Search Characteristics and Reporting of Systematic Reviews of Animal Experiments: A Cross-Sectional Study

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Research Article

Keywords: systematic review (SR), meta-analysis (MA), PubMed, OVID-Embase, Biosis Previews, CNKI, CBM, Wanfang Data

Posted Date: August 24th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-832957/v1>

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Abstract

Background

The formulation and implementation of a comprehensive search strategy is the basis for ensuring the quality of a systematic review (SR) and/or meta-analysis (MA). All published SRs/MAs of animal experiments were comprehensively identified, to evaluate how each search strategy was formulated, and how the search process and reporting were implemented, in order to represent a reference and provide suggestions for the future development of search procedures and reporting guidelines for SRs/MAs of animal experiments which should, ultimately, allow translation of the results of animal experiments into clinical practice.

Methods and Findings

PubMed, OVID-Embase, Biosis Previews, CNKI, CBM, Wanfang Data, and VIP databases were searched to identify the SRs/MAs of medical-related animal experiments. The literature was independently screened and basic information extracted. The search characteristics (including search methods and their reporting) of each included study were analyzed in accordance with pre-established evaluation criteria. A total of 813 animal experiment SRs/MAs published in 503 different journals from 52 countries and regions were included. PubMed, Embase, and Medline were the three most commonly searched English-language databases for animal experiment SRs/MAs, although in 28.8% (234/813), fewer than 3 databases were searched. A supplementary search had been conducted in only half (52.2%, 424/813%) of the studies. In terms of search reporting, only 47.4% (385/813) reported search methods and 31.6% (243/813) described the search strategy. Only 4.8% (39/813) of the animal experiments SRs/MAs reported the qualifications of the search personnel.

Conclusions

The quality of search methods and reporting of the search process for published SRs/MAs of animal experiments are inadequate and substandard. Therefore, the search process should be standardized in future to improve efficiency and ensure the integrity and universality of the search, thereby allowing the development of SR/MA search strategies and reporting guidelines for animal experiments, and ultimately promote improvements in the quality of animal experiment SRs/MAs.

1 Introduction

Performing a systematic review and/or meta-analysis (SRs/MAs) of animal experiments has multiple challenges, among which is the process of formulation and implementation of an extensive and comprehensive search strategy ^[1], without which the quality of an SR/MA cannot be guaranteed ^[2]. Previous studies have demonstrated that publication bias is likely to decrease the likelihood that the results of preclinical studies are translated into clinical practice ^[3–5]. Such a risk can, to a certain extent, be reduced by conducting a search using a comprehensive and systematic strategy ^[6].

Although complete search guidelines for SRs/MAs of clinical trials^[7] currently exist, they are not fully applicable to animal experiments. In addition, researchers in the field of basic medical research have little understanding of SR/MA methodology^[8]. Thus, almost universally, the formulation of search strategies for published SRs/MAs of animal experiments is problematic, causing omissions and misidentification to a varying extent^[9, 10]. For example, Chen *et al.*^[10] found that only 6.63% (12/181) of SRs/MAs of animal experiments in international journals reported the complete search strategy in at least one database. Vriezen *et al.*^[11] found that only 39.5% (15/38) of reviews additionally supplemented the search with reference lists in the study, and only 36.8% (14/38) supplemented with grey literature. Nesdill *et al.*^[12, 13] briefly described the basic characteristics of databases commonly used for searching animal studies but did not elaborate on the specific methods for formulating the search strategies or implementing the SRs/MAs of animal experiments. In addition, although a number of researchers have set forth suggestions for the search procedure for the SRs/MAs in animal research^[14], they have generally only utilized their accumulated experience of searching without elaborating a standardized search process in detail, nor systematically explaining the problems within the search process and improvements in the integrity of the results. In 2010, Hooijmans *et al.* from the SYRCLE Animal Experimental Center of Radboud University Medical School in the Netherlands successively published animal experiment search filters for the PubMed^[1] and Embase databases^[15]. Although these increased the sensitivity of the searches to a certain extent, the specificity for animal experiments requires improvement, in addition to those filters being limited to the PubMed and Embase databases^[15]. In addition, no standardized reporting guidance for searching for animal experiment SRs/MAs exists which also affects search quality to a large extent^[16]. Therefore, methods of formulating and implementing extensive and comprehensive searches for the SRs/MAs of animal experiments, and standardization of the reporting of the search results remain an important challenge.

