Evidence-Based Medicine (EBM) Essay

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Evidence based medicine; (EBM[i]) is the conscientious, explicit, judicious and reasonable use of modern, best **evidence** in making decisions about the care of individual patients. EBM integrates clinical experience and patient values with the best available research information. It is a movement which aims to increase the use of high quality clinical research in clinical decision making. EBM requires new skills of the clinician, including efficient literature-searching, and the application of formal rules of evidence in evaluating the clinical literature. The practice of evidence-based medicine is a process of lifelong, self-directed, problem-based learning in which caring for one's own patients creates the need for clinically important information about diagnosis, prognosis, therapy and other clinical and health care issues. It is not "cookbook" with recipes, but its good application brings cost-effective and better health care. The key difference between evidence-based medicine and traditional medicine is not that EBM considers the evidence while the latter does not. Both take evidence into account; however, EBM demands better evidence than has traditionally been used. One of the greatest achievements of evidence-based medicine has been the development of systematic reviews and meta-analyses, methods by which researchers identify multiple studies on a topic, separate the best ones and then critically analyze them to come up with a summary of the best available evidence.
The EBM-oriented clinicians of tomorrow have three tasks:
a) to use evidence summaries in clinical practice;
b) to help develop and update selected systematic reviews or evidence-based guidelines in their area of expertise; and…
c) to enroll patients in studies of treatment, diagnosis and prognosis on which medical practice is based.

Essay;[ii] In a reflective essay, you recount something that you have experienced, and say what you learned or how the experience changed you. The language used in a reflective essay should be first person, primarily past tense, primarily concrete, with a coherent tone and level of diction.

Semantics can be important. Words & terms can be weaponized, taken out of context. The implication that this new emphasis on EBM can be subverted to imply that we have not been practicing with an evidence basis to the current point. Taken to an extreme, the implication can be that we're practicing no better than the Obeah of the newly colonized West Indies[iii] as they burned chicken feathers to effect both healings and curses.

Contrast the Obeah to the practitioners of Ayurveda medicine on the subcontinent of India—this practice was established around 5,000 BCE[iv]. Traditional Chinese medicine began around 2,000 years ago.[v] Homeopathy was initially practice around 1796 in Germany with strong influences ranging back to Hippocrates in 400 BC[vi]. I'm unaware of any self-evaluation of "EBM" being done in any of these fields.

While voodoo and Obeah is still being practiced to some degree in the Caribbean, the other types of medicine listed above are also still being practiced.

Why is that?

Because they work!

Louis Pasteur & Robert Koch developed the germ theory of disease in the late 1850's[vii] which is arguably the birth of "modern (western) medicine" as we have come to know it.

"Modern Medicine" should not be the final accreditor of what does and does not work. The approaches, philosophies and practices of healing mentioned above look at illness from a much different perceptual vantage than our traditional western culture uses. Many of them don't even share the same perspectives amongst themselves—all look at the problems of human illness differently and all get results.

Attempting to "step out of line" or "think outside of the box" can be detrimental to the individual practitioner's career.

Medical discovery, presumably in ancient as well as modern times likely begins with a hypothesis, hunch, gut feeling or possibly merely a desire to do something, *anything*, to provide relief to a suffering person. If it works, it's likely to be tried again when a similar situation presents itself. The initial sample of N=1 may become N=dozens over time as a practitioner repeats the pattern seeking success. Continued success is likely to have the information passed on, initially, perhaps by word of mouth to colleagues and possibly students (depending on the setting).

This newborn theory remains at high risk at this point; denizens of the Ivory Tower may feel threatened by a discovery that they did not make, attempting to discredit the idea. Medical advances historically have begun as simple observations as mentioned above. Knowledge spreads, by word of mouth, informal "curbside consults" in hospitals and other settings, at lectures, conferences, in journals. Eventually studies may be funded. An Institutional Review Board (IRB) must be convened and consulted before any (no matter how loosely defined) form of "experimentation" may be done on patients—even including retrospective reviews in which researchers "look back" at what was done and what happened.

