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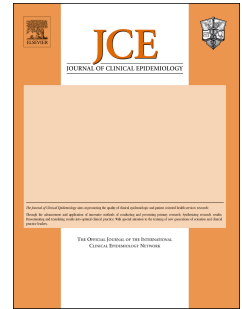
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Systematic review finds that appraisal tools for medical research studies address conflicts of interest superficially

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Objective: To identify and summarise 1) appraisal tools and other guides which address conflicts of interest in medical research studies; and 2) top journals with policies on managing conflicts of interest in journal papers.

Study Design and Setting: Systematic review. We searched bibliographic databases, other sources and websites of 30 top medical journals. Two authors selected documents and extracted data.

Results: We included 27 appraisal tools. None were designed specifically for addressing conflicts of interest and they included only 1-2 short items on conflicts of interest. We also included eight other types of guides. Of 27 appraisal tools, 23 addressed study funding and 19 authors' conflicts of interest. Nine tools addressed availability of conflicts of interest information, 13 reported conflicts of interest, and five influence from conflicts of interest. Twelve of 30 top journals had conflicts of interest managing policies (beyond disclosure). One journal restricted non-research papers (e.g. editorials) to authors without financial conflicts of interest and ten only restricted under certain circumstances.

Conclusion: Appraisal tools that address conflicts of interest typically do so superficially and rarely address how conflicts of interest may influence studies. Less than half of top medical journals have explicit policies on managing conflicts of interest.

Keywords: Conflicts of interest; Industry funding; Critical appraisal tools; Medical journals; Journal policies; Systematic review

Key findings

- We identified no appraisal tool designed specifically to address conflicts of interests in medical research studies. Twenty-seven tools included 1-2 short items mainly focusing on whether conflicts of interest information was available or if any conflicts of interest were reported. There was little guidance on assessing how conflicts of interest may influence studies.
- In a small sample of 30 top medical journals more than half had no explicit policies on managing conflicts of interest in journal papers beyond standard disclosure practices. Journals with policies to manage conflicts of interest mainly placed some form of restriction on non-research papers, publishing only those where authors did not have financial conflicts of interest.

What this adds to what is known?

- Conflicts of interest are considered important, but the focus in both appraisal tools and journals is on how conflicts of interest are disclosed; not on how conflicts of interest may influence studies or how journal policies may minimise such influence.

What is the implication, what should change now?

- There is need for more comprehensive evidence-based guidance for addressing conflicts of interest in research studies.
- The International Committee of Medical Journal Editors and medical journals could consider developing, revising and harmonising explicit policies on managing conflicts of interest in their journal papers.

1. Introduction

More than half of medical research funding originates from the drug and device industry [1] and around two-third of drug trials are industry-funded [2–4]. Similarly, more than half of clinical trials include investigators with financial ties to companies producing interventions tested in the trials [2,3]. Such relationships create conflicts of interest and introduce a risk that the primary scientific interest of an impartial investigation may be compromised by secondary commercial interests [5]. Similarly, specialist interests and academic relationships may create non-financial conflicts of interest [4,6].

While it is generally agreed that conflicts of interest pose an important threat to the integrity of science, it has been much debated how to tackle the problem [5,7]. Currently most medical journals request that authors report sources of study funding transparently and disclose any relationships that may be perceived as conflicts. Readers are then left to assess whether and to what degree such conflicts of interests could have influenced study findings. This assessment is often a challenge, when reading a single research paper, when reading several papers to guide a clinical decision, or when critically appraising multiple studies in the context of developing a clinical practice guideline or conducting a systematic review [8,9]. While numerous tools are available for appraising research studies of different designs [10–12] they seem to address conflicts of interest differently.

Another journal strategy is to manage conflicts of interest by restricting publication of journal papers to authors without conflicts of interest. The majority of medical journals require transparently reporting funding source and authors' conflicts of interest using the International Committee Medical Journal Editors' (ICMJE) criteria [13], but little is known on how journals manage conflicts of interest beyond disclosure.

We therefore undertook a systematic review to identify and summarise 1) appraisal tools and other guides which address conflicts of interest of funders and authors in medical research studies; and 2) top medical journals with policies on managing conflicts of interest in journal papers.

2. Methods

2.1 Protocol and registration

A protocol was written and registered prior to study conduct (August 3, 2017; PROSPERO record: CRD42017070208).

2.2 Eligibility criteria – appraisal tools and other guides

We included appraisal tools and other guides, in any language, which address conflicts of interest in any type of medical research study. This included methodological checklists with items related to conflicts of interest, other guides such as handbooks for conducting systematic reviews which contained specific recommendations for addressing conflicts of interest in included studies, and journal guidance for assisting peer reviewers. We excluded reporting guidelines, and appraisal tools and other guides which address conflicts of interest in clinical practice guidelines (Appendix 1).

