



Writing and presenting a systematic review emphasizing the Cochrane Handbook for systematic reviews

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Abstract

BACKGROUND: The systematic review is a scientific method for identifying and presenting early research, quality assessment, and integration of their results. This study aimed to describe the principles of systematic reviews and inscribe related articles emphasizing the Cochrane Handbook, for using of medical and health students.

METHODS: This study was a library review and a compilation of materials on how to conduct review studies in medical sciences and health with emphasis on the Cochrane Handbook.

RESULTS: The findings of this study indicated that review studies have different types, most notably systematic reviews. The Cochrane Handbook provides valuable information collections for conducting these studies in medical sciences, and allows systematic reviews to step by step facilitate and publish relevant articles.

CONCLUSION: Writing a systematic review involves defining the purpose and protocols, systematically searching for primary studies, critical assessment, selection of the studies, and then, analysis and integration of the final results.

KEYWORDS: Meta-Analysis, Systematic Review, Public Health

Review Article

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Introduction

The systematic review is a scientific method of searching and finding the results of primary studies and evaluating and integrating their results on a certain topic, and it is considered to summarize and combine quantitative and qualitative studies. This method is different from the traditional review study which includes explanation of studies, but not the systematic identification of studies, qualitative evaluation, and integration of results.¹ In other words, the systematic review is an allocation process, critical review, and systematic

integration of evidence retrieved from scientific studies in order to obtain a general, short, and reliable description of an issue.²

A systematic review is not a mere list of studies, but it integrates and interprets the results of studies in a way that increases understanding. Moreover, it is a key method for bridging over the gap between research and practice.³ It is a special methodology for the evaluation and synthesis of the results of primary studies and foundations to improve evidence-based policies and performance.⁴

Review studies comprehensively cover a certain biomedical subject and justify the path to future studies for successful master, doctorate, and postgraduate programs.⁵

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Unlike narrative reviews, the feature of the systematic review is that all its procedures and methods are designable and clear, and if other researchers adopt the same procedures and methods to review the same set of data, they will obtain identical results. In other words, such reviews are reproducible without the effect of the researcher, which indicates the internal consistency of such studies.⁶

Systematic reviews can lead to more reliable scientific achievements by saving time for researchers, therapists, and planners. It has been estimated that over 2 million articles are published in over 20,000 journals every year (2014), and it is impossible for a researcher to be aware of all scientific developments and productions even in a limited field of specialty. The systematic review, however, summarizes the best accessible evidence and provides a conclusion to help therapists and planners choose the right treatment for patients.⁷ Therefore, the systematic review aims to respond to a question based on the most scientific published or unpublished evidence available¹ and is the basis for evidence-based medicine.⁷ On the other hand, a systematic review can not only provide good reasons for clinical decision taking, but can also play an important role in determining future research needs. In this regard, the most important advantages of systematic reviews are:

1. Having certain methods to select and reject studies, which reduce biases or deviant results and increase the reliability of results,
2. Generalizability of results, consistency, and lack of dispersion of results by comparing the results of different studies⁸ and increasing the statistical strength of smaller studies⁹,
3. Comprehensive access of researchers, health services providers, or policymakers to exploitable information⁸,
4. Updating the results of the most recent studies,
5. The possibility of designing evidence-based guidelines (action guides) to provide

therapeutic and preventive interventions⁷, and

6. Avoiding duplication and waste of time and resources on issues whose evidence has been clarified before.

Given the difference between decision making and decision taking, scholars usually help with decision taking, and executives and policymakers are responsible for taking the final decision. Like other health and healthcare decisions, policymaking should be based on the best and latest evidence available, and review studies are also useful in this field.

In this regard, the Cochrane Collaboration is an international organization which primarily aims to help individuals take informed healthcare decisions by preserving and enhancing access to systematic reviews of evidence. The Cochrane Collaboration was founded in 1993 and currently includes over 15,000 contributors from more than 100 countries, easily making it the largest organization involved in this kind of work. The international collaboration was launched one year after the establishment of the Cochrane Centre in Oxford (now the UK Cochrane Centre), founded by Sir Iain Higgins and Green and named after British epidemiologist Archie Cochrane. The Cochrane Collaboration is now an internationally renowned initiative.¹⁰

The present writing aims to introduce the principles of conducting systematic reviews in medicine and health. Such studies are highly reliable among other scientific articles. Given the development of knowledge in Iran and researchers' need for extensive studies in a certain field, it is expected that researchers take steps toward summarizing and providing effective scientific achievements by becoming familiar with the principles of review studies.