Therefore, the present study aimed to review the following aspect of all published SRs/MAs of animal experiments: (1) Systematic evaluation of how each search strategy was formulated and its implementation, including the problems within the search process, so that the search methods could be standardized, preventing the relevant literature being overlooked, reducing the risk of bias, and improving the credibility of the evidence reported in animal experiment SRs/MAs; (2) Analysis of the reporting of search on animal experiment SRs/MAs and its problems, and to provide a reference for the development of animal experiment SRs/MAs reporting guidelines in the future, thereby promoting the translation of preclinical evidence to clinical utilization.

2 Methods

2.1 Eligibility Criteria

Inclusion criteria Medical-related SRs/MAs of animal experiments published internationally were included in the study, with no restrictions on animal species and publication language. SRs/MAs involving the results of both humans and animals were included. "Animal experiments" were defined as *in vivo*

experiments in which an intervention was performed on a living animal, without limiting whether the outcome was measured *in vivo* or not. The definition of "Systematic review and/or Meta-Analysis" included studies in which "systematic review" or "meta-analysis" was clearly mentioned in the report, or the nature of the study could be determined by reading the results based on the summary of the multiple research reports it was reviewing, the methods used for literature review, and the reporting of exclusion criteria and quality evaluation methods, *etc.*

Exclusion criteria Studies of basic biology such as genetics studies, cellular molecular studies, physiological mechanisms, or behavior unrelated to human medicine were excluded, as were studies in which duplicate results were published. Conference papers or academic reports were excluded.

2.2 Search Strategy

The search strategies of Peters and Korevaar *et al.* [17, 18] were used but adjusted for the search platform utilized. A comprehensive search was conducted on the PubMed, Ovid-Embase, Biosis Previews, CNKI, CBM, Wanfang Data, and VIP databases from the inception of each to December 2019. An updated search of the period to December 31, 2020 was also conducted. The search string used was: (animal experimentation OR animal experiments OR animal experiment OR animal study OR animal studies OR animal research OR Mice OR Mus OR Mouse OR Murine OR Rats OR Rat OR Pigs OR Pig OR Swine OR Swines OR guinea pigs OR guinea pig OR Cavia OR Rabbits OR Rabbit OR Dogs OR Dog OR Canine OR Canines OR Canis OR Sheep OR Sheeps OR Goats OR Goat OR Monkey OR Monkeys OR Ape OR Apes OR orangutan OR Paniscus OR pan paniscus OR Bonobo OR Bonobos OR pan troglodytes OR Chimpanzee OR Chimpanzees OR gorilla OR gorillas OR pongo OR Frog OR Frogs OR Ranidae OR Toad OR Toads OR Bufonidae) AND (Meta-analysis OR Meta-Analysis OR systematic review OR systematic reviews). In addition, the reference lists of all included studies were searched for eligible studies. The search strategy for each database is listed in Appendix Table S1.

2.3 Methodological quality control

Prior to document screening, all researchers (Bing Zhao, Fei Chen, Qianqian Gao, Fan Mei, Li Zhao, Jinwei Yang, Mingyue Jiao, and Yanbiao Jiang) underwent professional training, which included understanding the eligibility criteria, the literature screening process, and data extraction. Data were extracted on 10% of the included studies after training and before the formal search process to evaluate researcher consistency via calculation of the Kappa statistic. If Kappa was > 0.75, the training could be considered effective and researchers suitably qualified.