We used the Institute of Medicine conflicts of interest definition: “a set of circumstances that creates a risk that professional judgment or actions regarding a primary interest will be unduly influenced by a secondary interest” [5]. This included financial conflicts of interest (e.g. study funding or authors’ ties) and non-financial conflicts of interest (e.g. specialist or academic conflicts of interest) [6,14].

2.3 Eligibility criteria – journals

We included medical journals with policies on managing conflicts of interest among funders and authors of journal papers that went beyond simple disclosure. This included restrictions on publishing studies related to specific funding sources (e.g. not permitting funding by tobacco companies) or conflicts of interest related to certain types of papers (e.g. only publishing editorials by authors without financial conflicts of interest).

We excluded journals with policies that focused only on managing conflicts of interest among editors or peer reviewers.

2.4 Search strategy

We searched MEDLINE and Embase via Ovid and the Cochrane Methodology Register (up to November 1, 2017), and Google Scholar (in November 2017). The search strategy was developed for MEDLINE and adapted for the other databases (Appendix 2).

We searched the websites of the EQUATOR Network, and Cochrane including all review groups. Furthermore, we searched the reference lists of included documents and relevant systematic reviews, and searched Web of Science for any studies citing the included documents (in August 2018). We contacted 20 content experts (in December 2018) and searched for relevant unpublished conference abstracts from previous Cochrane Colloquia, Evidence Live and the Congress on Peer review and Scientific Publication (in August 2018).

We searched the websites of 30 top medical journals (10 general medical journals and 20 specialty journals with the highest impact factors) for any guides for peer reviewers and journal policies on managing conflicts of interests (Appendix 3). In our study we describe this sample of journals as top journals and other journals as regular journals. We contacted the journals to ensure that relevant guides and policies were identified (20 of 30 journals replied after one email and two reminders).

2.5 Inclusion process

One author (LØ) screened titles and abstracts (i.e. publications or website information) for obvious exclusions. In a second round two authors (LØ and KR) independently assessed full text documents and disagreements were resolved through discussion with a third author (AL) as arbiter.

2.6 Data extraction

One author (AL) extracted data into a pilot tested and standardised data sheet with verification by a second author (KR).

We extracted general characteristics of documents, how they were developed and how conflicts of interest were addressed (Appendix 1). We defined appraisal tools using a modification of Higgins and colleagues [11], as any structured instrument aimed at aiding

the user to assess quality or susceptibility to bias in research studies or to assess the quality of the body of evidence based on a synthesis of studies. For other guides we divided them into: 1) guidance questions: any list of guidance questions aimed at assisting readers in appraising a study, that did not contain specific categories for answers (such as yes, no and unclear); and 2) set of recommendations: documents providing readers with recommendations which did not fit the definition of the categories above (e.g. handbooks for conducting systematic reviews).

For appraisal tools we extracted additional information on tool development and divided them into groups: simple checklist, checklist with overall rating and scale (i.e. containing summary numerical scores typically derived from scores of individual items). We used a hierarchical approach to describe how conflicts of interest were addressed in each tool based on the categories: 1) availability of conflicts of interest information (i.e. assessment of whether study publication contained disclosure statements); 2) reported conflicts of interest (i.e. assessment of whether any conflicts of interest were reported in the study); and 3) influence from conflicts of interest (e.g. assessment of whether a study included procedural elements minimising influence from conflicts of interest or if certain types of conflicts of interest were judged to have a higher risk of influencing study results).

2.7 Usage of appraisal tools with items addressing conflicts of interest

For published appraisal tools we noted the total number of citations, and citations since 2018, of the main tool publication using Google Scholar (May 8, 2019).

3. Results

In total, we included 27 appraisal tools [12,15-35], eight other types of guides which address conflicts of interest [36–43] and 14 journals (12 top journals and two regular journals from our database search) (Figure 1). Of the eight other types of guides three were journal papers with specific guidance questions for journal readers to be used when appraising research papers [36–38] and five were guides which addressed conflicts of interest in the context of conducting systematic reviews [39–43]. To enhance readability,

we focus on the content of appraisal tools in the main text, and report the content of the other guides in the appendix (Appendix 1 and 4-7).

3.1 Appraisal tools with items addressing conflicts of interest

Eighteen tools were designed to appraise primary research studies of various design, seven tools to appraise systematic reviews and two tools to rate the quality of the body of evidence. None had been developed specifically to address conflicts of interest (Table 1; Appendix 1 and 8). The tools were published from 1989 to 2017 (median: 2014) and included from 7 to 56 items (median: 13).

