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**Cover Picture:**  
Enhanced axial T1-w MR image shows  
a enhancing right temporal lobe cyst.  
(Refer to pages 590-593)

## How hard should we look for the evidence?

K H Pwee

The second article in the SMJ series on evidence-based medicine and healthcare covers useful resources and skills for locating information from the medical literature<sup>(1)</sup>. Susan Bidwell has provided an excellent and practical introduction to many convenient and easily-accessible information resources. These resources go some way toward facilitating the search for the evidence to help answer your clinical questions. If your question is a common one, it is likely that someone else has already examined the issue rigorously, perhaps through a systematic review of the topic. If so, why not benefit from the work they have done?

A subsequent article in this series will discuss systematic reviews and how these can be a useful summary of the evidence from the medical literature. Looking at a systematic review, it is instructive to observe the care with which the reviewers searched the medical literature. You will usually see a description of the databases that were searched for primary clinical studies and they may also describe their search terms and strategy.

Why do systematic reviewers do this? Beyond demonstrating the rigour with which they have conducted their literature search, such a level of detail supports the reliability and validity of the review's findings. By being explicit in their study methods, the reviewers allow readers to satisfy themselves that a comprehensive search has been conducted, and the search can be duplicated if necessary to verify its findings. We can draw an analogy with a paper on a primary study, such as a randomized controlled trial. No serious study today would be published in a reputable journal without a section describing the methodology of the trial: in the same way, the methodology of a systematic review, especially the search strategy, needs to be described.

There are various factors to consider when evaluating a search that has been done for a systematic review, or for that matter, when you do a search yourself. Comprehensiveness is a fundamental factor. The net needs to be cast wide enough to ensure that you catch what you are fishing for.

MEDLINE is the default bibliographical database for many people, but as has been noted, there are other databases of the primary literature, which contain references that may not be found in MEDLINE. For example, whereas MEDLINE has a heavier concentration of North American publications, EMBASE has more European references. The overlap between the two databases has been estimated at only 30% to 50%<sup>(2)</sup>. Specialist databases, such as PsychINFO for psychological medicine, may have references that do not make it into general databases like MEDLINE. Databases of publications in other languages or geographic regions (e.g. LILACS for Latin American and Caribbean publications) may contain useful references not indexed in the English language databases.

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One more factor to consider: searching in the previously-mentioned resources will usually turn up studies that have been published. What about unpublished studies? The phenomenon of publication bias may arise when medical journals do not publish the results of clinical studies that do not show a difference between an intervention and its comparator, because it is felt to be of little interest to its readers. Another possibility is when medical industries do not publish the results of studies involving their products, for whatever reason<sup>(3)</sup>.

One way to address this is to register all clinical trials at their inception – then reviewers will know that the trial has been done, even if the results are not subsequently published<sup>(4)</sup>. And the reviewer can contact the investigators to see if the unpublished results can be made available. Reviewers should also include searches of the grey literature (e.g. conference proceedings, government reports, graduate theses) to seek out unpublished trials<sup>(5)</sup>. Unfortunately, the rigour of a literature search is proportional to the time and resources that go into performing the search. As always, there is a trade-off between how thorough you want to be and how quickly you need it. How hard do we need to look for the evidence?

Egger et al<sup>(6)</sup> studied 159 systematic reviews of therapeutic or preventive interventions that were based on comprehensive literature searches. The authors examined the effect of trials that were difficult to locate (i.e. unpublished trials, trials published in languages other than English, non-MEDLINE indexed trials) on the results of the systematic reviews. They found that unpublished trials tended to be smaller, less likely to produce statistically significant results and showed less beneficial effects than published trials. Conversely, non-English language and non-MEDLINE indexed trials were more likely to produce statistically-significant effects and larger treatment effects despite smaller sample sizes. However, in the majority of systematic reviews, if unpublished, non-English language and non-MEDLINE indexed trials were excluded, the exclusion had relatively small effects on estimates of treatment effects and the precision of the estimates (although more substantial changes were observed in some instances). The authors concluded that systematic reviews based on a search of the English language literature that is accessible in the major bibliographical databases will often produce results that are close to those obtained from reviews with more comprehensive searches that are free of language restrictions. They recommended that when planning a review, investigators should consider the type of literature review and the degrees of comprehensiveness that are appropriate for the review in question, taking into account budgetary and time constraints.

Moher et al's<sup>(7)</sup> study on the effect of including or excluding trials in languages other than English in systematic reviews concluded that language restrictions do not appear to bias the estimates of a conventional intervention's effectiveness. However, there was substantial bias in the results of a complementary and alternative medicine systematic review if trials in languages other than English were excluded.

While those with limited resources may take comfort from Egger et al's study, it has to be borne in mind that the characteristics of scientific studies are not the same as biological characteristics. The former is much more mutable than the latter, and scientific studies are also a heterogeneous group. As the quality of non-English language and non-MEDLINE indexed publications improve, their importance will

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correspondingly rise. Hopefully, initiatives like clinical trial registration<sup>(4)</sup> and "author pays" open access publication<sup>(8)</sup> will reduce the effects of publication bias.

There is no easy answer on how hard we need to look. Ultimately, it should depend on the purpose to which the information is to be put. More often than not, the time you have to reach your decision based on the information is a limiting factor. "Quick and dirty" methods may not be so "dirty" as to be useless, but neither should they be the only option all the time. Fortunately for the medical practitioner, many resources exist that represent the expenditure of more time and effort than any one person can spare – systematic reviews, critically appraised topics, clinical practice guidelines and health technology assessments are all evidence-based information sources that are easily accessible and usually freely available. All it takes is the small effort to search for and find them. **SMD**

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