REVIEW ARTICLE

UNDERSTANDING SYSTEMATIC REVIEW AND META-ANALYSIS : TO GENERATE BEST EVIDENCE BASED PRACTICE

ABSTRACT

The aim of this article is to provide an understanding to systematic review and meta-analysis and to explain its various steps. A systematic review is intended to appraise and synthesize the best available research evidence on a defined research question by using explicit methods to search, critically appraise and synthesise the available literature systematically. After a systematic review, data from individual studies may be pooled quantitatively and can be re-analysed using established statistical method which is called meta-analysis. The purpose of pooling searched literature is to improve the statistical power of the analysis as well as the precision of the estimates of treatment effects.

KEYWORDS: Systematic review, meta-analysis, evidence-based practice

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INTRODUCTION

Multiple research studies are available on a single research question by different researchers at various locations. Many of these may have different findings making a clinician puzzle what is best answer of the research question. It is very demanding for researchers and medical professional to keep up dated with the best available literature. So reviews, summarizing the outcomes of various experimental studies are therefore effective and efficient method for obtaining the best evidence related to specific research question/ problem. Systematic review is the best method to get confidence in level of evidence[1] amongst all research methods (figure 1).

A systematic review attempts to collect and analyze all evidences that answer a specific clearly defined question. Systematic reviews typically involve a detailed and comprehensive plan and search strategy, with the goal of reducing bias by identifying, appraising, and synthesizing all relevant studies, sometimes with conflicting findings on a particular topic or research question.[2] A systematic review is a review of a clearly formulated question that uses systematic and reproducible methods to identify, select and critically appraise all relevant research, and to collect and analyse data from the studies that are included in the review. [3]

Following a systematic review, data from individual studies may be pooled quantitatively and re-analysed using established statistical methods. This technique is called meta-analysis.[4] The rationale for a meta-analysis is that, by combining the samples of the individual studies, the overall sample size is increased, thereby improving the statistical power of the analysis as well as the precision of the estimates of treatment effects.

aMeta-analysis is a two stage process. The first stage involves the calculation of a measure of treatment effect with its 95% confidence intervals (CI) for each individual study. Next step is summary statistics that are usually used to measure treatment effect include odds ratios (OR), relative risks (RR), and risk differences.[5]

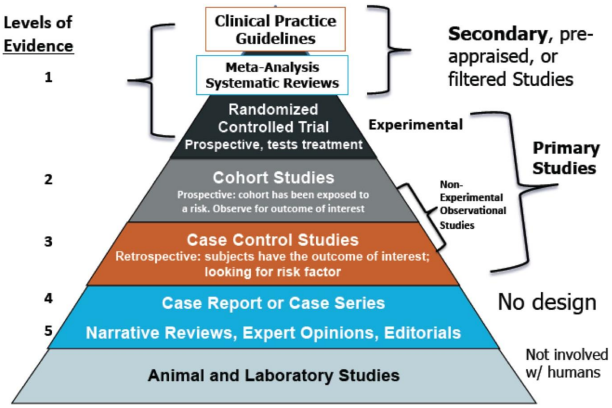

Figure 1: Showing Systematic review and meta-analysis on the top in levels of research evidence

The characteristics of a systematic review:

- Clearly stated set of objectives with predefined eligibility criteria for studies;
- Explicit, reproducible methodology;
- Systematic search that attempts to identify all studies that meet the eligibility criteria;
- Assessment of the validity of the findings of the included studies; and
- Systematic presentation and synthesis of the attributes and findings from the studies used.

Although systematic reviews are published in academic forums, there are also organizations and databases specifically developed to pro-mote and disseminate them. For example, Campbell and Cochrane are widely used in the medical field that promotes, supports, and disseminates systematic reviews and meta-analyses on the efficacy of interventions.[6]

A systematic review can be two types:

- A quantitative systematic review will include studies that have numerical data.
- A qualitative systematic review derives data from observation, interviews, or verbal interactions and focuses on the meanings and interpretations of the participants. It will include focus groups, interviews, observations and diaries.

