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ORIGINAL ARTICLE

Comparison of non-Cochrane systematic reviews and their published protocols: differences occurred frequently but were seldom explained

Nadja Koensgen[a,1], Tanja Rombey[a,*,1], Katharina Allers[b], Tim Mathes[a], Falk Hoffmann[b], Dawid Pieper[a]

[a]*Faculty of Health, School of Medicine, Institute for Research in Operative Medicine, Witten/Herdecke University, Ostmerheimer Str. 200, 51109 Cologne, Germany*
[b]*Department of Health Services Research, School of Medicine and Health Sciences, Carl von Ossietzky University Oldenburg, 26111 Oldenburg, Germany*

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Abstract

Objective: To quantify the prevalence of differences in the reported methods between non-Cochrane systematic reviews (SRs) and their protocols and the extent to which these were reported and explained.

Study Design and Setting: We searched MEDLINE and Embase to identify protocols of non-Cochrane SRs published in 2012 and 2013. Using various methods, we searched for their corresponding SRs up to December 2016. The SRs and protocols were compared with respect to the methods-related "*Preferred Reporting Items for Systematic review and Meta-Analysis Protocols*" (PRISMA-P).

Results: We included 80 SRs and their protocols. Almost all SRs (92.5%) differed from their protocols in at least one of the methods-related PRISMA-P items (no. 7−17) and their subcategories. Half the SRs (48.8%) had a major difference in at least one item. On average, each SR differed from its protocol in 3.2 items, of which one comprised a major difference. Only 10% of all differences were reported in the SR, two-thirds with an explanation (7.0% in total).

Conclusion: The reporting quality and transparency of non-Cochrane SRs requires further improvement. Authors should report and explain all important changes made to the protocol in the SR publication. The updated PRISMA statement should include guidance regarding this matter.

Keywords: Systematic review; Protocol; Methodology; Transparency; Reporting quality; PRISMA

1. Introduction

Systematic reviews (SRs) are only truly systematic if their methods have been established a priori. Two transparent ways to do so are 1) to prospectively register the SR, for example, in the international prospective register of SRs, PROSPERO, the only open access database for this purpose [1], or 2) to publish a protocol in a peer-reviewed journal. An advantage of publishing a protocol is that through peer-review the risk of researcher bias might be reduced [2,3] and the methodological quality of the SR might be improved [4]. If study eligibility criteria, review outcomes and their prioritization, or analyses are not determined a priori, they may be modified post hoc according to the observed results or the available evidence. The selective inclusion of studies [5] or selective reporting [6], for example, biases the results of SRs.

Over the past years, there has been a strong increase in the number of published protocols [4] and PROSPERO records [7] for non-Cochrane SRs, although publishing a protocol for health-related secondary research is currently only required by some organizations, including Cochrane [8] and the Joanna Briggs Institute (JBI) [9].

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Conflict of interest: DP became an associate editor of "*BMC Systematic Reviews*" in August 2018. The other authors declare that they have no competing interests.

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Availability of data and material: The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

[1] Authors contributed equally.

* Corresponding author. Institute for Research in Operative Medicine, Witten/Herdecke University, Ostmerheimer Str. 200, 51109 Cologne, Germany. Tel.: +49 221 989 5742; fax: +49 221 989 5730.

E-mail address: tanja.rombey@uni-wh.de (T. Rombey).

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What is new?

Key findings

- We found that, on average, non-Cochrane systematic reviews (SRs) differed from their published protocol in three methods-related PRISMA-P items, but that changes of the methods were seldom reported and explained.

What this adds to what was known?

- Most existing studies focused on selective inclusion and reporting of outcomes in Cochrane SRs, whereas this study adds knowledge with regard to non-Cochrane SRs and further methodological aspects.

What is the implication and what should change now?

- To ensure high reporting quality and transparency of SRs, authors should report and explain any changes they made since the protocol was published in the SR and update their PROSPERO record (if available).
- The updated PRISMA statement should include guidance for authors of SRs regarding how and where to report changes made to the protocol.
- Editors and peer-reviewers should compare manuscripts of SRs with their protocols and check back with the authors if changes have not been reported and explained.

Publishing a protocol is not enough, however. Reviewers need to follow it, too, and report and explain any amendments they made during the process [8,10,11]. Existing empirical studies investigated differences between Cochrane SRs and their protocols [3,12–14] or between non-Cochrane SRs and their PROSPERO records [1]. Most of these studies only focused on selective outcome reporting, though [1,12–14]. Our primary objective was to quantify the prevalence of differences in all aspects of the reported methods between non-Cochrane SRs and their protocols. Our secondary objective was to quantify the extent to which these were reported and explained in the SR.

