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Basing medical practice on the best available scientific evidence does have its critics. Some, for instance, assert that this philosophy of practice has major limitations when considering the care of individual patients. On the other hand, 'outcomes research' has documented that patients who received evidence-based therapies often have better outcomes than those who don't [1-5]. However there are several areas of disagreement between evidence-based medicine (EBM) supporters and detractors as well as unanswered questions about the role of EBM in modern healthcare. Opponents says that EBM does not provide a means to integrate other, non statistical, forms of medical information, such as professional experience and patient specific factors and the usefulness of applying EBM to individual patients is limited [6].

POLARIZATION OVER EVIDENCE-BASED MEDICINE

The polarization over EBM is the most current manifestation of a classic debate over the "soul" of medicine: Is medicine a science or an art? [7]

CRITIC POSITIONS. Critics of EBM mostly come from within the medical professions. In addition to the many scientific problems of creating sound guidelines when evidence is weak, they stress the destructive effects of standards at the local level. In an age of mandated cost control and resource limitation under managed care, this group tends to see medicine in traditional terms: It is a "craft" or "art," in which individual expertise and technique are allowed to shine through and ultimately result in a higher standard of patient care. Instead of revolutionizing care, EBM therefore threatens to bring about stagnation and bland uniformity, derogatorily characterized as "cookbook medicine".

Interested readers are referred to two comprehensive articles: 'Evidence based medicine in primary care: perils and pitfalls' by Upshur & Tracy [8] and 'A categorization and analysis of the criticisms of Evidence-Based Medicine' by Cohen *et al* . [9]. The latter identifies the major criticisms and limitations of EBM appearing in the literature over the past decade, summarized and categorized into five recurring themes. The themes include: *reliance on empiricism, narrow definition of evidence, lack of evidence of efficacy, limited usefulness for individual patients, and threats to the autonomy of the doctor/patient relationship.*

SUPPORTER POSITIONS. If we draw out the positions at the extremes, supporters tend to see standards as a panacea for the problems of rising costs, inequity, and variability plaguing the health care field. For this group, the promised benefits of EBM are self-evident: It ties clinical practices to scientific standards of evidence, thereby providing a means of measuring the efficacy of those practices. Instead of relying solely on accumulated personal experiences to determine which clinical techniques are most effective, individual clinicians using EBM will be able to draw up on the objective experience of many researchers working with accepted scientific standards of evidence and relate this evidence to an assessment of the patient's circumstances and the practitioner's clinical experience. Improved efficacy should also promote greater efficiency by allowing doctors and hospitals to filter scarce resources away from ineffective clinical practices and toward practices whose effectiveness has been conclusively shown. In addition, EBM promises to create better-informed patients and clinicians by offering collectively agreed-upon and publicly available information about treatment options. Finally, EBM should provide a scientific basis for the construction of public policy. Instead of relying on the opinions of interested parties, policymakers and insurers will be able to supplement these perspectives with objective evidence.

THE BENEFIT OF EVIDENCE-BASED MEDICINE

Taking an evidence-based approach to practice, teaching, and research can help you address some of the limitations of current medical practice. It can help you:

- stay up to date with the current literature
- communicate effectively with consultants
- make the best use of information from the history, physical examination, and diagnostic testing
- avoid common pitfalls of clinical decision-making

USING THE BEST EVIDENCE IN SYSTEMATIC REVIEWS

The term 'evidence-based medicine' means integrating individual clinical expertise with the best available external clinical evidence from systematic research. An important source for those who wish to practise evidence-based medicine is the systematic review. Systematic reviews, however, are not without their pitfalls. There are several steps in completing a systematic review. These include developing the clinical question, searching for all available literature, study selection, assessment of study quality, data extraction, data analysis, interpreting the results, implications for practice and further research, and finally updating the review in a timely manner.

TABLE 1. THE ESSENTIAL STEPS IN THE EMERGING SCIENCE OF EBM

1. To convert our information needs into answerable questions
2. To track down evidence - searching for evidence which may come from the clinical examination, the diagnostic laboratory, the published literature, searching database, or other sources
3. To appraise the evidence critically to assess its validity and usefulness – clinical applicability
4. To implement the results of this appraisal in our clinical practice
5. To evaluate our performance

Central to an evidence-based approach is the ability to ask the right question. You might ask questions, for example, about a patient's symptoms at the preoperative visit (in a 65 year old man with left sided chest pain, what is the probability that there is a serious heart problem, and if there is, what is the chance that complications will show up during the perioperative period?), about treatment (in a surgical patient with recent acute myocardial infarction scheduled to epidural anaesthesia are the risk associated with thrombolytic drugs outweighed by the benefits, whatever the patient's age, sex, and surgical diagnosis?), and about a host of other aspects of patient care.

