How to appraise a systematic review

Systematic reviews are a vital tool in evidence-based practice, allowing a comprehensive synthesis of research evidence. This article provides guidance for appraising systematic reviews and resources for more detailed assessments.

Systematic reviews are the cornerstone of evidence-based medicine (Higgins and Green, 2011). Healthcare literature represents a large and heterogeneous resource, from which professionals must be able to obtain sufficient information to guide their practice (Mulrow, 1994). Traditional narrative reviews, which would involve a non-systematic assessment of a literature base, have significant scope for bias; a famous example of such an approach is a work on vitamin C and health, published by a Nobel laureate, which was later found wanting by a systematic review (Knipschild, 1994; Greenhalgh, 2010a).

The purpose of this article is to provide guidance for appraising systematic reviews. A brief overview of the nature and aim of a systematic review is provided, followed by a discussion of the concept of bias, the elimination of which is a central purpose. After this, a summary of key points to consider when appraising reviews is outlined. Finally, the broader aspects of a review that relate to implementation of findings are discussed.

Numerous publications and resources exist to guide the conduct of reviews. Familiarity with these resources is essential to appraisal. They are used here to guide the broad topics that should be considered when appraising a systematic review.

What is a systematic review?

A systematic review is a synthesis of available research literature on a given topic, designed so that the data incorporated are obtained and analysed in a structured, transparent and reproducible manner (Mulrow, 1994; Greenhalgh, 2010a; Higgins and Green, 2011). In the same way that a scientific researcher uses a structured method and experiment to elicit information from observation, so a systematic review uses a structured method to elicit information from the raw evidence base (Mulrow, 1994; Egger et al, 1997a). A systematic review begins with a focused, justified research question (Greenhalgh, 2010a). It involves a structured approach to selecting and searching databases, obtaining papers, selecting or rejecting papers for inclusion, appraising the quality of these papers, and synthesizing the findings to generate a coherent answer to the original question (Higgins and Green, 2011). A key consideration at every point in this process is the presence of bias, which is assessed and, where possible, eliminated.

Bias

Bias represents the potential of an unsystematic study or literature review to skew included data so that the findings reported do not accurately represent reality (Song et al, 2000). In a systematic review, bias is relevant at two levels. The first is at the level of paper selection (Song et al, 2000, 2010) and the second focuses on bias within individual studies. Such biases should be considered and incorporated into the study inclusion and assessment process (Higgins and Green, 2011).

A key strength of a well-conducted systematic review is the minimization of bias at the level of study inclusion, so that the overall synthesis accurately reflects research undertaken in the field. For example, a reviewer with pre-conceived ideas about an intervention may select papers for inclusion that support his/her own ideas (selection bias) (Ahmed et al, 2012). Similarly, a tendency to include only papers in a given language will restrict international research (language bias) (Egger et al, 1997b). As a result, the reviewer(s) must have clearly defined inclusion and exclusion criteria at the outset of the review, should aim to include all relevant work and, ideally, should have each study assessed by more than one person.

Beyond the bias that is present through the selection of published studies, further bias may exist through the fact that studies with positive findings are more likely to be published (publication bias) (Song et al, 2010; Ahmed et al, 2012), and are likely to be published more rapidly (time-lag bias) (Song et al, 2010). Active steps should therefore be taken by reviewers to minimize these forms of bias (through actively seeking out non-published findings), or to test for their presence.

By clearly defining study inclusion criteria at the outset, and by systematically and transparently applying them to the studies being considered, the scope for these forms of bias is reduced. Furthermore, specific statistical tests exist to assess for certain types of bias (Song et al, 2000; Dwan et al, 2008; Ahmed et al, 2012) in a review, which are key to conduct and reporting of the conducted study.

In addition to bias occurring through study selection, it may exist at the level of the individual study.

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Techniques to attenuate such bias depend on the study type. For randomized controlled trials (a common study type for incorporation in systematic reviews) these include systematic sampling, recruiting, randomization, follow up, outcome reporting and analysis (Torgerson and Torgerson, 2008). A further area of bias, which overlaps somewhat between the review-level and study-level biases, is outcome bias (Dwan et al, 2008; Moher et al, 2009; Song et al, 2010); published articles may only include data that showed significant findings, and fail to report other measures. A summary of the main sources of bias in systematic reviews is given in *Table 1*.

