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Quo Vadis Medicina Ex Testimoniis? Part 1. A Quarter Century after Its Inception, Where is Evidence-Based Medicine (EBM) Today? More Questions than Answers

Jenicek M*

Department of Health Research Methods, Evidence, and Impact, Faculty of Health Sciences, McMaster University, Hamilton, ON, Canada

***Corresponding author:**

Milos Jenicek,
Faculty of Health Sciences,
McMaster University, Hamilton,
ON, Canada,
Tel: 1 - 519 - 856-1324,
Email: jenicekm@mcmaster.ca

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Summary

The domain of 'Evidence-based medicine' (also known as 'EBM') is increasingly ubiquitous across the medical literature and experience. It is just about one generation old and worthy of further refinements. Five related insights are outlined here:

- Among others, clinical epidemiology, fundamental and field epidemiology and biostatistics have led to EBM.
- EBM is still defined in multiple ways and its objectives are based on these multiple EBM definitions.
- Only the meaning of 'evidence' and its uses in health sciences and professions have changed. Steps of the EBM practice have simply expanded.
- Applications of EBM have also expanded and currently move beyond their essential use in cause-effect relations. EBM is also increasingly dependent on modern critical thinking, argumentation, decision making, and communication while grading of evidence supports the development of clinical guidelines. Scientific method follows such lines of thought.
- Evaluation of EBM practice as an activity requires the best possible understanding of its structure, process, impact, efficacy, effectiveness, efficiency, and equity. Such an evaluation is still rare today.

This article is the first in a series of two. It outlines what has been done so far in the EBM domain. The second article directly follows the first and discusses what remains to be done in the future.

Medicine has always been evidence-based and its evolution depends on its current nature and development, as well as on its evaluation, which all depend on us as professionals in health sciences and practice. Further training in the EBM domain should help progress our mutual understanding as developers and users.

A note about references: Transient and often temporary value are inherent to electronic references and websites. Many are worth quoting here, but Reader bewares!

To mistrust science and deny the validity of the scientific method is to resign your job as a human. You'd better go look for work as a plant or wild animal. *P.J. O'Rourke* 1947- Parliament of Whores (1991) Philosophy aside, isn't the practice of EBM a health program of sorts, an activity to be known, evaluated, and understood as such?

Just as Peter asked Jesus in the New Testament about two thousand years ago, Domine, quo vadis? (Where do you go, Master, i.e.to be crucified again?), we may ask ourselves today where we are a quarter century or so since the birth of evidence-based medicine within the context of medicina ex testimoniis [1], i.e. evidence-based medicine. We may also wish to know where we should and probably will go from here. Thirteen years ago, we examined similar questions, Quo vadis Medicina ex testimoniis? And concluded then that the evidence-based medicine (EBM) glass remained half-full and half empty [2]. Current use of 'evidence' in logic and critical thinking still

requires clarification.

Historically, medicine has always been evidence-based! Today, what is new then? It is the meaning of 'evidence' itself which appears as a new asset and entity to explore, use, and further develop. Is it more than 'that's what I have seen' or 'that's what our most experienced Colleagues say'? Is it perhaps more objective, more pragmatic, more focused, more reproducible, and more evaluable?

Let us try in this essay to outline some challenges and questions pertaining to EBM today and to highlight the best ways to define, pragmatize and solve them now and in the future.

As for EBM and evidence itself, we still must determine systematically across an ever-increasing number of book and article titles if we are speaking of the same thing to be integrated and interpreted across a widening experience. A systematic review of Amazon-listed book titles (numbering these days in the thousands) might bring surprising results and itself constitute a relevant research project!

As a matter of fact, among other resources today, Amazon compresents several lists with up to six thousand books and other publications bearing 'evidence-based' titles (monographs) of which over one hundred have their cover pages reproduced. The latter pertain not only to evidence-based medicine, evidence-based dentistry, evidence-based nursing and evidence-based public health, but also to various specialties and activities including palliative medicine, obstetrics and gynecology, infectious diseases, geriatric medicine, newer medicines like complementary and alternative medicine, clinical activities like patient history physical diagnosis, communication disorders, rehabilitation, as well as specialties and subspecialties or specific activities within them.

