Reporting a Systematic Review

Beate Wieseler and Natalie McGauran

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Reporting a Systematic Review

Beate Wieseler, PhD; and Natalie McGauran

A systematic review (SR) is “[a] review of a clearly formulated question that uses systematic and explicit methods to identify, select, and critically appraise relevant research, and to collect and analyse data from the studies that are included in the review. Statistical methods (meta-analysis) may or may not be used to analyse and summarise the results of the included studies.”¹ In contrast to SRs, narrative reviews summarize evidence in a nonsystematic fashion and are, therefore, more likely to be affected by bias.

SRs help clinicians keep up to date with medical research findings and are used in the development of clinical practice guidelines and patient information, as well as in health policy decision making. They are also being increasingly applied to plan future research agendas (eg, some funding agencies require SRs as a condition for study sponsorship).²,³

About 2,500 new SRs are indexed in MEDLINE each year, predominantly concerning the effectiveness of interventions.⁴ Poor reporting of SRs may produce biased results and thus diminish their usefulness.⁵ To be of use to clinicians and other stakeholders, SRs must meet minimum criteria (ie, be “complete, accurate, and transparent”).⁶ Further-

more, SRs should describe to which patient populations their findings apply. Finally, SRs are most useful when they are up to date.⁴

Guidelines for Reporting SRs

Well-executed SRs constitute the highest level of evidence for medical decision making.⁶ However, although some improvement has been noted in the reporting of SRs, the quality of reporting is still inconsistent,⁷,⁸ which underlines the need to follow reporting standards. The recently published Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement aims to help improve reporting, focusing on SRs of randomized trials.⁹ The Statement consists of a checklist of 27 essential items for transparent reporting and a flow diagram for the phases of study selection and is accompanied by the PRISMA Explanation and Elaboration Document, which, among other things, provides examples of good reporting for the various review sections.¹⁰ All documents are available online (www.prisma-statement.org). The PRISMA Statement replaces the Quality of Reporting of Meta-analyses statement.¹¹ Many journals, including CHEST, require that manuscripts follow the PRISMA checklist. Further guidance on the reporting of SRs has been published by the Cochrane Collaboration,¹² an international organization that prepares, updates, and publishes SRs of the effects of health-care interventions following a standardized format.¹² The quality of reporting in Cochrane reviews is superior to that of non-Cochrane reviews.⁴

Aim of This Article

The production of a systematic review is a research project. The main steps in the process and a summary of the corresponding items for reporting SRs are presented in Table 1.⁵,⁹,¹¹-¹⁸ This article focuses on the reporting of SRs in journal publications, and, taking account of PRISMA and other recommendations, aims to provide SR-related and general medical writing tips to researchers and medical writers.
### Table 1—Steps in the Conduct of a Systematic Review and the Corresponding Items for Reporting

<table>
<thead>
<tr>
<th>Steps of an SR</th>
<th>Details</th>
<th>Sections and Content in the SR Publication</th>
<th>PRISMA Items</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1) Formulate the research question (and develop the protocol)</td>
<td>Research questions should be stated precisely and explicitly, and may be narrowly focused or broad, depending on the overall objectives of the SR._components of the question: PICOS (participants, interventions, comparisons, outcomes, and study design). A protocol minimizes the risk of bias caused by post hoc changes in methods. Additional components of the protocol: eligibility criteria (following PICOS), the search strategy, and the methods for screening, data extraction, and analysis.</td>
<td>Objective: State objective of the review (research question with reference to PICOS).</td>
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<tr>
<td></td>
<td>Methods: Indicate whether protocol exists. Define inclusion/exclusion criteria (following PICOS) for studies and documents. Further methods are presented below.</td>
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<tr>
<td>(2) Search for evidence</td>
<td>A systematic search in various information sources reduces the risk of bias in study selection. Potential sources to search or contact: -bibliographic databases (CENTRAL, MEDLINE, and EMBASE). -national, regional, and subject-specific databases. -conference abstracts and other gray literature. -reference lists in primary studies, reviews, guidelines, and other related articles. -trials registers and trials results registers (to find ongoing and unpublished trials). -study authors, other experts, and manufacturers (to identify unpublished data).</td>
<td>Methods: Describe all information sources (including period covered by search). Present main keywords of search strategy, and include full search strategy for one database in a web appendix.</td>
<td>7</td>
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<td></td>
<td>8</td>
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<tr>
<td>(3) Select the studies</td>
<td>Two reviewers should perform the screening process independently of one another to minimize the risk of bias. Disagreements should be resolved by consensus or third party (procedures also apply to steps 4 and 5). Procedure: -screening of titles and abstracts -screening of the full texts -exclusion of nonrelevant/selection of relevant studies.</td>
<td>Methods: State the process of study selection (from screening to inclusion in SR). Results: State the number of retrieved citations, studies excluded (with reason) and included (PRISMA flowchart).</td>
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<td>10</td>
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<tr>
<td>(4) Extract the data and other information</td>
<td>Study information and data are extracted from journal publications or other documents; study authors or manufacturers might be contacted to obtain missing information or clarify open questions. Data extraction forms should be pilot tested on a representative sample of studies before using them in the entire review. Items typically extracted: study citation, objective, follow-up period, sample size, PICOS, study results, and funding source.</td>
<td>Methods: Describe methods for obtaining and extracting data. List and define items for which data were extracted (see left column). Results: For each study, present study characteristics, study results, and other items extracted (see left column).</td>
<td>11</td>
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<td>12</td>
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<td>(5) Appraise the risk of bias in individual studies and across studies</td>
<td>Various scales and checklists for appraising the quality of studies are available, however, reporting appraisal scores alone does not provide sufficient detail to understand the origin of the bias.</td>
<td>Methods: Describe methods for risk of bias assessment of individual studies and across studies, as well as how the assessments were subsequently used in the data synthesis.</td>
<td>13, 14</td>
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</tbody>
</table>

