Review Article

How to Write a Systematic Review: A Narrative Review

Abstract

In recent years, published systematic reviews in the world and in Iran have been increasing. These studies are an important resource to answer evidence-based clinical questions and assist health policy-makers and students who want to identify evidence gaps in published research. Systematic review studies, with or without meta-analysis, synthesize all available evidence from studies focused on the same research question. In this study, the steps for a systematic review such as research question design and identification, the search for qualified published studies, the extraction and synthesis of information that pertain to the research question, and interpretation of the results are presented in details. This will be helpful to all interested researchers.

Keywords: *Narrative review, review, systematic review*

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Background

A systematic review, as its name suggests, is a systematic way of collecting, evaluating, integrating, and presenting findings from several studies on a specific question or topic.[1] A systematic review is a research that, by identifying and combining evidence, is tailored to and answers the research question, based on an assessment of all relevant studies.[2,3] To identify assess and interpret available research, identify effective and ineffective health-care interventions, provide integrated documentation to help decision-making, and identify the gap between studies is one of the most important reasons for conducting systematic review studies.[4]

In the review studies, the latest scientific information about a particular topic is criticized. In these studies, the terms of review, systematic review, and meta-analysis are used instead. A systematic review is done in one of two methods, quantitative (meta-analysis) and qualitative. In a meta-analysis, the results of two or more studies for the evaluation of say health interventions are combined to measure the effect of treatment, while in the qualitative method, the findings of other studies are combined without using statistical methods.[5]

Since 1999, various guidelines, including the QUORUM, the MOOSE, the STROBE, the CONSORT, and the QUADAS, have been introduced for reporting meta-analyses. But recently the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement has gained widespread popularity.[6-9] The systematic review process based on the PRISMA statement includes four steps of how to formulate research questions, define the eligibility criteria, identify all relevant studies, extract and synthesize data, and deduce and present results (answers to research questions).[2]

Systematic Review Protocol

Systematic reviews start with a protocol. The protocol is a researcher road map that outlines the goals, methodology, and outcomes of the research. Many journals advise writers to use the PRISMA statement to write the protocol.[10] The PRISMA checklist includes 27 items related to the content of a systematic review and meta-analysis and includes abstracts, methods, results, discussions, and financial resources.[11] PRISMA helps writers improve their systematic review and meta-analysis report. Reviewers and editors of medical journals acknowledge that while PRISMA may not be used as a tool to assess the methodological quality, it does help them to publish a better study article [Figure 1].[12]

The main step in designing the protocol is to define the main objectives of the

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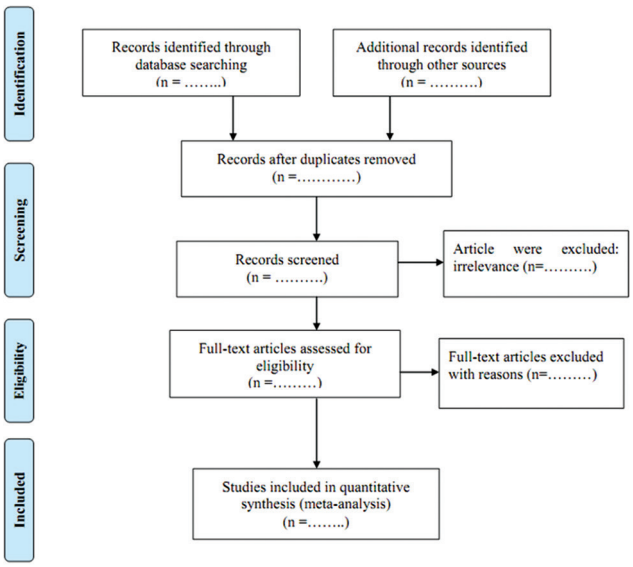

Figure 1: Screening process and articles selection according to the PRISMA guidelines

study and provide some background information. Before starting a systematic review, it is important to assess that your study is not a duplicate; therefore, in search of published research, it is necessary to review PREOSPERO and the Cochrane Database of Systematic. Sometimes it is better to search, in four databases, related systematic reviews that have already been published (PubMed, Web of Sciences, Scopus, Cochrane), published systematic review protocols (PubMed, Web of Sciences, Scopus, Cochrane), systematic review protocols that have already been registered but have not been published (PROSPERO, Cochrane), and finally related published articles (PubMed, Web of Sciences, Scopus, Cochrane). The goal is to reduce duplicate research and keep up-to-date systematic reviews.[13]

