Quality and reporting completeness of systematic reviews and meta-analyses in dermatology

Short title: Quality of systematic reviews in Dermatology

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ABSTRACT

We sought to assess the quality of dermatological systematic reviews and to identify factors that predict high methodological quality. We searched for all systematic reviews published in 2017 using PubMed, Epistemonikos, and the Cochrane Database of Systematic Reviews. We included studies identified as systematic reviews or meta-analysis in the title or abstract and dealing with a dermatological topic. Study selection, data extraction, PRISMA and AMSTAR 2 rating were carried out independently by two authors. Based on AMSTAR 2, confidence in systematic reviews results was classified as high, moderate, low or very low. We included 732 studies. We describe a random sample of 140. The overall rating of confidence in the results according AMSTAR 2 tool was high or moderate for nine reviews (6%). Twenty (15%) had a registered protocol. Independent factors associated with AMSTAR 2 moderate or high rating were publication in a journal where PRISMA is mandatory (odds ratio (95% confidence interval) = 27.0 (1.4-528) and journal impact factor (OR 1.9 (1.3-3)) for each increase in one more point. The observation that 90% of published dermatology systematic reviews are of very low quality is alarming. Review registration in PROSPERO and full reporting according to PRISMA should be mandatory for publication.

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INTRODUCTION

A systematic review (SR) is a review of a precisely defined subject using systematic methods to identify, select and analyze relevant research (Higgins et al. 2019). SRs have become over the years one of the main tools for clinicians, guideline authors and public health agencies to make more informed decisions. The number of SRs published each year is constantly increasing (Chalmers and Fox 2016). Ioannidis reported an increase of 2,728% for systematic reviews between 1991 and 2014, almost 20 times greater than the increase in all indexed publications (Ioannidis 2016). The results and conclusions of SRs are relevant for helping in the decision-making process only if their reporting is complete enough to guarantee transparency and if the quality is good enough to prevent bias.

The Preferred Items for Systematic Reviews and Meta-Analyses (PRISMA) statement is an evidence-based minimum made of 27 items for reporting in systematic review and meta-analysis (Moher et al. 2009). Many journals have endorsed the PRISMA statement and request authors submitting a SR to follow PRISMA and in some cases include a PRISMA checklist. The methodological counterpart is covered by the AMSTAR 2 tool (Shea et al. 2017). This tool is made of 16 questions covering different aspects of methodology of systematic reviews.

The aims of *a priori* registration of systematic reviews are to prevent reporting bias and duplication of efforts, and to promote transparency in the review process. PROSPERO is the international register for systematic reviews protocols (Page et al. 2018). Protocol registration of the systematic review requires a precise research question, inclusion criteria and prespecified primary and secondary outcomes. Protocols of Cochrane Reviews are published in both the Cochrane Library and PROSPERO.

Deficiencies in the conduct and reporting of SRs have been highlighted in general (Pussegoda et al. 2017) as well as in specific specialties such as pediatric surgery (Cullis et al. 2017) or

urology (Xia et al. 2017). A recent analysis of quality of reporting of SRs according to PRISMA published from 2013 to 2017 in the five highest-impact dermatology journals concluded that reporting was often inadequate but had improved over time (Croitoru et al. 2019). Reporting quality is important, but it is not the same as study quality. Although the two are related in that good reporting is a pre-requisite to assess study quality, it does not mean that a well reported review is necessarily a good quality review. It is important therefore to assess the quality of published dermatology systematic reviews as well as the completeness of reporting.

The main objective of this study was to assess study quality using the AMSTAR 2 tool and explore the relationship between study quality and reporting completeness using PRISMA.

RESULTS

Search results

For the 6,117 SRs retrieved through database searching, 951 duplicates were removed, and 4405 were excluded. Among the 732 (386 intervention; 346 others) corresponding to our selection criteria, a sample of 140 SRs was randomly selected (68 interventional and 72 non-interventional) and included in the final analysis. The selection process and reasons for exclusion are summarized in Figure 1. A list of excluded studies after full text analysis is listed in appendix S2.

Characteristics of included systematic reviews

The characteristics of the randomly selected SRs are summarized in Table 1. The majority of the 140 SRs did not include a MA (n=73, 53%). The most frequent type of non-interventional reviews were epidemiological reviews (n=49, 35%). The most frequent topic was inflammatory skin diseases (n=49, 35%). The median number of authors was 5 (1-29). Determined by the country of first author, reviews were most commonly from European countries 43 (31%).