(Continued)
The PRISMA statement and accompanying documents are > 30 pages long; our article provides only a rough outline of the content. Readers looking for indepth information, for example on the details of reporting statistical analyses, should refer to the PRISMA materials. It should also be kept in mind that the target journal’s instructions for authors should be followed, and previous SRs of the journal should be checked, to ensure adherence to the journal’s style.

As the same basic writing principles apply both to primary publications and to SRs, previous medical writing tips in CHEST by MaryAnn Foote and others, which are all available online, provide many useful general tips that are also relevant for SRs.19-24

### Sections of an SR

Structuring the paper according to PRISMA makes the paper easier to write and to read. However, although PRISMA suggests subheadings for abstracts, it does not specifically suggest subheadings for the full text. Because not all PRISMA checklist items are necessarily suitable subheadings, we propose the structure outlined in Table 2.
The title is a signpost that tells readers what the paper is about and encourages them to invest time in reading it. It should ideally follow the participants, interventions, comparisons, outcomes, and study design (PICOS) approach, and include the terms “systematic review,” “metaanalysis,” or both. In general, indicative titles are preferred to declarative titles (ie, titles including the conclusion). Nonstandard unexplained abbreviations should be avoided.

The main purpose of an abstract is to summarize the key elements of a paper so that the reader can decide whether to read the full text or not. Abstracts should be stand-alone documents. Authors need to be aware that the abstract may be the only part of the paper available to many readers, and should therefore provide a balanced presentation of the review content. Neither links to other parts of the review nor trade names nor nonstandard unexplained abbreviations should appear in the abstract. Both the PRISMA Explanation Document and the Cochrane Handbook include sample abstracts (a proposal for a structure following PRISMA is included in Table 2).

Introduction

The main purpose of an introduction is to establish the rationale for the research. Journal reviewers often complain about overlong introductions. This section should include only the essential information and citations. A simple structure for an introduction is: (1) the clinical problem (what is known and what is not), which leads to (2) the rationale (why the SR was conducted), and (3) the objective (the formulation of the research question with reference to PICOS).

Methods

The main purpose of a methods section is to allow readers to assess the validity of the research. Failure to provide detailed methods is a frequent cause of manuscript rejection. The PRISMA checklist provides a detailed step-by-step procedure, which, if completed, ensures a minimum standard of methods reporting. PRISMA recommends indicating whether a protocol exists and providing additional information, such as where it can be accessed and the registration number (if applicable). Deviations from the protocol should be noted and justified.

Eligibility Criteria: Both types of eligibility criteria should be described: (1) study characteristics (PICOS and minimum length of follow-up), and (2) report characteristics (ie, years and language considered and publication status, eg, inclusion of unpublished data).