STEPS OF A SYSTEMATIC REVIEW

A systematic review involves the following steps:

1. **Check for existing reviews.**

The first step for conducting a systematic review is to get and go through with the existing reviews on the topic and assess their depth and quality. It helps to refine and formulate review question.

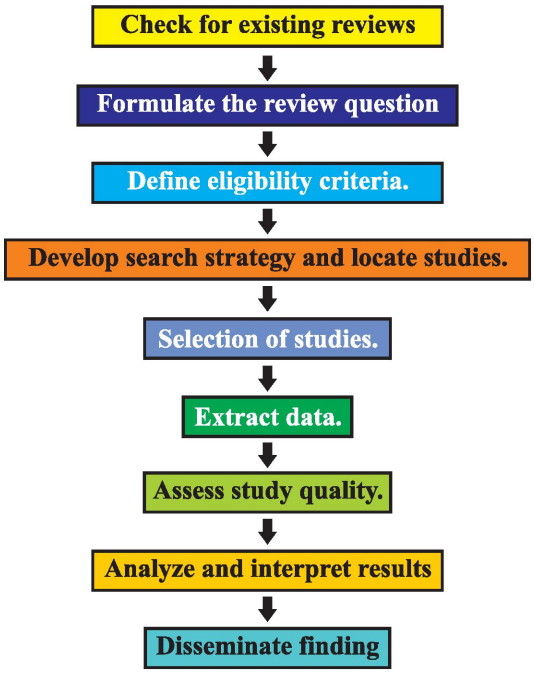

Figure 2: Steps of systematic reviews

2. **Formulate the review question.**

This step involves defining the review question, forming hypotheses, and developing a review title. It is often best to keep titles as short and descriptive as possible, by using the following formula: Intervention for population with condition (e.g., Dialectical behavior therapy for adolescent females with borderline personality disorder). If authors decide to conduct their systematic review through the Cochrane Collaboration, they need to register their title in the appropriate review group and can get access to further Cochrane support.

3. **Define eligibility criteria.**

The Cochrane acronym PICO which stands for population, intervention, comparison, outcomes can be useful to ensure that one decides on all key components prior to starting the review. For example, authors need to decide a priori on their population age range, conditions, outcomes, and type(s) of interventions and control groups. It is also critical to operationally define what types of studies to include and exclude (e.g., randomized controlled trials-RCTs only, RCTs and quasi-experimental designs, qualitative research), the minimum number of participants in each group, published versus unpublished studies, and language restrictions. For Cochrane Reviews, this information gets prepared, peer-reviewed, and published in a Protocol format first, which is then replaced with the full Review once it is completed.

P	I	C	O
Population Patient Problem	Intervention Or Exposure	Comparison	Outcome
Who are the patients? What is the problem?	What do we do to them? What are they exposed to?	What do we compare the intervention with?	What happens? What is the outcome?

4. **Develop search strategy and locate studies.**

This step involves developing and running electronic searches. Generally, it is important to come up with a comprehensive list of key terms (i.e., "MeSH" terms) related to each component of PICOC to be able to identify all relevant trials in an area. For example, if the age range is 13-18 year old females, search terms may need to include any of the follow-ing: adolescents, teenagers, youth, female, women, girls, etc. The key in developing an optimal search strategy is to balance sensitivity (retrieving a high proportion of relevant studies) with specificity (retrieving a low proportion of irrelevant studies). Searches generally include several relevant electronic databases but can also include checking article refer-ence lists, hand-searching key journals, posting requests on listservs, and personal communication with experts or key researchers in the field.

5. **Selection of studies.**

Once a comprehensive list of abstracts has been retrieved and

reviewed, any studies appearing to meet inclusion criteria would then be obtained and reviewed in full. This process of review is generally done by at least two reviewers to establish inter-rater reliability. Authors are advised to keep a log of all reviewed studies with reasons for inclusion or exclusion, and it may be necessary to contract study authors to obtain missing information needed for data pooling (e.g., means, standard deviations).

6. Extract data.

It can be helpful to create and use a simple data extraction form or table to organize the information extracted from each reviewed study (e.g., authors, publication year, number of participants, age range, study design, outcome, included/excluded). Data extraction by at least two reviewers is important again for establishing inter-rater reliability and avoiding data entry errors.