Materials and Methods

This was a review study on how to conduct review studies in medical sciences and health, with especial emphasis on the Cochrane Handbook.

Introducing and categorizing review studies: Review studies, which are also called secondary studies, are the result of scientific review, synthesis, and integration of several primary studies and are classified into the following methods.

In a classification, they were divided into two types: systematic articles and unsystematic (narrative) articles. These two types have different features and aims. The systematic review utilizes precise and extensive searches for texts on the subject in question using a critical investigation, and due to its precise methods of evaluating the available texts, it is considered as the gold standard of reviews. Systematic reviews are divided into qualitative and quantitative reviews. In both qualitative and quantitative reviews, authors try to retrieve all primary studies, search multiple databases, search the relevant studies manually, contact the authors of grey (unpublished) studies, examine the texts systematically, and critically evaluate the studies included in the review.

An unsystematic review is an overview of materials that are easily readable.¹¹ This type of review is more traditionally seen in nonmedical sciences, and is usually extensively used by the main practitioners in a field and generally on an issue. They use informal, unsystematic, and mental methods to search, collect, and interpret data that are mostly summarized through a hypothesis, without critical evaluation, and with an easy narration. Although review studies in every field are carried out by experts, they may be based on biased views.¹² Unsystematic review articles do not list the varieties of databases and methodological approaches used to carry out studies and the inclusion criteria of the retrieved articles, while searching the databases.¹³ The results of such studies are more qualitative than quantitative.¹⁴

In another classification, review studies are classified as follows:

A) Narrative review articles (categorized as editorials, commentaries, and unsystematic narrative reviews),

B) Qualitative review articles or systematic review, and

C) Quantitative review or meta-analysis

A) Narrative and unsystematic review articles were explained above. An editorial is a kind of article which explains the view of an individual¹⁵ or a group of individuals.¹⁶ An editorial can be on any topic, but it usually deals with social issues. In order for editorials to be validated, they need to be supported by realities and evidence.¹⁵ Similar to a lawyer on a debate that has already been made, the author of an editorial tries to convince the reader of a current result. Therefore, an editorial is a viewpoint with a predictive orientation.¹⁷

A commentary is a kind of review study in which individuals express their opinions about a person, thing, or event (for example, a sports event).¹⁸ In the Cambridge Dictionary, it is stated that this type of review is used in radio or television or it is the comments written on an event, a book, or a person, which deal with the topic of that book or event.¹⁹

B) As stated, a qualitative systematic review is a comprehensive review that is based on primary research studies and has obtained certain standards with regard to its methodology. These studies should be clear and possess appropriate inclusion and exclusion criteria.²⁰ Systematic reviews are mainly characterized by searching all main reports on the topic in question, evaluating the reports of studies critically, and concluding based on integration of studies that have the qualitative features in question.²¹ Other key features of such studies are developing clear goals and predetermined criteria and designing explicit methodology which leads to the reproduction of systematic reviews.¹⁰

C) The meta-analysis is regarded as equal to systematic review, but researchers use meta-analysis that has a quantitative scientific

analysis method to combine and summarize the results of studies in a quantitative way.¹ Therefore, conducting a meta-analysis is a step beyond review studies and is neither necessary nor possible in all systematic reviews, because conducting complex statistical comparisons requires similarity among the participants, trials, and interventions and their outcomes.⁶ In other words, it is a mathematical combination of the results of at least two primary studies with similar hypotheses and methods.⁹ According to the Cochrane Handbook, meta-analysis is using statistical methods to summarize the results of independent studies by combining the data from relevant studies. The meta-analysis can provide a more accurate assessment of the effects of health care compared to the case in which such assessments are conducted alone. Meta-analyses also increase the strength of evidence and facilitate the revelation of discrepancies among studies.

The method of conducting a systematic review: The systematic review is similar to primary scientific researches in which an instruction including the research question needs to be answered and the proposed methods should be developed.¹ In order to achieve and present the results of a systematic review to be published in the Cochrane Database of Systematic Reviews (CDSR), it is necessary to minimize bias, which is possible when the researchers do not allow their personal judgments to interfere with the selection and report of the studies. Protocol development is the first step in writing systematic reviews, which is like the proposal in primary studies and clarifies the path of the next steps. In addition, bias in selecting the studies to be included in a systematic review and reporting the data of all articles and studies, the results of which may include bias, need to be minimized. Since writing the protocol before reviewing the texts determines the research question and the characteristics of

the included studies, it minimizes the probability of bias to a large extent. To write a systematic review, first, its protocol should be registered and agreed on in one of the thematic groups of the Cochrane subset. Protocols that are not converted into systematic reviews 2 years after confirmation will be eliminated from the Cochrane groups.