The proportion of tool items related to conflicts of interest ranged from 1 in 5 items to 1 in 43 items (Table 2; Appendix 9). Twenty-three tools addressed study funding source and 19 addressed authors' conflicts of interest. Nine tools included assessment of whether conflict of interest information was available for a study, 13 assessed whether any conflicts of interest were reported in a study and five assessed whether conflicts of interest might have influenced study results or interpretation. Seven tools described conflicts of interest as a separate type of bias. Six of 27 tools were developed using systematic methods (i.e. based on a literature search, used a defined process, and were both pilot and reliability tested).

The five tools addressing influence from conflicts of interest did so differently. Three tools, AMSTAR 2 and DART for systematic reviews, and PQAQ for paediatric health economic studies, focused on management of conflicts of interest with different criteria for what was considered appropriate methodology [15,19,29]. The AMSTAR 2 tool required a description of how the conflicts of interest were managed and the DART tool required exclusion of individuals with substantial conflicts of interest from study involvement, though without describing a threshold. The PQAQ tool had one item requiring that the role of the sponsor should be explicitly stated and another item requiring study authors to have had independent control over the methods and right to publish, but did not take conflicts of interest of study authors into account. Two tools, IPM-QRB and IPM-QRBNR for trials and observational studies of pain management interventions, focused on judging the degree of conflicts of interest [24,25]. Both tools used a scale approach assigning negative scores if,

for example, industry employees were involved or if conflicts of interest disclosure information was misleading.

3.2 Usage of appraisal tools with items addressing conflicts of interest

GRADE, AMSTAR and AMSTAR 2 were the three most cited appraisal tools both in total and since 2018 (Figure 2; Appendix 10).

3.3 Journals with policies on managing conflicts of interest

Five of 12 top journals with policies on managing conflicts of interest were general medical journals and seven were specialty journals. Six of these 12 top journals were from the *Lancet* group (Table 3; Appendix 11).

One top journal, *BMJ*, restricted publication of non-research papers (e.g. editorials) to authors without financial conflicts of interest and ten top journals restricted it to authors without certain types of financial conflicts of interest. For two of these ten journals this was based on editorial judgement (*CMAJ* and *PLoS Medicine*), for one journal it was based on a certain monetary threshold (*NEJM*) and for the last seven journals it was based on specific types of financial conflicts of interest (*Blood* and the six *Lancet* journals). Three journals, *American Journal of Critical Care and Respiratory Medicine*, *BMJ* and *PLoS Medicine*, did not permit publication of any study with funding from the tobacco industry.

None of the identified top journals had conflicts of interest managing policies in research papers or addressed non-financial conflicts of interest. However, one regular journal, *Cochrane Database of Systematic Reviews*, did not permit commercial funding of any research paper, required that the majority of authors should be without financial conflicts of interest and that editors should check data if a review included studies by review authors.

4. Discussion

We identified no tools developed specifically for addressing conflicts of interest, and 27 general appraisal tools including 1-2 short items addressing conflicts of interest, and 8

other guides. No tools addressed conflicts of interest comprehensively as they mainly focused on whether conflicts of interest information was available or any conflicts of interest were reported and provided little guidance on assessing how they might influence studies. Less than half of top journals had explicit policies on managing conflicts of interest beyond disclosure, e.g. restricting publication of non-research papers to authors without financial conflicts of interest.

4.1 Strengths and weaknesses

We undertook a comprehensive literature search. However, as we found that some specific tools were developed as part of an evaluation of a sample of studies and not described in the abstract and some tools were only available on websites [18,28,32] we might therefore have missed relevant tools and other guides. We investigated only a small sample of top journals with policies on managing conflicts of interest and half of top journals with policies were from the *Lancet* group. This may limit the generalisability of our findings particular in relation to low impact medical journals.

4.2 Context

This is to our knowledge the first study to specifically investigate how conflicts of interest are addressed in appraisal tools and other guides. A previous systematic review of epidemiological appraisal tools reported that three of 86 tools included items addressing conflicts of interest [11]. A more recent systematic review reported this to be the case for seven of 62 tools for human epidemiological studies [44]. Similar to our study the tools included in the systematic reviews varied in relation to how and for which context they were developed. However, none of the systematic reviews investigated how conflicts of interest were addressed in the included appraisal tools.

