



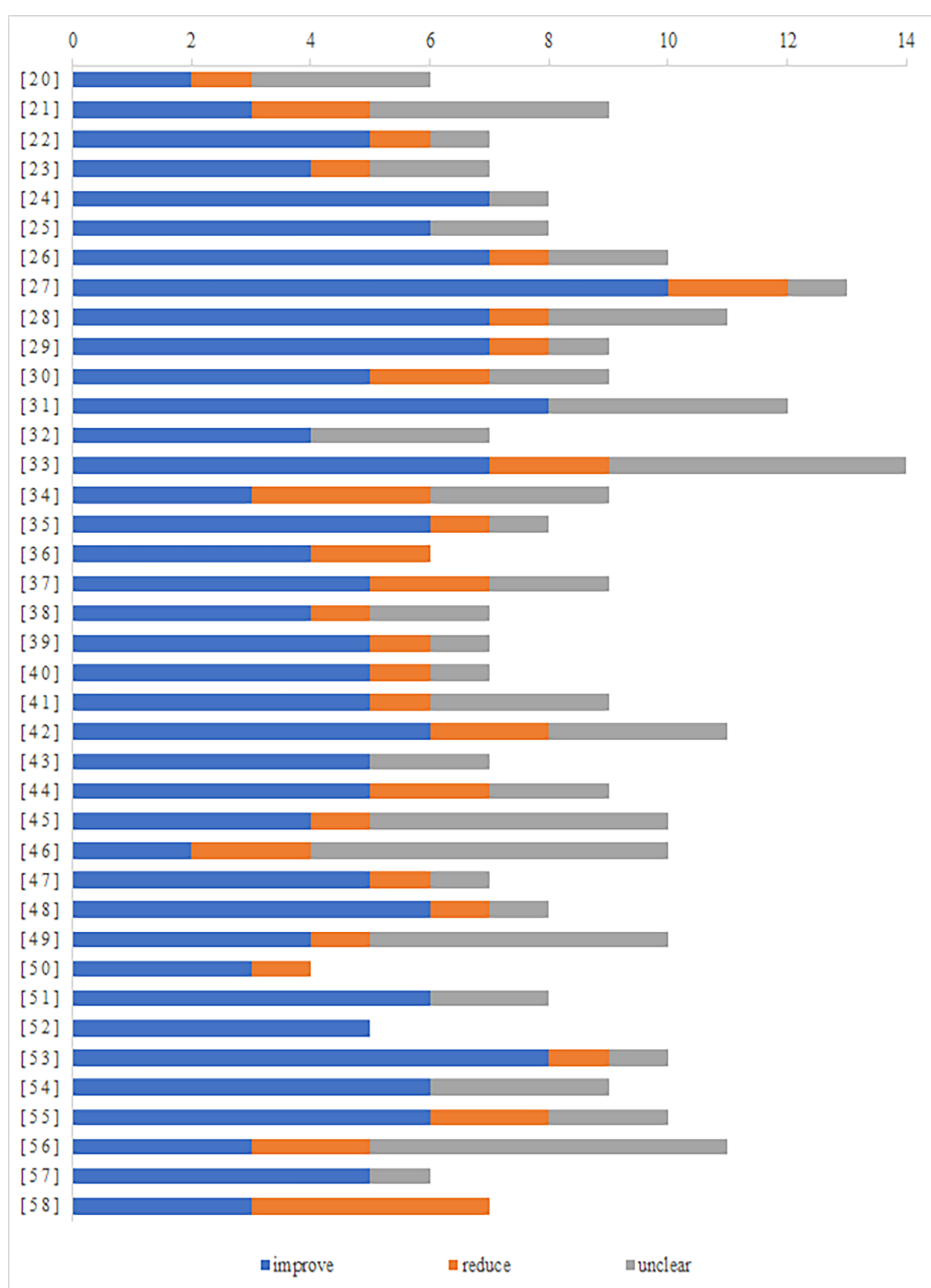
Inconsistencies are common between non-Cochrane systematic reviews and their protocols registered in PROSPERO but were seldom explained

The Problem

Determined what changed were made between non-Cochrane reviews and their protocols in PROSPERO and how likely these changes impacted the quality of systematic review.