2.4 Screening and Data Extraction

Three researchers (Bing Zhao, Fei Chen, Qianqian Gao) independently screened and cross-checked the literature in accordance with the eligibility criteria. In the case of disagreement, disputes were resolved through discussion or adjudication by a third party (Ma Bin).

Four researchers (Bing Zhao, Jinwei Yang, Mingyue Jiao, and Yanbiao Jiang) independently extracted and cross-checked the relevant data. The following information was extracted: ☐ Epidemiological

characteristics, year and country of publication, publication journal, type and number of included studies, sample size of the included studies, disease involved, scope of intervention, and funding, *etc.* ☐ Methodology of search: search characteristics (number of databases, number of search strategies, whether a supplementary search had been conducted, whether the publication language of searched articles had been restricted). ☐ Reporting characteristics: whether the search terms/search methodology had been reported, whether complementary search methods had been reported, whether the search strategy of at least one database had been reported, how the search strategy had been presented, or whether a flow chart describing literature screening, *etc.* had been reported.

2.5 Data Analysis

Microsoft Excel® software (2019 version; <http://office.microsoft.com/zh-cn/>) was used for statistical analysis. Count data (for example, whether it is included in SCI, number of authors, number of retrieved databases, *etc.*) were described statistically using "number of cases (percentage)". Measurement data (such as the number of included studies, size of samples in the included studies, *etc.*) were described statistically by medians and interquartile range.

3 Results

3.1 Search results

A total of 19,716 potentially relevant studies were initially selected. After excluding duplicates and those that did not fulfill the inclusion criteria, 813 studies were ultimately included in the present review. The selection process and results are displayed in Fig. 1.

Fig. 1 Flow diagram describing the identification, screening, and inclusion of SRs.

3.2 Epidemiological characteristics of the included SRs/MAs

The first systematic review of animal experiments was published in 1996 ^[19], and since then, the number of published review articles has increased, with 813 having been published by the end of 2020 (Fig. 2). A total of 813 animal experiment SRs/MAs were published in 503 different journals, from 52 countries and regions, of which the top three were China (226, 27.8%), the United States (80, 9.8%), and Brazil (70, 8.6%) (Fig. 3).

Fig. 2 Numbers of SRs/MAs included in the present review by year of publication.

Fig. 3 Ranking of journals and nationalities of origin of published SRs/MAs included in the present review.

Of the 813 published SRs/MAs of animal experiments, 81.4% (662/813) were published in SCI-indexed journals. The majority were intervention studies (82.9%, 687/813). The three diseases ^[20] most commonly studied were those of the nervous system (23.5%, 191/813), the musculoskeletal system and connective

tissue (15.0%, 122/813), and those relating to the digestive system (10.6%, 86/813) (Fig. 4). Of the 813 SRs/MAs, 25.9% (215/813) also included different types of research, such as clinical research and cellular experiments. The median number of trials included per SR/MA was 16 (interquartile range: 10-29), and the median number of animals included in each SR/MA was 398 (interquartile range: 232-712). In addition, only 13.2% (107/813) of the SRs/MAs were registered on an official database (Table 1).

Fig. 4 Types of diseases included* (* classifications in accordance with WHO ICD-11 ^[20]).

Key: 8: Diseases of the nervous system; 15: Diseases of the musculoskeletal system or connective tissue; 13: Diseases of the digestive system; 11: Diseases of the circulatory system; 5: Endocrine, nutritional or metabolic diseases; 2: Neoplasms; 16: Diseases of the genitourinary system; 12: Diseases of the respiratory system; 22: Injury, poisoning, and certain other consequences of external causes, and external causes of morbidity and mortality; 6: Mental, behavioral or neurodevelopmental disorders; 1: Certain infectious or parasitic diseases; 14: Diseases of the skin; 18: Pregnancy, childbirth or the puerperium; 24: Factors influencing health status or contact with health services; 21: Symptoms, signs or clinical findings, not elsewhere classified; 4: Diseases of the immune system; 18: Pregnancy, childbirth or the puerperium; 19: Certain conditions originating in the perinatal period; 10: Diseases of the ear or mastoid process; 25: Codes for special purposes; 3: Diseases of the blood or blood-forming organs; 9: Diseases of the visual system; 17: Conditions related to sexual health

Table.1 Epidemiological characteristics of the included SRs/MAs.

