

Quo Vadis Medicina Ex Testimoniis? Part 2. After A Quarter of Century, What Now? Some Questions and Answers

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Received: 01 Nov 2020

Accepted: 17 Nov 2020

Published: 19 Nov 2020

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Citation:

Jenicek M. Quo Vadis Medicina Ex Testimoniis? Part 2. After A Quarter of Century, What Now? Some Questions and Answers. Japanese Journal of Gastroenterology and Hepatology. 2020; V5(3): 1-7.

Summary

Despite being a young domain with a one-generation history or so, evidence-based medicine has benefitted from thousands of contributions, as reflected in numerous book titles and subjects, and original articles.

EBM-related philosophical insights are increasing as are endeavours in reasoning, modern argumentation, considerations of causality, and grading of evidence.

The scientific method is in focus in most communications including research projects and ensuing medical articles.

Quantitative and qualitative methods will further expand across evidence-based methodology and applications.

The more the future is obscure, the more promising it may be for some. How promising is evidence-based medicine?

The last quarter of century created today's evidence-based medicine, focused mostly on various beneficial (clinical trials) and noxious effects of various non-clinical and clinical factors on health. Clinical epidemiology and biostatistics methodologically prevail. In addition to this historical experience the ways of thinking, exchanging experience with various interested parties and peers as well as the ways of communicating such experience develop and rightly so. In other terms, we may be asking ourselves if today EBM today isn't more than the production of high-quality evidence in quantitative and qualitative terms. Yes, it is. But shouldn't it be more?

EBM relies also on high quality, pragmatic reasoning, informal logic, critical thinking, and decision making in the context of modern

philosophy.

1. Some Philosophical Contributions to Cherish and Develop in The Future

How can we define such concepts in this context?

Thinking, across the literature, is a mental action which, if verbalized is a matter of combining words in propositions [1-5].

Critical thinking (from several definitions) is the intellectually disciplined process of actively and skillfully conceptualizing, applying, synthesizing and/or evaluating information gathered from, or generated by observation, experience, reflection, reasoning, or communication as a guide to belief and action [1-3].

Critical thinking components are an integral part of epidemiology, clinical epidemiology, and decision making in practice and research. Isn't evidence-based medicine a medicine of critical thought? it also is.

Critical thinking in medicine deserves more detail and discussion, as also presented elsewhere [4, 5].

Reasoning in general is thinking leading to a conclusion. Judgments (inferences) are derived from facts, observations, and/or hypotheses. In other words, it is a tool to form conclusions, judgments, or inferences from facts or premises [6].

Clinical reasoning is a context dependent way of thinking and decision making in professional practice to guide practice actions [7].

We discussed fallacy-free reasoning in medicine in more detail elsewhere [8].

An argument in medicine is a connected set of statements originating from a lived situation, experience, or research in medicine intended

to establish a position in medical problem solving, understanding, and decision making.⁷

A modern form of an argument [9, 10] is the Toulmin et al. model as a multi element process of reasoning to reach valid conclusions. We discussed this kind of modern argumentation and its application in more detail elsewhere [4-6, 11].

Modern medical argumentation is useful (if not necessary) not only in the production and evaluation of evidence in research and practice. A considerable volume of information in health sciences and professions is also communicated the argumentative way, even in medical journal articles today [12-14].

Should we go beyond evidence-based medicine within this context or within a larger framework incorporating informal logic, critical thinking and modern argumentation in a kind of cognitive medicine or cognitive medical thinking? [15].

Yes, we should.

So far, grading evidence continues to focus mainly on cause-effect relationships. This is still not supported by a systematic review of past and current experience. Far reaching consequences include clinical and community medicine guidelines.

As an example of the most frequent evidence grading, let us take the 'pyramid of evidence' which illustrates graphically the hierarchy of evidence strength for causal proofs: the weakest evidence is at the base of the pyramid while increasingly stronger evidence is found towards the top:

- Synopses.
- Meta-analyses,
- systematic reviews.
- Experimental studies
- (clinical trials).
- Analytical cohort studies (observational).
- Analytical case-control studies (observational).
- Observational descriptive studies.
- Single clinical case reports, case series reports.
- Hearsays, anecdotes, narratives, plain ideas, opinions.

With minor modifications and expanded sources of information, such a hierarchy of evidence may be found across the literature [16-18].