2. Methods

2.1. Study design

This was a retrospective, observational study comparing non-Cochrane SRs and their protocols. There was no a priori protocol for this study.

2.2. Search for eligible protocols and their systematic reviews

The study was based on a sample that we have generated in a previous study [4]. Protocols were identified through a search in MEDLINE (via PubMed). For the present study, we performed an additional search in Embase (via Embase), but it did not retrieve any additional protocols. All protocols for SRs that were titled as such or met the "*Preferred Reporting Items for Systematic review and Meta-Analysis Protocols*" (PRISMA-P) definition of SR protocols [15] were eligible for inclusion, regardless of the SR type or publication language.

Protocols had to be published in 2012 or 2013 so that their corresponding SRs would have been published by December 31, 2016, when we performed our final searches for the corresponding SRs. This was judged to be a sufficient period of time as it usually takes about 6 months to 2 years to complete an SR (median 66 weeks) [16,17]. We excluded any articles that were not protocols for SRs, such as protocols for primary studies or for literature reviews other than SRs (e.g., overviews, scoping reviews, or realist reviews). Protocols published in "*The JBI Database of Systematic Reviews and Implementation Reports*" were also excluded because, similar to Cochrane reviews, it is mandatory to publish a protocol for SRs to be published in this journal [18].

The corresponding SRs were identified as follows: One author (K.A.) searched for the protocol in PubMed and then used the similar and citing article functions. If that was unsuccessful, we searched for the first and last author's names in PubMed (in combination with a key word related to the protocols topic). If that was unsuccessful, too, we ran a forward citation search in Web of Science and Google Scholar. These steps were independently performed by a second author (F.H.) if necessary. As a last instance, the authors of the corresponding protocol were contacted via email (no reminders were sent).

2.3. Data extraction

The protocols' and SRs' basic characteristics had been extracted into a piloted, standardized Excel sheet as part of the previous study [4]. One author (N.K. or K.A.) extracted all text passages relating to the methods-related PRISMA-P items (no. 7–17) and their subcategories from the protocols and SRs into a second piloted, standardized Excel sheet. All data were verified by a second author (T.R.). Discrepancies were resolved through discussion until consensus was reached.

2.4. Reporting of protocols and comparison of protocols with systematic reviews

First, we assessed to which extent protocols for non-Cochrane SRs were reported in compliance with PRISMA-P [15]. Because PRISMA-P does not offer a scoring guidance, two authors (D.P. and N.K.) developed an internal

Table 1. Internal guideline for judgment of differences

PRISMA-P item specified in protocol and systematic review?	Possible judgment(s)	Explanation/example
Yes, item specified in protocol and systematic review	No difference	Information regarding the item is identical in protocol and systematic review.
	No difference as item not applicable	In protocol, a funnel plot was announced under specific preconditions. In systematic review, it was explained that these preconditions had not been fulfilled.
	Unclear, item not fully specified in protocol	Eligibility criteria fully reported in systematic review but only briefly in protocol.
	Unclear, item not fully specified in review	Eligibility criteria fully reported in protocol but in only briefly in systematic review.
	Unclear, item not fully specified in protocol/review	Some aspects of an item were only specified in the protocol (e.g., search strategy) and other aspects of the same item only in the systematic review (e.g., search limits).
	Minor difference	In protocol, nine databases were listed as information sources. In systematic review, a database was added/omitted.
	Major difference	In protocol, independent data extraction by two reviewers and consultation of a third reviewer was announced. In systematic review, single data extraction was reported.
No, item specified in protocol but not in systematic review	No difference as item not applicable	A funnel plot was mentioned in protocol but not again in systematic review as no meta-analysis had been performed.
	Unclear, item not specified in review	An item that presents an inevitable aspect of the methods, e.g., the literature search, was specified in protocol but not in systematic review.
	Major difference	An item that presents an optional aspect of the methods, e.g., GRADE assessment, was mentioned in protocol but not again in systematic review.
No, item specified in systematic review but not in protocol	No difference as item not applicable	Funnel plot not mentioned in protocol as meta-analysis was not expected to be feasible. However, meta-analysis could be performed and a funnel plot was created.
	Unclear, item not specified in protocol	An item that presents an inevitable aspect of the methods, e.g., the literature search, was specified in systematic review but not in protocol.
	Major difference	An item that presents an optional aspect of the methods, e.g., GRADE assessment, was not mentioned in protocol but in systematic review.
No, item not reported at all.	No difference as item not reported	Study selection process not described in protocol nor in systematic review.

guideline (Supplement 1) on how to judge if a PRISMA-P item was reported. Independently, they pilot-tested the guideline in a subset ($n = 10$ protocols) of the sample and revised it accordingly. Then, one author (N.K. or K.A.) assessed every protocol regarding all PRISMA-P items (no. 1–17) and judged whether they were reported or not.