We found that tools used variable approaches to address conflicts of interest, likely reflecting a lack of consensus on how best to handle conflicts of interest in medical research. Industry funding and authors' financial ties have been associated with more frequent reporting of statistically significant results and favourable conclusions in trials [2,45], and also more favourable conclusions in systematic reviews [46]. However, it has

been debated whether this association should be interpreted as conflicts of interest being an independent bias-inducing mechanism or if conflicts of interest should be viewed as a proxy for underlying differences in study characteristics, such as more frequent use of inferior comparators and surrogate outcomes in industry trials compared with non-industry trials [47–49]. Seven of the tools we reviewed described conflicts of interest as a separate type of bias and one study found that 28% of Cochrane Reviews included conflicts of interest in the risk of bias assessment despite the Cochrane Handbook advocating against this practice [49,50]. This recommendation has been debated within Cochrane [47,48] and the recent version of the Cochrane Handbook now propose that in addition to reporting trial conflicts of interest review authors should also assess conflicts of interest as part of study appraisal, though without considering it as a separate type of bias [51].

In relation to journals with conflicts of interest managing policies Bero surveyed 10 top general medical journals and found results similar to ours [52]. However, our study also extends to top specialty journals. Only two of 15 top specialty journals that did not belong to the *Lancet* group had policies to manage conflicts of interest. This could suggest that such policies are adopted less frequently in top specialty journals compared to top general medical journals, but our sample is too small to make a robust comparison.

4.3 Implications

Most tools focused on whether conflicts of interest information was available or if any conflicts of interest were reported. These approaches do not take into account the degree of conflicts of interest (e.g. a trial sponsored by a drug company compared to a trial where one investigator had received a single sponsored conference trip) or the potential influence from collaborators with conflicts of interest (e.g. an industry-initiated trial run by the company compared to an investigator-initiated trial with industry funding, but run by a university based clinical trial unit).

Only five tools addressed whether conflicts of interest might have influenced study results or interpretation either by focusing on whether conflicts of interest were managed in some form, or by focusing on the degree of conflicts of interest in a study. The AMSTAR 2 tool (for assessing quality of systematic reviews) addressed whether conflicts of interest were managed thereby addressing conflicts of interest in a more comprehensive manner.

However, the tool provided no assessment as to whether conflicts of interest were managed in an adequate way. Similarly, while the four other tools addressing influence from conflicts of interest (DART, IPM-QRB, IPM-QRBNR and PQAQ) did so in a more detailed manner compared to other tools, they did not provide adequate assessment to how conflicts of interest might have influenced a study.

There is therefore a need for a tool aimed at addressing conflicts of interest in a more detailed manner and developed using evidence-based principles. One way forward could be the Tool for Addressing Conflicts of Interest in Trials (TACIT) which is currently in development under the auspices of the Cochrane Bias Methods Group [51,53,54]. The tool aims at judging concern for conflicts of interest in trials included in systematic reviews and works in conjunction with other review tools such as Risk of Bias 2, Risk of Bias due to Missing Evidence and GRADE [22,55,56] and TACIT may stimulate the development of appraisal tools aimed at other study designs.

Our results also highlight a striking contrast between the importance given to conflicts of interest by medical journals and how journals currently address and manage such conflicts of interest. As an example, we did not identify any guidance for peer reviewers for addressing conflicts of interest in research papers. Furthermore, while there has been a move towards managing conflicts of interest in clinical guidelines with major guidelines issuing organisations such as US Preventive Services Task Force, WHO and NICE having policies excluding or limiting the role of authors with certain types of conflicts of interest [57–59] this is not the case for research papers in top medical journals.

Journals may be reluctant to introduce restrictive conflicts of interest policies for research papers as it may be commercially disadvantageous due to loss of revenue from reprint sales and lowering of impact factors [60,61]. One solution could be to introduce future policies across multiple journals simultaneously, for example at the level of publishers or under the auspices of ICMJE. Such policies should also address conflicts of interest of editors and peer reviewers as they may similarly influence the content of papers published in medical journals [62,63].

5. Conclusions

We identified no tools that specifically addressed conflicts of interest, and 27 general appraisal tools addressed conflicts of interest in 1-2 short items. No tools addressed conflicts of interest comprehensively as they mainly focused on whether conflicts of interest information was available or if any conflicts of interest were reported and offered little practical guidance to users on assessing how conflicts of interest might influence studies. Less than half of our small sample of top journals had explicit policies on managing conflicts of interest beyond disclosure, most often restricting non-research papers to authors without financial conflicts of interest. There seems to be a striking contrast between the considerable attention given to conflicts of interest in medical research and the lack of adequate guidance for addressing and managing such conflicts.

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Author contributions

AH and AL conceived the idea for the study. All authors were involved in developing the study protocol. LØ performed database searching and LØ and KR included studies. AL, AH, KR and LØ performed data extraction, AL performed data analysis and all authors were involved in interpretation of results. AL drafted the manuscript and all authors were involved in writing of the manuscript and approved the final version of the manuscript. AL is the guarantor and accepts full responsibility of the work; all authors were involved in the decision to publish.