"Properly" doing studies to obtain the vaunted "EBM" moniker is an extremely expensive process. The best chance of success is to have a recently patented molecule that will be able to be marketed in a manner that will allow funding of the necessary studies.

The "golden child" of research is the Randomized Controlled Trial (RCT) which is generally double-blinded (neither researchers nor patients know who is receiving the experimental treatment vs. being used as a control). Sometimes patients serve as their own controls with specific time points being used to collect data for analysis regarding benefits & harm/risk.

The sine quo non after the double-blinded RCT will be "meta-analysis" in which numerous research studies are combined, reviewed and the results are (ideally) published.

There are a variety of types of bias that can confound and confuse medical research[viii]:

1. Bias in concepts — Lack of clarity about the concepts that are to be used in the proposed research. This gives an opportunity to the investigators to use subjective interpretation

that can vary from person to person. Sometimes the logic used can be faulty and sometimes the premise itself of the logic can be incorrect.

2. Definition bias — The study subjects should be sharply defined so that there is no room for ambiguity. For example, if the cases are of tuberculosis, specify that these would be sputum positive, Monteux positive, radiologically established, or some combination
3. Bias in design — This bias occurs when the case group and control group are not properly matched, and the confounding factors are not properly accounted for at the time of analysis.
4. Bias in selection of subjects — This occurs when the subjects included in the study are not truly representative of the target population. This can happen either because the sampling was not random, or because sample size is too small to represent the entire spectrum of subjects in the target population.
5. Bias due to concomitant medication or concurrent disease — Selected patients may suffer from other apparently unrelated condition but their response might differ either 2 because of this condition itself or because of medication given concurrently for that condition.
6. Instruction bias — When unclear or no instructions are prepared, the investigators use discretion and this can vary from person to person, and from time to time.
7. Length bias — A case-control study is generally based on prevalent cases rather than incident cases. Prevalence is dominated by those who survive for a longer duration. And these patients are qualitatively different from those who die early.
8. Bias in detection of cases — Error in the diagnostic or screening criteria, e.g., being able to use a laboratory investigation properly in the hospital setting but not in the field setting where the study is to be actually done.
9. 'Lead-time' bias — All cases are not detected at the same stage of the disease. In cancers, some may be detected at the time of screening such as by pap smear, and some may be detected when the disease has started clinical manifestation.
10. Bias due to confounder — Failure to take proper care of the confounders so that any difference or association cannot be fully ascribed to the antecedent factors under study.
11. Contamination in controls — Control subjects are generally those that receive placebo or the usual therapy. If these subjects are in their homes, it is difficult to know if they have received some therapy that can affect their status as a control.
12. Berkson's bias — Hospital cases when compared to hospital controls can have bias if the exposure increases the chance of admission.
13. Bias in ascertainment or assessment — Once the subjects are identified, it is possible that more care is exercised by the investigators for cases than for controls.
14. Interviewer bias or observer bias — Interviewer bias occurs when one is able to elicit better response from one kind of patients (say, those who are educated) relative to the other kind (such as illiterates).
15. Instrument bias — This occurs when the measuring instrument is not properly calibrated.
16. Hawthorne effect — If a subject knows that he is being observed or being investigated, his behavior and response can change.
17. Recall bias — There are two types of recall bias. One, arising from better recall of recent events than those occurring long time ago. Also, serious episodes are easy to recall than the mild episodes. Two, cases suffering from disease are able to recall events much more easily than the controls if they are currently healthy subjects.