Research questions

Writing a research question is the first step in systematic review that summarizes the main goal of the study.[14] The research question determines which types of studies should be included in the analysis (quantitative, qualitative, methodic mix, review overviews, or other studies). Sometimes a research question may be broken down into several more detailed questions.[15] The vague questions (such as: is walking helpful?) makes the researcher fail to be well focused on the collected studies or analyze them appropriately.[16] On the other hand, if the research question is rigid and restrictive (e.g., walking for 43 min and 3 times a week is better than walking for 38 min and 4 times a week?), there may not be enough studies in this area to answer this question and hence the generalizability of the findings to other populations will be reduced.[16,17] A good question in systematic review should include components that are PICOS style which include population (P), intervention (I), comparison (C), outcome (O), and setting (S).[18] Regarding the purpose of the study, control in clinical trials or pre-poststudies can replace C.[19]

Search and identify eligible texts

After clarifying the research question and before searching the databases, it is necessary to specify searching methods, articles screening, studies eligibility check, check of the references in eligible studies, data extraction, and data analysis. This helps researchers ensure that potential biases in the selection of potential studies are minimized.[14,17] It should also look at details such as which published and unpublished literature have been searched, how they were searched, by which mechanism they were searched, and what are the inclusion and exclusion criteria.[4] First, all studies are searched and collected according to predefined keywords; then the title, abstract, and the entire text are screened for relevance by the authors.[13] By screening articles based on their titles, researchers can quickly decide on whether to retain or remove an article. If more information is needed, the abstracts of the articles will also be reviewed. In the next step, the full text of the articles will be reviewed to identify the relevant articles, and the reason for the removal of excluded articles is reported.[20] Finally, it is recommended that the process of searching, selecting, and screening articles be reported as a flowchart.[21] By increasing research, finding up-to-date and relevant information has become more difficult.[22]

Currently, there is no specific guideline as to which databases should be searched, which database is the best, and how many should be searched; but overall, it is advisable to search broadly. Because no database covers all health topics, it is recommended to use several databases to search.[23] According to the A MeaSurement Tool to Assess Systematic Reviews scale (AMSTAR) at least two databases should be searched in systematic and meta-analysis, although more comprehensive and accurate results can be obtained by increasing the number of searched databases.[24] The type of database to be searched depends on the systematic review question. For example, in a clinical trial study, it is recommended that Cochrane, multi-regional clinical trial (mRCTs), and International Clinical Trials Registry Platform be searched.[25]

For example, MEDLINE, a product of the National Library of Medicine in the United States of America, focuses on peer-reviewed articles in biomedical and health issues, while Embase covers the broad field of pharmacology and summaries of conferences. CINAHL is a great resource for nursing and health research and PsycINFO is a great database for psychology, psychiatry, counseling, addiction, and behavioral problems. Also, national and regional databases can be used to search related articles.[26,27] In addition, the search for conferences and gray literature helps to resolve the file-drawn problem (negative studies

that may not be published yet).[26] If a systematic review is carried out on articles in a particular country or region, the databases in that region or country should also be investigated. For example, Iranian researchers can use national databases such as Scientific Information Database and MagIran. Comprehensive search to identify the maximum number of existing studies leads to a minimization of the selection bias. In the search process, the available databases should be used as much as possible, since many databases are overlapping.[17] Searching 12 databases (PubMed, Scopus, Web of Science, EMBASE, GHL, VHL, Cochrane, Google Scholar, Clinical trials. gov, mRCTs, POPLINE, and SIGLE) covers all articles published in the field of medicine and health.[25] Some have suggested that references management software be used to search for more easy identification and removal of duplicate articles from several different databases.[20] At least one search strategy is presented in the article.[21]