Conflicts of interest

Four of the authors (AH, AL, IB and LAS) are members of the TACIT Steering Group involved in developing a Tool for Addressing Conflicts of Interest in Trials.

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Journal Pre-proof

Table 1. Characteristics of 27 appraisal tools with items on conflicts of interest

Appraisal tool characteristics	Tools intended for appraising			
	All tools (n = 27)	Primary research (n = 18)	Systematic reviews (n = 7)	Body of evidence (n = 2)
	Number (percentages)*			
Items related to conflicts of interest included in appraisal tool				
1 item	20 (74%)	14 (78%)	6 (86%)	0 (0%)
2 items	4 (15%)	3 (17%)	1 (14%)	0 (0%)
No separate item (addressed as part of another item)	3 (11%)	1 (6%)	0 (0%)	2 (100%)
Content of items related to conflicts of interest				
addressed study funding	23 (85%)	15 (83%)	6 (86%)	2 (100%)
addressed author conflicts of interest	19 (70%)	13 (72%)	4 (57%)	2 (100%)
considered conflicts of interest as a separate type of bias	7 (26%)	6 (33%)	1 (14%)	0 (0%)
Appraisal tool identified from				
Journal publication	24 (89%)	17 (94%)	6 (86%)	1 (50%)
Website	3 (11%)	1 (6%)	1 (14%)	1 (50%)
Appraisal tool developed using systematic methods**	6 (22%)	3 (17%)	2 (29%)	1 (50%)
Type of appraisal tool				
Simple checklist	7 (26%)	5 (28%)	2 (29%)	0 (0%)
Checklist with overall rating	15 (56%)	9 (50%)	4 (57%)	2 (100%)
Scale	5 (19%)	4 (22%)	1 (14%)	0 (0%)
Quality issues addressed in appraisal tool				
Generalisability	10 (37%)	7 (39%)	1 (14%)	2 (100%)
Methodological	27 (100%)	18 (100%)	7 (100%)	2 (100%)
Reporting	21 (78%)	14 (78%)	7 (100%)	0 (0%)
Statistics	23 (85%)	14 (78%)	7 (100%)	2 (100%)

*Percentages do not always add up to 100 due to rounding.

** If tool was developed based on a literature search, using a defined process, and both pilot and reliability tested.

Table 2. Addressing of conflicts of interest in 27 appraisal tools with items on conflicts of interest

Name*	Number of items on conflicts of interest/ total number of items	Addressed study funding	Addressed author conflicts of interest	How conflicts of interest were addressed	Conflicts of interest described as a separate type of bias
<i>Primary research tools</i>					
AXIS	1/20	Yes	Yes	Reported conflicts of interest	No
Berra	1/27	Yes	Yes	Reported conflicts of interest	No
Cochrane Hepato-Biliary Group	1/8	Yes	No	Reported conflicts of interest	Yes
Cowley-case series	1/17	No	Yes	Reported conflicts of interest	No
Cowley-non-randomised studies	1/13	No	Yes	Reported conflicts of interest	No
Cowley-RCT	1/12	No	Yes	Reported conflicts of interest	No
Faillie	2/10-32**	Yes	Yes	Reported conflicts of interest	Yes
Guo	1/20	Yes	Yes	Availability of conflicts of interest information	No
IPM-QRB	2/22	Yes	Yes	Influence from conflicts of interest	No
IPM-QRBNR	1/16	Yes	No	Influence from conflicts of interest	No
Moncrieff	1/23	Yes	Yes	Availability of conflicts of interest information	No
Navigation Guide-human	1/8	Yes	Yes	Availability of conflicts of interest information	Yes
Navigation Guide-non-human	1/7	Yes	Yes	Availability of conflicts of interest information	Yes
PQAQ	2/56	Yes	No	Influence from conflicts of interest	No
QCC-non human	1/10	Yes	Yes	Reported conflicts of interest	Yes
QCC-primary research	1/10	Yes	Yes	Reported conflicts of interest	Yes
Reisch	0/12***	Yes	No	Availability of conflicts of interest information	No
Viswanathan	1/29	Yes	No	Availability of conflicts of interest information	No
<i>Systematic review tools</i>					
AMSTAR	1/11	Yes	No	Availability of conflicts of interest information	No
AMSTAR 2	2/16	Yes	Yes	Influence from conflicts of interest	No
DART	1/14	No	Yes	Influence from conflicts of interest	No
Higgins	1/43	Yes	No	Availability of conflicts of interest information	No
QCC-reviews	1/10	Yes	No	Reported conflicts of interest	Yes
R-AMSTAR	1/11	Yes	Yes	Reported conflicts of interest	No
SIGN	1/13	Yes	Yes	Availability of conflicts of interest information	No
<i>Body of evidence tools</i>					
GRADE	0/8***	Yes	Yes	Reported conflicts of interest	No
OHAT	0/10***	Yes	Yes	Reported conflicts of interest	No

* If tool did not have an official short or abbreviated name we used the name of the first author of the main publication.