18. Response bias — Cases with serious illness are likely to give more correct responses regarding history and current ailments compared to the controls. Some patients such as those of STDs may intentionally suppress sexual history
19. Repeat testing bias — In a pretest-posttest situation, the subjects tend to remember some of the previous questions and they may remove previous errors in posttest—thus do better without the effect of the intervention.
20. Mid-course bias — Sometimes the subjects after enrollment have to be excluded if they develop an unrelated condition such as injury, or become so serious that their continuation in the trial is no longer in the interest of the patient.
21. Self-improvement effect — Many diseases are self-limiting. Improvement over time occurs irrespective of the intervention.
22. Digit preference — It is well known that almost all of us have special love for digits 0 and 5. Measurements are more frequently recorded ending with these digits. A person of age 69 or 71 is very likely to report his age 70 years.
23. Bias due to non-response — Some subjects refuse to cooperate, injure, die, or become untraceable. In a prospective study, there might be some dropouts for various reasons. Non-respondents make two types of effects on the responses. First, they are generally different from those who respond, and their exclusion can lead to biased result. Second, nonresponse reduces the sample size.
24. Attrition bias — Differential nonresponse in various groups. The pattern of nonresponse can differ from one group to the other in the sense that in one group more severe cases drop out whereas in another group mostly mild cases drop out.
25. Bias in handling outliers — No objective rule is available to label a value as outlier except a guideline that the value must be far away from the mainstream values.
26. Recording bias — Two types of errors can occur in recording. One arising due to inability to properly decipher the writing on case sheets. Physicians are notorious for illegible writing.
27. Bias in analysis — This again can be of two types. First, gearing the analysis to support a particular hypothesis. Second can arise due to differential P-values. When P = 0.055, one researcher can straight refuse to say that it is significant at 0.05 level and the other can say that it is marginally significant. Some researchers may change the level of significance from 5 percent to 10 percent if the result is to their liking
28. Bias due to lack of power — You will soon notice that statistical tests are almost invariably used to check the significance of differences or associations. The power of these tests to detect difference or association depends to a large extent on the number of subjects included in the study—the sample size.
29. . Interpretation bias — The tendency among some research workers to interpret the results in favor of a particular hypothesis ignoring the opposite evidence.
30. Reporting bias — Researchers are human beings. Some can create a report such that it gives a premonition result yet based on evidence. It is easy to suppress the contradictory evidence by not talking about it.
31. Bias in presentation of results — Scale for a graph can be chosen to depict a small change look like a big change, or vice-versa. The second is that the researcher may 5 merely state the inconvenient findings that contradict the main conclusion but does not highlight them in the same way as the favorable findings.

32. Publication bias — Many journals are much too keen to publish reports that give a positive result regarding efficacy of a new regimen, compared to the negative trials that did not find any difference.

Many of the above forms of bias can be honestly unintentional. There's another class of bias however that is much more subversive; intentional bias.

"There oughta be a law…" that research should be regulated to some degree. If a pharmaceutical corporation runs a head-to-head study of its product against the competitors product, findings that don't support the desired result won't be reported at all, anywhere.

Another form of bias is the fault of the practitioner: we didn't choose to practice medicine with the hope of becoming statisticians! Subtle variations in study design, result reporting etc. can have significant effects on whether or not a claim is believable. One of my personal favorites is the "non-inferiority" result; "our product isn't worse than the other guys!". Really? When in a busy practice setting, taking time to stop and see a drug rep so that samples can be obtained for the "latest and greatest" requires that we give up a bit of our precious daily patient-contact time… For "non-inferiority"?!! Our options at this point are to smile, sign the rep's receipt and get on with our day, or stop and ask more questions, argue a few points and possibly get the rep to agree that they are in fact, throwing fertilizer… Why waste the time? It's like wrestling with a pig---you both get muddy, but the pig enjoys it!

There are also what I would deem "wasted time & talent" studies. The American Academy of Family Physicians publishes "Smartbriefs" Monday through Friday that have "soundbite"-type reports with valuable information along the line of "who is buried in Grant's tomb?". It turns out that lack of physical activity and a calorie dense/nutrient light diet is linked with obesity in children. Wow, I'm sure glad our tax dollars funded THAT study!

EBM reflects the problems listed above.

Looking at the problem from another perspective can bring in a new set of problems to consider; time is money!