Study Design and Setting

In this retrospective comparative study we electronically searched for protocols and their corresponding reviews in the PROSPERO platform that were “completed and published” from January to December, 2018. Two reviewers independently identified and classified changes between the protocols and reviews then evaluated the impact of these change on the quality of reviews.



Key Results

- This study has demonstrated that 100% of published non-Cochrane reviews (n=39) with a protocol in the PROSPERO underwent alterations during the research process, and these alterations involved all 13 compared method-related section
- All changes to only a single review were considered to improve the reporting/methodology quality, and the remaining 97% of systematic reviews (n=38) contain changes that were considered to reduce the methodology/reporting quality or have an unclear impact on systematic reviews.
- Only 8% of the reviews analyzed included reviews (n=3) that provided reasonable explanations for individual changes in the published full text.

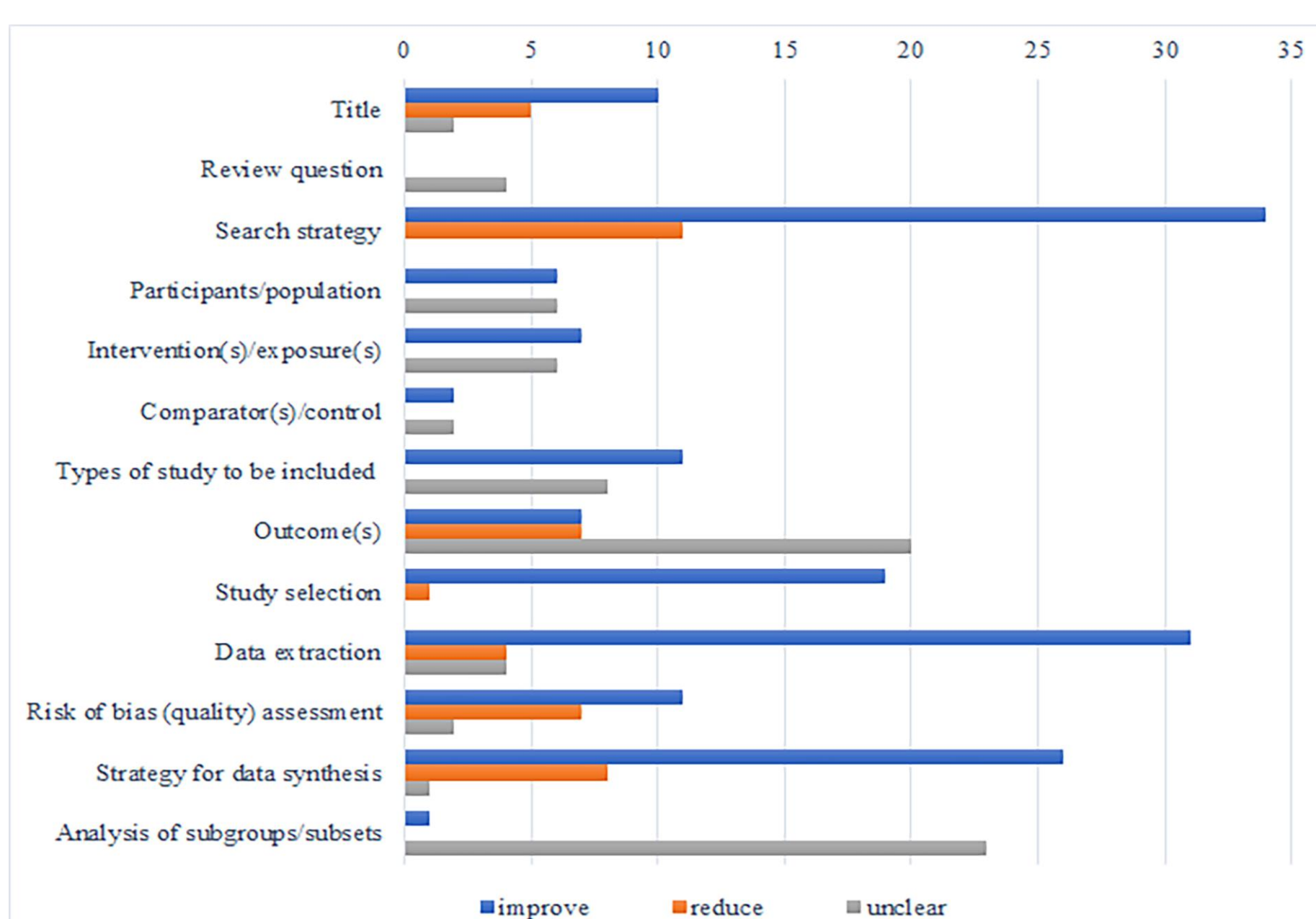


Table 1. Categories and impact of changes (n=39).