Original articles on EBM further extend this count. However, do they all address the same topic?

In this paper, which is an essay, and not a systematic review and analysis of EBM today (although this should also be done sooner rather than later),

- Let us discuss EBM and its past and present contributions and definitions (background, history and definitions, methods, limits and criticism, applications, and education).
- Let us also reflect here on what we should or shouldn't do in EBM in the years to come.
- This is not a classical research paper or article, but rather a reflection paper or position paper.

In the past two or three decades, new medicines have appeared, namely Evidence-Based Medicine, Personalized Medicine, Cognitive Medicine, Functional Medicine, Precision Medicine, Patient-Centered Medicine, Person-Centered Medicine, Interpretive Medicine, and others. How can we perceive and understand them?

- What are such entities more precisely?
- Are all these medicines entirely new, evolutionary, revolutionary, exclusionary, or complementary?
- Are they based on different underlying philosophies, research methodologies, or subjects of interest?
- Are they practiced sufficiently? Do we have enough experience with them to evaluate their structure, process, and impact?
- Are they relevant both for research and practice?
- What might we consider for their future use, expansion, and refinement?

In this essay, let us focus first on evidence-based medicine (EBM). Hence, what kinds of medicine shall we see, practice, and develop in this millennium? Will some or all these new forms of medicine be involved?

To answer such questions, let us first examine some remarkable advancements in medicine and other health sciences as well as experiences achieved by past generations, especially in the last two centuries. The number of new paradigms, associated methodologies and their wide applications and uses are steadily increasing. Where we are today and what can we anticipate in the near future?

As always, we want to practice a medicine that is not only rational, effective, patient-oriented, ethical, and human, but also that make senses. This essay should open the debate about what we want, what we should do now and later and the framework we should use.

In this spirit, let us argue that:

- Today's medicine is not simply experience- and scientific method-based. As always, patients and their communities matter, and serve as a basis and terrain for such experience and scientific method uses.
- Initiatives and contributions of evidence-based medicine (EBM), as remarkable as they may be, do not provide satisfactory answers and solutions to all major challenges in health professions.
- In addition to epidemiology, biostatistics and other probability and uncertainty focused methodologies, the recent development of several branches of modern philosophy offers an increasingly operational and usable methodology to rationalize both understanding and decision making in medicine, particularly through formal and informal logic, and argumentation, in addition to well-established, even broader ethics-related notions.
- Our modern ways of understanding and making decisions about health phenomena and their management will only benefit from such developments, provided they are mastered, used and integrated within basic sciences, clinical experience and skills, clinical and fundamental epidemiology,

biostatistics, management and decision-making methodology.

- The above considerations apply not only to medicine, but also to all health professions and sciences if increasing experience and use support such paradigm extensions in dentistry, nursing, veterinary medicine, chiropractic, physical therapy, clinical psychology and the broadest spectrum of alternative and complementary medicines and other health professions.
- Reasoning, decision making, and critical thinking supported by epidemiology, biostatistics, healthcare management sciences (administration, economics, and others) must fundamentally be a learned clinical and community medicine experience. To fully benefit from them, do we need a new, integrated fundamental discipline to be taught and mastered by all from the undergraduate level up? We believe so.

Several distinct periods of development in recent medicine allow us to expand our knowledge of many topics beyond medicine, namely the definition of any entity of interest (domain of orismology), perception, cognition, error and harm detection, explanation, and control and avoidance (lathology), or organization and management of our clinical or community activities or both, and their evaluation. These topics and activities apply to all levels of prevention and to health promotion. Ideally, physical and biological factors as well as social factors, dependent or independent, should be taken into account.