According to the Cochrane Handbook, a protocol includes the following parts: topic, background, aims, methods, characteristics of the studies that are selected for review including the type of study, participants, interventions, scales of results, search methods to determine the studies, data collection, analyses, acknowledgments, references, and additional information in appendices.¹⁰

A systematic review is carried out in a number of phases.

King's College London (2014) has introduced the following 8 phases: specifying the topic and whatever is needed to be known (developing an answerable question), searching articles (finding relevant studies), selecting articles based on the inclusion and exclusion criteria to enter into the review study, evaluating the selected articles with regard to bias, statistical analysis (summarizing and integrating the relevant studies), controlling bias in the inclusion method of studies (for example, whether the emphasis is on positive results and negative results receive less attention, and vice versa), introducing the statistical outline, presenting the results and their summary in tables, expressing and interpreting the results and the conclusion.⁷ Similar phases have been introduced in other references including the Cochrane Handbook.^{1,3,9,10,13}

Main and important stages of a review study

A) Specifying the topic and developing an answerable question: One of the most important characteristics that differentiate systematic reviews from typical studies is that, in systematic reviews, the review topic and inclusion and exclusion criteria or qualification criteria are precisely determined. These criteria

are usually a combination of the clinical question and characteristics of different varieties of studies that deal with the clinical question.¹⁰ However, if the research question is more specifically posed, the study will be carried out more scientifically. Therefore, more useful and relevant data can be filtered from useless data.¹⁴

The proposed method to review the text of most questions can be divided into 4 main sections which are determined based on the PICO framework.

P (Patient/Population/Problem): This section determines the individuals related to the problem in question.

I (Intervention or exposure): This is related to the method of management, intervention, or test of what is aimed to be obtained. This section can include a method of therapy, surgery, or diet or factors that may affect the health outcomes.

C (Comparison or control): This is related to the method of control, replacement, placebo, or conducting of the test in order to compare in a correct and exact manner.

O (Outcome): This section shows what is more important than others or what the patient is most concerned about.² The first three parts of the clinical question (population, interventions, and comparisons) are usually the decisive criteria for selecting the studies to be

entered into the review study, while the results of a study do not play a decisive role in the inclusion or exclusion of a study in the review.¹⁰

It is important that the study question is posed based on the abovementioned components to the extent possible; however, sometimes it is not necessary to consider all of them.

B. Searching and finding relevant studies: The best evidence is obtained from the studies whose method has minimized the probability of bias.² Based on the type of question (in fact, the type of problem that is to be resolved), the type of the selected articles can differ (Table 1).

In order to ensure the discovery of all of the conducted studies related to a topic, it is necessary to develop a systematic strategy to search the texts. The first step is to determine whether the systematic review can be conducted or not. After making sure that there is no review on the topic in question in the Cochrane Library, searching into the desired references will begin. The easiest way for this is to utilize bibliographic databases of studies.

In all systematic Cochrane reviews, the three databases of MEDLINE, Embase, and the Central Register of Controlled Trials (CENTRAL) need to be searched to find the required studies.¹⁰ Moreover, appropriate for the topic under research, specialized thematic databases like the Cumulative Index of Nursing and Allied Health (CINAHL),

Table 1. Types of questions related to public and clinical health, types of ideal studies, and types of major evaluations¹

Type of question	Types of ideal studies	Types of major evaluations
Intervention	Randomized clinical trial	Randomization, completion with follow-up, and blinding (patients and clinical factors)
Frequency/rate (disease)	Cross-sectional study or sequential sample	Sample framework, case affirmation, sufficient follow-up, or appropriate reaction
Etiology and risk factors	Cohort study	The groups are only different in terms of presentation, evaluation of the consequences, and acceptable evidence of the causes.
Prediction and precaution	Cohort study	Main cohort, and sufficient follow-ups
Diagnosis precision	Randomized or sequential sampling	Independent blind comparison using "gold standard", and correct selection of patients
Hypothesis	Qualitative research	Appropriate selection of topic and research methods

Information Center (ERIC) can be utilized. Searching a single database is not sufficient, and different databases should be used. There is no formal law that determines how many databases are required for searching; however, a view beyond the standard databases of health care is needed in interdisciplinary topics. In fact, the whole process of a good search is to find the best balance between sensitivity (finding the highest number of articles possible) and feature (ensuring that the articles are relevant).⁷

