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Systematic Review of Observational Studies

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Introduction

The biomedical literature is constantly growing, and it can be difficult to keep abreast of the large amounts of research relevant to one's practice [1, 2]. Systematic reviews and meta-analyses are evidence-based approaches that are often applied to both observational, retrospective and cohort studies, as well as to randomised controlled trials. They provide a means of synthesising this large body of biomedical evidence [2]. Furthermore, they overcome many of the shortcomings of less rigorous reviews. This article provides a brief overview of the systematic review process.

The Need for Literature Reviews

The literature comprises a large amount of evidence relating to particular health problems. This information is not of equal quality and so not all provide the same level of evidence. The information is also often conflicting. Review articles synthesise a large amount of information on a particular health problem, and as such are useful for students, researchers, health professionals and policy makers.

Although useful, traditional reviews are subject to a number of biases [2]. Firstly they are influenced by selection bias. It may be that the author's perspective on the overall body of evidence is limited to highly cited or more commonly available literature. When the results of these studies are different to the results of studies less commonly cited or in less available literature, biased results can occur. Another problem is that the weighting of study results may be undertaken in a subjective manner, meaning that the authors may weight the evidence of a particular study based on their own interpretation or bias. In addition, the authors may provide a misleading interpretation of the study findings. In many of these reviews, there may also be a failure to examine whether particular characteristics of some studies may explain inconsistencies between study findings [2]. Such characteristics may relate to geographic region or even age and sex distribution.

Systematic Reviews

The rationale for conducting a systematic review is to provide a summary of a health issue that is free from the biases raised above. The Cochrane Collaboration has developed methods for conducting systematic reviews of interventions and some observational studies [3]. These methods can be equally applied to reviews of descriptive studies. The steps in conducting a systematic review are outlined below, and the specific criteria for a systematic review are summarised in table 1. At each step, the corresponding approach used in a review of stroke incidence studies has been provided to demonstrate how these principles can be applied to a descriptive study [4].

Review Question and Eligibility

The first step in conducting a systematic review is to define the review question and to outline the eligibility criteria for including studies. For descriptive studies, the review question will state the types of participants included, such as age, gender, disease, diagnostic criteria and setting. Feigin et al. [4] proposed to update knowledge of stroke morbidity and early case-fatality and to review secular trends in stroke incidence and case fatality. All population-based studies with comprehensive case ascertainment were included. Most of the criteria related to those of 'ideal' stroke incidence studies [5], but the authors also needed to calculate specific rates. This necessitated a decision to include only those studies that published the appropriate raw numbers to calculate these figures. Adding to the rigour of the analysis by increasing the number of studies that could be used, Feigin et al. [4] obtained some of these missing data from the authors of the original articles.

Finding Studies That Meet the Eligibility Criteria

A systematic approach to finding eligible studies is required. In their review, Feigin et al. [4] searched Medline, Scopus, PubMed, and Science Direct from 1950 to May 2008 for publications in the English language. The search strategy included words such as 'stroke', 'ischaemic stroke', 'population-based', 'incidence' and 'case fatality'. The search strategy was likely to unearth the majority of studies relevant to their topic. However, because studies published in languages other than English were not included, there may be some bias introduced if the findings from studies published in other languages differ to those studies that were included.

Tabulate Characteristics

Each study should be tabulated using a specifically designed data collection form. This enables systematic extraction of study methods, including an assessment of eligibility and quality. It is also necessary in some instances to justify why some studies are excluded. In the Feigin et al. [4] review of stroke incidence studies, 3 authors independently graded the articles for eligibility, and any disagreements were resolved by discussion. They excluded data from incidence studies conducted prior to 1970, because only 1 study had been conducted prior to this, and so there were no other population-based studies for comparison [4]. Providing details of studies that are excluded is an important part of the review process.

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Table 1. Criteria for a systematic review

– Usually focussed on one clinical question
– Comprehensive search of many databases including the grey literature
– Search strategy is explicitly stated in the study methods
– Selection process is based on explicit criteria that are uniformly applied
– Rigorous appraisal of articles, usually including the use of a data extraction form
– Usually includes an assessment of data quality on the data extraction form
– When possible, quantitative meta-analysis is undertaken to synthesise data from different studies
– Interpretations are usually evidence-based

Assessing Bias

It is important to assess potential biases of studies that are to be included in the review [6]. This usually comprises assessing whether treatment assignment was random, the allocation group was concealed, participants and study personnel were blinded to the treatment group, and outcome data were complete or near complete with all outcomes being reported. In observational studies, the bias may instead be an assessment of whether incident cases are obtained from all potential sources, or whether they are biased to the more or less severe cases.

Conduct a Meta-Analysis

The data from eligible studies should be analysed and a meta-analysis undertaken where possible. The advantage of conducting a meta-analysis is that it enables one to determine the direction and size of the average effect, and the precision and robustness of the effect. Similar analysis can be undertaken in descriptive studies, including the assessment of differences between subgroups. When assessing incidence of stroke subtypes, Feigin et al. [4] found that the incidence of intracerebral haemorrhage in low- and middle-income countries was approximately double that in high-income countries. This type of analysis is different to a sensitivity analysis where different methods might be used to assess the same outcome.

Assess Reporting Bias

Different sorts of reporting bias may occur in the literature [7]. These include biases resulting from non-publication of research findings, lack of access to particular journals, restriction to particular languages, or because of selective reporting of particular outcomes. Studies with larger effects tend to be published more often than those with no effect or where the effect is in an opposing direction. Funnel plots can be used to assess selection bias from these sources [8, 9].

Presenting Results and Summaries

The results of systematic reviews are usually summarised using forest plots. These summarise data from individual studies as well as the combined findings. These forest plots include tabulation of the number of events in each group, the study weight, heterogeneity and summary effect. Summary tables are also provided for the overall findings of the review.

Interpreting the Results

When interpreting results, it is important to consider and report the overall quality of each outcome reported [3, 10]. These are based on a number of factors including the types of studies included in each outcome assessment, the variation of effects between studies, the presence of potential bias and the presence of a dose-response relationship.

Further details on how to report meta-analyses of observational studies are provided in a very nice overview by Stroup et al. [10].

Conclusions

The Cochrane approach to conducting systematic reviews includes a number of techniques to minimise bias. The systematic approach is applied to randomised controlled trials and observational studies. The approach can be further extended to include descriptive studies. Meta-analyses involve a statistical summary of the results of the separate studies and the calculation of an overall summary effect. The studies are weighted according to their size, so that the larger studies that contribute more information have a greater influence.

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