In the current western medical world, payment for services is commonly separated to some degree from the recipient of those services. Numerous European countries & Canada have "socialized" medicine, covered by the government as a necessary means of caring for it's citizens. In the US the Accountable Care Act was instituted to mixed reviews and results and is now failing as more physicians refuse to participate while costs climb and care quality (often as obstacles to care) decline.

Healthcare & medical education have become major industries and drivers of the current economy. Disillusioned practitioners refer to "mangled care" organizations with good reason. It seems that we're all practicing on a treadmill with ever-increasing speed, demands on our time, bureaucratic obstacles hindering quality care, etc.

To attempt to "think outside of the box" in a careful, thoughtful manner is actively discouraged in such an environment; it requires time, wisdom and judgement. Wisdom and judgement take time to acquire before one is likely to be able to fully evaluate alternative ideas and approaches to healthcare.

Thinking outside of the box threatens the large "establishment" that has ensconced itself in the thick of things as the final arbiter of all things medical and healthcare. There is a lot of money & power in academia & healthcare-related industry; the two are locked in a tight symbiotic embrace. Industry pays academia for study results, academia provides results that industry can quote for marketing purposes.

The number and percentage of independent practicing physicians has been plummeting for the last decade or more. This means that most physicians are now in employed positions, answering to "higher-ups" who may or may not have medical training. This healthcare industry should not be confused with the healthcare-related industry mentioned above. Running the treadmill under their taskmasters with ever-decreasing reimbursements (and increasing managed care organization profits) does little to encourage stepping out of line to try something different for patients who are not getting better quickly on the standard therapies.

This leaves us with several distinct groups;

1. Academia; or academic medicine, teaching students while receiving funding from health-care-related industries such as pharmaceuticals to publish academic, peer-reviewed articles touting the benefits and necessity of the new products coming out of the industrial pipeline—expensive, new, patented medications & devices that generate a lot of income for industry and further academic awards, doctorates, etc. for those in the ivory towers.
2. Industry; pharmaceuticals, implantable devices, surgical instruments, vaccines, the list goes on…
3. Healthcare as industry; Hospitals & Healthcare Systems, Accountable Care Organizations, Managed Care Organizations, large bureaucratic organizations that employ "providers" (formerly physicians, now with an ever-increasing group of "mid-level providers").

These groups are comfortable with the predictable status quo. If there is knowledge to be acquired, it's expected to originate in the ivory tower and progress downward and outward to the practitioners in the trenches. Insurance companies don't want to pay for any more than they must pay for, often deeming new techniques & therapies "experimental" so that they can be "non-covered services".

This is the practice model that has given us such great diseases as "fibromyalgia", "chronic fatigue", "irritable bowel syndrome" and their like. Our lack of a "health care *system*" does little to encourage innovation!

Is "EBM" really new? I maintain that it's been practiced right along, but the term is just a "sound byte" that sounds great! It's a term that can be used to restrict progress as well.

We HAVE been practicing EBM since before I obtained any of my degrees or Board Certifications. By thinking outside the box, I was able to help many suffering people who had been marginalized by "the system". It took time. Time that cost me money.

I started seeing patients in 1990 with a computer keyboard instead of pen and paper. I designed my own electronic medical record (EMR) in 1990, revising it several times along the way. That took time & money. There were many other losses as well; reputation among colleagues who lacked my enthusiasm for new ideas, distrusted the changes required, perhaps felt that their autonomy was being threatened. Medicine tends to be very conservative and evolves slowly. Very few physicians think of the establishment of EMR's as a good thing. Some of us have seen the potential, embracing it early, smoothing some of its rough edges along the way. It improved care of my patients; I was willing to do that extra work. We are in a service industry. My patient is my boss in a sense. I'm at their disposal to serve them to the best of my ability.

Another example of how EBM can be used as a weapon to keep individual practitioners "in their place" and not interfere with the "comfort zone" of organized medicine is in order. I had a personal run-in with an organization that I had previously held in high regard after I innocently dared to suggest to them an area that I felt deserved more exposure. An explanation is in order for the reader to understand the issue.

