# SYSTEMATIC REVIEWS OF THE LITERATURE

# The Overview and Meta-analysis

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## INTRODUCTION TO THE INFORMATION PROBLEM

The process of being a continual learner in this information age is a significant challenge. This challenge is especially significant for the health care provider who realizes that patient care is not a stagnant undertaking but an evolving process in which the responsibility to act in the patient's best interest requires continual infusion of new knowledge and skills. For others, who are possibly less motivated to stay upto-date, state licensure organizations impose expectations of continuing education that strongly suggest it is in the publics' best interest for professionals to improve their knowledge continually to provide adequate patient care. For all dental practitioners, staying up-to-date is a challenge because of the vast amount of clinical research available. At the heart of the problem is the difficulty in finding a focused answer that has the best chance of truthfully informing clinicians to act in the patient's best interest regarding a specific clinical dilemma.

The dilemma associated with the sheer volume of the literature available is illustrated by a recent publication<sup>15</sup> that focused on a specific area of dental care, the dental implant literature. In this study, the authors wanted to estimate the quantity of dental implant literature available from the MEDLINE database between the years 1989 through 1999 that could be used to guide evidence based decisions. The search

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strategy was designed to identify the best evidence related to the categories of etiology, diagnosis, therapy, and prognosis in implant care. The results for this single area of dentistry reinforced the notion of an information explosion. The search provided an amount of clinically relevant information regarding implants that would require a clinician to read between one and two articles a week for 52 weeks out of the year just to stay current with the progress in dental implants. For the practitioner also interested in staying current in other areas, such as prosthetic, surgical, periodontal, endodontic, and direct restorative procedures, staying current could indeed be difficult.

To determine whether this volume of literature is characteristic of all aspects of dentistry or only of special dental subjects such as dental implants, another study<sup>16</sup> investigated trends in dental and medical research publications and the proportion of high-quality clinical studies (randomized, controlled trials [RCTs]) of relevance to general dentistry. In this study, the authors conducted a MEDLINE search of the literature published between 1969 and 1999 and found that clinical trials in dental research had increased to 7% and RCTs had increased to 5% of all dental research during this period. Although the overall number of research publications decreased during this period, the proportion specifically related to outcomes of patient care had increased. Thus, more of the literature currently published focuses directly on patient care and might be important for clinicians to read. Between 1979 to 1999, the authors found that one of every 200 research publications was an RCT, studies which by nature of their design have the best chance to provide valid and reliable information. These trials were relevant to between 60% of the dental care activities for adults and 80% of those for children.

Together these findings suggest that more high-quality information is available to clinicians than ever before. In a professional life that leaves little time for reviewing the increasing numbers of potentially useful research reports, how does the conscientious clinician of today find the highest quality and most relevant reports among the hundreds of others.

# A SOLUTION FOR THE BUSY PRACTITIONER

One solution is for the clinician to seek reports that synthesize numerous sources of clinical information into summary statements or recommendations regarding specific clinical questions or controversies. These articles can save the clinician time and effort spent sorting through numerous primary research reports. Such research syntheses go by various names and can take a variety of forms. The familiar literature review is a narrative summary of some clinical topic or group of topics, often provided by an expert in the field and usually characterized as an unsystematic compilation of opinion and evidence. Although it intuitively seems correct that experts should be able to inform clinicians about a topic they have studied intensively, it has been shown that they are less able to produce objective reviews of the literature in their subject than are nonexperts.<sup>11</sup> More reliable are the reviews that take a systematic approach in providing an overview of the relevant and important primary research regarding a specific clinical question. (In this context, *primary research* refers to the research reports that contain the original information on which the review is based.) Such a systematic review is an overview of the primary research that has an explicit statement of the objectives, materials, and methods and has been conducted following a previously established rigorous and reproducible methodology.<sup>5</sup> When the systematic review includes a statistical synthesis of the numerical results of several trials that examined the same question it is termed a meta-analysis.