In total, the 140 SRs were published in 89 different journals; the four most frequent journals were The British Journal of Dermatology, The Journal of the American Academy of Dermatology, The Journal of the European Academy of Dermatology and Venereology, and The Cochrane Database of Systematic Reviews (n=7 each). The mean impact factor of journals was 3.3 (0.46; 14.1). One third of SRs (n= 46; 33%) were published in journals that explicitly required authors to follow the PRISMA statement, and 29 (21%) were in journals that suggested authors followed the PRISMA statement. In 85 SRs (61%), authors reported that they had reported the review according to PRISMA but five (4%) provided the checklist.

Quality of the methodology of systematic reviews according to AMSTAR 2

The overall rating of confidence in the results of the SR according to the AMSTAR 2 tool was high (none or one non-critical weakness) for eight reviews (6%), moderate (more than one non-critical weaknesses) for one (1%), low (one critical flaw with or without critical weakness) for five (4%) and very low (more than one critical flaw with or without critical weakness) for 126 (90%). All Cochrane Reviews were associated with a high overall rating of confidence in the results. The proportion of review with a moderate to high level of confidence (nine out of 140, 6%) was similar when limiting the analysis to SRs including a MA (five out of 56, 7%). When limited to intervention reviews, the proportion of reviews with a moderate to high level of confidence was 12 % (8 /68).

In 69% (n=97/140), of the SRs, four or more steps considered as one of the seven critical domains (Q2, 4, 7, 9, 11, 13 and 15) of the AMSTAR 2 tool were not performed adequately. A statement of the establishment of review methods prior to the conduct of the review (Q2) was given for 21 SRs (15%). Concerning the search strategy (Q4), 38 (27%) of the reviews provided a comprehensive search strategy, and of these 11 (8%) searched in other sources,

including grey literature. A list of excluded studies and justification of exclusion (Q7) was provided in 26 (19%) of SRs. Risk of bias assessment of individual studies (Q9) was done with a satisfactory technique in 44 SRs (31%) and 36 SRs (26%) assessed the impact of risk of bias in individual studies on the results of the review (Q13). Finally, among the 67 SRs with MA, 45 (32%) used an appropriate method for combining data (Q11), and 38 (27%) carried out an adequate investigation of publication bias and discussed its likely impact on the results of the review (Q15).

Figure 2 represents the rate of yes or partial yes for each AMSTAR 2 question. Results for each question are available in table S4.

Factors associated with a moderate to high level of confidence in the results of SRs according AMSTAR 2

In univariable analyses, PRISMA endorsers, journals with an EBM section, Cochrane Reviews, higher impact factor journals, registered protocol and interventional SRs were associated with a moderate to high AMSTAR 2 overall rating (Table 2). After testing the correlation between these variables, journals with an EBM section, Cochrane Reviews and protocols were excluded ($r>0.5$). In a multivariable analysis, independent risk factors associated with a moderate to high level of confidence were publication in a journal where PRISMA was mandatory (odds ratio (95% confidence interval) = 27 (1.4-528) and journal impact factor (OR1.92 (1.3-3) for each higher point of impact factor).

We did not include PRISMA adherence as a potential associated factor because there is no method for assessing an overall score as there is for AMSTAR. All SRs with a moderate to high AMSTAR 2 score had fulfilled 20 or more items. The distribution is wider for SRs with low to very low AMSTAR. Indeed 42 % fulfilled more than 20 items, 67% between 10 and 20 and 22% less than 20 items.

Quality of reporting of systematic reviews according PRISMA checklist

Seventy-two (51%) of the 140 analyzed reviews reported at least two thirds of the required items of the PRISMA checklist. All the items of PRISMA checklist were reported in only three SRs. For intervention reviews, 42 out of 68 (62%) reported at least two thirds of the required items of the PRISMA checklist. Figure 3 shows the proportion of SRs that reported each PRISMA item. The five items reported in less than one third of the reviews were: Item five related to protocol redaction, Items 15 and 22 corresponding respectively to methods and results of publication bias and outcome reporting bias assessment; and I16 and I23 corresponding respectively to methods and results of sensitivity or subgroup analyses. A clear definition of the question (I4) was reported in 72 (51%) of the SRs. A table with the results for each item is available in table S3.

