally poorly articulated in RoB tables [11]. Our analysis shows that this is not limited to judgments of high risk, but that the problem is much larger for trials assessed with low risk of selective reporting bias.

For some trials, it is possible that Cochrane authors may have made an unintentional error. However, it is unlikely

that such errors are behind the majority of inadequate assessments, based on the comments Cochrane authors provided.

In about 10% of trials judged as having a high risk of selective reporting bias, Cochrane authors indicated that those trials were available as only abstracts or unpublished data. Often it was unclear whether these were conference abstracts or journal article abstracts when the full text was not available. Likewise, when SR authors use unpublished data, their authors may be unwilling or unable to provide data on all outcomes that were mentioned, and for this reason, it appears harsh to judge that kind of data with high RoB.

All missing data may not be equally relevant, and therefore, without in-depth knowledge about a specific clinical field, it may be difficult to judge whether missing information or outcome is a key outcome. If using stricter criteria, we could consider that all cases of missing data are associated with high risk of selective reporting; in that case, our results would be even worse, indicating that further 19% of judgments among trials that were judged with unclear risk were inadequate.

Next relevant finding of our study is a considerable number of trials where there was no ‘‘selective reporting bias’’ domain in their RoB table. It is unclear why Cochrane authors do this because this leads to incomplete and incomparable Cochrane reviews, which miss relevant and complete RoB information.

Currently, training and support for Cochrane authors include reading Cochrane Handbook, attending online courses, learning by doing, and attending workshops. It would be worthwhile to explore new educational and methodological interventions that will help SRs authors to improve in this respect.

It also needs to be emphasized that the new version of the Cochrane RoB tool 2.0 has been announced, and its use is anticipated in the future [12]. The version 2.0 includes domain ‘‘bias in selection of the reported result,’’ for which the authors are encouraged to try to retrieve the prespecified analysis intentions for each trial and consult relevant sources, including the trial registry entry, trial protocol, or design paper [12]. Therefore, even the revised Cochrane RoB tool 2.0 tool instructs authors to search for relevant source data. Based on our analysis of the usage of the first version of the Cochrane RoB tool, authors seldom reported that they searched for a trial protocol.

Limitations of this study include restricted time in which analyzed Cochrane reviews were published. This kind of analysis is time consuming because it involves an analysis of several tens of thousands of data units; our aim was to make an in-depth analysis for a recent period. For efficiency, after initial piloting and high agreement, one author made assessment, and another author verified it; independent evaluation with subsequent consensus phase could have been superior methodological approach. Furthermore, we did not account for potentially overlapping trials included in Cochrane reviews; it has been shown before that RoB judgements of RCTs included in more than one Cochrane review may differ substantially [13].

We analyzed Cochrane reviews only, and non-Cochrane reviews can also use Cochrane RoB tool [14]. Although we expect that Cochrane should be more stringent with applying its own tool, compared with non-Cochrane reviews, we also hope that the findings of our study can help authors of both Cochrane and non-Cochrane reviews to improve their future assessments of selective reporting bias.

In conclusion, assessments for risk of selective reporting bias in Cochrane reviews are often not in line with the Cochrane Handbook. Cochrane authors often use insufficiently informative supporting comments, which do not justify given judgments of risk. Interventions for helping Cochrane authors to make an adequate RoB assessments should be considered.

CRediT authorship contribution statement

Frano Saric: Formal analysis, Writing - review & editing, Writing - original draft, Visualization. **Ognjen Barcot:** Investigation, Formal analysis, Writing - review & editing, Writing - original draft, Visualization. **Livia Puljak:** Methodology, Formal analysis, Writing - review & editing, Writing - original draft, Visualization.

Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jclinepi.2019.04.007.

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