Search Strategy and Study Selection: All information sources used should be presented (Table 1, step 2), including the dates of coverage for databases, the date last searched, and any contact with study authors or sponsors. PRISMA recommends presenting the full electronic search strategy for at least one major database so that readers can replicate the search. The procedure of study selection includes reporting the stages of screening (title/abstracts and full texts), and the number and identity of the people involved in each stage. Whether the screening process was performed in duplicate and independently should be reported, as well as how disagreements were resolved (this also applies to the procedures for data extraction and assessing the risk of bias presented below).

Data Extraction: The section on data extraction describes the methods used to extract data from reports and obtain and confirm data from investigators.

Table 2—Possible Structure for a Publication of a Systematic Review

<table>
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<th>PRISMA Items</th>
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<tr>
<td>Methods</td>
<td>5</td>
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<tr>
<td>Eligibility criteria</td>
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<td>Search strategy and study selection</td>
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<td>Data analysis</td>
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<td>Results</td>
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<tr>
<td>Description of studies</td>
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<td>Risk of bias</td>
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<td>Discussion</td>
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<td>Summary of evidence</td>
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<td>Strengths and limitations of the review</td>
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<td>Comparison with previous research</td>
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<td>Conclusions</td>
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<td>Funding</td>
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</table>

See Table 1 for expansion of the abbreviation.

Abstract: following one of the proposals in PRISMA; body of text: in part based on the Cochrane Handbook and PRISMA.

Add to end of abstract: information on funding and the registration number of the review (if applicable).

Structure to achieve the most transparent presentation of data (eg, per intervention, per outcome, per comparison, per patient group).
are usually extracted using standardized extraction forms; an example of such a form is available online.\textsuperscript{28} Whether piloted forms were used should be noted.\textsuperscript{9} Data items typically extracted and reported are listed in Table 1 (step 4).

**Assessment of Risk of Bias:** For assessing the risk of bias in individual studies, PRISMA recommends a component approach, such as the Cochrane method. A summary of risk-of-bias items usually reported is included in Table 1 (step 5). Authors should explain the procedure applied and specify whether this was done at a study or outcome level.\textsuperscript{9} How the results of the bias assessment were used in the data analysis (eg, exclusion of studies with a high risk of bias, implementation of sensitivity or subgroup analyses related to bias assessments) should also be stated.\textsuperscript{9} Methods applied to investigate the risk of bias that might affect the cumulative evidence should also be described (Table 1, step 5).\textsuperscript{9}

**Data Analysis:** The principal summary measures should be reported, for example, the odds ratio, risk ratio or risk difference for dichotomous data, and the (standardized) mean difference for continuous data.\textsuperscript{29} If metaanalysis is performed authors should specify the effect measure, the statistical method, and the type of model (eg, fixed or random effects).\textsuperscript{9} Methods to determine statistical heterogeneity should be reported (eg, the I^2 test). Any additional analyses should be presented (eg, subgroup analyses, sensitivity analyses, meta-regression), including the information as to whether they were prespecified.\textsuperscript{9} The handling of missing data should be explained, which mainly refers to participants lost to follow-up and missing statistics.\textsuperscript{28}

**Results**

The main purpose of a results section is to give specific answers to the aims outlined in the introduction.\textsuperscript{30} The results text should provide a summary of main findings and trends. Repetition of detailed information from the tables and figures in the text should be avoided. Instead, readers should be given the messages derived from them (and not have to interpret the data themselves).\textsuperscript{30} Basic introductions for the effective use of tables and figures are available online, although not specifically targeted toward SRs.\textsuperscript{24,31} It may be more appropriate to place detailed comments on individual studies in table footnotes rather than in the text.

**Description of Studies:** The first section of the results section provides the number of studies screened, assessed for eligibility and included, and should contain a flowchart of study selection (see PRISMA flowchart at www.prisma-statement.org), which in the case of excluded studies should also note the reason for exclusion.\textsuperscript{9} Study characteristics and baseline characteristics are typically presented in tables and briefly summarized in the text. If the amount of information on these two items is limited, it can be presented in a single table. Study characteristics typically include the study citation, the follow-up period and study size, the location and setting, and the PICOS components. Reviews of drug interventions should include the drug name, dosage, duration (if not already stated), and mode of administration (if not obvious).\textsuperscript{27} Baseline demographics typically include the mean age and age range, the male to female ratio, and relevant medical information.