Second, we judged whether there were any differences between the SRs and their protocols regarding the methods-related PRISMA-P items (no. 7–17) and their subcategories. Again, an internal guideline that was developed, independently pilot-tested (in $n = 10$ pairs), and revised by two authors (D.P. and N.K.) was used as a decision aid (Table 1). The pairs were categorized as follows: no difference (when the SR matched the protocol or when an item was not applicable or not reported), unclear difference (when an item was not (fully) specified in the SR or in the protocol, or when one part of an item was specified in the SR and another part in the protocol), and difference (minor difference, major difference).

If more than one judgment applied to an item, we chose the "worst case" (e.g., when we observed a minor and a major difference, we judged the pair as having a major difference). If there were multiple minor differences concerning one and the same item, we also judged the pair as having a major difference regarding this item. All judgments were done by one author (N.K. or K.A.) and verified by another author (T.R.). Discrepancies were resolved through discussion until consensus was reached.

Third, if there was a difference between an SR and its protocol, two authors (N.K. and T.R.) independently checked if these had been reported and explained in the SR. Discrepancies were resolved through discussion until consensus was reached.

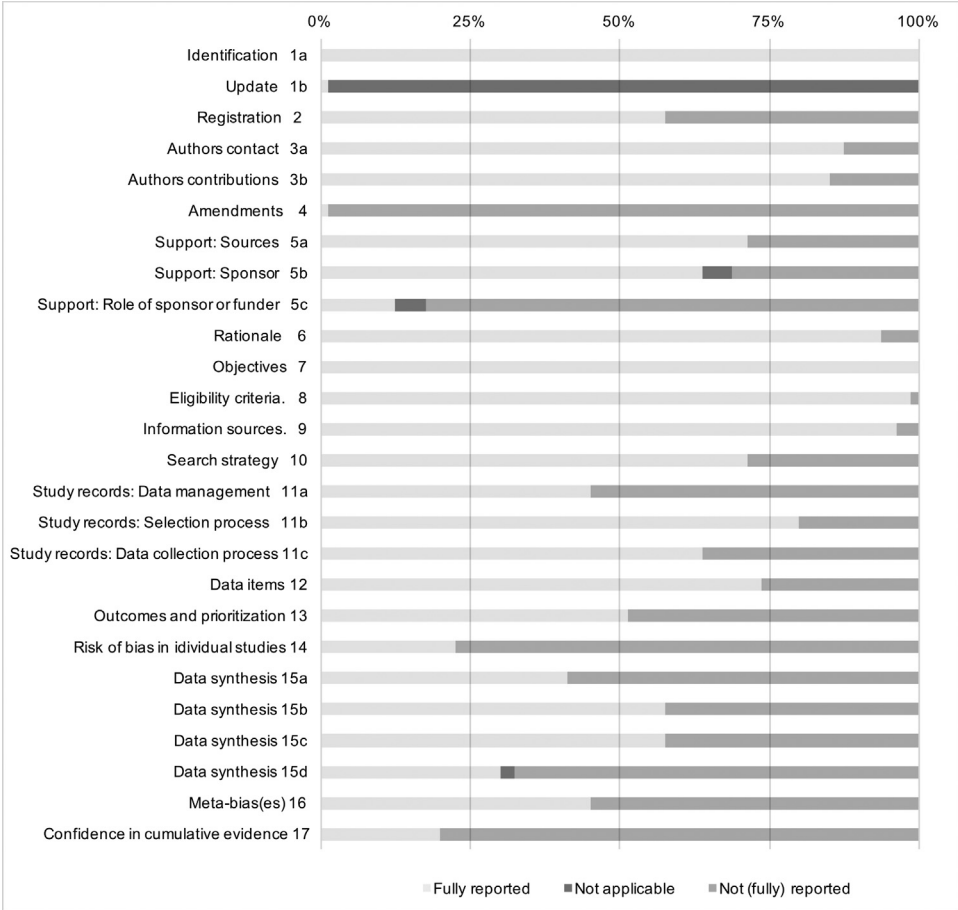

Fig. 1. Compliance with PRISMA-P (n = 80 protocols).

