WHAT IS EVIDENCE-BASED MEDICINE?

A Discussion of the Pros and Cons of the Trend Towards Statistical Evidence Guiding Medical Practice

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The term "Evidence-Based Medicine" (EBM) is a recent concept, designed to improve medical practice through decision making being guided by more rigorous medical and scientific data. Although works such as "*Effectiveness and Efficiency* " by Archie Cochrane were published well before the 1990s, it was not until this decade that the methodology and definition of EBM was formulated.

The term "Evidence-Based Medicine" (EBM) itself was coined in 1990 by Guyatt[i], a professor from McMaster University in Canada. A commonly touted definition, from Sackett[ii] (another McMaster University professor) et al, reads "The conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients".

Following is an example of how evidence may be gathered at different levels; If we take the assertion "all rubber tires are round", we may decide to believe it on the basis of general experience and common sense. On the other hand, we may not believe it blindly and decide to gather relevant data such as definitions and systematically gather observations. Further still we may seek to test whether the evidence supports the assertion by testing the hypothesis under certain controlled conditions to see if the hypothesis stands up to scrutiny.

Evidence, broadly construed, is anything presented in support of an assertion. In these terms the concept of "Evidence-Based Medicine" seems somewhat self-evident. Taking the devil's advocate position, we may consider that any practitioner who compiles a history, examination and clinical tests on a patient and uses this information for a diagnosis is essentially practising EBM.

Therefore could one really be practising medicine of any sort without practising a form of evidence-based medicine?

"Yes" promptly replies the proponent of EBM. "One can in fact practice medicine on the basis of supposition, tradition, heresay or on the basis of theories of causation that don't belong to the world of science. Perhaps one could even attribute disease to magic or supernatural causes."

"So then, we need to have some hard data for a hypothesis we develop regarding any patient, and an even stronger basis for the treatment we plan to administer?"

"Absolutely."

"So as long as I have some basis to believe what I believe in terms of a hypothesis for why a patient is ill and for what treatment I am going to administer, I am practising EBM?"

"No" echoes the stalward proponent of EBM. "The best evidence, implies use of randomised controlled trial (RCT) evidence, and even more preferably meta-analyses of randomised controlled trials as the best available evidence, with other forms of evidence is considered inferior on the basis of methodological considerations."

It has been proposed that it is only when we get to randomised controlled trials that we start to eliminate confounding factors which theoretically plague the observational study. Randomisation of variables in a RCT setting should theoretically eliminate such confounding factors.

However on closer examination, the advantages offered by the RCT seem to dwindle when we start examining the different forms of bias which can confound the situation.

The first is what I call *inclusion bias*. This essentially refers to the fact that certain types of treatment are much more likely to be included in RCTs while others are not. The first category includes patented medicines, as the pharmaceutical companies who brandish them are much more likely to be able to afford the expense of RCTs which generally now average $12 million per trial. On the other hand, non-patented medicines such as nutrients, or lifestyle changes, such as exercise or healthy living, or medications which are no longer on patent, are much less likely to attract sponsorship for RCTs due to their much lower profitability.

Secondly is what is known as *publication bias.* This relates to what is and is not accepted for publication in journals. For instance, Dickerson et al[iii] demonstrated that trials with a positive result were three times as likely to be published as studies with a negative result. Is some cases, investigators may not submit results for publishing if not thought to be of interest or significant enough for publication.

And finally we have what is known as *reporting bias.* This relates to the tendency to under-report unexpected or undesirable experimental results, and may partly related to disclosed or non-disclosed conflict of interest in studies.

In-line with this reporting bias, two highly significant papers by Bekelman et al[iv] and Bhandari et al[v], suggested that there is a direct correlation between industry-funding of trials and a positive outcome of trials. In other words, there was a trend for studies regarding interventions in which the sponsor of the trial had a financial interest in the product or intervention being studied, tending to be positive.

Moreover these types of conflict of interest are not always disclosed, as a 2011 study showed. Out of 509 randomised controlled trials studied, 219 were industry funded. Only 113 of these reported conflict of interest disclosures, and importantly these disclosures rarely were discussed in meta-analyses which included their data[vi].

Other types of bias also exist in the area of randomised controlled trials and meta-analyses of these trials. A discussion of these forms of bias are outside the scope of this article.

Further to this discussion, a 2000 NEJM study by Benson & Hartz[vii], found that randomised controlled trials and observational studies give significantly similar results overall, suggesting a higher level of validity of observational trials than is generally attributed to this study type.

So perhaps we need to lay aside the absolute insistence on data from RCT and meta-analyses of published data and realise that all many forms of experimental and even basic science data is likely to be useful in certain situations. Perhaps the key benefit to EBM may be more in the rigour in the application of the data, rather than insistance on one form of study type.

One could liken the use of RCTs in medicine as peering in one window of a house. A certain view of the house can be obtained by looking in that particular window, however a more comprehensive view of the whole house could likely be obtained by looking at all forms of data, from basic sciences to observational data, to randomised trials and meta-analyses.

The question also arises that in the context of a newly developing area of medicine, where few or no randomised or even observational trials have been performed, how does one practice EBM?

I believe the answer is by rigorous application of the diagnostic process, including thorough clinical history taking, examination, investigations and differential diagnoses. Furthermore it is desirable to track the results of treatment closely including normalising of pathology markers.

Consider for example the new field of Chronic Inflammatory Response Syndromes (CIRS) which are triggered by biotoxins such as those present in water-damaged buildings. Dr Ritchie Shoemaker has shown that one can apply an evidence-based approach to diagnosing and treating this condition, by rigorous data collection.

A database is completed on each patient treated, with demographic information, symptoms reported, laboratory values, treatment administered and progressive changes in symptoms and laboratory values with treatment. This is a form of case-by-case observational study which eventually can form the basis for a published observational trial.

Another question arises in how we can balance the scientific rigour espoused by EBM with the increasing consumer-driven needs of modern medicine? How can we balance the tendency for a conveyor belt approach to medicine to be the outcome of EBM, with an individualised approach?

In the case of the new area of functional medicine, as do many other physicians working in this area, often find that in any given condition, there may be a number of imbalances in core areas of physiology that may be underlying the condition. These may be different for each patient with a particular condition.

For instance in a case of rheumatoid arthritis, there could be a mild deficiency of vitamin D3, a slight undergrowth of beneficial intestinal bacteria, a slight decrease in conversion of thyroid hormone to T3 (the active form of thyroid hormone) and a lowering of ACTH and cortisol to the lower end of the reference ranges.

Another patient with the same condition could have exactly opposite disturbances.

An evidence-based approach to intervening on a functional level may be to keep a clear handle on basic physiology at all times; to supplement a dosage of vitamin D3 that is well-established in the peer-reviewed literature, to use probiotic preparations with a body of evidence to support their use, supplementing selenium or other nutrients known to enhance thyroid hormone conversion and to perhaps ignore the cortisol imbalance.

However these imbalances need to be followed up in time to ensure they are normalising and that symptoms are improving concomitantly. This could be considered a more individualised form of evidence-based medicine. Of course a patient should be informed of any treatments which are available based on RCT and meta-analysis evidence, however all options should be offered to the patient.

EBM used under this context, provides a powerful way for patients to have options presented for their disease management, with the level of experimental data for these options disclosed at each point.

This form of EBM can help us move forward towards a more unified and individualised practice of medicine, that discards "magical thinking" as well as shallow insistence on randomised trials and can perhaps be best defined as "the rigorous use of data from basic science, observational and clinical trials for the benefit of the patient in any given situation."

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