Note: * : Continuous variables represented by medians (interquartile range). A total of 329 studies did not specify sample sizes in the included studies, and 62 studies provided incomplete data or only stated the range, so data from only 422 studies were used in this calculation.

3.3 Methodological characteristics of searches in the animal experiment SRs/MAs included in the present review

3.3.1 Characteristics of search databases

Of the 813 SRs/MAs included in the present review, 28.8% (234/813) searched fewer than 3 databases, and fewer than 20% (18.9%, 154/813) searched more than 5. The median number of databases searched was 3 (interquartile range: 2-5). The three databases most commonly used for searching were PubMed (72.4%, 589/813), Embase (55.6%, 452/813), and Medline (41.7%, 339/813) (Figs. 5 & 6).

Fig. 5 Numbers of databases used by SRs/MAs to identify animal experimental studies

Fig 6. Most commonly searched databases by SRs/MAs of animal experiments

3.3.2 Basic characteristics of search strategies

3.3.2.1 Search terms

Of the 813 published SRs/MAs of animal experiments, 98.3% (799/813) reported search terms, among which 736 (90.5%, 736/813) were related to patients or populations (P), 736 (90.5%, 736/813) were related to interventions (I), 9 (1.1%, 9/813) were related to comparisons (C), 137 (16.9%, 137/813) were related to outcomes (O), and 12 (1.5%, 12/813) were related to study design (S) (Fig. 7).

Fig. 7 characteristics of search terms

3.3.2.2 Search methodology

Of the 813 SRs/MAs, P plus I was the most common combination for search terms (78.5%, 638/813), followed by PIO (8.5%, 71/813) and IO (5.4%, 44/813) (Fig. 8).

Fig. 8 Distribution of Search Term Combinations for Animal Experiment SRs/MAs

3.3.3 Supplemental literature searches

Of the 813 SRs/MAs included in the present review, only 52.2% (424/813) conducted a supplementary search, among which 89.9% (392/424) searched the reference lists of included reviews, 8.9% (38/424) included the gray literature, while 7.3% (31/436) searched relevant journals, 4.7% (20/424) contacted the authors or experts, 7.5% (32/424) searched conference abstracts or other reports, and 3.8% (16/424) consulted Google and other search engines (Table 2).

Table 2 Supplemental literature searches

3.4 Characteristics of the reporting in the included animal experiment SRs/MAs

3.4.1 Basic search characteristics reported

Of the 813 animal experiment SRs/MAs included in the present review, the proportions reporting database sources, search terms, and the searched publication period were 99.4% (808/813), 98.3% (799/813), and 98.9% (804/813), respectively. In total, 78.7% (640/813) of SRs/MAs provided a literature screening flow chart, 67.4% (548/813) restricted the publication language of articles, and only 47.4% (385/813) reported the search methodology. In addition, only 8.0% (65/813) reported the database search platform and 4.8% (39/813) stated the qualifications of the search personnel (*e.g.*, assistance from library-related professionals in formulating the search strategy or conducting the search) (Fig. 9).

Fig. 9 Basic search characteristics reported

3.4.2 Reported search strategies

Of the 813 SRs/MAs, only 31.6% (243/813) reported search strategies, of which 68.7% (167/243) reported 1-2 strategies and only 23.9% (58/243) reported 3. The majority of the search strategies were described within the text (119/243, 49.0%), while strategies were presented at an internet link in 36.6% (89/243) and in the appendix after the text in 14.1% (34/243) (Table 3).