A quarter of century or so has already elapsed since the first initiatives in evidence-based medicine (EBM) and the refinement of EBM's identity, objectives, content, methodology, and applications. Remarkable monographs, papers and sources of information, electronic and otherwise, on the subject continue to multiply in number. In this context, we may now consider the following questions:

- Historically, what preceded and led to EBM? Is EBM actually new?
- What is EBM today, how might it be defined, and what are its objectives?
- Do we know what we are talking about? What are EBM's methodological strengths and weaknesses, especially regarding definitions, as an example?
- What are its applications and uses across the health sciences?
- What might we expect and possibly do with EBM in the future?

1. Historically, What Preceded and Led To EBM?

As previously mentioned, medicine has always been evidence-based! Only the definition of evidence and the uses of evidence have changed over time, since the word and experience of a respected authority no longer suffice.

Historical development, rich practice and numerous contributions in fundamental, field, and clinical epidemiology and biostatistics throughout generations remain core EBM methodologies today. However, as discussed in the following pages, these methodologies and experiences are also coupled with the methodology of EBM in terms of modern philosophy, its informal logic, argumentation, or critical thinking in managing health problems, decision making and communication as scientists and practitioners.

2. What Is EBM Today, How Might it be Defined, and what are its Objectives?

Shouldn't we agree not only on what EBM is, but also on what we mean by evidence and qualitative attributes in this domain?

2.1. Are We All Speaking and Thinking About The Same Concepts?

Two papers triggered the current EBM trend. In 1992, the Evidence-Based Medicine Working Group proposed a new approach to teaching in practice and medicine3, and in 1996, Sackett's et al.'s reflection4 proposed what EBM should be:

- Evidence-based medicine is the process of systematically finding, appraising, and using contemporaneous research findings as the basis for clinical decisions about the care of individual patients [3].
- Evidence-based medicine is the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients [4].
- Dixon et al [5] consider EBM to also be the application of the scientific method:
- In its broadest form, evidence-based medicine is the application of the scientific method in healthcare decision making. … Evidence-based medicine (EBM) is an approach to medical practice intended to optimize decision-making by emphasizing the use of evidence from well-designed and well-conducted research. Although all medicine based on science has some degree of empirical support, EBM goes further, classifying evidence by its epistemological strength and requiring that only the strongest types (coming from meta-analyses, systematic reviews, and randomized controlled trials) can yield strong recommendations; weaker types (such as from case-control studies) can yield only weak recommendations [5].
- In addition to more recent lists of definitions, other definitions (indicated below) somewhat loosely follow the original explanations of what EBM should be:
- The consistent use of current best evidence derived from

published clinical and epidemiologic research in management of patients, with attention to the balance of risks and benefits of diagnostic tests and alternative treatment regimens, taking account of each patient's unique circumstances, including baseline risk, comorbid conditions and personal preferences [6, 7].

The integration of the best research evidence with clinical expertise and patient values [6]. The process of systematically finding, appraising, and using contemporaneous research findings as a basis of clinical decisions [8]. Consistent use of the best available evidence, preferably from current peer-reviewed sources in electronic and print media, to inform decisions about optimum patient management; decisions should consider the needs and preferences of individual patients [6].

The integration of the best research evidence with clinical expertise and patient values [6].

It's about integrating individual clinical expertise and the best external evidence. … Evidence based medicine is the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients. The practice of evidence-based medicine means integrating individual clinical expertise with the best available external clinical evidence from systematic research. By individual clinical expertise, we mean the proficiency and judgment that individual clinicians acquire through clinical experience and clinical practice. … By best available external clinical evidence, we mean clinically relevant research, often from the basic sciences of medicine, but especially from patient-centered clinical research into the accuracy and precision of diagnostic tests (including the clinical examination), the power of prognostic markers, and the efficacy and safety of therapeutic, rehabilitative, and preventive regimens [8, 9].