2.5. Statistical analysis

We performed a descriptive analysis using SAS for Windows, version 9.4 (SAS Institute Inc, Cary, NC). Results were expressed as proportions or as frequencies, which were reported as mean and standard deviation (SD) or as median and interquartile range (IQR).

3. Results

3.1. Search results

Our systematic literature search in MEDLINE retrieved 214 records. Of those, 89 were excluded, leaving a total of 125 (58.4%) eligible protocols. We found the corresponding SR for 65.6% (n = 82) of them but had to exclude two JBI SRs. Consequently, we included 80 protocols and 80 SRs. Their basic characteristics can be found in Supplements 2 and 3.

3.2. Reporting of protocols

The PRISMA-P items were fully reported by 1.3% to 100% of the protocols (Fig. 1. For numerical data, see Supplement 4). There were five items (1b, 4, 5c, 14, and 17) that were reported by less than 25% of the protocols. The items most often not fully reported were number 1b: "Update" and number 4: "Amendments" (1.3% each). Effectively, however, item 1b was reported in 100% of the protocols as it only applied to one protocol, which has reported it. Another item that was rarely fully reported was item 5c: "Role of sponsor or funder." It was only reported in about one-fifth of all protocols where it was applicable (in total 12.5%), although most protocols (71.3%) provided information regarding funding sources (item 5a) and named a sponsor (item 5b) if applicable (in total 63.8%).

Inter-rater agreement was high; discrepancies between the raters had occurred in 3.2% of the initial judgments.

3.3. Comparison of protocols and systematic reviews

We observed at least one difference between the SR and the protocol across the methods-related PRISMA-P items (7–17) and their subcategories in 74 of the 80 analyzed pairs (92.5%). At least one minor difference occurred in 71 pairs (88.8%), and at least one major difference in 38 pairs (47.5%).

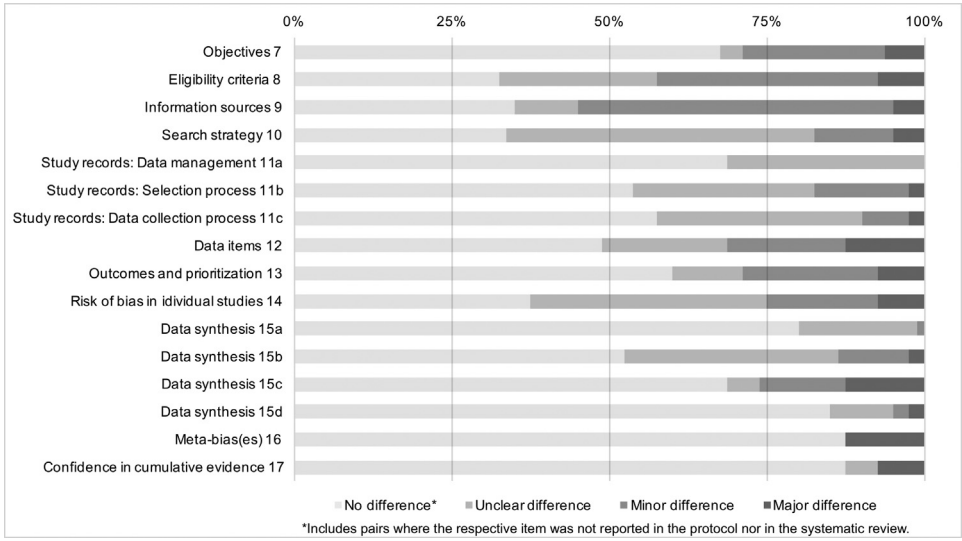

Fig. 2. Differences in reported methods between protocols and systematic reviews (n = 80 pairs).

On average, there was a difference between an SR and its protocol in 3.2 items. In 2.3 items, this difference was minor, and in 0.9 items, it was major. Major differences between protocol and SR occurred most frequently with regard to item 12: "Data items," item 15c: "Additional analyses," and item 16: "Meta-bias(es)" (in 12.5% of the pairs in each case). There was a minor difference in half the pairs (50.0%) regarding item 9: "Information sources" and in every third pair (35.0%) regarding item 8: "Eligibility criteria" (Fig. 2. For numerical data, see Supplement 5).