Table 3 Reported search strategies in the SRs/MAs included in the present review

4 Discussion

Although the methodological quality ^[17, 21] and reporting quality ^[22, 23] of animal experiment SRs/MAs have previously been discussed in the literature, the formulation of search strategies and the reported information have not been analyzed in detail. The present study is the first to have evaluated these aspects in all 813 published animal experiment SRs/MAs. The search methodology and reporting quality were comprehensively analyzed, to provide the basis for evaluation of the search process and the standardization of reporting of animal experiments in the future.

4.1 Epidemiological characteristics of the included SRs/MAs

A total of 813 animal experiment SRs/MAs were identified in 503 journals, from 52 countries and regions, with a trend of increasing numbers year on year. However, compared with similar clinical systematic reviews and meta-analyses, the total number was nevertheless quite small ^[24]. The included studies covered almost all the diseases categorized by the WHO ICD-11^[20]. The distribution of diseases researched by animal SRs/MAs is essentially similar to those that are clinically research-based ^[24], which to some extent reflects the fact that preclinical research tends to provide the evidence for clinical research to be conducted. Therefore, the publication of animal experiments of SRs/MAs should be continuously encouraged so that sufficient evidence is provided to support the clinical transformation of animal research in the future.

Numerous investigations have confirmed that registration of studies or publication of protocols may reduce the risk of specific research being unnecessarily repeated, and reducing or avoiding selection bias in systematic reviews, such as the inclusion of retrospective adjustments, selective reporting bias, such as using good or positive outcome indicators only, and therefore provides the basis for evaluating the results of other researchers' studies ^[25, 26]. In addition, it is also helpful so that researchers can update their studies in the future.^[27] However, the present review found that only 13.2% (107/813) of animal experiment SRs/MAs were pre-registered, considerably fewer than clinical trial-based SRs/MAs study protocols ^[28, 29]. We believe that this may be associated with the lack of publication of animal experiment SRs/MAs until recently, the imperfect methodology used, the lack of understanding of the significance of registration, and the lack of relevant guidelines. As early as 1993, the Cochrane Collaboration required authors to pre-register clinical SRs/MAs^[30]. A study published in 2004 confirmed that the publication of the Cochrane Handbook of Systematic Reviews significantly promoted such SR/MA registration ^[31, 32]. However, it was not until 2018 that International prospective register of systematic reviews (PROSPERO) allowed the registration of animal-based SRs/MAs ^[33, 34], and by the end of 2020, 781 had been registered ^[33], although this is still a relatively small number compared with clinical trial-based SRs/MAs registrations. Nevertheless, there is already a focus on the registration of animal experiment SRs/MAs.

4.2 Methodological characteristics of searching in the animal experiment SRs/MAs included in the present review

There are a number of limitations in the search methods used by published animal experiment SRs/MAs. Here, we discuss source database searches, the formulation of search strategies, implementation of the search procedure, and supplementary searches, respectively.

▣ The range of searched databases is large

The present study demonstrated that the number of databases searched ranged from 1 to 16. For clinical trial-based SRs/MAs, the Cochrane Handbook of Systematic Reviews^[30] requires that Medline, Embase, and the Cochrane Library should be searched. In addition, databases from the country or region of the investigator should also be searched, and specific additional databases selected relevant to the study topic. Although no standards exist for database searches for animal experiment SRs/MAs, the present study demonstrated that 28.8% (234/813) of the reviews searched fewer than 3 databases, while fewer than 20% (18.9%, 154/813) searched more than 5.