Other definitions are more general, going beyond the "research – clinical expertise – patient or community" trio of considerations:

- The practice of medicine in which the physician finds, assesses, and implements methods of diagnosis and treatment on the basis of the best available current research, their expertise, and the needs of the patient. The expertise here means special skills or knowledge acquired by a person through education, training, or experience. (Expertise also includes the respect and practice of medical ethics) [9].
- The practice of medicine in which physicians find, assess, and implement methods of the best available risk assessment, diagnosis, and treatment and prognosis; on the basis of the best available current research, inline with medical ethics consideration within a specific setting of practice and society [10].
- From an epistemological perspective, EBM can be defined also as a set of principles and methods to ensure that decisions regarding the individual patient as well as population-based policies regarding groups of individuals are consistent with the most credible evidence while relying on both type 1 (fast, automatic, intuitive, experiential, affect-based) and type 2 (slow, analytical, research-based logical and probabilistic cognitive processes) to weigh the trade-offs involved in alternative understandings of questioned phenomena and decision-dependent courses and results of action [11-13].
- Evidence-based medicine is the practice and research of medicine and other health sciences in which the physician and health professional find, assess and implement methods of diagnosis and treatment on the basis of the best available current research, their expertise, and the needs and values of the patient and the community [10].

Other definitions are also worthy of attention, some based on the three elements mentioned above, some going beyond them.

As we have seen above, evidence-based medicine and other evidence-based sciences and professions are still the subject of multiple, and often heterogeneous, definitions. Is there a common way to define the evidence-based domain in health sciences and professions? Let us try to do so in the nearest possible future.

3. Do we know exactly what we are talking about? What are EBM's methodological strengths and weaknesses, especially regarding definitions, as an example?

- To this day, we still do not know if everyone means the same thing when referring to 'evidence-based medicine', 'evidence' within the context of EBM, and other terms in the EBM vocabulary. Could our certainty in this matter increase in the future?
- The following content, definitions, classifications, and characterizations may be considered by some to be repetitive. However, they provide additional information on many aspects of our thoughts.
- The emerging domain of orismology (from the Greek "orismos" meaning definition and "logos" meaning study) emphasizes the relevance of the best possible definitions of whatever we are doing and interested in.
- From a more detailed coverage of this topic elsewhere14,15, let us examine briefly how orismology applies to the EBM domain. Orismology in EBM is not overstated, but it is certainly highlighted here.
- Not everything is well defined in EBM, which limits its relevance and calls for further improvements and developments.
- As an example, is the basic definition of EBM as formulated by Sackett et al. an adequate motivational definition or is it something more? They proposed [4]:

- Evidence-based medicine is the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients [4].

Could and Should This Definition Have been Formulated Better?

This original definition is a composite definition. To make it usable, we must specify what each individual component means to us: What is 'evidence'? What is 'conscientious' and what isn't? What is 'explicit' or 'judicious' offering to help us decide what EBM is and who is its practitioner and who isn't? Such a definition may be valuable from a motivational perspective, but something more is needed to make it operational.

As a matter of fact, definitions still may be [16]:

- No definition at all (missing, absent definitions)
- Inspirational and motivational, strategy-motivated, value (judgment)-based, cause-based and cause-containing, content-listing, context specifying, uncertain or evolving, a posteriori developed, specialty-bound or type of care-dependent, subject-missing, purpose missing, patient/physician centered, those of other scientific endeavours and entities, and
- Operational.

Needless to say, as practicing professionals we would prefer all relevant definitions to be operational, moving successfully from one proponent and recipient to another.

In medicine, ideally, the definition of any variable, entity or observation should allow proper measurement, classification, decision making, action, and evaluation. It should also reflect changes (by changing itself).

In addition to the above definition types, composite definitions also require definitions of each of their constituting elements in order to make them as operational as possible. Starting with the definition of EBM, what should be considered, improved, implemented, and evaluated?

