



REVIEW

Digging for evidence: Is the answer available?



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S U M M A R Y

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Evidence based practice has become a golden standard in modern medicine. Before searching for evidence, a clinical question including the population in focus, the intervention and maybe control treatment and the relevant outcomes must be posed. Hereafter a comprehensive search will yield the published evidence to enlighten the question. The papers must be critically evaluated and bias assessed.

Published material will tend to overestimate the treatment effect because of publication bias, language bias, the fact the authors and journals strive for significance instead of true results and the fact that for many interventions the evidence is low quality trials. Methods and challenges are discussed.

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1. Introduction

As clinical work becomes increasingly complex and the number of possible interventions continues to evolve, and as patients become increasingly aware of possibilities and start to surf the internet on their own, clinicians need to be able to find answers to their clinical questions. But what is a clinical question and is it possible to find answers to all kinds of problems? No doubt the last decades have made it easy to access information.¹ However, are clinicians in general educated in the process of searching for evidence and even more importantly, to filter and evaluate the yielded results? After more than 20 years practising evidence based medicine as an integrated part of clinical practice, and increasing quality of research methodology the question still remains: Is the answer out there, and if so, can it be trusted?

The aim of this paper is to explain a way to pose the clinical question, to perform a comprehensive search and to point out some of the problems that arise in the process of interpreting the search results.

2. Defining the clinical question

Before starting the search process, it is important to be absolutely sure what you are looking for. Defining the clinical question may be the most important part of the search process. The clinical question consists of three parts: the population, the intervention/

comparison and the outcomes. This is sometimes called the PICO, as a short name for the parts of the question. Time spent on the process of defining and limiting the question will facilitate the rest of the process by clearing your mind and focussing on what it really is, you want to know. The clinical question can be about a single patient with a specific condition, or it can be about a group of patients. It can be narrow and very specific or it can be wide and sensitive. A well-defined question will later help in designing the search strategy.²

Defining the population is an important part of the process. If the population is very precisely defined, a potential answer to the question can be very precise. However, the chances are that no answer is out there for this narrow population and even if there are trials looking at the narrow population, it may not be appropriate to extrapolate the results to other patients groups. If, on the contrary the group is widely defined, the chances of finding relevant literature increase. On the flip side is the risk that the population contains a subgroup of patients, for which the results can be different. The subset of patients can “hide” within the broadly defined group.

The intervention is what is done to the patient. This can be a surgical procedure, a type of anaesthetic, preoperative smoking counselling or whatever else is in focus. The key point is, whether it is well defined and feasible. The comparison depends on the intervention. Examples of relevant comparisons can be no treatment, standard treatment, placebo medication or two types of surgery that can be compared to each other. If the intervention is well described from the beginning the process of finding relevant papers is facilitated.

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The outcomes must be something the patient feels, functions or survives in order to be clinically relevant. Examples of clinically relevant outcomes in anaesthesia are pain, postoperative nausea and vomiting, complications after surgery, postoperative cognitive dysfunction and mortality. Outcomes such as length of stay in the postanaesthetic care unit, length of hospital stay and intensive care admittance are relevant, but difficult to deal with, as they are dependent on a wide range of organizational factors, not necessarily related to the question in focus.

It is important to beware of surrogate outcomes in research. Surrogate outcomes are sometimes believed to “reflect” real outcomes, to be a marker of serious disease or complications. A surrogate outcome is most often a biochemical marker or a physiological measurement that can be obtained with relative ease.

However, surrogate outcome measures are not necessarily a true surrogate for what is really sought and there is a high risk that the believed correlation is unreliable and they should be avoided or used with extreme care.

3. Searching for answers

In principle, all available information is considered evidence. The obvious place to look for scientific papers is via a database on the internet, but in fact books, journals and newspapers may hold valuable information. Before starting the search it is important to define a search strategy. The clinical question defined above is an integral part of this strategy. How much time and energy put into the development of the search strategy depends on the purpose. If you are going to need a fast but imprecise idea of what the answer may be, it is possible to do a quick and dirty search, using a few keywords and a related article search.

However, if you are going to use the answers to write a clinical guideline or a systematic review, or if you want a comprehensive answer to your question, you will have to perform a thorough and comprehensive search.