In order to reduce bias, it is necessary to search grey studies¹³ such as synopses of conferences, technical or governmental reports, dissertations, and theses. In order to find grey literature, the websites of relevant organizations can be searched and the experts can be contacted.¹

With regard to search strategy, first, it is useful to formulize the topic under search into smaller topics, and search the components and combine them with each other, and second, to utilize synonymous and relevant words. Specialized glossaries available in databases or keywords of articles can also be used for this purpose. Medical Subject Headings (MeSH) are the most famous of these glossaries. Moreover, it should be noticed that using keywords of glossaries should be as a supplement to free keywords not their substitute.

- Using Boolean operators: Using the operators "AND", "OR", and "NOT" make the search more limited, wider, or more specific.

- Using limiters and filters: On databases, filters such as language and year can be used. Moreover, searching the keywords can be restricted in a special field such as title, author, and abstract, and the types of retrieved documents, type of study, and age can be utilized according to the features of each database in order to make the searches more specialized.

C. Evaluating the quality of the retrieved studies and selecting them: The Cochrane systematic

review is reviewing studies that possess the inclusion criteria.¹⁰ The method of selecting the articles is typically presented as a diagram⁸ and their specifications, including the method, the population, interventions, and various outcomes, are determined.⁶

The following measures are taken in order to select the required studies:

- The search results are entered into resource management software (such as Reference Manager and Endnote) and repeated articles are crossed out.

- The topics and abstracts of the articles are checked, and irrelevant cases are specified.

- The full text of the relevant articles is retrieved, and different reports of a single research are integrated.

- In the case of incomplete articles, the full text of the articles is requested from their authors in order to evaluate the rate of relevance regarding the topic of the review.

- The final decision on selecting or rejecting the study is taken.¹⁰

First, the abstract of the article should be reviewed. Subsequently, if it is relevant to the topic in question, its methodology is taken into account, and if the methodology is accepted, the results are considered. There is typically no need to study the introduction, discussion, and conclusion.²² Due to the importance of the correct selection of the studies, at least two analysts should independently read and score all of the relevant studies. Then, the analysts find a solution for the probable discrepancies between the given scores by discussing and justifying every single score that they have given.¹

In addition to the tool introduced in the Cochrane Handbook, the methods proposed by Jadad *et al.*²³ and Moher *et al.*²⁴ are among other ways to evaluate the quality of articles. These two standard methods are utilized to evaluate the quality of interventional studies, especially clinical trials, and the method of their report. Other available tools to assess and evaluate the quality of meta-analyses and systematic reviews

are QUORUM²⁵ and PRISMA²⁶, and to measure the quality of observational studies such as cross-sectional studies, case-control studies, and cohort studies are STROBE²⁶ and MOOSE.²⁴

Since using predetermined and abridged scales can be problematic in assessing the quality of trials, it is recommended that authors evaluate trials from 5 perspectives: making sure that the trial has employed a randomized method, the therapeutic interventions are secretly distributed among the subjects, the study is double-blind, the patients are followed up for a long period of time, and the results of the intervention are analyzed.⁶

D. Extracting the data of the selected articles: In this phase, it is helpful to prepare a (paper or electronic) form in order to extract and summarize the data of the selected articles. This form should include the following parts:

- Reference (including journal name, title, author, volume, and page number),
- Topic of the study (as written by the author),
- Design of the study (trial),
- Population (the participants' demographics)
- Control (explaining the control group or the alternative intervention), and
- Results (the results of the intervention and the method of measuring them).^{9,10}

E. Summarizing and combining the studies: If the studies are homogenous enough with regard to their questions and methods, it is appropriate to combine the results in order to present a summarized assessment, and a meta-analysis will be carried out, which has various statistical methods. The method of combining the studies can differ based on the type of their questions and the criteria of assessing the outcomes.

Various factors can lead to the emergence of differences in the results of a systematic review. For example, it is possible that the effect of a type of therapy appears different in different studies. These differences can be due to the patients or the disease (e.g., the phase or

severity of the disease), intensity or duration of the intervention, simultaneous interventions (e.g., other treatments or measures that the patient is going through), evaluating the outcomes, and timing.