The present study found that PubMed, Embase, and Medline are currently the three most commonly searched English-language databases for animal experiment SRs/MAs, although these databases do not cover all data resources causing some articles to have been omitted. A number of studies have shown that a search of PubMed/Medline or Embase databases will identify only 55% or 49% of relevant studies, respectively^[35]. In addition, Biosis Previews is currently the largest life science and biomedicine database^[36,37], with a wide collection of related literature, such as in biology, medicine, pharmacy, *etc.* The Web of Science can be searched through known relevant source literature and references, and so it represents an important aid to database searching^[38]. However, the present study found that only 29.8% (242/813) searched Web of Science and 4.6% (37/813) consulted Biosis Previews. Therefore, following a search of PubMed/Medline and Embase databases, it is also recommended that the search is supplemented using Biosis Previews and Web of Science databases so that fewer relevant articles are omitted caused by incomplete searching.

▣ Problematic formulation of search strategies and implementation of search processes

Prior to the implementation of a search, research issues for animal experiment SRs/MAs should be summarized in accordance with PICOS (Participants, Intervention, Comparisons, Outcomes, and Study Design) principles using a methodology similar to that of clinical trial SRs/MAs^[39]. Previous studies have demonstrated that a structured PICOS search strategy allows the definition of a more specific and detailed research problem and, additionally, improves the accuracy of a search^[40]. During the search procedure, sensitivity (recall) and accuracy (positive predictive value) are often used to evaluate the search results^[41]. A number of researchers have found that the sensitivity (recall) of the P and I in the PICOS-based element search in SR/MA abstracts of clinical trials were 37–84% and 26–80%, respectively^[42–43]. In addition, it has been shown that the sensitivity (recall) of P, I, and O were 62%, 47%, and 75%,

respectively ^[47] when using an entity recognition model tool to analyze 191 biomedical articles. The results above indicate that the most commonly used elements in PICO for searching for clinical trial-based SRs/MAs are P, I, and O. In the present study, we found that the PICOS elements utilized in the search terms of the 813 studies included here were essentially the same as that observed in clinical trial-based SRs/MAs searching ^[48], although P and I were higher, while O was lower. This may be associated with the number of outcome indicators for animal experiments. Where a particular outcome is included in the search process, it may lead to the omission of relevant articles. High sensitivity for a target comprehensive search is considered standard practice for systematic reviews ^[49] although the ideal search strategy should be a balance of recall and precision ^[50]. As a result, for searches for animal experiments, we still recommend using the PICOS principle to formulate a search strategy, with P and I elements as the basic choice, and depending on the research purpose, adding C or O, prior to implementation of a search.

Irrelevant literature can to a certain extent be filtered out when addressing limitations of study design. Therefore, appropriate development and use of search filters could improve search efficiency ^[51] and reduce workload. There has been a rapid growth in the trend for the use of search filters since 2012 ^[52]. Medline, Embase, PubMed, and Cinahl have developed their own subject search filters, which are different in their implementation. For example, search filters designed for Ovid Medline typically take advantage of the database's advanced search capabilities, such as field search, subject search, and location operators, but the user must add them precisely, one line at a time, so commonly used search filters are saved to a personal account. However, search tools in individual accounts can only be used personally which prevents their widespread use in research teams ^[52]. In contrast, PubMed (including the free version of Medline) provides the means to add a long and complex search filter as a single detailed search string ^[1] that researchers can copy and paste into a database search box. In addition, its open accessibility allows search filters to be constructed behind hyperlinks and embedded into any HTML environment so that clicking a link or selecting a drop-down menu option can trigger a real-time, up-to-date PubMed search. For animal experiments, only PubMed and Embase have developed such search filters for their respective databases ^[1, 15], indeed improving search efficiency to a certain extent. The two are not universal for the identification of articles when searching, and researchers are not limited to these two databases when searching for animal experiment SRs/MAs, which undoubtedly increases the burden on researchers to identify other relevant databases to search. Therefore, the development of general search filters suitable for all databases for animal experiments is recommended for future research.