*** Tool intended for appraisal of RCTs, cohort studies, case-control studies and systematic reviews with some items tailored for specific study designs. Considered to be a single tool.*

**** Indirectly included conflicts of interest in an item on publication bias.*

***** Conflicts of interest addressed in one of five subquestion in an item on purpose of study.*

Journal Pre-proof

Table 3. Managing of conflicts of interest in 12 top medical journals

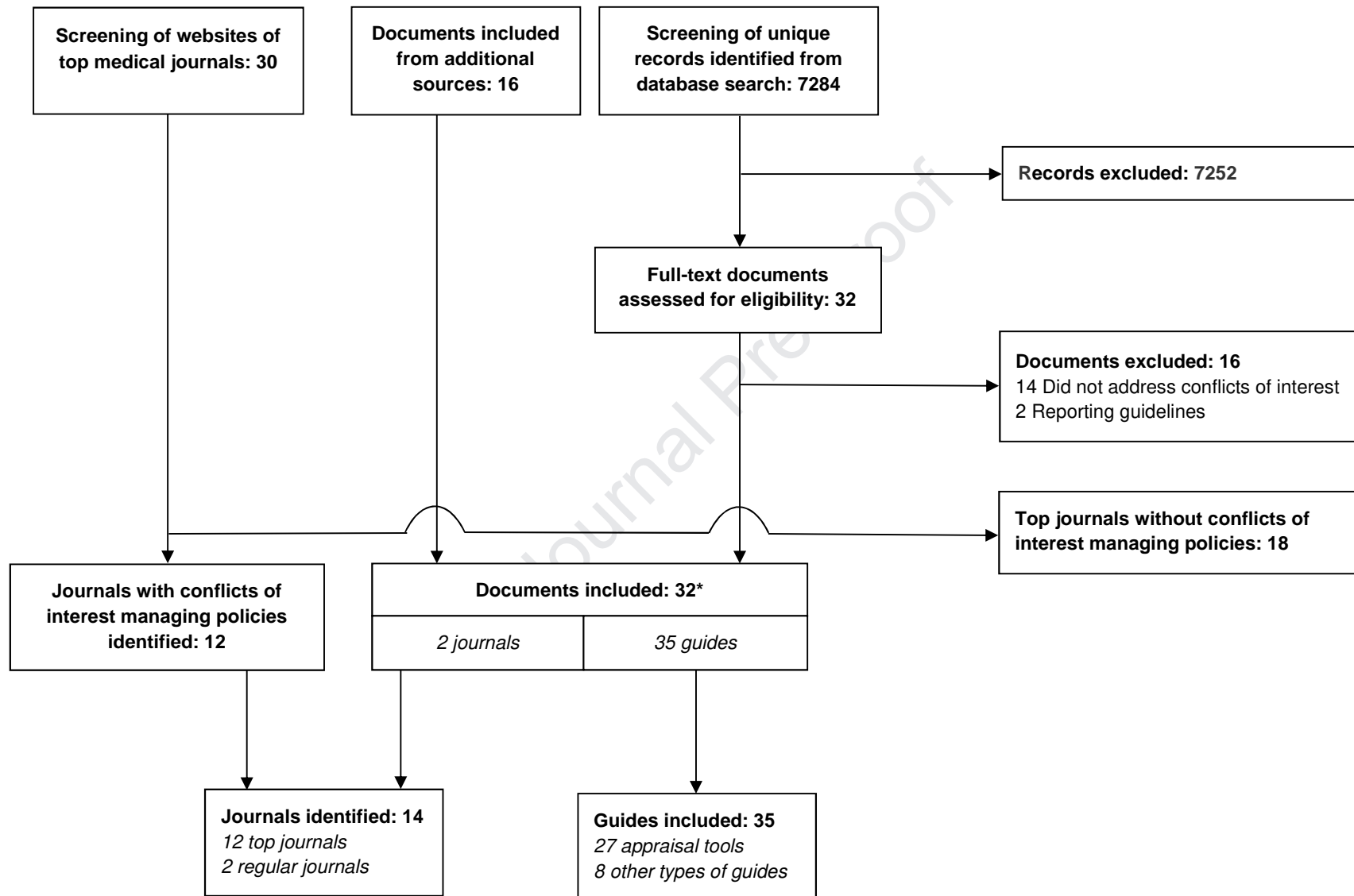
Journal	Description of management	Restrictions related to				Types of industries	Mentions non-financial conflicts of interest
		Study funding	Employment	Author conflicts of interest*	Specific types of publications		
American Journal of Respiratory and Critical Care Medicine	Does not publish any paper funded by tobacco companies or by authors with relationships with tobacco companies. Corresponding authors must have full access to data and take responsibility for integrity of data if study is commercially funded.	Yes	Yes	Yes	Partly**	Relevant industries	No
Blood	Authors with pharmaceutical or medical device company employment and medical writers supported by these industries must not have any role in writing Review, Perspective, How I Treat, Blood Spotlight, or Evidence-based Focused Review articles.	Partly***	Yes	No	Yes	Drug and device	No
BMJ	Does not permit authors with relevant financial ties to drug, device, test, medical education or other relevant industries for writing editorials, clinical reviews, minerva pictures, endgames and practice articles. Prohibits any study that is partly or wholly funded by the tobacco industry.	Yes	Yes	Yes	Partly**	Relevant industries	No
CMAJ	Editor may exclude authors with financial conflicts of interest or industry employment from writing commentaries and narrative reviews.	No	Yes	Yes	Yes	Relevant industries	No