**Risk of Bias:** Graphs or tables provide a better overview of the risk of bias than presentation solely in text form. Examples of graphic and tabular presentation are available online.\textsuperscript{9,16,32}

**Effects of Interventions:** General recommendations on data presentation should be followed (eg, Lang and Secic\textsuperscript{25}). All outcomes should be presented following the sequence of outcomes in the methods section. If no data are available, this should be stated. Regarding individual studies, simple summary data should be presented for each intervention group, as well as effect estimates and confidence intervals (ideally with a forest plot).\textsuperscript{9}

Metaanalyses are typically presented in forest plots. Their results should be reported as an estimated effect across studies with confidence intervals and include measures of consistency (eg, the I^2 statistic).\textsuperscript{9} Great heterogeneity indicates a risk of bias across studies, and in this case, conclusions should not be drawn. Individual results of studies that could not be included in the metaanalysis should ideally be summarized in tables, providing the reason for noninclusion. All additional analyses should be reported to help avoid selective outcome reporting and Web appendices should be used to present extensive analyses.\textsuperscript{9}

**Discussion**

The main purpose of a discussion is to explain how results answer the research question and to compare and contrast them with previous relevant research.\textsuperscript{21} Many authors find the discussion section the most difficult to write.\textsuperscript{25} Common problems include verbosity and the repetition of results.\textsuperscript{26} In order to facilitate the structuring of this section, it might be useful to add further subheadings to the ones below, which may later be deleted. In the following text, we also present potential topics for consideration in this section.
Summary of Evidence: The review’s “take-home” message should be summarized in two to three sentences. The strengths and weaknesses of the evidence should be discussed by addressing issues such as whether a sufficient number of patients were analyzed and whether the studies included were of sufficient quality to be able to draw robust conclusions, whether the magnitude of effects was clinically relevant, what type of patients the findings were applicable to, and how relevant the results are to policy makers, clinicians, and patients.

Strengths and Limitations of the Review: The strengths of the SR should not be overemphasized and limitations should be described in detail. Both the limitations of the individual studies and of the SR itself should be addressed. For instance, if only data on specific patient populations are available, the SR might have limitations regarding the applicability of findings to wider patient populations. Other limitations might include language bias (eg, restriction to English-language publications) and poor reporting in the studies included. Limitations of metaanalyses should be addressed; they may be misleading if they do not consider factors such as “specific study designs, within-study biases, variation across studies, and reporting biases.” If statistical tests show low heterogeneity between studies, this can support the validity of the pooled results.

The issue of publication bias, which is a major problem in SRs, should be addressed, as published studies tend to overestimate the effects of interventions. Therefore, if the studies included in the SR are a biased sample of the evidence, then the results of the review will also be misleading. If the SR included only published studies, then publication bias should be presented as a potential limitation. If extensive efforts were made to identify unpublished data and previously unpublished data were provided, then the minimization of publication bias can be presented as a strength.

Comparison With Previous Research: The comparison with previous research should only cite the relevant previous work in the field investigated (ie, similar SRs and/or major randomized controlled trials contradicting or supporting the findings of the SR). Any criticism of other authors’ work should be expressed in an objective manner.

Conclusions: Conclusions should answer the research question stated in the objective. However, if conclusions cannot be drawn on the basis of the evidence, then this should be stated. Unsupported conclusions are commonly criticized by journal reviewers. Potential implications and recommendations for clinical practice should be presented with caution, keeping the degree of generalizability of the SR’s results in mind. Recommendations should avoid general statements, such as “further studies are needed.” Instead, specific suggestions should be made, for example, by following the proposals by Brown et al, whose suggested format for research recommendations includes the current state of the evidence, the PICOS components, and the date of recommendation as core elements.

Funding

The provision of information on funding allows readers to judge the SR’s credibility. Although few SRs are funded by commercial sources, it is nevertheless mandatory to state the funding source and its role, and fully disclose any potential conflicts of interest of the authors.

Quality Control of the Manuscript

In addition to the usual quality control and content review of a manuscript before submission, a researcher not involved in the conduct or reporting of the SR should ideally perform an additional quality control using the PRISMA checklist and a quality appraisal tool for SRs, such as the Assessment of Multiple Systematic Reviews tool, which is available online. The Assessment of Multiple Systematic Reviews tool was developed to assess the methodological quality of SRs; however, answering the 11 checklist questions also helps to identify deficiencies in reporting, such as missing information on key methodological aspects.

In summary, detailed guidance and appraisal tools are available to support the writing of SRs. Using these aids and following basic medical writing principles will help to create a high-quality paper, thus increasing the usefulness of SRs in supporting medical decision making.

Acknowledgments

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References

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