Despite the existing methods for addressing individual biases, and statistical tests to assess for their presence, published systematic reviews do not always make reference to them (Song et al, 2010; Ahmed et al, 2012). As a result, in the same way that a reader must be prepared to appraise the conduct of a study before accepting the outcomes, so the same approach should be taken to a systematic review. An outline approach to appraisal is provided below, based on the key resources cited above.

Structured approach to appraising systematic reviews

As with any piece of scientific research, the key to appraisal is a critical assessment of the overall work, assessing the research question and design, appropriateness of specific decisions made, and with consideration to the impact of the work on practice (Greenhalgh, 2010b). Nevertheless, checklists, which allow a structured approach to assessment, and prompt consideration of key concepts according to study type, are valuable (Critical Appraisal Skills Programme, 2010). Three such checklists follow; a simple 'overview' list from the Cochrane collaboration, a series of important questions from the Critical Appraisal Skills Programme and a more detailed series of specific prompts, derived from the PRISMA statement (PReferred Items for reporting Systematic reviews and Meta-Analyses).

The Cochrane collaboration is an international body that conducts, coordinates and archives systematic reviews of interventions in a consistent and structured manner. The organization's handbook, which contains instructions for conduct and reporting of systematic reviews, is available online and in hard copy (Higgins and Green, 2011). In appraising the conduct of a review, the Cochrane collaboration recommends considering five basic characteristics, presented in *Figure 1*, which provide a broad overview of the main aspects for consideration in appraisal.

A second initiative, Critical Appraisal Skills Programme, is an international network of health-care researchers and organizations which aims to help students and health-care professionals appraise research and implement findings. Critical Appraisal Skills Programme documents, principles of appraisal and checklists are readily available online, for a number of different research techniques (Critical Appraisal Skills Programme,

Figure 1. Key characteristics of a well-conducted systematic review. From Higgins and Green (2009).

Does this review have:	A clearly stated set of objectives with pre-defined eligibility criteria for studies
	An explicit, reproducible methodology
	A systematic search that attempts to identify all studies that would meet the eligibility criteria
	An assessment of the validity of the findings of the included studies, for example through the assessment of risk of bias
	A systematic presentation, and synthesis, of the characteristics and findings of the included studies

Table 1. Key biases affecting systematic reviews

Name of bias	Description	How addressed
Selection (Ahmed et al, 2012)	Occurs when a non-systematic approach to article inclusion is used, so that obtained studies do not accurately reflect the research literature	A systematic approach to study inclusion
Publication (Song et al, 2010)	Decisions to publish research may be influenced by whether findings are positive, interesting or timely. Focusing only on published literature ignores potentially useful negative or dated research	Consulting the 'grey' literature, corresponding with researchers to obtain non-published data
Language (Egger et al, 1997b)	Limiting returned articles to English language has the potential to ignore useful research published in other languages, and skews the population to whom the research may be applied	Through avoiding language limits, and translating articles in other languages
Outcome (Dwan et al, 2008)	Within published studies, the included results may be limited to those with positive outcomes, limiting the reported data	As for publication bias, correspondence with researchers and consulting the grey literature may attenuate outcome bias
Study level biases (Higgins and Green, 2009)	Biases associated with conduct of trials, such as sampling bias, allocation bias, placebo effect	Individual studies assessed for the presence of these biases

2010). The Critical Appraisal Skills Programme checklist for systematic reviews includes ten questions in three sections, intended to help a reader 'make sense of a review', and further considers the wider application and local relevance of research findings. These questions are presented in *Table 2*.

A third, more detailed and structured approach to assessment of a systematic review may be found through the PRISMA statement. This is an expansion of the preceding QUOROM statement (QUality Of Reporting Of Meta-Analyses) (Moher et al, 2009), resulting from an international meeting of researchers, and presents a detailed list of factors that should be considered when conducting or reporting a systematic review. The statement and structured list can be found in journal sources (Moher et al, 2009) and are available online. These points are summarized in *Table 3*.

Types of studies included in a systematic review

Randomized controlled trials and meta-analysis

Systematic reviews are frequently associated with randomized controlled trials: studies in which the impact of an intervention on a population is assessed, while using randomization and blinding to alleviate bias. A clear review question exploring the evidence for the effect of an intervention may draw on randomized controlled trial data; studies use a common methodology and hence can be readily and meaningfully combined.