DISCUSSION

Main findings

Our study showed that methods and reporting of a large number of systematic reviews published in 2017 in dermatology field were poor. In 2017, 732 dermatological publications were named as systematic reviews and /or a meta-analysis by their authors in the title or abstract. In our random sample of 140 reviews, the proportion with an AMSTAR 2 overall rating of moderate to high confidence in the results was 6% (n=9), and of these 140 SRs, half reported two thirds of the items in the PRISMA checklist. These disappointing results have to be balanced by the fact that we considered all types of SRs, not only intervention SRs, and reviews published in all journals whatever the impact factor. Indeed, intervention SRs had slightly better results, with 12% achieving moderate to high AMSTAR 2 overall ratings and 68% (42/68) reporting two thirds of PRISMA items.

The two independent factors associated with a moderate to high confidence in the results of a SR according AMSTAR 2 were publication in a journal where PRISMA was mandatory and

a higher journal impact factor. We did not identify registration of a protocol as an independent risk factor in this study. A recent study assessing adherence to PRISMA of SRs published between 2013 and 2017 in the five highest impact dermatology journals found an improvement of reporting over time and an independent association between protocol registration and better reporting (Croitoru et al. 2019).

Each of the seven methodological steps considered as critical in the AMSTAR 2 tool was adequately performed in a maximum of 32% and a minimum of 13% of the reviews. Registration allows reviewers and readers to verify the concordance between what was planned and what was done. Indeed, it has been previously demonstrated that *post hoc* alterations in the choice of inclusion/ criteria and analytical models for meta-analysis can result in major changes in the results (Palpacuer et al. 2019). Rigorous searching of all relevant articles regardless of language is also critical in order to avoid including only published studies having more frequently positive results (Le Cleach et al. 2016). A previous study that re-analyzed meta-analyses that including unpublished FDA data almost always modified the results (Hart et al. 2012). In our study, 27 SRs (19%) searched for studies in at least two databases and provided key words and/or search strategy and justified publication restriction.

Strengths and limitations

Strengths of our study were the registration of our protocol, a wide search for studies, and a double independent study selection and data extraction. In addition, we used the AMSTAR 2 tool that is associated with an overall rating algorithm based on a distinction between critical and non-critical methodological points. The inclusion of all type of SRs based on the title or abstract with no limitation (language, type of SR, journal) ensured strong external validity of our results. Our study had some limitations. For practical reasons, we analyzed a sample of

the SRs published in 2017. However, this sample was randomly selected and thus likely to be representative. Regarding deviation from the protocol, we added in an analysis of publication in a journal with PRISMA mandatory request, protocol registration and interventional SR. These items should be considered as *post hoc* analyses. It is also worth pointing out that although PRISMA and AMSTAR 2 are used for all types of SR/MA, they were initially more dedicated towards intervention review and adaptation of some questions of for non-intervention reviews was done. A new version of PRISMA taking account of these new developments in systematic reviews is in on the way (Page et al. 2020).

Relationship between quality and quality of reporting

The discrepancies of results between PRISMA and AMSTAR 2 highlighted that adequate reporting did not mean that methodology was appropriate. For example, we considered that information was reported in 86% of SRs for the PRISMA item "Describe all information sources in the search and date last searched", but only 27% were rated Yes or partial Yes for the related question of AMSTAR "Did the review authors use a comprehensive literature search strategy", because of absence of justification of publication restriction and of absence of search for unpublished studies.

How our results compare with other medical disciplines

A study assessing SRs in orthodontics published between 2012 and 2016 found that the 37/182 (20.3%) of reviews associated with a registered protocol were associated with a higher AMSTAR score compared to those with non *a priori* registered protocol (Sideri et al. 2018). Our results (13% of SR with a registered protocol) were comparable to those in the orthodontic fields, and to those of a study assessing a sample of all SRs published from 1996

to 2010 that found 6% (102/1741) of SRs providing information on protocol (Le Cleach et al. 2016; Pussegoda et al. 2017).

What needs to be done?

Given the confidence that readers and guideline writers often place in systematic reviews based on the quoted position of systematic reviews on the top of evidence hierarchy, journal reviews of this type of article should be especially stringent, and should always include prospective registration and a review of PRISMA and at least a reviewer with experience in SR methodology. For full presentation of methods and results of systematic reviews, journals should allow and encourage additional important data to be presented in an online supplementary appendix that should include PRISMA checklist as a mandatory item.

It would be useful for harmonization for any future versions of PRISMA to include some key items of AMSTAR such as searching for unpublished studies, justification of deviations between protocol and review, a list of excluded studies and justification and source of funding of included studies.

