ScienceDirect

Available online at www.indianjrheumatol.com and www.sciencedirect.com

Review Article

Systematic reviews and meta-analysis demystified

Vinod Ravindran [a], Subramanian Shankar [b,*]

[a]Center for Rheumatology, Kozhikode, Kerala, [b]Dept of Medicine and Clinical Immunology, Medical Division, Command Hospital (Air Force), Bangalore 560007, India

ARTICLE INFO

Article history:
Received 10 April 2015
Accepted 14 April 2015
Available online 8 May 2015

Keywords:
Databases
Heterogeneity
PRISMA
Jadad score
Forest plot
Funnel plot

ABSTRACT

Systematic reviews and meta-analysis both form essential research in today's scientific world with plethora of primary research in every filed. A systematic review is an overview of primary studies which contains an explicit statement of objectives, materials, and methods and is conducted according to the explicit and reproducible methodology. When systematic reviews provide a quantitative (statistical) estimate of net benefit aggregated over all the included studies, it is termed meta-analysis. In this review important individual components of systematic review and meta-analysis have been discussed for the benefit of our readers.

1. What is a systematic review?

A systematic review attempts to collate all empirical evidence that fits pre-specified eligibility criteria to answer a specific research question. It uses systematic methods that are selected with a view to minimising bias, providing reliable findings from which appropriate conclusions can be drawn and decisions made.[1] The key features of a systematic review are (a) a clearly stated set of objectives with an explicit, reproducible methodology; (b) a well defined search strategy to identify all studies that would meet the eligibility criteria; (c) an assessment of the validity of the findings of the included studies and (d) systematic presentation and synthesis of the characteristics and findings of the included studies. Knowledge regarding the methodology of systematic reviews is an essential requirement to appraise published literature.[2]

2. What is the difference between a systematic review and a narrative review?

A systematic review, in contrast to a narrative review, provides a summary of medical reports on a specific clinical question, using explicit methods to search, critically appraise, and synthesise the available literature systematically. It is very useful in bringing together the vast number of independently conducted studies, often with conflicting findings, and synthesising their results. By providing a summary of all the studies addressing a specific clinical question in a clear explicit fashion, systematic reviews allow us to take into account the entire range of relevant findings from research on a particular topic, and not just the results of a couple of studies. They can be used to establish whether the scientific findings are consistent and generalisable across different populations, settings, and treatment variations, or whether they vary significantly by

* *Corresponding author.*
E-mail address: Shankarsid@gmail.com (S. Shankar).
http://dx.doi.org/10.1016/j.injr.2015.04.003

particular subgroups. The explicit methods used in systematic reviews reduce bias and permit reliability and accuracy of conclusions. By their ability to deal effectively with large amounts of information, systematic reviews can examine variations in treatment effectiveness or relationship strength and examine differences due to study methods, variation in settings or types of participants. They are thus superior to narrative reviews by being more objective and replicable.

3. How to perform a systematic review?

The aim of systematic reviews is to present a balanced and impartial summary of the existing research, enabling decisions on effectiveness to be based on all relevant studies of adequate quality. One has to take great care to find all the relevant studies (both published and unpublished), and assess the methodological quality of the design and execution of each one of them.

3.1. *Defining the clinical question*

Firstly, the research question should be clearly stated at the outset. It should include the relevant population or patient groups being studied, the intervention of interest, any comparators (where relevant), and the outcomes of interest. A structured approach for framing questions using the five components may help facilitate the process. This approach is commonly known by the acronym "PICOS" where each letter refers to a component: the patient population or the disease being addressed (P), the interventions or exposure (I), the comparator group (C), the outcome or endpoint (O), and the study design chosen (S). Keywords from the research question and their synonyms are usually used to identify studies for inclusion in the review. The question addressed by a systematic review needs to be defined very precisely, since the reviewer must make a dichotomous (yes/no) decision as to whether each potentially relevant paper will be included or, alternatively, rejected as "irrelevant." Thus, for example, the clinical question "Do glucocorticoids cause adverse events in patients with rheumatoid arthritis (RA)?" should be refined as an objective: "To assess the safety of glucocortioid therapy in patients with RA: comparison with placebo."

3.2. *Search strategy*

3.2.1. *Selection/exclusion of studies*

The validity of a systematic review or meta-analysis depends primarily on the validity of the studies included. The authors should state explicitly the type of studies they have included in their review, and the readers of such reports should decide whether the included studies had the appropriate study design to answer the clinical question. Further, all other attributes of the studies which would be included has to be pre-specified. For example; in a recent systematic review which determined the safety of glucocorticoids in RA, the investigators included only studies which; (i) were randomised controlled trials (RCTs), (ii) enrolled adult patients with RA, (iii) had at least one of the treatment groups was placebo, (iv) had double-blinded assessment, (v) lasted 1 year or longer, (vi) used prednisolone (or equivalent) and (vii) was published in English.[3]

3.2.2. *Databases*

It is well appreciated that single electronic database searches lack sensitivity and may miss relevant articles. It has been shown that only 30–80% of all known published RCTs would be identified using MEDLINE. A comprehensive search is therefore important, not only for ensuring that as many studies as possible are identified but also to minimise selection bias for those that are found. Relying exclusively on one database may retrieve a set of studies that might be unrepresentative of all studies that exist and that could have been identified through a comprehensive search of multiple sources. Hence, in order to retrieve all relevant studies on a given topic, several sources should be searched to identify relevant studies (both published and unpublished), and the search strategy should not be limited only to the English language. The aim of an extensive search is to avoid the problem of publication bias which occurs when trials with statistically significant results get published and cited, preferentially in English language journals and indexed in Medline. For example in a systematic review and meta-analysis of the therapy for psoriatic arthritis the investigator's search consisted of searching the Medline, PubMed and EmBase databases, Cochrane clinical trials register and Cochrane database for systematic reviews and manual search of bibliographies of articles thus found and of previously published reviews.[4]

3.2.3. *Data extraction*

The data extraction should be done using a predefined proforma. There is evidence that using at least two reviewers has an important effect on reducing the possibility that relevant reports will be discarded. In case of a disagreement, consensus through discussion could be aimed at or a third reviewer may give final judgement. For missing data the protocol may prespecify contacting the corresponding author of included study.

3.3. *Quality assessment*

Once all relevant studies have been identified, decisions must be taken about which studies have been sufficiently well conducted to be worth including. This process can introduce bias, hence good meta-analyses will use explicit and objective criteria for inclusion or rejection of studies on quality grounds. A minimum of two reviewers should independently assess the quality of the included studies to reduce the risk of selection bias. Among the several scales for assessing the quality of the individual clinical trials, two scales that are commonly used are those developed by Chalmers et al.[5] and Jadad et al.[6] Perhaps more important than the scale used is whether a scale has been used at all. Once a quality score has been assigned, the impact of excluding low quality studies can be assessed by sensitivity analysis when doing meta-analysis.

3.4. *Tabulation and depiction*

Included studies should be tabulated in most comprehensive manner possible. All relevant details such as study identifier (name of the first author and year), study details (e.g. number of patients, disease duration, interventions, dose of drug etc.), quality (e.g. Jadad score) should be included in the table. This helps the reader at a glance to get the gist of key study characaristics. This type of all inclusive table is also essential to