Systematic reviews are now considered the most reliable method for summarizing large volumes of research evidence. These reviews are less prone to subconscious and subjective forms of bias often seen in reports by experts because they follow principles of research design similar to those found in primary research. The fundamental difference between the primary research study and the systematic review is the unit of study. The scientific principles of a systematic review-documentation of methods before beginning, a comprehensive search identifying all relevant studies, and the use of rigorous methods for appraisal, collection, and synthesis of data-limit the bias in identifying and rejecting studies and provide more reliable and accurate conclusions. The usefulness of overviews and meta-analyses is reflected in the increasing numbers of review publications and in the efforts of groups, most notably the Cochrane Collaboration, to prepare, maintain, and disseminate results of systematic reviews of health care. The Cochrane Collaboration is an international initiative for systematic review management and currently has an Oral Health Group that encourages participation by interested individuals.

## ANATOMY OF A SYSTEMATIC REVIEW

The specific features that illustrate the systematic approach and improve the chance of providing the best synthesized evidence are

- Preparation of a detailed research protocol that outlines the clinical question of interest
- · Selection of criteria for inclusion of articles in the review
- Systematic search of relevant published and unpublished research
- Determination (by two reviewers) of articles that meet predefined inclusion criteria
- Critical appraisal of the quality of selected articles
- · Extraction of outcome data from the selected articles
- Data combination (where appropriate) to synthesize and summarize the best evidence
- Report of findings relative to the knowledgebase and new questions raised by the findings

A systematic review has distinct advantages over an unsystematic approach.<sup>6</sup> The authors must describe where the data (the published trial) come from and how they were processed to arrive at the conclusions. Being explicit about the methods taken to identify and select the appropriate trials for processing is important in limiting bias and provides more accurate and reliable synthesized information from the volumes of related literature. Also, with a systematic review, large amounts of information can be assimilated in a timely manner, resulting in shorter delays between research discoveries and implementation of demonstrated effective patient-management methods. Results of different studies can be more formally compared, inconsistencies among studies can be identified, and the causes for the inconsistencies can be evaluated. When possible, quantitative systematic reviews, or meta-analyses, can provide more precise answers by combining overall results of many similar trials, increasing confidence in the clinical application of the results.

A summary of some recent dental systematic reviews illustrates the important steps in this process. The importance of the search for uncovering all potential sources (articles) that can contribute to the results is highlighted by recognizing that a simple MEDLINE search alone is inadequate for this phase of the systematic review process. One recent report<sup>9</sup> describes a process that included a review of 25 electronic databases, the Worldwide Web, relevant journals that were also hand-searched, and authors in the field who were personally contacted for additional information. Personally contacting authors is an important attempt to address potential publication-bias problems. This form of bias, which results from the selective publication of studies based on the direction and magnitude of their results, is harmful if important negative studies are not published.<sup>10</sup> Because systematic reviews pool results, conclusions derived in the absence of truthful negative studies could lead to overestimation of treatment effectiveness.

Another review provides a good illustration of several key features of the systematic process. In this recent report of the effectiveness and cost-effectiveness of prophylactic removal of wisdom teeth, the authors wanted to provide a summary of existing evidence on prophylactic removal of wisdom teeth in terms of the incidence of surgical complications and the morbidity associated with wisdom tooth retention.<sup>18</sup> The inclusion criteria were in three main categories: design (RCT, literature review, or decision analysis), patient characteristics (unerupted or impacted wisdom teeth, or those having wisdom tooth extraction prophylactically or because of disease), and reported outcomes (either pathologic changes associated with retention of wisdom teeth or postoperative complications following extraction). The data sources included an existing review that formed the basis for the report, six electronic databases, paper sources (including Clinical Evidence), web-based resources, and relevant organizations and professional bodies that were contacted for further information. For non-English papers, translators were recruited to assist with study selection and data extraction. Decisions regarding study selection, data extraction, and validity assessments were made by two independent reviewers; when the reviewers disagreed, discussion took place to gain consensus. The process of assessing validity followed a previously established checklist that was used to evaluate data organized into structured tables. This process resulted in 40 studies being included in the review: two RCTs, 34 literature reviews, and 4 decision analysis studies. The authors' method of dealing with such a mix of data sources is instructive. Specifically, it was stated that the methodologic quality of the literature reviews (no systematic reviews were included) was generally poor. Although most of the reviews suggested that prophylactic removal was not warranted, the three reviews that did suggest such removal was justified were of poorer methodologic quality than most other reviews. When reviews include primary research with less-than-optimal designs, Slavin<sup>17</sup> emphasizes the need to report more details about the studies.