2. Is Evidence of Causality the Sole Evidence to be considered in Relation to Grading?

Based only on Bradford Hill's criteria¹⁹, evidence of causality appears as a basic way to consider relationships between care and cure or prevention and staying healthy. More than causality assessment may be needed in the world of clinical guidelines. Is grading of evidence becoming a tool beyond the clinical guidelines' domain? The GRADE approach also assumes qualitative considerations and expert individual and team opinions in clinical guidelines and recommendations development and uses [20-23]. It is the subject of an increasing number of developments, reflections, and opinions.²⁴⁻²⁵Clinical

guidelines remain an evolving system, reflecting or not the GRADE approach [21-26].

The GRADE Working Group underlines several advantages of GRADE, like clear separation between the quality of evidence and strength of recommendations, explicit evaluation of the importance of outcomes of alternative management strategies, or transparent process of moving from evidence to recommendations among other GRADE characteristics.²¹Numerous rating evidence and grading systems exist, under other acronyms like the SORT system (Strength of Recommendation Taxonomy) or OCEBM (Oxford Centre for Evidence-Based Medicine) recommendations. numerous evolving OCEBM websites

Hierarchy of evidence, levels of evidence, or GRADE systems of evaluation are evolving fields and have weaknesses. Critical and independent evaluation of GRADE and other approaches, management of intellectual interests, encouragement of critiques of existing approaches and testing new ideas, and willingness to recognize deficiencies in methods and to address them may, and will be, subject to change. Without these changes, GRADE is not sustainable as a leading approach for developing guidelines [27].

Shouldn't grading, meta-analyzing, and systematic reviewing of evidence go well beyond the evaluation of cause-effect relationships? Certainly! It all depends on how broad our vision of EBM is in the future.

3. Scientific Method and Its Place in EBM

Production and uses of evidence, as well as its evaluation, are domains of uses of qualitative and quantitative research. We reason deductively, inductively, or additively depending on the nature and objectives of the health problem. The scientific method underlies research projects, research reports in medical articles and elsewhere, and it is behind various types of communication.

As (Table 1) shows, the scientific method includes the following expanded steps:

(Table 1): Sequence of Steps Summarizing the Scientific Method

I. Creating research on the basis of currently available experience and evidence and identification of the problem of interest

- Observation, description, definition, and identification of the problem, formulation, and reformulation (if needed)to be studied and solved
- Operational definition of variables and other entities of interest
- Examination of currently available background knowledge in a search for elements that might help to solve the problem

II. Formulation of a hypothesis to explain the problem (most often a cause-effect relationship)

- Hypothesis development and formulation
- Conceptual evaluation of the hypothesis and its compatibility with currently available knowledge

- Establishing testable consequences, whether the hypothesis is accepted or rejected
- Using the hypothesis to make predictions of other phenomena and/or to predict in quantitative terms the results of new observations

III. Conducting experimental or observational studies to test hypotheses and predictions

- Building the design of an empirical (experimental or observational) test of the hypothesis and/or a consequence of the hypothesis (specifying types of studies)
- Actual empirical test of the hypothesis, involving a search for both favorable and unfavorable evidence (examples and counterexamples)

IV. Analyzing results, drawing conclusions, reporting the experience

- Critical examination and statistical processing of the data (errors, outlying data, and inferences)
- Detection and control of errors, biases, and fallacies
- Evaluation of the hypothesis in light of its compatibility with both the background knowledge and the new evidence produced by the study
- Formulating meaningful conclusions in light of the study results
- Identification of falsifiability (cases when conclusions do not apply)
- Proposing future directions on the basis of the newly acquired experience, i.e. making decisions, recommendations, and directions regarding what to do in future research and practice
- Replication of study to confirm the consistency of what was found (if need to be)

V. Taking actions and evaluation of what was done and its results

Source: As assembled from philosophy at large for health sciences and professions in References 7 and 9.

Let us remember that such steps of the scientific methods contain several elements common to modern argumentation (Toulmin's model) [10, 11] already mentioned above and expanded here:

- the claim or conclusion of our argumentative reasoning,
- grounds as the basis from which we reason,
- backing by a body of evidence supporting a warrant,
- a warrant as a general rule or experience,
- understanding the nature of the problem of interest

a qualifier, i.e. an expression which quantifies the certainty with which we make our claim in light of the preceding blocks and connections between them,

- rebuttals as conditions or circumstances under which our claim does not apply, and
- Connectors between various statements.

Such commonality of scientific method and modern argumentation makes sense [4].