Implications for future research

The poor overall quality of dermatology systematic reviews warrants the development of a constructive intervention study to encourage dermatology journal editors that accept systematic reviews to improve the quality and reporting of systematic reviews, and following up that intervention with a repeat of the present study to monitor whether things then improve. It is also important to define by consensus what the minimum criteria should be to call a review a systematic review.

MATERIALS AND METHODS

This review is reported according to the Preferred Reporting Items for Systematic reviews and Meta-analyses (PRISMA) statement. The PRISMA checklist is available in table S1. The study protocol was registered in PROSPERO on 23/05/2018, [CRD42018093856].

Literature search

The search was performed on 11th May 2018 on PubMed, Epistemonikos, and the Cochrane Database of Systematic Reviews for articles published in 2017.

For PubMed, relevant MeSH terms relating to dermatology and skin disease were included in the search. As well as exploding the MeSH term "Skin and Connective Tissue Diseases" to include all the subsidiary MeSH Terms, MeSH terms for other skin diseases not covered by this MeSH term were used, including terms for the major skin cancers. In addition, for all three databases a list of free text terms relating to dermatology and major skin diseases was compiled based on the major skin disease terms included in the British Association of Dermatologists (BAD) Diagnostic Index.

In PubMed, the search was combined with the built-in Clinical Queries systematic review filter, command systematic[sb], with an additional free text term for “systematic review” (Appendix S1).

Inclusion criteria

All published studies identified as an SR or MA in their title and/or abstract and concerning a dermatologic disease were included. Both reviewers followed the table of contents of the Rook’s Textbook of Dermatology in order to determine if the reviews dealt with dermatology (Griffiths et al. 2016). There were no exclusion criteria for the type of studies included in the SR. There was no exclusion on language of publication.

Study selection and data extraction

Each selection and extraction step was performed by two reviewers independently (LLC, CM, SA, SS, IGD, CP), with referral to a third reviewer in case of disagreement. Using Covidence (https://www.covidence.org/home), reviewers first screened each title, then abstracts, and then full text articles. For feasibility reasons, we undertook a sample size calculation, using a binomial exact test. We chose a random sample of 140 as it would lead to reasonable precision in terms of 95% confidence intervals for most of the anticipated outcomes. We classified the included reviews as interventional or non-interventional, and performed a stratified random sampling (interventional and non-interventional) of 20 per cent of the included reviews by assigning a computer-generated random number to each SR.

The data extraction on the 140 randomly selected studies was carried out a standardized extraction form.

Quality assessment

PRISMA and AMSTAR 2 checklists (Table S2) were completed independently by two authors. For PRISMA, we gave a rating of non-applicable (NA) for items concerning MA if there was no MA in the review. For AMSTAR 2, for non-interventional reviews we rated question 1 regarding PICO as "yes" for reviews with a clear and precise research question, and for reviews including studies others than RCTs or NRSIs we rated "yes" for question 9 on risk of bias assessment if a validated tool with a reference was used.

Outcomes

Our primary outcome was the proportion of SRs with a high, moderate, low or very low overall confidence rate in their results according to the AMSTAR 2 tool. High level of confidence is defined as none or one non-critical weakness, moderate level is defined as more than one non-

critical weakness, low level is defined as one critical flaw with or without critical weakness, and finally critically low level of confidence is defined as more than one critical flaw with or without critical weakness.[5]Seven items of AMSTAR 2 are considered as critical domains: registered protocol, adequacy of the literature search, justification for excluding individual studies, individual studies risk of bias, appropriateness of meta-analytical methods, consideration of risk of bias when interpreting the results and assessment of presence and impact of publication bias.

Our secondary outcome was the proportion of SRs that fulfilled the required PRISMA items (27 for SRs including a MA and 23 for SRs without MA).

We also assessed factors associated with high or moderate in comparison to low or very low levels of confidence according to the AMSTAR rating. Prespecified factors were pharmaceutical funding Y/N, EBM or systematic review section, Cochrane systematic review Y/N, and journal name. We added a further two non-prespecified factors during the analysis: we changed journal name for impact factor (because of the very high number of distinct journal names precluding any analysis) and we added PRISMA endorsement, protocol registration, and intervention reviews that were considered during the review process as other strong potential factors.

Data synthesis

Data were described as mean± standard deviation (SD) or median (interquartile range, 25th-75th percentiles) for continuous data, depending on distribution normality, and as number (%) for categorical data.