☒ Insufficient supplementary searches

When identifying articles for an SR/MA, searching only database resources may result in failing to detect some that are relevant ^[53, 54]. Supplementary searches can reduce this occurrence ^[336, 55]. In addition, scientific evaluation of publication bias is of considerable importance for the interpretation of the credibility of the conclusions of animal experiment SRs/MAs ^[56–57]. Insufficient and incomplete searches undoubtedly increase the possibility of publication bias ^[58]. Furthermore, manual searches are considered

the least efficient of all search methods ^[59]. The results of the present study indicate that only a half (52.2%, 424/813) of the included 813 animal experiment SRs/MAs had conducted a supplementary search. Although no standard for supplementary searches has been published for the field of basic medicine, Chris Cooper *et al.* ^[60] summarized more effective methods of supplementary searches by referring to 4 existing systematic review methodology manuals, which included referring to references and journals, contacting authors, *etc.* This can also represent a reference for researchers to develop and implement supplementary searches for animal experiment SRs/MAs.

In conclusion, for search methodology for animal experiment SRs/MAs, we suggest that: (1) Databases should be selected that are pertinent and reasonably appropriate for the specific research problem. In addition to the PubMed and Embase databases, it is necessary to also search the Web of Science and/or Biosis Previews. For studies involving specific topics such as pharmacological toxicology, TOXNET and other databases should be reviewed ^[61]; (2) Using PICOS principles, the P and I should be selected as the main elements for searching, while C or O should be added in accordance with the research purpose when selecting search terms; (3) Development of effective supplementary search strategies and methods that avoid missing relevant literature, while reducing the risk of publication bias; (4) Identify relevant information from experts in the field or ask library personnel to participate in the entire search process to ensure the accuracy and scientific nature of the search strategy; (5) Use appropriate animal experiment search filters to improve search efficiency; (6) Development of guidelines for the search procedure for animal experiment SRs/MAs, that will ultimately promote improvements in the quality of SRs/MAs.

4.3 Reporting of search strategies of the animal experiment SRs/MAs included in the present study

A complete and transparent search strategy helps readers understand the credibility of SRs/MAs by allowing analysis of the methodology and assessment of quality ^[62], but journal editors, often because of page limitations, but also because of the poor understanding of the importance of reporting the full search strategy, allow only a partial list of search words or search methodology, preventing readers ascertaining the full details, which thus affects their ability to properly interpret the results. PRISMA ^[63] and MOOSE ^[62] are international reporting guidelines for SRs/MAs for clinical trials which explicitly requires that the complete search strategy of at least one database to be reported when conducting an SR/MA. Additionally, in terms of reporting the search strategy, the sources of search information, search strategies, search restrictions, and other literature must also be reported. In the results section, in accordance with the above guidelines, a flow chart describing the screening of the literature for an SR/MA must also be presented, indicating the total number of animal experiments included in the meta-analysis. Of course, the encouraging thing is that the proportion reporting database names, search terms, and publication dates of searched articles was found to be more than 98%. However, of the 813 SRs/MAs included in the present review, only 47.4% (385/813) reported the search methodology and 31.6% (243/813) described the search strategy, possibly due to limitations of the journals. As a result, the methodology for the majority of databases has not so far been fully presented. However, as there are

currently no reporting guidelines specifically for animal experiment SRs/MAs, the authors only refer to similar published research guidelines (such as PRISMA ^[61]) or published formats for SRs/MAs or lists of content for reporting, resulting in incomplete data and large differences in the quality of reporting. Furthermore, Medline and Embase have different platforms ^[64, 65], which increases the burden for researchers in terms of implementing specific search strategies. In addition, the lack of familiarity with multiple search platforms can result in omitting relevant articles and conducting flawed searches ^[66]. In the present review, only 8.1% (67/813) of studies reported the database search platform. The participation and guidance of trained search experts or library personnel will improve the comprehensiveness, accuracy, and reliability of relevant literature searches for SRs/MAs ^[10, 67]. However, the present results demonstrated that only 4.8% (39/813) of animal experiment SRs/MAs reported the qualifications of the researchers. Therefore, we suggest that: (1) On the premise of standardization of the search process, details of the entire search procedure, such as search database and platform information, publication date range and limitations, at least one search strategy and a supplementary search method, and details of all those participating in the search process (including information experts) should be reported; (2) Clinical researchers master the skills of literature searching by providing universal education and consultations in evidence-based medicine, enabling a technical guarantee of the practice and production of high-quality evidence-based medicine; (3) Develop animal experiment SR/MA reporting guidelines, allowing the entire search process and its reporting to be standardized, ensuring the transparency of the research, and ultimately promoting improvements in the overall quality of animal experiment SRs/MAs.