What then is 'Evidence' Itself in Our Context?

Here are some definitions of evidence itself:

- Any data or information, whether solid or weak, obtained through experience, observational research or experimental work. These data or information must be relevant and convincing to some (if not full) degree either to the understanding of the problem (case) or to the clinical decisions (diagnostic, therapeutic or care oriented) made about the case. 'Evidence' is not automatically correct, complete, satisfactory and useful. It must be first evaluated, graded and based on its own merit [14, 17].
- A fact or body of facts on which a proof, belief or judgment is based. Evidence does not mean certainty. Rather, it represents an available proof with varying degrees of certainty [18].
- In medicine, evidence itself is a broad entity encompassing any data or information, whether solid or weak, obtained through experience, observational research or experimental work (trials). This data or information must be relevant and convincing to some (best possible) degree either to the understanding of the problem (case) or the diagnostic, therapeutic, or otherwise care oriented clinical decisions made about the case [17].

And what about the other components cited above that constitute one of Sackett et al.'s EBM definitions [4]?

- What is 'conscientious'?
- What is 'explicit'?
- What is 'judicious'?

How can we identify who is or isn't a practitioner of EBM? Many definitions are remarkably motivational, but maybe otherwise useless.

What kind of methodology has been developed so far and to what extent?

The steps of EBM practice further define this domain, however indirect such specifications might be.

The five original steps, as proposed, may be reworded as follows:

- Converting clinical information of interest (about prevention, prognosis, therapy, causation, etc.) into answerable questions; defining the problem; (what kind of evidence are we interested in?).
- Searching for wanted sources of information; tracking down, with maximum efficiency, the best evidence with which to answer them, whether from clinical examination, diagnostic laboratory, research evidence, or other sources; (obtaining the best evidence to fit our needs and interest).
- Critically appraising the evidence for its validity (closeness to the truth) and usefulness (clinical applicability); critically evaluating the information; (what is such evidence worth?).
- Applying the results of this appraisal in our clinical practice to the patient; integrating the critical appraisal without our clinical expertise and with our patient's unique biology, values, and circumstances; (using valid and useful evidence obtained); and
- Evaluating our performance; efficacy, effectiveness and efficiency in executing steps 1-4; evaluating this application on a patient and seeking ways to improve for next time (was it worth it?) [6, 19].

These five original steps may be expanded to include namely [17]:

- Converting the need for information into an answerable question; formulating the question that needs to be answered concerning the problem, patient, or community (identifying the need for evidence);
- Tracking down the best evidence with which to answer that question; searching for evidence (producing the evidence);
- Critically appraising the evidence for its validity, impact, and applicability;
- Integrating the critical appraisal with our clinical expertise, and with our patient's unique biology, values, and circumstances (linking the evidence);
- Selecting the best evidence available for clinical and community health decision making (using the evidence);
- Connecting the evidence to clinical and community health knowledge, experience, and practice with the patient's and/or community values and preferences (integrated uses of evidence);
- Implementing useful findings in clinical (clinical care) and community (public health policies and programs) medicine's decisions and practice (implementation of evidence);
- Using the evidence in clinical and/or community care to solve the patient's or community problem (uses of evidence in specific settings);
- Evaluating the effectiveness of uses of evidence in this case and situation (weighing the impact); evaluating our effectiveness and efficiency in executing steps 1-8 and seeking ways to improve them both for next time;
- Evaluating the implementations and the overall performance of evidence-based medicine and/or evidence-based public health practitioner and activity (evaluating structure, process and impact of evidence-based actions, economical, and managerial real and desired characteristics); and
- Teaching and expanding EBM practice and research (going beyond what was already achieved).

In other and shorter terms, EBM does not consist of and focus on the production of high-quality evidence only. It also encompasses its uses, and the effects such uses bring to the patient, their health care provider (not just doctors!), the health system, community, and society.

4. What are EBM's Applications and Uses across the Health Sciences? Is Our Understanding of EBM The Same Across The Literature and Current Experience?