TABLE 2. THE CLINICAL QUESTION

The formulation of the clinical question helps focusing the question, is the basic of literature search and helps appraising the papers critically.

A clinical question consists of three parts

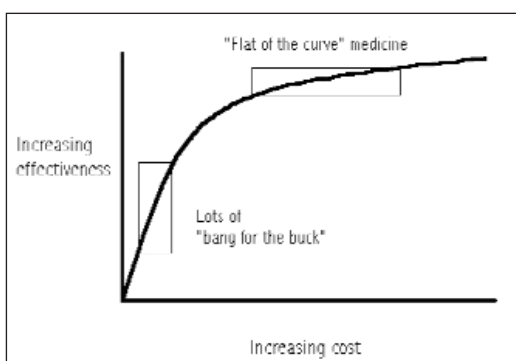
- The patient/population/problem
- The interventions/exposures considered
- The relevant outcomes

A narrow question yields specific results that are hard to extrapolate. A broad question yields sensitive results that are easier to extrapolate, but carries the risk of overlooking differences in subgroups

We all operate within constraints imposed by economics, health systems, patient preferences, culture, and availability of resources. Remember, external evidence requires context.

An evidence-based approach is sometimes confused with cost-effectiveness. Not necessarily although an evidence-based approach should increase effectiveness, it may also result in higher costs. The curve below plots increasing effectiveness against increasing cost:

FIGURE 1



Once a more effective intervention is identified, the decision to implement may depend on where it lies on the “health-policy” curve shown above. If near the lower left corner, where you get a large improvement in benefit for a small cost, it may make sense. If near the “flat of the curve”, you may decide that the incremental benefit is not worth the additional cost.

RANDOMISED CONTROLLED TRIAL AND META-ANALYSES: BENEFIT AND PITFALLS

The real value of randomisation is that, if it is done properly, it reduces the risk of serious imbalance in unknown but important factors that could influence the clinical course of the participants. No other study design allows investigators to balance these unknown factors. When the method of randomisation is not described, or is open to manipulation (through allocation by birth-date, for example), treatment effect can be overestimated by 30-50% [10-12]. There is also a clear tendency to overestimate effect in the control groups of historical studies, and in studies that are un-blinded [10, 12]. This overestimation can be between 30 and 40% [13], or even greater if there are very few patients in the study [14]. When observational cohort studies are subjected to strict epidemiological principles, this discrepancy can be partially offset. The results can also undervalue the treatment effect, which means that the newer techniques do not make the observational studies more reliable [15,16].

In the past meta-analyses (MA) has been criticized as a silly synthesis of disparate data. This criticism continues. Specific examples of discrepancies between meta-analytic summary statistics and subsequent large RCTs have been noted; in one report about one third of the outcomes in the latter trials were discordant with the previous MA [17]. This has leads some prominent statisticians to still favour the narrative review [18]. Other statisticians have emphasized the need for a careful exploration of heterogeneity by sub-category and sensitivity analyses in every MA [19].

How can you determine if you would be able to use the results of a randomised controlled trial and avoid pitfalls in EBM? Garbage in, garbage out. This is a phrase that you may have heard in relation to systematic reviews. What people are worried about is that a reviewer might be collecting together poor quality studies and then presenting the results as if they are high quality. This is a real concern – putting together a group of biased studies is likely to give a biased answer. So, having selected which studies are included in your review, you need to look at the quality of them.

By looking for information on how the trial was executed, you will be able to judge how well it was executed and whether you could use its results. To judge the execution of a trial, you should focus on the following:

Size

Were the trials big enough and was duration of follow-up long enough to make the results believable and clinically relevant? The main goal of using statistical methods to calculate the sample size is to maximise the chance of detecting a statistically and clinically significant difference between the interventions when a difference really exists.

Drop outs

In reality most trials have missing data. Data can be missing because some of the patients loss their motivation, or because some outcomes are not measured correctly or cannot be measured at all at one or more time-point, or withdrawal by clinician for clinical reasons. Regardless of the cause, inappropriate handling of missing information can lead to bias.

Methods

What were the interventions? How and by whom were they given? The article should include detailed information on the characteristics of the intervention, the profile of the individuals in charge of administering them, and the regimens used to administer the interventions. The article should also include information on important co-interventions (for example, the number of patients in each group who received adjuvant therapy) that could influence the outcomes of the trial.