The scientific method and its steps represent, to a variable degree of completeness, building blocks of research grant applications, reports of research results, ensuing medical articles, as well as various guides and guidelines to activity both in research and practice: implicitly or explicitly. We have discussed in more detail such necessary efforts elsewhere [4-5, 8].

(Table 2) illustrates connections between the scientific method of thinking, elements of modern argumentation and critical thinking as well as their reflex across the elements of a medical article.

Formulation and uses of the scientific method in general, as well as in medicine, evolve and they are subject of continuous attention.

If we want our practice and research to be more rigorous and “scientific research-based”, shouldn't we know and practice EBM itself

Table 2: illustrates connections between the scientific method of thinking, elements of modern argumentation and critical thinking as well as their reflex across the elements of a medical article. Connections between the scientific method, arguments, and medical articles

Scientific method	Argument	Medical article
Characterizations backing, warrant		Problem in context, Introduction, literature review, (external evidence), external evidence
Research question, assumptions		Original idea, thesis, Introduction proposition, backing, warrant
Hypothesis, Original idea, information input		Introduction backing, warrant
Prediction		Backing, warrant Introduction
Experiment (data input: Grounds, data, Material and methods collection and analysis)		(internal evidence) Results
Conclusions made (accept or modify hypothesis)		Support (adducts), Discussion and qualifier, claim conclusions
Contradictions, errors, Attenuators, rebuttals	Discussion	biases, fallacies, review of limitations, hypothesis rejection
Falsifiability considerations	Attenuators, rebuttals	Discussion
Replications considered	Depending on rebuttals	Discussion and qualifier
Decisions made recommendations	Claim, conclusions	conclusions and Action considered, taken, Additional study, evaluated proposed corrective measures
Revision of the theory, New argument	Discussion/conclusion, new theory proposed	developed and recommendations

in a similar way?

To some degree, we already do. The five basic steps of EBM line up with the scientific method as indicated above.

4. Let us Conclude by Stating What we Might Expect and Do with EBM in The Future: An Expanded Consideration and Practice of Evaluation of How Do We Do It and What Have We Achieved in Health Professionals and in our Patients and any Other Target Community?

Evidence-based medicine, *medicina ex testimoniis*, is still a very young domain compared to its historical components and contributors, such as epidemiology, clinical epidemiology, biostatistics, ethics, and other related areas of philosophy.

It is perhaps too early to undertake a systematic review and research synthesis of EBM endeavours and activities themselves. However, it may and should be, considered in the future.

As with any other activity in the domain of health, we are interested in our evaluations of health phenomena and activities in:

- Structure (how it is all organized),
- Process (how does it work as designed), and
- Impact (what is the effect of such an activity)

So far, we know:

- how EBM activity is organized (its structure),
- less about its functioning (the process of an organized system), and
- Almost nothing about positive or negative impacts on our patients and on us, as health professionals.

If we examine through the eyes of health economists the practice of EBM as a health activity with a specific program and objectives^{7,6}, we may consider evaluating what the practice of EBM medicine is in terms of a health program:

- Efficacy, i.e. result under ideal conditions (a “can it work” question),
- Effectiveness, i.e. result under prevailing, ordinary or customary conditions and patients (a “does it work” question),
- Efficiency, i.e. effects in proportion to the effort (human, material resources, time) in healthcare activity (a “what does it cost for what it gives” question), and
- Equity, i.e. fairness and impartiality of EBM care (as one of its possible causes). In other words, we want to know “how well the costs and benefits of EBM are distributed”.

It may still take time to develop and better understand such aspects of care.

No one is to blame for the lack of knowledge regarding the impact of EBM. More time is simply needed for the process and impact of EBM to develop with all its measurable effects. Knowing EBM's structure better than its process and impact is reassuring as it marks the completion of an important step.

Is the practice of EBM more beneficial for patients, health professionals, or the community? Despite all information currently avail-

able, we still should know more. EBM itself should still be better defined in more operational terms as a technique of practice. Any definitions of other types of practice to which it can be compared should also be improved.

In 2015, Empananza, Cabello, and Burls²⁷ published an analysis of a natural experiment in a Spanish hospital, inquiring if evidence-based practice improves patient outcomes. In this case and elsewhere, operational and reproducible definitions of patients, health professionals involved, interventions, care, or outcomes constituting groups to compare are essential, allowing researchers to conclude if EBM practice is better than its alternative(s) and if so, where, when, in whom, and by whom. This study focused mainly on patients.