7. Assess study quality.

Although there are short checklists available such as the 5-point Oxford Quality Rating Scale (Jadad et al., 1996)[7] commonly used in Cochrane reviews, this measure is heavily influenced by double-blinding which is appropriate for drug trials but generally not for psychological or non-pharmacological interventions. There are other more comprehensive recommended guidelines and standards available such as the Consolidated Standards of Reporting Trials (CONSORT Statement), as well as articles providing recommendations for improving quality in RCTs and meta-analyses for psychological interventions (e.g., Uman et al., 2010).[8]

8. Analyze and interpret results.

There are various statistical programs available to calculate effects sizes for meta-analyses, such as the Review Manager (RevMan) program endorsed by the Cochrane Collaboration available online. Effect sizes are stated along with a 95 % confidence interval (CI) range, and presented in both quantitative format and graphical representation (e.g., forest plots).

A forest plot, also known as a blobbogram, is a graphical display of estimated results from a number of scientific studies addressing the same question, along with the overall results. It visually depict each trial as a horizontal diamond shape with the middle representing the effect size (e.g., SMD) and the end points representing both ends of the CI. These diamonds are presented on a graph with a centre line representing the zero mark. Often the left side of the graph (< zero) represents the side favoring treatment, while the right side (> zero) repre-sents the side favouring the control condition. At the bottom of the graph is a summary effect size or diamond representing all of the individual studies pooled together. Example of a forest graph is shown below:

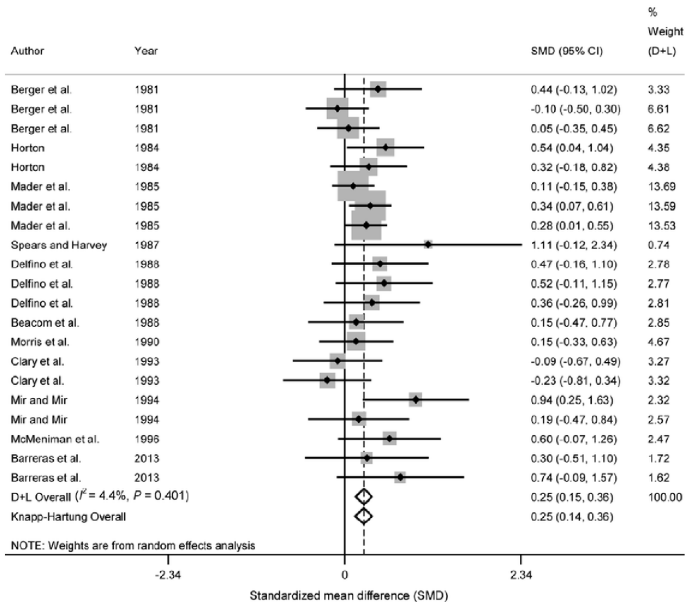

Figure 3: Example of a forest graph

Ideally, researcher would like to see this entire diamond (effect size and both anchors of the CI) falling below zero, indicating that the inter-vention is favoured over the control. In addition, most programs also calculate a heterogeneity value to indicate whether the individual studies are similar enough to compare. In this case, it is preferable to have non-significant findings for heterogeneity. It is still possible to pool studies when significant heterogeneity exists, although these results should be inter-preted with caution or reasons for the heterogeneity should be explored. As with all papers, the last step in the writing process involves summarize the findings, and providing recommendations for clinical work (e.g., which interventions are efficacious, for whom, and under what conditions) and research (e.g., what areas/topics/interventions require further research.

9. Disseminate finding

Although reviews conducted through the Cochrane Collaboration get published in the online Cochrane Database of Systematic Reviews, they are often quite lengthy and detailed. Thus, it is also possible and encouraged to publish abbreviated versions of the review in other relevant academic journals. Plain language summaries for families and patients are also commonly provided, and there is an expectation that reviews should be regularly updated to ensure they are always up-to-date and relevant. Indeed, participating in a review update or joining a well-established review team, can be a helpful way of getting involved in the systematic review process.

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