Section (Change amount/Total)	Categories of change	Improve the reporting/methodology quality	Reduce the reporting/methodology quality	Unclear (Having the potential risk of introducing bias)
Title (16/33)	Inclusion of the terms “systematic reviews” and “Meta-analysis” in the title	[33] [43] [45]		
	More accuracy key information (PICOS) about the scope of the reviews was provided	[23] [25] [31] [34] [38] [47] [49] [50]		
	Exclusion of the terms “systematic reviews” and “Meta-analysis” from review title		[40] [46]	
	The key information (PICOS) about the scope of the reviews was deleted		[45] [48] [55]	
	The key information (PICOS) about the scope of the reviews was changed			[46] [56]
Review question (5/33)	Modification of the review question by changing the intervention			[25]
	Narrowing the review question by deleting the exposures or interventions			[33] [46]
	Expanding the review question by considering safety in addition to efficacy			[49]
Eligibility criteria				
Participant (12/33)	Modifying the eligibility criteria of participant, like age, diagnosis			[31] [32] [34] [45] [49] [56]
	Adding the exclusion criteria of included participant to reduce confounders	[23] [24] [27] [48] [53] [57]		
Intervention(s)/exposure (15/33)	Modifying the intervention/exposure and thus changing the scope of review			[25] [33] [46]
	Modifying the eligibility criteria of intervention, like duration of treatment, drug dose, administration way			[23] [33] [45]
	Adding the exclusion criteria of intervention/exposure, like additional co-interventions and other inapplicable interventions or exposures	[27] [41] [44] [55]		
	Adding the definitions/measures of exposure	[22] [24] [50]		
Comparator(s)/control (4/33)	Modification the intervention of control group and thus changing the scope of review			[33] [35]
	Adding the inclusion/exclusion to increasing the comparability of the control group	[44] [57]		
Outcome (28/33)	Modifying the outcome			[28] [32] [33] [41] [44] [46]
	Deleting the distinction between primary and secondary outcome			[20] [21] [42] [43] [45] [49]
	Adding/deleting primary or secondary outcome			[20] [21] [22] [23] [27] [28] [30] [31] [37] [41] [42] [43] [44] [45] [54]
	Adding the measures/definition of outcome	[25] [29] [37] [43] [53] [54] [55]		
	Deleting the measures/definition of outcome			[22] [27] [34] [37] [38] [41] [49]
Types of study to be included (13/33)	Modifying the study type and thus expanding/narrowing the scope of included studies			[30] [31] [32] [34] [39] [49] [54] [55] [56]
	Adding exclusion criteria of some special study type, like conference abstract, review, case report, commentary, editorial, etc and improve the transparency of systematic review	[24] [26] [27] [31] [33] [35] [36] [40] [50] [51]		
Others (7/33)	Adding inclusion/exclusion criteria that studies reported/didn't report interested outcome and improve the transparency of systematic reviews (having readers ascertain whether the systematic review may be biased as a consequence of selective reporting)	[24] [27] [39] [48] [50]		
	Modifying the eligibility criteria, including sample size of included studies			[41] [46]
Search strategy (16/33)	Adding search term/language restriction/time range of retrieval/database/filters of retrieval to increase research transparency and repeatability	[30] [33] [24] [25] [26] [28] [30] [31] [32] [33] [35] [36] [38] [40] [42] [43] [44] [45] [46] [47] [48] [49] [50] [51] [52] [53] [55]		
	Deleting method to ensure the accuracy and comprehensiveness of retrieval, including including the database of retrieval, narrowing the time range for retrieval, deleting the re-run retrieval before the final analysis, deleting the manual search of grey literature etc.			[20] [21] [22] [23] [24] [25] [26] [27] [28] [29] [30] [31] [32] [33] [34] [35] [36]
	Adding methods to ensure the accuracy and/or comprehensiveness of retrieval, including increasing the database of retrieval, expanding the time range for retrieval, adding the manual search of grey literature etc.	[22] [23] [25] [26] [27] [28] [29] [30] [31] [32] [33] [34] [35] [36] [37] [38] [39] [40] [41] [42] [43] [44] [45] [46] [47] [48] [49] [50] [51] [52] [53] [54] [55]		