Lancet	Does not permit authors with relevant employment or certain types of financial conflicts of interest for writing Comment, Seminars, Reviews, and Series articles.	No	Yes	Yes	Yes	Relevant industries	No
Lancet Diabetes & Endocrinology	Does not permit authors with relevant employment or certain types of financial conflicts of interest for writing Comment, Seminars, Reviews, and Series articles.	No	Yes	Yes	Yes	Relevant industries	No
Lancet Infectious Diseases	Does not permit authors with relevant employment or certain types of financial conflicts of interest for writing Comment, Seminars, Reviews, and Series articles.	No	Yes	Yes	Yes	Relevant industries	No
Lancet Neurology	Does not permit authors with relevant employment or certain types of financial conflicts of interest for writing Comment, Seminars, Reviews, and Series articles.	No	Yes	Yes	Yes	Relevant industries	No
Lancet Oncology	Does not permit authors with relevant employment or certain types of financial conflicts of interest for writing Comment, Seminars, Reviews, and Series articles.	No	Yes	Yes	Yes	Relevant industries	No
Lancet Respiratory Medicine	Does not permit authors with relevant employment or certain types of financial conflicts of interest for writing Comment, Seminars, Reviews, and Series articles.	No	Yes	Yes	Yes	Relevant industries	No
New England Journal of Medicine	Does not permit authors with significant financial interests (i.e. > 10.000 US \$ or stock or patents) for writing editorials and review articles.	No	Yes	Yes	Yes	Relevant industries	No
PLoS Medicine	Does not publish any paper with any degree of funding of research costs or authors' salaries by a tobacco company. Does not permit commissioned or other non-research articles by authors with conflicts of interest which according to editors could introduce bias or reasonable perception of bias.	Yes	Yes	Yes	Partly**	Relevant industries	No