Meta-analysis refers to a group of statistical techniques in which comparable data across studies are pooled to produce a result for the whole set (Egger et al, 1997a). This may provide evidence of an effect that is not yet supported by any of the individual studies. A seminal example demonstrating the value of this approach was published by Antman et al (1992), with respect to β-blockers for secondary prevention of myocardial infarction. Combined data from a number of individual studies showed evidence for improved survival before any individual randomized controlled trial had provided sufficient evidence.

Table 2. Ten questions to help make sense of a systematic review

Section	Specific questions
Section A: Are the results of the review valid?	Did the review address a clearly focused question?
	Did the authors look for the appropriate sort of papers?
	Do you think the important, relevant studies were included?
	Did the review's authors do enough to assess the quality of the included studies?
	If the results of the review have been combined, was it reasonable to do so?
Section B: What are the results?	What are the overall results of the review?
	How precise are the results?
Section C: Will the results help locally?	Can the results be applied to the local population?
	Were all important outcomes considered?
	Are the benefits worth the harms and costs?

From Critical Appraisal Skills Programme (2010)

Other study types

A well-conducted systematic review with a meta-analysis is a gold standard approach to answering a specific research question relating to an intervention in a clearly

Table 3. Key points for consideration according to the PRISMA statement

Section	Sub-headings
Title	Title
Abstract	Structured summary
Introduction	Rationale
	Objectives
Method	Protocol and registration
	Eligibility criteria
	Information sources
	Search
	Study selection
	Data collection process
	Data items
	Risk of bias in individual studies
	Summary measures
	Synthesis of results
	Risk of bias across studies
	Additional analysis
Results	Study selection
	Study characteristics
	Risk of bias within studies
	Results of individual studies
	Synthesis of results
	Risk of bias across studies
	Additional analysis
Discussion	Summary of evidence
	Limitations
	Conclusions
Funding	Funding

PRISMA = PReferred Items for reporting Systematic reviews and Meta-Analyses. From Moher et al (2009)

defined population (Egger et al, 1997a). Nevertheless, systematic reviews are also conducted to explore other research questions, and hence may include other study designs such as observational (Higgins and Green, 2011) or qualitative methods (Thomas and Harden, 2008), or mixed methods study designs (Thomas et al, 2004).

While these approaches may not readily allow a meta-analysis, the principles of appraisal remain the same (Greenhalgh, 2010b). Are the included study designs appropriate to the question being asked? Is the synthesis of data appropriate to the included results? For mixed methods synthesis, each aspect of the study may be assessed individually, and then synthesized using a recognized theoretical approach; for example, thematic analysis may be used to combine intervention and qualitative data (Thomas et al, 2004). While this has the potential to add a level of complexity, and will result in variation between reviews, the basic principles of a good systematic review remain. The principles of critical appraisal of systematic reviews apply equally to reviews of interventional studies, observational studies, qualitative studies and combined methods.

Clinical and research context

The aspects described so far cover the appraisal of a systematic review as a stand-alone piece of scientific work. The purpose of the research, however, is ultimately to influence clinical practice (Bero et al, 1998; Haynes and Haines, 1998; Greenhalgh, 2010a). When appraising a review as a clinician, therefore, the clinical context must be considered – is the review relevant, incorporating up-to-date, feasible interventions in a realistic population? As a researcher, the review must be placed into the wider literature – is it based on reasonable hypotheses and does it contribute to the clinical research base? To some extent, these considerations are covered as part of the rationale, appraised in the PRISMA checklist (Moher et al, 2009), and section C of the Critical Appraisal Skills Programme key questions (Critical Appraisal Skills Programme, 2010). The wider clinical and research context of a review should, however, be actively considered as part of appraisal.

KEY POINTS

- Systematic reviews allow a coherent synthesis of a broad research base.
- A key aim of systematic reviews is the elimination of bias.
- Several resources exist to support the structured appraisal of systematic reviews; the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement and the Cochrane collaboration are two main examples.
- While commonly associated with randomized controlled trials, systematic reviews may also incorporate data from other research methods.
- A systematic review should be appraised in the wider clinical and research context.

Conclusions

Systematic reviews are vital for evidence-based medicine, allowing coherent conclusions to be drawn from a wide research base. A chief aim is the elimination or attenuation of bias, and the use of a structured, rigorous methodology supports this. The Cochrane collaboration's guidance and the PRISMA statement provide two important resources for appraisal of systematic reviews, and facilitate a structured approach. Issues of clinical and research context provide further aspects for consideration, particularly when applying findings to practice. **BJHM**

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