Heterogeneity

Heterogeneity could be a pitfall in the clinician readers of the medical literature. Any kind of variability among studies in a systematic review may be termed heterogeneity. There is the clinical diversity of the participants (age, gender, associated illnesses, etc), the implementation of the interventions (dose, route, associated therapies, etc) and the measurement of outcomes (hospital mortality, 30 day mortality, etc); this is described as clinical heterogeneity. There is also variability in trial design and quality.

Surrogate outcomes

Were the outcomes clinical relevant? How were they measured?

A surrogate endpoint can be defined as a laboratory or physiologic measurement used as a substitute for an endpoint that measures directly how a patient feels, functions, or survives. Surrogate end points have several drawbacks. Firstly, a change in the surrogate end points does not itself answer the essential questions: What is the objective of treatment in this patient? Secondly, the surrogate end point may not closely reflect the treatment target. Thirdly, the use of a surrogate end point has the same limitations as the use of any other single measure of the success or failure of treatment – it ignores all the other measures. Reliance on a single surrogate end point as a measure of therapeutic success or intervention success usually reflects a narrow or naïve clinical perspective. When flipping through a variety of anaesthesia journals one will find surprisingly many articles, which measure only surrogates.

So why would investigators continue to perform trials that measure only surrogates – such as blood pressure, cardiac output, central venous pressure or a variety of laboratory findings?

The reasons are many. These trials are much easier to perform. Patients can be included, anaesthetised, outcome measures within one day and at a minimal cost and effort – even during the performance of daily clinical work. Being an anaesthetist makes you familiar with the registration and interpretation of various clinical signs. But beware. What is a great help in keep the anaesthetised patient stable and safe may well mislead you, if new intervention should rely on trials with just one, or a few clinical signs as outcomes.

Bias

Duplicate publications

Some studies result in more than one publication. Authors may publish the methods of the study, present preliminary data at a conference resulting in an abstract, then publish some results, and later publish longer-term follow-up. There's nothing wrong with this, as long as you can tell it's all about the same study. Sometimes, studies may be published more than once for other reasons – more publicity, more papers on the author's CV, or to allow different authors to be first authors. Sometimes, it's not easy to tell whether they are reports of the same study. This can cause problems for reviewers because we might count a study more than once and so give extra weight to it in our review. So, we need to be alert to the possibility of duplicates. Look for

- Same authors in different orders
- Similar study inclusion and exclusion criteria
- Many reports of a study done in the same place at the same time

Publication bias

Systematic reviews aim to find and assess for inclusion *all* high quality studies addressing the question of the review. But finding all studies is not always possible and we have no way of knowing what we have missed. Does it matter if we miss some of the studies? It will certainly matter if the studies we have failed to find differ systematically from the ones we have found. Not only will we have less information available than if we had all the studies, but we might come up with the wrong answer if the studies we have are unrepresentative of all those that have been done.

We have good reason to be concerned about this, as many researchers have shown that those studies with significant, positive, results are easier to find than those with non-significant or 'negative' results. The subsequent over-representation of positive studies in systematic reviews may mean that our reviews are biased toward a positive result.

Publication bias is just one type of a group of biases termed reporting bias. We have quite a lot of evidence that these biases exist, so it is fair to assume that most systematic reviews will be subject to reporting bias to some extent. Publication bias and other related biases can be summarised as statistically significant, 'positive' results being:

- More likely to be published (publication bias)
- More likely to be published rapidly (time lag bias)
- More likely to be published in English (language bias)
- More likely to be published more than once (multiple publication bias)
- More likely to be cited by others (citation bias)

However, some questions about therapy do not require randomised trials (successful interventions for otherwise fatal conditions) or cannot wait for the trials to be conducted. And if no randomised trial has been carried out for our patient's predicament, we must follow the trail to the next best external evidence and work from there.

CONCLUSION

Evidence-based medicine is about integrating individual clinical expertise and the best external evidence.

Evidence-based medicine using meta-analysis of randomised controlled trials has been criticized as an incautious synthesis of disparate data. Also, there are specific examples of discrepancies between meta-analytic summary statistics and the results of subsequent large randomised controlled trials evaluating the same therapies. The meta-analysis of a systematic review is a research tool; it is transparent and available. It can be used correctly or incorrectly. There must be a careful exploration of clinical heterogeneity in every meta-analysis. Systematic reviews can provide relevant evidence for policy decisions in medicine by estimating summary effect measures contrasting treatment choices. While the performance of a systematic review with analysis is original research, this is observational research. The data elements come from what has been done — which may differ from what should have been done. Therefore the results of meta-analysis are tentative and provisional.

The evidence (reviews) does not make decisions – people make the decision. So we must stress, these tools need to be combined with clinical experience and patient preferences.

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