Assessment of significant differences between a high or moderate AMSTAR 2 score and journals' characteristics (impact factor (2019, Journal Citation Reports), PRISMA

endorsement) were based on the Mann-Whitney test for quantitative data and on the χ^2 or Fisher's exact test for categorical data as appropriate.

Factors associated with a high or moderate AMSTAR 2 score were determined by a logistic regression model. In univariable analyses, the following factors were searched for association with high or moderate AMSTAR 2 rating: pharmaceutical funding vs none or institutional, inclusion of a protocol, journal that endorsed PRISMA, journal with Evidence Based Medicine (EBM section) or dedicated to SRs, Cochrane Review, and type of SR (intervention vs others). The strength of correlations between previous variables was determined by calculating Pearson's coefficient r; variables with $r<0.50$ were entered into the selection process for the final multinomial logistic regression model by upward stepwise method based on Akaike Information Criterion (AIC).

Two-tailed p values less than 0·05 were considered significant. Statistical analyses were performed using Stata software version 14.1 (StataCorp LP, College Station, TX, USA)

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Conflicts of interest:
L Le Cleach is Editor of the Cochrane Skin Group and Associated Editor of the British Journal of Dermatology
I Garcia-Doval is Section Editor of the British Journal of Dermatology
R Boyle is a Joint Co-ordinating Editor of Cochrane Skin
Hywel Williams is an editor of Cochrane Skin
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References

Chalmers I, Fox DM. Increasing the Incidence and Influence of Systematic Reviews on Health Policy and Practice. Am. J. Public Health. 2016;106(1):11–3

Croitoru DO, Huang Y, Kurdina A, Chan A-W, Drucker A-M. Quality of reporting in systematic reviews published in dermatology journals. Br. J. Dermatol. 2019;n/a(n/a) Available from: https://doi.org/10.1111/bjd.18528

Cullis PS, Gudlaugsdottir K, Andrews J. A systematic review of the quality of conduct and reporting of systematic reviews and meta-analyses in paediatric surgery. PLOS ONE. 2017;12(4):e0175213

Griffiths C, Barker J, Bleiker T, Chalmers R, Creamer D. Rook's Textbook of Dermatology. ninth. John Wiley & Sons, Inc; 2016.

Hart B, Lundh A, Bero L. Effect of reporting bias on meta-analyses of drug trials: reanalysis of meta-analyses. BMJ. 2012;344:d7202

Higgins J, Thomas J, Chandler J, Cumpston M, Li T, Page M, et al. Cochrane Handbook for Systematic Reviews of Interventions [Internet]. version 6.0 (update 2019). Cochrane. 2019 [cited 2020 Jan 25]. Available from: /handbook/current

Ioannidis JPA. The Mass Production of Redundant, Misleading, and Conflicted Systematic Reviews and Meta-analyses. Milbank Q. 2016;94(3):485–514

Le Cleach L, Doney E, Katz KA, Williams HC, Trinquart L. Research Techniques Made Simple: Workflow for Searching Databases to Reduce Evidence Selection Bias in Systematic Reviews. J. Invest. Dermatol. 2016;136(12):e125–9

Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. BMJ. 2009;339:b2535

Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann T, Mulrow CD, et al. Mapping of reporting guidance for systematic reviews and meta-analyses generated a comprehensive item bank for future reporting guidelines. J. Clin. Epidemiol. 2020;118:60–8

Page M, Shamseer L, Tricco A. Registration of systematic reviews in PROSPERO: 30,000 records and counting. Syst. Rev. 2018;7

Palpacuer C, Hammas K, Duprez R, Laviolle B, Ioannidis JPA, Naudet F. Vibration of effects from diverse inclusion/exclusion criteria and analytical choices: 9216 different ways to perform an indirect comparison meta-analysis. BMC Med. 2019;17(1):174

Pussegoda K, turner lucy, Garritty C, Mayhew A, Skidmore B, Stevens A, et al. Systematic review adherence to methodological or reporting quality. Syst. Rev. 2017;6:131
Shea BJ, Reeves BC, Wells G, Thuku M, Hamel C, Moran J, et al. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. BMJ. 2017;358:j4008

Sideri S, Papageorgiou S, Eliades T. Registration in PROSPERO of systematic review protocols was associated with increased review quality. J. Clin. Epidemiol. 2018;100

Xia L, Xu J, Guzzo TJ. Reporting and methodological quality of meta-analyses in urological literature. Palazón-Bru A, editor. PeerJ. 2017;5:e3129