Other evaluations of EBM focus primarily on the role, needs, and current achievements of health professionals, administrators and managers in public health, clinical medicine, and patient and community health and disease.

As for evaluating EBM itself:

- How much will its mastery and practice improve patient and/or community health?
- Will EBM practice make physicians feel more comfortable? Will EBM practice improve communication, understanding and sharing of health problems and interaction between patients and their surrounding professional environment of care?
- How can the quality of such above-mentioned EBM practice and research be methodologically evaluated to the satisfaction of clinical epidemiologists?
- It is probably too early to respond to these questions. Years from now, the answers they produce will most likely enrich our conviction that we are doing the correct and better thing. Will all this be more than a ‘it makes sense’ feeling?
- It will be interesting to see if developing and practicing EBM in the future will lead to improved patient health, physician professional practices and expertise, and patient values and preferences, as well as to the production of evidence itself.
- Professional training in EBM also requires professional teaching and training at the undergraduate and graduate levels in other disciplines and domains. Will this happen in current programs or new ones? Time will tell.

There are two reasons to teach and understand EBM and its expanded and still expanding methodology:

- Students should realize and understand ‘why, what and how they are being taught all this’.
- We, as their teachers, should know ‘how to teach and explain all this, and why’.

Given EBM's unquestionable attractiveness and relevance, we expect too much, too fast, and our expectations and goals may not be fulfilled without modern informal logic, argumentation and critical

thinking as contemporary ways of producing and sharing evidence for the benefit of individual patients and the community. Gathering such information will still take time.

This perspective is not only intellectually and professionally exciting, it is also possibly necessary.

Aren't evidence-based medicine and other evidence-based health professions today, such as nursing, dentistry, public health, as well as other initiatives and domains (often called 'complementary' or 'alternative' such as chiropractic, homeopathy, or naturopathy) subject to systematic rigor and expertise?

If we direct our attention in a balanced way not only towards research evidence, but also towards the physician's clinical experience and the patient as a beneficiary of such experience (as EBM is also defined), more will certainly be done in the domain of professional experience by taking into account, among other things, on the patient side, the patient's genetic content or other molecular and cellular analysis tools like molecular diagnostics, imaging and analytics. That is, for example, the focus of precision medicine [28].

Don't We All Share The Same Philosophy, Ways of Thinking, and Goals? We Believe So

Although further information regarding the role of clinical epidemiology, biostatistics, informal logic and reasoning in EBM is currently available, we have not found so far in the current literature more insights about the sharing of experience and the role of perception in the EBM domain. Also, we still do not know enough about whether EBM practice influences health professionals' perception, judgment, decision making and evaluation. And whether such and other kinds of EBM practice are better than their alternatives.

Besides a rigorous scientific approach and methodology, sensory perception (sensation) such as seeing, listening, palpating, smelling, vocally communicating and sharing may play a variable role in evidence study and its development, uses, effects and evaluation of evidence in EBM. What is the role of perception as 'the organization, identification, and interpretation of sensory information in order to represent and understand the presented information or the environment' [29] in the development and uses of evidence in EBM? Do we know? Our attention to what we are doing and thinking regarding the benefits of an increasingly beneficial modern philosophy and its domains as reflected above will certainly grow.

As for evidence itself, we know now more than ever about cause-effect relationships such as between treatment and cure or prevention, or between exposure to noxious factors and occurrence of disease. We know much less about diagnosis and health and disease courses. Shouldn't we work on this?

All our conclusions and recommendations are rooted in our current reflection. They are not yet supported by systematic follow-ups of EBM's state, past and present evolution, developments, completeness of information, and evaluation of its practice and effects across the larger or entire experience for health professions. This remains to be done. Let us try to enrich such valuable information together. It

will not be easy, given the sheer number of books, articles, and other reports about the EBM experience, but this should not discourage us.

Some ways to proceed are proposed in this essay. What could be added, expanded, and otherwise stated better? Readers may have their opinion in these matters.

Only a systematic review, analysis, and synthesis of current and evolving EBM experience (this has not yet been done) will bring us better 'evidence about evidence and its uses' and information regarding what to do and how to do it in the hopefully not too distant future.

EBM has reached the point where, as a still evolving attractive and relevant domain, it increasingly merits some kind of "midway" analysis, evaluation and tracing of future developments and refinements. This reflection does not replace EBM itself, but may bring us to think about the relevance of such a rigorous endeavor.