The Autism Research Institute (ARI)[ix] replaced the Defeat Autism Now (DAN) group due to name confusion with the "Divers Alert Network" involved in treating decompression sickness ("the bends"). The simple name change did not change the mission of the ARI. They have held numerous educational conferences that review proposed risk factors for autism and how to minimize autism spectrum illness. Disordered methylation & mitochondrial function has been observed in those with autism spectrum disorders[x]. Methylation greatly increases the toxicity of inorganic mercury[xi]. Thiomersal is essentially Ethyl-Hg-Thiolate in structure[xii]. In the body, it is metabolized or degraded to ethylmercury[xiii] ($C_2H_5Hg^+$) and thiosalicylate.[xiv] Cases have been reported of severe Mercury poisoning[xv] by accidental exposure or attempted suicide, with some fatalities.[xvi] Animal experiments suggest that thiomersal rapidly dissociates to release ethylmercury after injection; that the disposition patterns of mercury are similar to those after exposure to equivalent doses of ethylmercury chloride; and that the central nervous system and the kidneys are targets, with lack of motor coordination being a common sign. Similar signs and symptoms have been observed in accidental human poisonings. The mechanisms of toxic action are unknown. Fecal excretion accounts for most of the elimination from the body. Ethylmercury clears from blood with a half-life of about 18 days in adults by breakdown into other chemicals, including inorganic mercury. Ethylmercury is eliminated from the brain in about 14 days in infant monkeys. Risk assessment for effects on the nervous system have been made by extrapolating from dose-response relationships for methylmercury[xvii]. Methylmercury and ethylmercury distribute to all body tissues, crossing the blood–brain barrier[xviii] and the placental barrier, and ethylmercury also moves freely throughout the body.[xix] Concerns based on extrapolations from methylmercury caused thiomersal to be removed from U.S. childhood vaccines, starting in 1999[xx].

Having been educated in the DAN (pre-ARI) protocol I was aware of some information that I thought was pertinent in the Mercury-Thiomersol-vaccine debate. "Thiomersal-free" is a misnomer, the truth is that such preparations contain *lower amounts* of thiomeraol[xxi].

Preservatives tend to settle toward the bottom of the vial. If a multi-dose vial is being used to administer doses without proper resuspension of the solution prior to drawing a dose from the vial, the last recipient of that vial can receive a significantly higher dose of thiomersal. Literature provided at the DAN meeting relayed that documents linking thiomersal toxicity to autism development had been destroyed by the manufacturer.

Thiomersal content has been reduced in vaccines, but remains present[xxii]; concerns regarding mercury in vaccines were addressed in a letter published by the Journal Pediatrics on March 13, 2008 *(update 3/17/2016: letter is no longer available online)*. As noted in the letter, parents and pregnant women may want to consider the following data and make an informed decision.

- 0.5 parts per billion (ppb) mercury = Kills human neuroblastoma cells (Parran et al., Toxicol Sci 2005; 86: 132-140).
- 2 ppb mercury = U.S. EPA limit for drinking water.
- 20 ppb mercury = Neurite membrane structure destroyed (Leong et al., Neuroreport 2001; 12: 733-37).
- 200 ppb mercury = level in liquid the EPA classifies as hazardous waste.
- 25,000 ppb mercury = Concentration of mercury in the Hepatitis B vaccine, administered at birth in the U.S., from 1990-2001.
- 50,000 ppb Mercury = Concentration of mercury in multi-dose DTaP and Haemophilus B vaccine vials, administered 4 times each in the 1990's to children at 2, 4, 6, 12 and 18 months of age.
- 50,000 ppb Mercury = Current "preservative" level mercury in multi-dose flu (94% of supply), meningococcal and tetanus (7 and older) vaccines. This can be confirmed by simply analyzing the multi- dose vials.

How does this apply to EBM?