Table 1. Characteristics of the 140 appraised systematic reviews (SRs)

Type of SR	
Intervention	68 (49)
Epidemiological	49 (35)
Multiple reviews	15 (11)
Diagnostic test accuracy	3 (2)
Genetic reviews	2 (1)
Type of studies included in SR	
Only RCT	32 (23)
Only observational studies	42 (30)
RCT & observational studies	17 (12)
Only cases	19 (14)
All (RCT & NRSI & cases or NRSI & cases or others)	30 (22)
Presence of meta-analysis	
SR without MA	73 (53)
Classical MA	65 (46)
Network MA	2 (1)
Number of studies per SR (median, range)	29 (0-351)
SR without MA	20 (0-204)
SR with MA	14 (4-128)
Dermatologic diseases	
Inflammatory	49 (35)
Neoplastic, Proliferative and Infiltrative Disorders Affecting the Skin	20 (14)
Infections & Infestations	16 (11)
Skin Disorders Associated with Specific Cutaneous Structures (including acne, rosacea, hidradenitis suppurativa…)	16 (11)
Skin Disorders Caused by External Agents	13 (9)
Metabolic and Nutritional Disorders Affecting the Skin	6 (4)

Vascular Disorders Involving the Skin	5 (4)
Systemic Disease and the Skin	4 (3)
Skin Disorders Associated with Specific Sites, Sex and Age	4 (3)
Aesthetic Dermatology	2 (1)
Genetic Disorders Involving the Skin	2 (1)
Psychological, Sensory & Neurological	2 (1)
Multiple	1 (1)
Protocol	
Yes, and registered	21 (15)
Yes, but not registered	7 (5)
PRISMA statement	
Declared it was followed	55 (39)
Provided PRISMA checklist	5 (4)
Sources of funding	
Not declared	42 (30)
None	49 (35)
Institutional	39 (28)
Private	10 (7)
Number of authors /SR (median, range)	5 (1-29)
Country of first author	
Europe	43 (31)
USA	34 (24)
China	23 (16)
Others	40 (29)
Number of studies including as authors	
Institutional professionals	140 (100)
Employees of pharmaceutical companies	4 (3)
Private practitioners	4 (3)
COI	
Declared with COI	24 (17)
Declared without COI	103 (74)
Not declared	13 (9)
Number of SRs published in journals	
With EBM section	15 (11)
Dedicated to systematic review (not Cochrane)	1(1)
Cochrane	7 (5)
With PRISMA mandatory in guidelines for authors	39 (28)
With PRISMA suggested in guidelines for authors	29 (21)

Data are n (%), indicated when different
SR, systematic review; MA, meta-analysis; RCT, randomized controlled trial; COI, conflict of interest

Table 2. Factors associated with a moderate or high AMSTAR 2 overall rating

	Moderate or high AMSTAR overall rate N=9 N(%)	**Low or very low AMSTAR overall rate N=131 N(%)**	**OR 95% CI Univariable analysis**	**P**	**OR 95% CI Multivariable analysis**	**P**
Publication in a journal with PRISMA mandatory	8(89)	39(30)	19 (2.3-156)	0.006	27 (1.4-528)	0.03

No or institutional funding	8(89)	80(61)	0.2 (0.02-1.6)	0.1		
Protocol registered	9(100)	12 (9)	112 (16.3-inf)	0.0000		
Journal with EBM Section	8(89)	7(5)	142 (16-1297)	0.000		
Cochrane	7(78)	0(0)	391 (47-inf)	0.0000		
Interventional	8(89)	60 (46)	9.5(1.2-77.9)	0.004		
Impact factor (median)	7.7 (5.1-7.7)	2.7 (0.7-7.9)	1.9 (1.2-3)	0.003	1.92 (1.3-3)	0.001

Supplementary Material:

Table S1: PRISMA checklist of the review

Appendix S1: Search equation

Table S1: AMSTAR 2 tool

Appendix S2: List of excluded studies

Table S3: Rate of completion for each item of PRISMA checklist for the 140 analyzed SRs

Table S4: Rate of yes or partial yes for each AMSTAR question for the 140 analyzed SRs

Figure Legends:

Figure 1. Prisma Flow diagram
Figure 2. Rate of yes or partial yes for each AMSTAR question
Figure 3. Rate of completion for each item of PRISMA checklist for the 140 analyzed
Figure 4. Proportion of SRs according number of fulfilled PRISMA item