Building the search strategy will typically include the words from the clinical question as well as any synonym for any of the words.

The search should be rather sensitive than specific in order not to miss valuable information. The search strategy should therefore be comprehensive, sensitive and reproducible. It is often useful to include the search strategy in the resulting document.

There is a wide range of medical databases available across specialties and countries. The most commonly used are the following.

PubMed, which is a free web based database building on the Medline database of references and abstract of life sciences and biomedical topics. The United States National Library of Medicine (NLM) at the National Institute of Health maintains the database as part of the Entrez system of information retrieval. Although the database contains millions of references, its focus is on major medical journals and journals that publish in English. Limiting the search to PubMed will increase the risk of missing important papers, especially in languages other than English.

The Cochrane Library holds the large collection of Cochrane Systematic reviews, but it also holds many other resources. The most important of these is CENTRAL, which is a database of clinically controlled trials from almost all existing clinical databases. So searching CENTRAL is an absolute must in order to make the search comprehensive. Other papers available in the Cochrane Library are non-Cochrane systematic reviews, reports of Health Technology Assessment papers on scientific methodology and economic evaluations.

Embase is produced by Elsevier, is European in origin and is NOT free. Most institutions, however, have purchased access, so

normally there are no problems searching Embase. Embase covers around 7600 journals and has more European journals compared to PubMed. Search methods and the building of search strategies are slightly different in Embase compared to Pubmed and the Cochrane Library, so it is sometimes necessary to slightly remodel the search strategy. Searching Embase also reduces language bias – see later.

Other databases that might be searched include “Lilacs” (Literatura Latino-Americana e do Caribe em Ciências da Saúde), which is an on-line bibliographic database in medicine and health sciences, maintained by the *Latin American and Caribbean Center on Health Sciences Information* (also known as BIREME), located in São Paulo, Brazil. It contains bibliographic references to papers that have been published in a set of scientific and medical journals of the region, and that are often not covered by MEDLINE. “Cinahl” (Cumulative Index to Nursing and Allied Health Literature) is an index of English-language and selected other-language journal articles about nursing, allied health, biomedicine and healthcare. “Biosis”, is an English-language, bibliographic database service, with abstracts and citation indexing. It is part of the *Thomson Reuters Web of Knowledge* suite. BIOSIS indexes data from 1926 to the present. Besides journal articles, Biosis also covers meeting abstracts, conferences, literature reviews, U.S. patents, books, software, book chapters, notes and letters. There are more than 500 other, smaller and often narrower databases that can be sought, depending on the topic of interest.

4. How to search

Use the search strategy, based on the clinical question, with all available synonyms. The strategy ensures reproducibility and transparency. Do not make time restrictions. For some relevant clinical interventions, the original papers are old. As a general rule, older papers have less advanced methodology, but this is not always the case and too much may be missed, when applying time restrictions. If the intervention is modern, there will not be any old papers anyway. When evaluating the paper, it is always important to be aware of the details of the intervention and make sure it is applicable.

Other restrictions and limitations may also lead you astray. Language restriction will surely lead to language bias (see later). Including papers in foreign languages can be a challenge, but very often the paper includes an abstract in English, that will let you know whether the paper is relevant for your clinical question or not. And often it is possible to find a colleague or a friend who can help extract the data from a paper. If not, the least you can do is to point out that the paper exists, even if you cannot include it. The databases have a multitude of filter functions, which can be very useful for a “quick and dirty” search, but which is not always sensitive enough for a thorough search. For example, PubMed has a filter for randomised controlled trials. However, if the trial has been tagged as such, which is often the case; you may miss an important paper.

5. Evaluating search results

When the search is completed, you have (perhaps virtually) a pile of papers that deal with the clinical question you set out to answer. It is important to perform a critical evaluation of each paper in order to assess the methodological quality of the research process, identify potential bias and how this may influence the results. The themes that should be evaluated include: Trial design. Is this a randomised controlled trial, and if so was randomisation performed correctly? How was the allocation concealment achieved? How large was the sample size and how was it calculated? The inclusion and exclusion criteria must be appropriate and the

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