Evidence-Based Medicine

What Evidence-Based Medicine (EBM) is:

The original concept of EBM began in the 1980's with some investigators attempting to put medicine on a more solid scientifically based foundation. Ultimately, producing clinical guidelines based on current (at the time) related developing science. (1) The actual concept of EBM has been in the medical lexicon since the 1990's. Initially, EBM was being implemented to educate physicians/clinicians to understand the importance of integrating their understanding of the literature and science into clinical medicine. The currently accepted definition of EBM in medicine today is: "...the care of patients using the best available research evidence to guide clinical decision-making..." (2,3)

There are four basic elements of EBM. 1. Formulate a clinical question, 2. Finding the best available evidence, 3. Assessing the validity of the evidence (including internal and external validity), 4. Applying the evidence in practice, in conjunction with clinical expertise and patient preferences). (2,4)

1. Formulating a clinical question is a critically important part of EBM. This will allow the investigator and physician to zero-in on a specific area of scientific concern. This step is important to maintain focus on a specific area and not to become distracted by confounding outliers when searching for an answer. In medicine, a common method of maintaining this focus is to use the **PICO** method.

P: What is the relative **P**atient population? Is the study being considered related the individual patient(s) being treated? (5)

I: What **I**ntervention is being considered? A specific intervention must be considered. However, having an intervention (diagnostic test, medication, etc...) may cause the physician to rely too much on subgroup analysis. This reliance may have skewed results and not comport with the medical condition related to the study. Therefore, the scope of the intervention may need to be widened.

C: What is the **C**omparison intervention? When considering double-blind randomized controlled treatment trials, the comparison group in the study must be considered. For example, if the placebo control is not related at all to your patient population or treatment considerations, alternative interventions must be considered. (7)

O: What **O**utcomes are of interest? Outcomes should be well defined, measurable, reliable, sensitive to change and actually assess clinically relevant aspects of a patient's health. (2). There are three types of outcomes when consideration of clinical studies:

a. Composite endpoints – If there are multiple combined endpoints in a study, this may increase the studies reliability and statistical relevance. However, if these composite endpoints are not all equally relevant to your patient or treatment plan the endpoints are only marginally useful. In order to make sense of the studies endpoints, an analysis of the individual endpoints must be assessed to determine if the studies outcomes are relevant.

b. "Soft" outcomes – These outcomes are related to the more subjective measurements in a study (i.e. function, pain, quality of life, etc…). Soft outcomes are likely much more important to the patient and the empathic physician. However, they are subjected to expectation bias also known as the placebo effect.

c. Surrogate outcomes – are usually used when clinically important outcomes are either unable or too difficult to measure. Hence, these larger metrics tend to make the trials extremely expensive and make the cost of development prohibitive. (i.e., drug development). Surrogate outcomes are largely indirectly related to patients. This is akin to an associative effect not a cause and effect. Therefore, in the interest of using fewer patients and reducing costs, the studies results are subject to errors in interpretation of the outcomes. Ultimately, approving medications that produce either direct or indirect harm to patients. For example, if a drug was approved to address a specific medical problem and the drug did not have any effect on the population, the drug would not have a positive outcome. Consequently, if a drug was approved for the same medical problem and was the cause of increased morbidity or mortality, then that outcome would not be acceptable either.

2. Finding the best available evidence in today's technological environment is amazingly easy. In fact, the plethora of information available to physicians can be overwhelming. Since the advent of the internet, searching for information is quick, easy to search and most of the times at a reduced or zero cost to the user. There are many services available that sort and evaluate the volume of research available and will provide relevant summaries or abstracts for the physician's review.

In search of the evidence, there are three levels of complexity to be considered when reviewing the data.

a. Primary (original) research – this is data collected from groups of people that are defined by the researchers. Providing, the study is designed appropriately, this type of research will minimize the risk of bias. The best type of primary research studies are double-blind randomized control studies.
b. Systemic reviews – are designed to answer one specific question. Unlike traditional reviews, the systemic review is very specific in its selection of previously published studies and carefully evaluates if there are any bias or conflicting results.
c. Summaries and guidelines – are considered the highest level of complexity. This is due to the development of summaries and guidelines that are a synthesis of systemic reviews, original research, clinical expertise and patient preferences. (2). Subsequently, the guidelines are produced and vetted amongst multiple organizations and committees prior to publication.

3. Assessing the validity of evidence is using all the critical skills a physician has learned to evaluate the information presented to determine if the evidence is to be considered in the treatment of the medical problem the physician has in question. Critically evaluating the evidence is not only important but essential for the physician. To evaluate the evidence these areas must be assessed.

a. Internal validity – Is the study being reviewed, are the results of the study pertinent to the patients in the study. A few considerations will impact the internal validity. Bias and Chance to name two.
b. External validity – Are the results of a particular study applicable to patients outside the study being evaluated. (i.e. does the study apply to the patient the

physician is trying to treat). A few considerations will impact the external validity are: Indirect evidence, Subgroup analysis; Reporting bias, Multiple comparisons, Lower Statistical Power.

Assessing validity is a learned skill that improves with time and effort. The physician should work to develop their critical reading skills and work to maintain their knowledge in their respective fields of medicine.

4. Applying the evidence in practice is the ultimate goal with EBM albeit one of the most difficult tasks to undertake and implement.

a. The know-do gap – this is likely the most common problem implementing EBM in a clinical practice. This is due mainly to the gap in recommendations from best evidence and actual clinical practice. (8). As mentioned before, there is an overwhelming amount of research available. With only so many hours in an extremely busy day, sometimes there is little time to properly assess the evidence. Therefore, the know-do gap is created. The physician does not have a grasp on the evidence but implements a treatment based on gestalt or collegial input. It is incumbent on the physician to implement the appropriate treatment to the appropriate patient in the appropriate manner.

b. Difference in baseline risk – do the results in a particular study apply appropriately to the physician's population? The cliché of "every patient is different" is relevant and important in evaluating the baseline risk of your patient vs the baseline risks of the patients in a specific trial. Caution must be advised when using subgroup analysis of a study which may lead to unclear or improper conclusions.

What EBM is not:

EBM is not a substitute to violate our sacred and precious Hippocratic oath which includes Primum non nocere ('first do no harm'). As physicians, treating a patient blindly following guidelines without critically evaluating for a specific patient or patient population is risky. Especially, when knowingly or unknowingly there may be increased mortality or morbidity to the patient is unethical and unacceptable behavior. It is incumbent upon every physician to remember that once entering one of the most honorable professions, they are

committed to a lifetime of learning. EBM is an amazing method to apply research principles to the practice but only if the evidence is properly evaluated and then implemented.

Endnotes:

1. Progress in Evidence-based medicine: a quarter century on
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