	Deleting search term/language restriction/time range of retrieval/database of retrieval and thus reducing research transparency and repeatability			[39] [42] [56]
Study selection (20/33)	Adding a description of the literature selection process/method and thus improve transparency/accuracy	[22] [23] [27] [28] [29] [30] [31] [32] [33] [34] [35] [36] [37] [38] [39] [40] [41] [42] [43] [44] [45] [46] [47] [48]		
	Deleting a description of the literature selection process/method and thus reduce transparency/accuracy			[36]
Risk of bias (quality) assessment (17/33)	Adding the process/methods to ensure accuracy of assessment	[23] [26] [27] [28] [38]		
	Deleting the process/methods to ensure accuracy of assessment			[28] [30] [33] [43] [44] [58]
	Deleting the methodological components that they assessed			[33] [34] [36] [38]
	Adding the methodological components that they assessed	[35]		
	Adding the tool used to assess the risk of bias	[54]*		[26] [34]
	Adding the tool used to assess the risk of bias	[37] [52]		
	Adding description of how the strength of the body of evidence will be assessed (such as GRADE)	[26] [28] [52]		
	Adding report how the assessments of risk of bias are used subsequently in the data synthesis	[27]		
Data extraction (14/33)	Adding the data extraction process/method	[25] [27] [28] [29] [30] [31] [32] [33] [34] [35] [36] [37] [48] [51] [53] [54] [57]		
	Deleting the data extraction process/method			[26]
	Adding the list and definition of all variables for which data were sought or any assumptions/clarifications made	[20] [22] [24] [26] [27] [28] [29] [30] [31] [32] [33] [34] [35] [36] [37] [38] [39] [40] [41] [42] [43] [44] [45] [46] [47] [48] [49] [50] [51] [52] [53] [54] [55]		
	Deleting the list and definition of all variables for which data were sought or any assumptions/clarifications made			[34] [46] [47]
	Modifying the list and definition of variables for which data were sought or any assumptions/clarifications made			[38] [43] [51]
	Adding the algorithm that the author used to select data from overlapping reports and/or any efforts they used to solve logical inconsistencies across reports	[29]* [37] [42]* [47]* [41] [50]*		
	Modifying the algorithm that the author used to select data from overlapping reports			[56]*
Strategy for data synthesis (8/33)	Adding the principal summary measures (such as risk ratio, difference in mean)/the method of handling data and combining results of studies (including measures of consistency for each meta-analysis)/the assessment of risk of bias that may affect the cumulative evidence (such as publication bias, selective reporting within studies)/the methods of additional analysis (such as sensitivity analysis, meta-regression)/the tool of statistical analysis	[23] [22] [24] [25] [26] [28] [29] [30] [31] [32] [33] [34] [35] [36] [37] [38] [39] [40] [41] [42] [43] [44] [45] [46] [47] [48] [49] [50] [51] [52] [53] [54] [55] [57]		
	Deleting the principal summary measures (such as risk ratio, difference in mean)/the method of handling data and combining results of studies (including measures of consistency for each meta-analysis)/the assessment of risk of bias that may affect the cumulative evidence (such as publication bias, selective reporting within studies)/the methods of additional analysis (such as sensitivity analysis, meta-regression)/the tool of statistical analysis			[21] [23] [30] [36] [37] [44] [52] [58]
Analysis of subgroup/subsets (4/33)	Changing the method of combining results of studies			[40]
	Adding the subgroup analysis			[21] [26] [28] [29] [42] [46] [47] [48] [51] [53]
	Deleting the subgroup analysis	[43]*		[20] [26] [31] [54] [57] [44] [45] [49] [54] [55]
	Deleting the original subgroup analysis and adding a new subgroup analysis			[23] [33] [38] [57]

Conclusion & Suggestion

Differences between the non-Cochrane reviews and their protocols recorded in PROSPERO are widespread, and there have been many changes having an unclear impact on the quality of reviews. Guiding the author to report and explain the differences between protocol and reviews or even requiring authors to so at the level of journal are two fundamental solutions to further improve the transparency of the non-Cochrane reviews.

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