Quality assessment

The methodological quality assessment of articles is a key step in systematic review that helps identify systemic errors (bias) in results and interpretations. In systematic review studies, unlike other review studies, qualitative assessment or risk of bias is required. There are currently several tools available to review the quality of the articles. The overall score of these tools may not provide sufficient information on the strengths and weaknesses of the studies.[28] At least two reviewers should independently evaluate the quality of the articles, and if there is any objection, the third author should be asked to examine the article or the two researchers agree on the discussion. Some believe that the study of the quality of studies should be done by removing the name of the journal, title, authors, and institutions in a Blinded fashion.[29]

There are several ways for quality assessment, such as Sack's quality assessment (1988),[30] overview quality assessment questionnaire (1991),[31] CASP (Critical Appraisal Skills Program),[32] and AMSTAR (2007),[33] Besides, CASP,[34] the National Institute for Health and Care Excellence,[35] and the Joanna Briggs Institute System for the Unified Management, Assessment and Review of Information checklists.[30,36] However, it is worth mentioning that there is no single tool for assessing the quality of all types of reviews, but each is more applicable to some types of reviews. Often, the STROBE tool is used to check the quality of articles. It reviews the title and abstract (item 1), introduction (items 2 and 3), implementation method (items 4–12), findings (items 13–17), discussion (Items 18–21), and funding (item 22). Eighteen items are used to review all articles, but four items (6, 12, 14, and 15) apply in certain situations.[9] The quality of interventional articles is often evaluated by the JADAD tool, which consists of three sections of randomization (2 scores), blinding (2 scores), and patient count (1 scores).[29]

Data extraction

At this stage, the researchers extract the necessary information in the selected articles. Elamin believes that reviewing the titles and abstracts and data extraction is a key step in the review process, which is often carried out by two of the research team independently, and ultimately, the results are compared.[37] This step aimed to prevent selection bias and it is recommended that the chance of agreement between the two researchers (Kappa coefficient) be reported at the end.[26] Although data collection forms may differ in systematic reviews, they all have information such as first author, year of publication, sample size, target community, region, and outcome. The purpose of data synthesis is to collect the findings of eligible studies, evaluate the strengths of the findings of the studies, and summarize the results. In data synthesis, we can use different analysis frameworks such as meta-ethnography, meta-analysis, or thematic synthesis.[38] Finally, after quality assessment, data analysis is conducted. The first step in this section is to provide a descriptive evaluation of each study and present the findings in a tabular form. Reviewing this table can determine how to combine and analyze various studies.[28] The data synthesis approach depends on the nature of the research question and the nature of the initial research studies.[39] After reviewing the bias and the abstract of the data, it is decided that the synthesis is carried out quantitatively or qualitatively. In case of conceptual heterogeneity (systematic differences in the study design, population, and interventions), the generalizability of the findings will be reduced and the study will not be meta-analysis. The meta-analysis study allows the estimation of the effect size, which is reported as the odds ratio, relative risk, hazard ratio, prevalence, correlation, sensitivity, specificity, and incidence with a confidence interval.[26]

Estimation of the effect size in systematic review and meta-analysis studies varies according to the type of studies entered into the analysis. Unlike the mean, prevalence, or incidence index, in odds ratio, relative risk, and hazard ratio, it is necessary to combine logarithm and logarithmic standard error of these statistics [Table 1].

Interpreting and presenting results (answers to research questions)

A systematic review ends with the interpretation of results. At this stage, the results of the study are summarized and the conclusions are presented to improve clinical and therapeutic decision-making. A systematic review with or without meta-analysis provides the best evidence available in the hierarchy of evidence-based practice.[14] Using meta-analysis can provide explicit conclusions. Conceptually, meta-analysis is used to combine the results of two or more studies that are similar to the specific intervention and the similar outcomes. In meta-analysis, instead of the simple average of the results

Table 1: Effect size in systematic review and meta-analysis

Systematic review type	Primary studies	Measures of interest
Prevalence systematic review	Cross-sectional studies Descriptive studies	Prevalence Mean, correlation
Observational systematic review	Cohort studies Case-control studies Analytical descriptive studies	OR RR Mean difference Standard mean difference
Clinical trials systematic review	RCT Non-RCT	RR Risk difference NNT, NNH Mean difference
Diagnostic systematic review	Diagnostic accuracy studies	Sensitivity Specificity PPV, NPV PLR, NLR DOR