The Journal of the American Family Physician published an "Update on Routine Child and Adolescent Immunizations" in October 2015[xxiii]. I wrote a letter to the editors of the JAFP, clearly stating that I was a proponent of vaccination, but that having some experience with metal toxicology, I thought it would be wise to supplement vaccine recipients with reducing compounds such as high-dose Ascorbic Acid (Vitamin C)[xxiv] to bowel tolerance [xxv] (the dose at which diarrhea starts, indicating maximal dosing of an individual at that particular time due to their own need for the supplement). α-Lipoic Acid[xxvi], N-acetyl cysteine[xxvii], glutathione[xxviii] and it's precursor cysteine[xxix] all help with the excretion of this toxic metal. The JAFP deleted my post at the "comments" section at the end of the article and refused to allow it to be published. They hid behind the mantra of EBM as the basis for their decision, despite references such as those in the paragraph above.

In review of my experiences with "EBM":

I have been involved in all phases of clinical trials; I've seen first-hand what is involved with these studies. I was a principle investigator in the largest NIH-funded Complementary & Alternative Medicine study ever funded, the Trial to Assess Chelation Therapy (TACT). I have participated in numerous Phase I through IV clinical studies for a variety of types of medications. I've pursued studies in areas that were devoid of CME credits—simply because I wanted to be able to do more for my patients. I've had numerous successes, fought many battles and have

scars to prove it—scars that come from proponents of EBM who use the term as a weapon to defend themselves against what they don't understand (nor seemingly, care to study).

Managed care embraces the idea of EBM. There seems to be a perception in that industry that it will reduce medical care to easily coded check-lists without any appreciation of the nuances of atypical presentations of illness, concurrent factors involved in care, etc. They anticipate a more predictable revenue stream; care that does not fit the recipe is easy fodder to be a "non-covered service". Good for their stockholders, bad for the patient and provider. I was driven broke by "managed care". When I closed my practice, no single provider was able to provide the variety of care that I provided to my patients. It took six different physicians to do what I did for my patients. My wife and I have suffered from this "unknown illness". We then learned from Dr. Shoemaker what we didn't know. It became a "known illness" with hope for recovery. The steep learning curve has deterred every colleague I've tried to tell about this illness. I know that I am not alone in this observation. I persevere. It's the right thing to do for our patients.

Ritchie Shoemaker, MD is an example of somebody who came "before his time". An individual with rarified talent, drive, perspective, intuition & insight. He was presented with a problem. His mind was not held back by the idea of EBM and the "way we do things". He chose wisely at numerous points along his path.

I'm simply just another family doctor taking care of patients, giving them my best. I have been greatly encouraged by recognizing the talent that I've been shown. I am very honored to have the ability to cast my lot with the "Pied Piper of Pocomoke" and follow his lead!

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[i] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3789163/
[ii] http://classroom.synonym.com/language-use-writing-reflective-essay-3292.html
[iii] http://www.africaspeaks.com/articles/obeah.html
[iv] https://en.wikipedia.org/wiki/Ayurveda#History
[v] http://www.shen-nong.com/eng/history/chronology.html#origin
[vi] https://en.wikipedia.org/wiki/Homeopathy
[vii] https://en.wikipedia.org/wiki/Germ_theory_of_disease
[viii] http://www.medicalbiostatistics.com/Types%20of%20bias.pdf
[ix] https://www.autism.com/
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[xi] http://www.tandfonline.com/doi/abs/10.1080/20016491089226
[xii] https://en.wikipedia.org/wiki/Thiomersal
[xiii] https://en.wikipedia.org/wiki/Ethylmercury
[xiv] https://en.wikipedia.org/wiki/Thiomersal#cite_note-T-in-vaccines-13
[xv] https://en.wikipedia.org/wiki/Mercury_poisoning
[xvi] https://en.wikipedia.org/wiki/Thiomersal#cite_note-21
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[xviii] https://en.wikipedia.org/wiki/Blood%E2%80%93brain_barrier
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[xxiv] https://www.ncbi.nlm.nih.gov/pubmed/6940480
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