Another study faced a similar situation involving questions of study-design related to research synthesis. This study used an alternative method manner for selecting the articles to be included when the primary criteria were not met.<sup>14</sup> The aim of this review was to assess the clinical evidence for the ability of glass-ionomer restoratives to inhibit secondary caries. A total of 52 articles that met previously established inclusion criteria were evaluated. Primary and secondary lists of systematic criteria for methodologic quality were drawn up. After applying the primary list of 14 criteria to each article, none was found to be acceptable. The secondary list, which included design features of a prospective trial with an appropriate control group, was then applied to the 52 articles and yielded 28 suitable for data extraction and evaluation.

The methodology used in creating a systematic review and the syntheses such reviews provide make them useful for clinicians who do not have the time to review all the primary studies related to a clinical question of interest. Because systematic reviews offer the best chance for busy clinicians to act in their patient's best interest, it is important to know how to evaluate them.

#### WHAT TO LOOK FOR IN A USEFUL SYSTEMATIC REVIEW

A number of helpful descriptions for evaluating the validity of systematic reviews have been presented in the literature.<sup>3, 7, 13</sup> The important questions to consider when assessing a systematic review<sup>12</sup> are

- Was a clinical question clearly stated and addressed?
- Were the search methods comprehensive enough to find all relevant articles?
- Were explicit methods used to evaluate which articles to include in the review?

- Was validity of the articles assessed, and was this assessment reliable and free from bias?
- Were inconsistencies in the findings of the included studies analyzed?
- Were the findings of the primary studies combined appropriately?
- Were the reviewers' conclusions supported by the data?

Without a clear statement of the clinical question it addresses, clinicians have no idea if the review can help with their patients' needs. For clarity, questions must include specification of the patient population involved, the intervention or exposure studied (often with a comparison or standard treatment group), and the outcomes evaluated. Even a good question cannot be adequately answered if all pertinent articles are not found to evaluate. The reader therefore must be reasonably assured that all relevant and important literature has been included in the review. It is likely that comprehensive searches will include (1) use of one or more bibliographic databases, (2) a search for reports that cite the important papers found through a database such as Science Citation Index, (3) perusal of the references of all relevant papers found (and often the references of the references), and (4) personal communication with authors and organizations active in the area being reviewed.

A comprehensive search will probably yield many articles not useful for review. An article may be unsuitable because it does not directly relate to the question of interest or because a certain study design is methodologically too weak to provide valid information. The authors should clearly describe how the articles were chosen and, the method used may apply methodologic criteria. Such criteria will not always produce studies that are valid, so a validity assessment is also necessary so that the review will be based on data that are as free from bias as possible. Guidelines for such assessment have recently been published in dentistry for clinical questions that address diagnosis,<sup>2</sup> prognosis,<sup>1</sup> and treatment.<sup>4, 8</sup> Such guidelines should be applied and reported in sufficient detail to allow readers to assess the validity of the primary articles.

Even with the use of methodologic guidelines, assessments can be both unreliable and biased. Such assessments can affect both the inclusion and validity assessment of the primary studies. As a safeguard, the primary studies should be assessed by at least two reviewers, each blind to the other's decision. The level of disagreement should be known, and the rules to reach consensus should be reported. To protect from the bias associated with a lack of blindness, the information regarding the institution and authors associated with the primary research can be removed before assessment for inclusion and validity.

Variation in the findings from the assessed studies is inevitable. Reasons for this variation can include chance, study design, and differences in the three basic study components mentioned previously (population, exposure or intervention, and outcome). Authors of reviews who discuss the potential impact of all possible sources of variation have met their responsibility to the reader. Whether the review uses statistical methods of data synthesis or not, the author should clearly state the basis for any conclusions and explain any conflicting results. The primary studies included in the review should have been reported in sufficient detail to allow the reader to assess critically the basis for any conclusions.

#### SUMMARY

Systematic reviews in the form of overviews or meta-analyses offer a solution for busy practitioners who have difficulty keeping abreast of current literature. Because systematic reviews can condense numerous studies into reliable and valid summaries of the best available evidence for a specific clinical problem, they offer significant benefit to busy clinicians.

This article has summarized the major features and advantages of systematic reviews. It has distinguished those features that attempt to increase the usefulness of reviews by limiting bias, and it provided a summary of important questions clinicians can use to appraise such reviews critically. With this knowledge, clinicians should be able to use the literature more appropriately and in a timely fashion.

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