Evidence-based medicine, however accepted, has been criticized in general terms and in detail [20].

There are still multiple definitions of EBM as well as of its components in composite versions of EBM. In this context, can we evaluate how we do research in EBM, how we practice it, and what are the results of such practices across past and current experience?

For an example of the practice of EBM as it is currently defined, let us briefly look at the domain of causality. Causality so far is the main focus and topic of evidence-based medicine, and rightly so. However, this is not enough.

So far, it appears that cause-effect relationships such as those between exposure to a beneficial factor (treatment) and disease cure or prevention or between a noxious factor and the risk of disease occurrence and severity are subjects of considerable attention in EBM. And rightly so. However, other health phenomena and their management require further study.

(Table 1), below, illustrates a broader spectrum of possible questions in medical research, clinical domains of applications and types of research (only examples are given here), as well as fields of application and examples of practical problems to be solved.

The assessment of causality across the available information by

Table 1: Questions in medical research, clinical domains of application and examples of practical problems to be solved. Links and correspondences between the three.

Examples of questions in medical research	Clinical domain and Clinical domain and answer the question: examples.	Fields of application, examples of practical problems to be solved
DIAGNOSIS AND NEW EXPLORATORY TECHNOLOGIES		
What is the subject of diagnosis?	Forming clinical entities	Evaluation of internal and external validity of diagnostic and screening tests
How serious it is?	Measuring disease severity diagnostic criteria for Understanding the diagnostic process	Establishment of daily practice and disease surveillance
How do we arrive at diagnosis?		
HEALTH EVENT OCCURRENCE		

When, where, and in whom problems (health events)or cross-sectional appear?	Descriptive longitudinal of disease. studies at the hospital and in the community	Epidemiological portrait Disease spread
Studies of natural or Epidemiological	Epidemiological clinical course of cases	surveillance. Disease clustering
CAUSAL RESEARCH		
Why did it happen?	Etiological research byobservational studies.	Disease etiology research by comparative studies of exposure to various factors and disease occurrence using cohort and case-control studies
	Causes identification.	Elucidation of causes of disease spread.
INTERVENTION(Prevention and/or treatment)		
Can we control case(s) or disease?	Efficacy, effectiveness, and efficiency evaluation.	Phase 1-4 clinical trials.
Did we control case(s) of disease?	Systematic reviews and meta-analyses of interventions and their effect	Impact of secondary and tertiary prevention.(mainly)
Will it control, solve the problem?		Meta-analyses and systematic reviews of interventions effect
		Decision analysis.
PROGNOSIS Study of disease outcomes		
What might or will happen later on?	Survival studies. Descriptive and analytical studies of probabilities of events derived from case studies (disease course).	Epidemiological and clinical forecasting of exposures to beneficial or noxious factors Descriptive and disease occurrence and spread based on clinical follow-up and epidemiological surveillance.

way of Bradford Hill's criteria (strength of association, consistency, specificity, temporality, biological gradient, plausibility, coherence, experiment, analogy) and its grading [21] is essential, but does not suffice. Besides causality evidence, diagnosis evidence or prognosis evidence, among others, merit the same focus. If EBM wishes to be consistent with one of its major definitions, it is not enough to produce and evaluate the best evidence. We must also assess its uses and effect, as well as its links with clinical expertise, connecting (and how?) individual patient (or community) roles, needs, characteristics and preferences, in the framework of type 1 and type 2 ways of critical thinking and reasoning. Patient values are not forgotten and must not be forgotten either [22-32].

In conclusion to this first part of our discussion: The present achievements of Evidence-Based Medicine.

EBM was born and proposed with an attractive and relevant titre. Beneath its five basic steps of work and thinking lie more proven and used clinical epidemiology practices, biostatistics, health management and administration as we know and apply them today.

What will and should follow then? Let us take a closer look in the second article of this two-part series.

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