At least one unclear difference between the SR and the protocol was found in 73 of the 80 analyzed pairs (91.3%). On average, there were unclear differences in 3.2 items, most often because they had not (fully) been specified in the SR (mean 2.0 items) or in the protocol (mean 1.1 items). The item that was most frequently not (fully) specified in the SR was the search strategy (item 10, 32.5%), whereas item 15b: "Quantitative synthesis" was most frequently not (fully) specified in the protocol (25.0%).

Inter-rater agreement was moderate; discrepancies between the raters had occurred in 9.0% of the initial judgments.

3.4. Subgroup analyses

Post hoc subgroup analyses suggested that results may vary depending on the journal the protocol was published in ("BMC Systematic Reviews" vs. others) (Supplement 6), but not depending on the type of SR (therapy vs. other) (Supplement 7).

3.5. Reporting and explanation of differences

Of all 1,280 judgments (80 pairs times 16 items), 258 comprised a difference. Of those, 183 were judged to be minor differences and 75 to be major differences. Only 26 (10.1%) of all differences had been reported in the SR, 18 (9.8%) of the minor differences and eight (10.7%) of the major differences. Two-thirds of the reported differences (n = 18, in total 7.0%) had also been explained. This proportion was considerably higher for minor differences than for major differences (15/183 vs. 3/75) (Table 2).

4. Discussion

4.1. Summary of main findings

This was a descriptive study of 80 protocols for non-Cochrane SRs published in 2012 and 2013 and their corresponding SRs. In almost all pairs, at least one difference in the reported methods occurred, but only every tenth difference was reported in the SR.

Table 2. Differences reported in the systematic reviews (n = 80)

	Minor		Major		In total	
Differences[a]	**Absolute, *n***	**Relative**	**Absolute, *n***	**Relative**	**Absolute, *n***	**Relative**
Reported and explained	15	8.2%	3	4.0%	18	7.0%
Reported only	3	1.6%	5	6.7%	8	3.1%
Not reported	165	90.2%	67	89.3%	232	89.9%
In total	183	100%	75	100%	258	100%

[a] Each item was only counted once even if there was more than one difference regarding that item.

Some differences between protocols and SRs occurred because an item was only reported in the protocol and not in the SR. It was particularly the case for the items 11a: "Data management", 13: "Outcomes and prioritization", 15a: "Criteria under which study data will be quantitatively synthesized," and 17: "Confidence in cumulative evidence." This may be explained by the fact that they are not part of the "*Preferred reporting items for systematic reviews and meta-analyses*" (PRISMA Statement) [10], which is widely recognized as the gold standard for the reporting of SRs and which many journals request authors of SR to follow.

4.2. Comparison of our findings with other studies

To our best knowledge, this is the first study to compare non-Cochrane SRs with their published protocols regarding differences in the reported methods, which we structured after the PRISMA-P checklist.

There are four empirical studies that exclusively focused on selective outcome reporting [1,12–14]. Tricco et al. compared the primary outcomes reported in non-Cochrane SRs with those stated in their PROSPERO records and found that they differed in 32% of them [1]. Parmelli et al. [14], Kirkham et al. [13], and Dwan et al. [12] compared the outcomes reported in Cochrane SRs with those stated in their protocols. They found discrepancies in 47% [14], 22% [13], and 39% [12] of their samples because outcomes had been included/added, excluded/omitted, or changed (upgraded and/or downgraded). In our study, we assessed selective outcome reporting by looking at PRISMA-P item 13: "Outcomes and prioritization" and found that there was a difference or that it was unclear if there was a difference in 40% (28.8% and 11.3%, respectively).

Silagy et al. [3] compared Cochrane SRs with their protocols with respect to each of the, at that time, nine sections of protocols for Cochrane SRs. They found that there was a major difference between the types of outcomes stated in the protocol and reported in the review in almost half the pairs [3]. Regarding the methods, they observed a major difference in 68% of them [3].

Page et al. [19] synthesized the results of the aforementioned studies [3,12–14] except Tricco et al. [1]. The combined prevalence of Cochrane SRs with at least one discrepant (primary) outcome when compared with their protocol was 38% [19]. This is consistent with our finding.

4.3. Strengths and limitations

This was a comprehensive study of all protocols for non-Cochrane SRs published in 2012 and 2013 and indexed in MEDLINE or Embase that the corresponding SR was available for. Unlike most existing studies, we considered all relevant aspects of the methods, not only changes in the predefined outcomes. By assessing the aspects separately, we were able to identify those PRISMA-P items that differed most frequently between protocol and SR.