4.4 Advantages and limitations of the study

The principal advantages of the present study are the comprehensive analysis and systematic review of animal experiment SRs/MAs, analysis of the search methodology and reporting, with which multiple problems were identified in the published literature of basic research. This represents a reference to allow for the standardization of the search process, and the formulation of effective search guidelines and reporting standards in the future.

However, there are also a number of limitations. The results of the review are mostly based on those described by individual authors in the literature, which may have resulted in a degree of bias when judging some information, such as the partial steps completed in the implementation process but not reported. It would assist the quality of such SRs/MAs if journals would remove article length and other requirements.

5 Conclusions

The quality of search methodology and search process reporting of many published animal experiment SRs/MAs is incomplete and not standardized. Therefore, we suggest that: (1) Depending on the research problem, the most targeted and appropriate databases should be selected for searching, in addition to at least Medline, PubMed, and Embase, with supplementation of the searches with Web of Science and

Biosis Previews databases, where possible; (2) Develop search filters for animal experimental research suitable for different databases to improve search efficiency, to avoid the omission of relevant literature and reduce the risk of publication bias; (3) Experts in the search of relevant information or library searchers should participate in the entire search process to ensure the integrity and universality of search strategies; (4) Continuing education and information consultation for evidence-based medicine related to medical-related animal experimental research will assist researchers master the skills of literature searching and allow personnel to become technical guarantors of creating high-quality evidence for clinical translation; (5) On the premise of standardization of the search process, the research and development of animal experiment SRs/MAs search and reporting guidelines, standardization of the search process and reporting, will ensure the transparency of research, and promote its introduction in relevant journal contributions, and ultimately promote improvements in the quality of animal experiment SRs/MAs.

Declarations

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

Availability of data and materials

All data generated or analysed during this study are included in this published article [and its supplementary information files].

Competing interests

All authors declare that no competing interests exist.

Funding

The project was supported by the National Natural Science Foundation of China (project number: 81873184). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Author Contributions

B.Z., F.C. and B.M. were responsible for the conception and design of the study. B.Z. analyzed and interpreted the results in collaboration with F.M., Q.Q.G., L.Z., J.W.Y., M.Y.J., and Y.B.J., who were responsible for acquisition of the data. B.Z., F.C. and Q.Q.G., wrote the first draft of the article. All authors

critically revised the article for important intellectual content and approved the final version of the manuscript.

Acknowledgments

The authors would like to thank all the reviewers who participated in the review and MJEditor (www.mjeditor.com) for its linguistic assistance during the preparation of this manuscript.

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Tables

Table 1, 2 and 3 not available with this version

Figures

Figure 1

Flow diagram describing the identification, screening, and inclusion of SRs.

Figure 2

Numbers of SRs/MAs included in the present review by year of publication.

Figure 3

Ranking of journals and nationalities of origin of published SRs/MAs included in the present review.

Figure 4

Types of diseases included* (* classifications in accordance with WHO ICD-11 [20]).

Figure 5

Numbers of databases used by SRs/MAs to identify animal experimental studies

Figure 6

Most commonly searched databases by SRs/MAs of animal experiments

Figure 7

characteristics of search terms

Figure 8

Distribution of Search Term Combinations for Animal Experiment SRs/MAs

Figure 9

Basic search characteristics reported

Supplementary Files

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