Writing clinical guidelines with evidence-based medicine

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Most doctors spend a considerable amount of time reading, reviewing, assessing, updating or writing clinical practice guidelines. As a result, we are aware of the current philosophy of making these guidelines 'evidence based'. In so doing, we are attempting to improve the general practice of the science of medicine. A number of classification schemes have been developed to aid in this process, in an attempt, most often, to give an indication of the 'strength' of a recommendation. In general, peer-reviewed, published controlled clinical trials (level A) are considered to provide the best evidence for or against the use of a particular medication or therapeutic approach. Conclusions drawn from peer-reviewed, published epidemiological studies (level B) provide the next best evidence. The lowest rating is given to recommendations taken from the lessons of published case reports and the opinions based on the experiences of the individuals drafting the recommendations (level C).

Clearly there is benefit in knowing whether a recommendation is based on only an opinion or the results of a well designed, unbiased study published in a high ranking, peer-reviewed, scientific journal. With this information, a physician faced with a clinical decision can decide whether to follow a particular recommendation based, in part, on the assigned strength of the evidence on which the recommendation was made. However, there is a mindset that accepts only recommendations with a level A or B strength of evidence as being truly valid. This is a problem because there are a number of obstacles that make it difficult to have all current clinical practice guidelines based on these levels of evidence.

First, most of the published controlled clinical trials (level A evidence) are directly supported by the pharmaceutical industry. These are very expensive studies to do. Usually, they are conducted in relation to the development of a new therapeutic product, which the company is planning to market and from which they hope to profit financially. This is, after all, the primary goal of private industry, and we support that goal, particularly for those of us who own stocks or mutual funds. However, these studies are frequently conducted primarily to determine whether the efficacy of the new therapeutic product is similar, if not superior, to the current-

ly used product(s). If this is found to be the case, the results of the study are usually promptly published. If the product is not found to be at least equivalent in efficacy, are the studies published as readily? Also, the pharmaceutical industry only rarely supports clinical trials in which old drugs are studied unless the older drugs are used in the control groups to support the use of newer products or unless there are new diseases for which they could be used. Moreover, why would we expect the pharmaceutical industry to support studies designed to determine the minimum dosage of their products and, hence, reduce their profits when the current recommended dosage schedule cures or controls the patient's disease? Independent research funding to answer these questions is essentially nonexistent because most government and private funding agencies assume that these trials can be funded by industry and direct their limited funding support toward finding the answers to more basic science or epidemiological questions. The result is that, overall, we actually have very little independent level A quality evidence on which to base clinical practice guidelines. If this continues, the scientific basis for the delivery of health care will be determined primarily by private industry.

Another difficulty concerns evaluating older recommendations, many of which were originally based on case reports or limited clinical studies. It usually comes as somewhat of a shock to the individual, who is updating the recommendations and is trying to sort out exactly what the level of evidence to be assigned to it is, to find that the 'gold standard' of medical practice, which has been recommended for the past 30 years, is based on a retrospective case series involving 13 patients! Finding this information is not that easy because the studies were usually published before the dates covered by MEDLINE and may even be based on foreign literature, which is not readily available. Usually, one also finds that there has been no systematic research performed to confirm the validity of a recommendation once it had become 'standard practice'. How do we evaluate the evidence for its continued use? That patient outcomes were good indicates either that the recommendation was useful or that it, at least, caused no harm. However, some old recommendations

may be expensive or cumbersome, and often there is a desire to modify them. The problem now is how do we change them without any scientific evidence to justify the change?

Are recommendations based on opinion or case reports really that unreliable? In clinical practice, this is the type of evidence upon which the majority of decisions are based. If a treatment works and the patient is happy, the practitioner will tend to use it again. If there is a problem, another therapy will tend to be used. Unfortunately, this practice also forms the basis for most of the 'alternative medicine' success claims. In general, we do need to be cautious about recommendations based on this type of evidence. Case reports are useful, primarily because they alert us to potential problems. If the problem identified by the case report is serious enough, recommendations based on it may be necessary while awaiting the results of further confirmatory studies. Individual case reports are not usually useful for determining cause and effect, but reports of case series may be useful because they can indicate trends that support associations.

Recommendations based only on expert opinion can be difficult to evaluate. In these instances, there is usually little or no systematically gathered evidence on which to base the needed recommendation. Biases based on experiences in similar circumstances, knowledge of related fields of research, or contact with involved individuals or companies tend to influ-

ence this type of recommendation. Therefore, any overt biases should be identified and published along with the recommendation. There are circumstances when recommendations based upon expert opinion will not be challenged. For instance, three of 10 pregnant rabbits given a particular drug delivered anencephalic infant rabbits. Although this may be a phenomenon restricted only to rabbits, an accepted recommendation based upon expert opinion would be that this drug not be given to pregnant women.

Routine reporting of the evidence used to develop recommendations for clinical practice guidelines will improve their quality and their usefulness. At the very least, the lack of sufficient evidence to make strong recommendations highlights the areas of clinical medicine in which we need further research. Hopefully, this will also spur the federal and other medical research funding agencies to consider funding more clinical trials independent of the pharmaceutical industry. The need to quote the levels of evidence on which recommendations were based, although awkward when updating them, allows us to challenge openly our conventional thinking about the treatment of disease and to look closely at the reasons why we follow certain guidelines. Overall, the scientific basis for the practice of medicine will be enhanced by citing the levels of evidence. To improve the art of medicine, however, we will need to look elsewhere.