Difference among various studies is not only limited to these factors, but other characteristics, including the quality of the study, acceptance of the intervention, and suitability of the utilized criterion in assessing the outcome, can also lead to contradictions in the treatment results, which leads to differences in results.¹

At the end of this section, it should be noted that systematic reviews are carried out on both quantitative and qualitative studies. As opposed to quantitative studies, qualitative studies consider the patient as a complete human, and attempt to attain a correct understanding of the experiences of patients and reasons for which the patients perform some activities in certain conditions.²⁷ A qualitative study examines experimental, emotional, and social phenomena, and is defined as any type of study whose results are not obtained from quantitative investigations and statistical calculations.²⁸⁻³⁰ Qualitative synthesis is regularly used in the systematic review of professional health texts; however, it is mainly employed in general texts.³¹ It is evident that separate qualitative studies have limitations such as generalizability; therefore, combining these studies can help overcome such limitations. There are many methods for synthesizing qualitative evidence, which are appropriate for the aims and prospects of Cochrane interventional reviews. The synthesis of qualitative research is a controversial and developmental field, and the Cochrane Qualitative Methods Group has founded a committee to discuss the future methodological developments in this field.³²

F. The method of reporting systematic review articles: The structure of systematic review articles is as follows:

Title: The title should be short, interesting, clear, and general. The titles of such articles are usually shorter than those of research articles. Like research articles, using abbreviations is not allowed in this type of article. It is recommended that the terms “review” or “overview” be used in the title so that the type of article is clear.⁸ A title with more accurate and specific explanation is more likely to be referred to.⁵

Abstract: It is typically written as a structure and in the IMRAD framework (introduction, methodology, results, and discussion). In other words, it is written in the sections of introduction (aim), method, results, discussion, and conclusion. The content of this section is presented in about 250 to 400 words. The keywords range from 3 to 10 words, including the term systematic review.^{6,8}

Introduction: It includes background (epidemiological and clinical background of the topic) and different therapeutic approaches or interventions. In this phase, there is an attempt to convince the reader of the necessity or aim of the research.

Methodology: In this section, the method of retrieving the articles from the databases and the complete name of the utilized databases are included. The utilized keywords, time limit, and the language of the data references should also be specified. Moreover, the research question and inclusion and exclusion criteria should be included. In fact, it deals with the method of evaluating the methodological quality of the studies. If the systematic review article is accompanied with meta-analysis, statistical indicators and tests should also be included in this section.

Results: In systematic review articles, the results are actually the same as the selected articles obtained from the search and evaluation. In addition to referring to the number of the articles, the following sections are also included in the “Results” section.

Combining the data (studies): It should be

noticed that the studies are appropriately combined based on certain and valid criteria.

Similarity of the data: This section deals with examining the similarity among the populations under investigation, the administered interventions, and the outcomes of the articles.

Moreover, the reasons for discrepancy between studies should be taken into consideration.⁸ Furthermore, it is necessary to provide a short explanation of the main results, the level of the evidence, strengths and weaknesses of each study, and relationship with each section. Readability of a review can be improved by the inclusion of some tables without explanation, synthesis of the main data, and conveyance of the main messages.⁵

Discussion: In this section, a hypothesis is tested. The data, results, and analyses are summarized, and the application of the results is evaluated and interpreted according to the research question (aim).¹⁴ This section actually deals with the interpretation of the results. When the examined cases are more similar, there will be an increase in the probability of obtaining highly reliable results, which in turn enhances the generalizability of the results. The results of the content of the articles under investigation should be expressed with a logical sequence and in clear purposeful phrases. In the “Discussion” section, the issue of what concept has been obtained should be referred to. The author needs to deal with any certain opinion relevant to the issue, if there is any.

In addition to the criticisms and analyses presented in the text, the results obtained from examining and discussing different opinions should be linked with the study’s aims referred to in the introduction, but phrases and conclusions that are irrelevant should be avoided. In this section, the expenses, safety of the treatment (or intervention) compared to similar studies, limitations, and weaknesses should be included. Moreover, recommendations for future studies should be

provided based on the current study.⁸

Conclusion

The systematic review is a scientific method for searching, finding, evaluating, and combining the results of primary studies regarding a certain issue. The results of the present study show that review studies are of different types, and the most important type is the systematic review whose method of preparation and performance was presented in the current study. In order to optimally carry out review studies and prevent bias, developing the relevant protocol is the first step. Subsequent steps are searching systematically for primary studies, evaluating and selecting the right studies, and analyzing, combining, and interpreting the final results. The Cochrane Handbook is a collection of valuable information on how to carry out systematic reviews in medicine and health, and facilitates their performance and publication.

Conflict of Interests

Authors have no conflict of interests.

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