* By author conflicts of interest we mean any conflicts of interest in addition to direct employment (e.g. advisory board membership).

** Any type of publication in relation to tobacco funding, but specific types of publications in relation to other conflicts of interest.

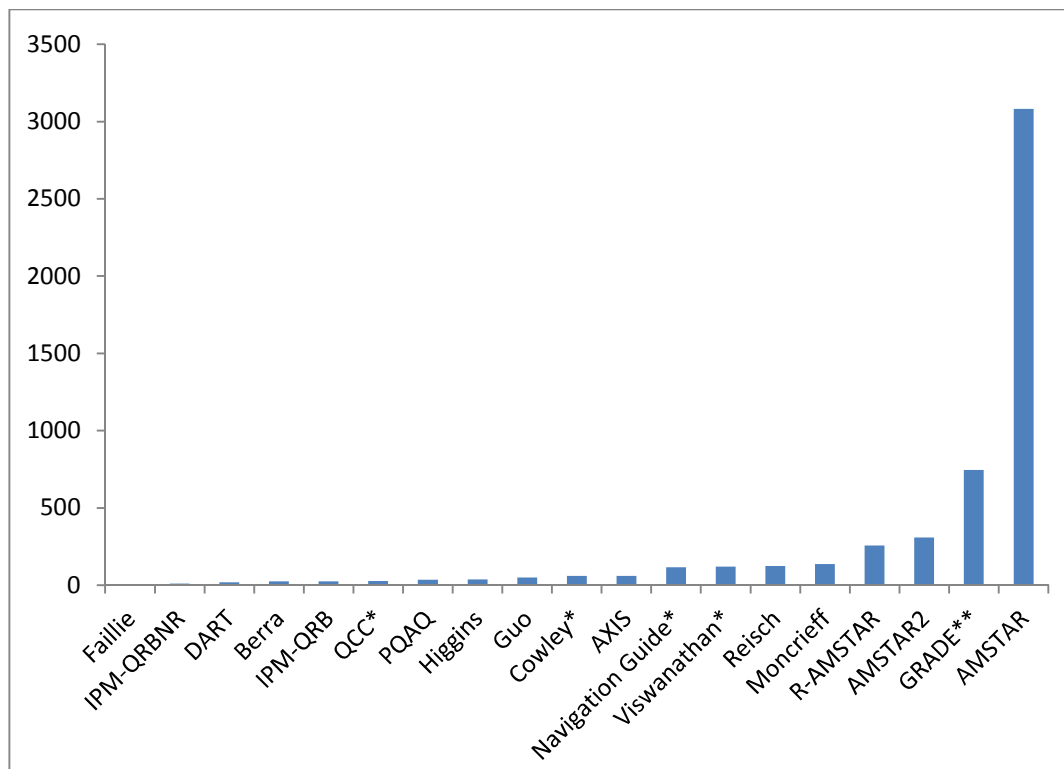
*** Indirectly by prohibiting industry funding of medical writers.

Figure 1. Study flow diagram of inclusion process



*Some documents contained more than one guide

Figure 2. Total number of citations of appraisal tools with items addressing conflicts of interest



* Some tools were available in formats tailored for specific study designs, but described in same publication. For these tools we reported citations to the overall tool publication.

** GRADE was described in multiple publications and we reported citations for the publication related to conflicts of interest.

Figure 3. Examples of how conflicts of interest were addressed in appraisal tool items

Availability of conflicts of interest information^{}*

Name of Tool	Item on conflicts of interest
AMSTAR	Was the conflict of interest stated?
Guo	Were both competing interests and sources of support for the study reported?

*Reported conflicts of interest^{**}*

Name of Tool	Item on conflicts of interest
Cowley-RCT	Independence of investigators (no vested interest) stated
QCC-Primary Research	Is bias due to study's funding or sponsorship unlikely? - were sources of funding and investigators' affiliations described? - was there no apparent conflict of interest?

*Influence from conflicts of interest^{***}*

Name of Tool	Item on conflicts of interest
DART	Were conflicts of interest stated and were individuals excluded from the review if they reported substantial financial and intellectual conflicts of interest?
PQAQ	Does the article present the relationship with the sponsor of the study? Does the article indicate that the authors had independent control over the methods and right to publish?

* Typically high quality if information was available regardless of whether conflicts of interest were reported or not.

** Typically high quality if active statement that no conflicts of interest were reported and low quality if conflicts of interest were reported or no information was available.

*** Typically high quality if some procedural elements were included in study minimising influence from conflicts of interest or if only conflicts of interest judged to be minor were reported.

What is new?

Key findings

- We identified no appraisal tool designed specifically to address conflicts of interests in medical research studies. Twenty-seven tools included 1-2 short items mainly focusing on whether conflicts of interest information was available or if any conflicts of interest were reported. There was little guidance on assessing how conflicts of interest may influence studies.
- In a small sample of 30 top medical journals more than half had no explicit policies on managing conflicts of interest in journal papers beyond standard disclosure practices. Journals with policies to manage conflicts of interest mainly placed some form of restriction on non-research papers, publishing only those where authors did not have financial conflicts of interest.

What this adds to what is known?

- Conflicts of interest are considered important, but the focus in both appraisal tools and journals is on how conflicts of interest are disclosed; not on how conflicts of interest may influence studies or how journal policies may minimise such influence.

What is the implication, what should change now?

- There is need for more comprehensive evidence-based guidance for addressing conflicts of interest in research studies.
- The International Committee of Medical Journal Editors and medical journals could consider developing, revising and harmonising explicit policies on managing conflicts of interest in their journal papers.

Author contributions

AH and AL conceived the idea for the study. All authors were involved in developing the study protocol. LØ performed database searching and LØ and KR included studies. AL, AH, KR and LØ performed data extraction, AL performed data analysis and all authors were involved in interpretation of results. AL drafted the manuscript and all authors were involved in writing of the manuscript and approved the final version of the manuscript. AL is the guarantor and accepts full responsibility of the work; all authors were involved in the decision to publish.

Declaration of interests

☐ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☒ The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Four of the authors (AH, AL, IB and LAS) are members of the TACIT Steering Group involved in developing a Tool for Addressing Conflicts of Interest in Trials.