Nevertheless, our study has some limitations. First, our study may not be representative of all published protocols for non-Cochrane SRs. Most protocols in our sample were published in "*BMC Systematic Reviews*" (Supplement 2). In a post hoc subgroup analysis, we found that these protocols were better reported than protocols published in other journals. Besides, the distribution of journals publishing most SR protocols has changed in recent years. Nowadays, about as many SR protocols are published in "*BMJ Open*" as in "*BMC Systematic Reviews*" [4].

Second, as PRISMA-P was published in 2015 and the included protocols in 2012 or 2013, it was not surprising that some items were poorly reported. The proportion of protocols fully reporting an item is probably higher in protocols published after 2015. Furthermore, the PRISMA-P checklist builds on the PRISMA Statement [15], which is aimed at SRs and meta-analyses of studies evaluating health care interventions [10]. Hence, our approach of using the PRISMA-P checklist to structure the methods of the protocols may not have been suitable for protocols for other types of SRs. However, in a post hoc subgroup analysis, we compared therapy SRs to other SRs and found no big differences between them. Besides, there are currently no reporting guidelines for protocols for other types of SRs that we could have used along PRISMA-P.

Third, we had to make subjective judgments regarding most endpoints. Owing to resource constraints, we were not able to contact the corresponding authors to resolve any ambiguities. So, although we developed and pilot-tested our own internal guidelines and one another author verified each judgment, it is possible that our judgments do not reflect "the truth" as experienced by the authors themselves or others. Our judgments were also affected by the reporting quality of the protocols and SRs. It was more likely to observe a difference between a protocol and an SR if they were both reported very detailed, which means that those pairs may wrongly have been penalized for being transparent.

Finally, as we did not quantify the total number of differences but counted the items with at least one difference, our results are a conservative estimate of the prevalence of differences in the methods between non-Cochrane SRs and their protocols. Because we also found many unclear differences, the true prevalence of differences between protocols and SRs might be even higher.

4.4. Implications for practice

We recommend to add the PRISMA-P items no. 11a, 13, 15a, and 17 in the updated version of the PRISMA Statement, which is currently under way. The updated version should also contain guidance of how and where to report changes made to the protocol.

Furthermore, we noticed that some review authors referred to the published protocol and did not fully report the methods again in the SR. It is important that the methods are still reported in sufficient detail so that readers can assess the SR's quality without having to read the protocol. We acknowledge that adequate reporting can be a challenge under a given word limit, though.

The purpose of methodological changes to the protocol should be to improve the methodological quality of the SR, although, realistically, they might be done for pragmatic reasons, too. It is important that the process is made transparent regardless. SR authors could publish a new version of their protocol, label it as an amendment of their previously published protocol, and list all changes made.

Because this may be unrealistic for different reasons, authors of SRs that are registered in PROSPERO may prefer to simply update their PROSPERO record [20]. Nevertheless, at least important changes should be reported and explained in the SR [21]. We encourage editors and peer-reviewers to compare manuscripts for SRs with their protocols and check back with the authors if changes have not been reported and explained.

4.5. Implications for further research

Future studies should focus on protocols published after the publication of PRISMA-P and their corresponding SRs to analyze trends over time (pre− vs. post−PRISMA-P era). In addition to the present analyses, future studies should investigate if there is an association between the frequency of methodological changes and the methodological quality of an SR. It should also be investigated if changing a specific PRISMA-P item is associated with lower/higher methodological quality. Furthermore, future studies should investigate the reasons for changing aspects of the methods and for not reporting changes in the SR.

5. Conclusion

It is important that published protocols for non-Cochrane SRs fulfill their purpose, namely to increase the quality and transparency of SRs. Authors of SRs should always report and explain any changes made to the methods after the protocol was published in the SR publication and update the PROSPERO record of their SR, if available. The updated PRISMA statement should include guidance on how and where to report changes made to the protocol.

CRediT authorship contribution statement

Nadja Koensgen: Methodology, Investigation, Writing - review & editing. **Tanja Rombey:** Validation, Investigation, Visualization, Writing - original draft. **Katharina Allers:** Methodology, Formal analysis, Investigation, Writing - review & editing. **Tim Mathes:** Data curation, Formal analysis, Writing - review & editing. **Falk Hoffmann:** Conceptualization, Formal analysis, Methodology, Writing - review & editing. **Dawid Pieper:** Conceptualization, Methodology, Supervision, Writing - review & editing.

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Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.jclinepi.2019.02.012.

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