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Abstract

Each year millions of papers are published reporting the results of medical research, making it virtually impossible for clinicians to keep up to date with the latest developments. However, it is important that clinical practice is based on the best available evidence and that effective treatments should be introduced as quickly as possible for the benefit of patients. Systematic reviews are different from traditional literature reviews because they aim to identify all studies (published and unpublished) that address a specific question and their methodology has been developed to minimize the effect of selection, publication and data extraction bias. In this guide to systematic literature reviews, the methods of conducting systematic reviews are discussed in relation to minimizing bias, searching the literature and investigating heterogeneity.

Introduction

In 1992 Lau et al.¹ published a cumulative meta-analysis of randomized controlled trials of thrombolytic therapy following acute myocardial infarction (AMI) and then compared the results of this analysis to the recommendations for the management of AMI.² Using cumulative meta-analysis they found that by 1973 there was clear, statistically significant evidence from 33 randomized

clinical trials (RCTs) that thrombolytic therapy reduced mortality following AMI (odds ratio 0.73 (95% confidence interval 0.59, 0.92)). Yet it was not routinely implemented in clinical practice until 13 years later. One of the reasons for this delay was that many of the studies included in the meta-analysis had small sample sizes and consequently the individual trials were underpowered for detecting a statistically significant treatment effect. By combining the results of the small trials together using meta-analysis it was possible to detect a statistically significant protective effect of thrombolytic therapy.

Section snippets

The Cochrane Collaboration

In 1993, Archie Cochrane founded the Cochrane Collaboration, an independent, not-for-profit organization that produces systematic literature reviews of interventions in healthcare³ that are published in the Cochrane Library. It has over 10,000 reviewers internationally⁴ and is organized into review groups, each with a specific area of interest. Each review group has an editorial board and a number of researchers responsible for supporting reviewers in the process of conducting their review.

What makes systematic reviews different from other literature reviews?

Literature reviews appear in most introductions and discussion sections of research reports, case reports and expert opinion papers. All of these types of literature review may be affected by selection bias because the authors are likely to include only major studies in a particular area, and only those that are most consistent with their personal opinion or the results of their research. Moreover, it is known that positive studies (those with statistically significant findings either of

Minimizing bias in systematic reviews

Selection bias in systematic reviews can arise when the inclusion and exclusion criteria for the review are not clearly established a

priori or where they restrict inclusion of studies in a way that might bias the findings; for example, by excluding papers not published in English. The first stage in conducting a systematic review is to develop a protocol that clearly defines: 1) the aims and objectives of the review; 2) the inclusion and exclusion criteria for studies; 3) the way in which

Searching the literature

Search strategies for systematic reviews must be designed to identify *all* studies that have been conducted addressing a specific question. This means that the search strategy needs to be sensitive rather than specific. A specific search strategy identifies more relevant than irrelevant papers but might miss some important papers. A sensitive search strategy is less likely to miss relevant studies but might identify a reasonably large number of irrelevant studies as well. Search strategies for

Meta-analysis

Meta-analysis is a statistical method for combining the results of studies identified using systematic review methodology, to give a pooled measure of treatment effect. It is particularly useful when there are a large number of small, underpowered studies where combining the results increases the power and therefore precision of the estimate of treatment effect. There are a number of different methods of conducting meta-analysis and the method used will depend on the type of outcome data,

Heterogeneity

The term heterogeneity generally refers to the variability in the results of studies included in a meta-analysis. Heterogeneity may arise from differences in study populations or interventions (clinical heterogeneity) or from differences in study methodology (methodological heterogeneity). It is usually possible to see on a forest plot if there is statistically significant heterogeneity because the 95% confidence intervals (the horizontal lines) of individual trials will not overlap to any

There is a lack of studies meeting your inclusion criteria – what next?

With the popularity of systematic reviews increasing dramatically over the past 15 years there seems to be an increasing number of published reviews concluding that only one study was identified, or that there were no studies fulfilling the inclusion criteria. This is not an uncommon problem in reviews of the effectiveness of surgical interventions that are aiming to identify RCTs. In a 'gold standard' systematic review of intervention, authors would report a lack of evidence from RCTs and

Summary

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Systematic reviews are designed to identify all research related to a specific subject, which might be effectiveness of interventions, incidence or risk factors for disease, diagnostic test accuracy or patient experience.
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Systematic reviews are protocol-driven and rigorously conducted.
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Methods used in conducting systematic reviews have been developed to minimize the risk of selection, publication and data extraction bias in the review.
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Meta-analysis can be used to combine the result of individual