OR=Odds ratio; RR=Relative risk; RCT= Randomized controlled trial; PPV: positive predictive value; NPV: negative predictive value; PLR: positive likelihood ratio; NLR: negative likelihood ratio; DOR: diagnostic odds ratio

of various studies, the weighted average of studies is reported, meaning studies with larger sample sizes account for more weight. To combine the results of various studies, we can use two models of fixed and random effects. In the fixed-effect model, it is assumed that the parameters studied are constant in all studies, and in the random-effect model, the measured parameter is assumed to be distributed between the studies and each study has measured some of it. This model offers a more conservative estimate.[40]

Three types of homogeneity tests can be used: (1) forest plot, (2) Cochrane's Q test (Chi-squared), and (3) Higgins I^2 statistics. In the forest plot, more overlap between confidence intervals indicates more homogeneity. In the Q statistic, when the P value is less than 0.1, it indicates heterogeneity exists and a random-effect model should be used.[41] Various tests such as the I^2 index are used to determine heterogeneity, values between 0 and 100; the values below 25%, between 25% and 50%, and above 75% indicate low, moderate, and high levels of heterogeneity, respectively.[26,42] The results of the meta-analyzing study are presented graphically using the forest plot, which shows the statistical weight of each study with a 95% confidence interval and a standard error of the mean.[40]

The importance of meta-analyses and systematic reviews in providing evidence useful in making clinical and policy decisions is ever-increasing. Nevertheless, they are prone to publication bias that occurs when positive or significant results are preferred for publication.[43] Song maintains that studies reporting a certain direction of results or powerful correlations may be more likely to be published than the studies which do not.[44] In addition, when searching for meta-analyses, gray literature (e.g., dissertations, conference abstracts, or book chapters) and unpublished studies may be missed. Moreover, meta-analyses only based on published studies may exaggerate the estimates of effect sizes; as a result, patients may be exposed to harmful or ineffective treatment methods.[44,45] However, there are some tests that can help in detecting negative expected results that are not included in a review due to publication bias.[46] In addition, publication bias can be reduced through searching for data that are not published.

Systematic reviews and meta-analyses have certain advantages; some of the most important ones are as follows: examining differences in the findings of different studies, summarizing results from various studies, increased accuracy of estimating effects, increased statistical power, overcoming problems related to small sample sizes, resolving controversies from disagreeing studies, increased generalizability of results, determining the possible need for new studies, overcoming the limitations of narrative reviews, and making new hypotheses for further research.[47,48]

Despite the importance of systematic reviews, the author may face numerous problems in searching, screening, and synthesizing data during this process. A systematic review requires extensive access to databases and journals that can be costly for nonacademic researchers.[13] Also, in reviewing the inclusion and exclusion criteria, the inevitable mindsets of browsers may be involved and the criteria are interpreted differently from each other.[49] Lee refers to some disadvantages of these studies, the most significant ones are as follows: a research field cannot be summarized by one number, publication bias, heterogeneity, combining unrelated things, being vulnerable to subjectivity, failing to account for all confounders, comparing variables that are not comparable, just focusing on main effects, and possible inconsistency with results of randomized trials.[47] Different types of programs are available to perform meta-analysis. Some of the most commonly used statistical programs are general statistical packages, including SAS, SPSS, R, and Stata. Using flexible commands in these programs, meta-analyses can be easily run and the results can be readily plotted out. However, these statistical programs are often expensive. An alternative to using statistical packages is to use programs designed for meta-analysis, including Metawin, RevMan, and Comprehensive Meta-analysis. However, these programs may have limitations, including that they can accept few data formats and do not provide much opportunity to set the graphical display of findings. Another alternative is to use Microsoft Excel. Although it is not a free software, it is usually found in many computers.[20,50]

A systematic review study is a powerful and valuable tool for answering research questions, generating new

hypotheses, and identifying areas where there is a lack of tangible knowledge. A systematic review study provides an excellent opportunity for researchers to improve critical assessment and evidence synthesis skills.

Authors' contributions

All authors contributed equally to this work.

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