Let us reiterate: medicine has always been "evidence-based". Only the notion of evidence, its scope, uses, and practice have evolved with time. Therefore, we should seek to continue to contribute to it, as many of us have for more than a generation.

How can we answer our introductory question: *Quo Vadis Medicina Ex Testimoniis?* Contrary to the biblical question, *Domine, quo vadis?*, also mentioned at the beginning of this article, the future of evidence-based medicine appears optimistic. Several beneficial initiatives have already taken place and many more will surely come. As a relatively new domain with a truly appealing name, EBM remains an evolving field to be further developed, used, and evaluated as this essay suggests. The evaluation methodology must go well beyond any kind of individual expert opinion or position, however solid they may be.

EBM foundations were built by clinical epidemiologists, field epidemiologists, and biostatisticians, among others. Modern philosophers²⁹ are pragmatists who join the first two generations of EBM builders. We do not always fully realize this.

Less seriously, beyond health sciences and professions, even horsemanship may be considered today "evidence-based"! [30] (N.B. Why not?)

Even less seriously, the author of this essay fondly remembers an informal chat about fifteen years ago with David Sackett, one of the author's intellectual accomplices, where it was mentioned that "if you wish to publish a donkey's ass, stamp 'evidence-based' on its buttocks"!

EBM will not be crucified! Let us all continue to move forward in this context and to the best of our abilities.

Some basic books and textbooks³²⁻³⁴ quoted in this paper have been brought into a broader context. Many others are beyond this reading.

So where should we go from here?

If we are considering EBM as another specialty or methodology domain, do we need a fundamental and broad dictionary like John Last's *A Dictionary of Epidemiology* [36] in the epidemiology domain?

- Do we need a formulation of its teaching, research and practice objectives, as structured as it is in existing, more traditional specialties and subspecialties?
- Do we need a more complete methodology as well as techniques of practice? Excellent books which first introduced the EBM domain, mostly in medicine³²⁻³⁴ and public health [35] have given way to ever-expanding coverage in all health sciences and professions. The websites quoted at the end of the References section in this article reflect the trend.
- Do we need to evaluate the success of the above both as teachers and students?
- Besides the mostly quantitative methodology integrated within EBM essentially by clinical epidemiology and biostatistics, should we expand the mostly qualitative domain of modern argumentation, critical thinking, reasoning and decision making as occurs already progressively in the EBM domain?
- Do we need the development and practice of evaluation systems and methods more specific to the EBM domain to know if we have been successful both as teachers and the recipients of our message? It all depends on whether we consider EBM as a health program and activity to improve health professions (and compared to what?), and/or the health of patients and community, or just an alternative way of thinking for health professionals. Patient health and community health improvements evaluation studies are just the beginning. What can we improve in the EBM domain beyond all the above?

Our perspective regarding EBM matters:

- Is it just an exceptional intellectual exercise and practice to be further refined, or
- Is it also a health program and intervention to be built, practiced, and evaluated as such? If so, what control (non-EBM) health program and intervention should be used as a comparison?

Evidence-based medicine (and other evidence-based health sciences and professions) is perhaps still too young to answer these questions. Should we not contribute to it and advance it as much as we can? Yes, we should. Evidence-based texts are still open and unfinished.

References

1. Ennis RH. *Critical Thinking*. Upper Saddle River, NJ: Prentice Hall, 1996.
2. Bowell T, Kemp G. *Critical Thinking. A Concise Guide*. London and New York: Routledge/Taylor and Francis, 2002.
3. Hughes W, Lavery J, Doran K. *Critical Thinking. An Introduction to the Basic Skills*. Seventh Edition. Peterborough, ON / London, UK / Moorebank, NSW: Broadview Press, 2015.
4. Jenicek M. *A Primer on Clinical Experience in Medicine. Reasoning, Decision Making, and Communication in Health Sciences*. Boca Raton / London / New York: CRC Press / Taylor & Francis Group / Productivity Press Book, 2013.
5. Jenicek M. *Fallacy-Free Reasoning in Medicine. Improving Communication and Decision Making in Research and Practice*. Chicago, IL: American Medical Association, 2009.
6. Jenicek M, Hitchcock DL: *Evidence-Based Practice. Logic and Critical Thinking in Medicine*. Chicago, IL: American Medical Association, 2005.
7. Majumder AA, Sa B, Alateeq FA, Rahman S. *Teaching and Assessing Critical Thinking in Clinical Reasoning Skills in Medical Education*. Chapter 12, Pp. 213-233 in the *Handbook of Research on Critical Thinking and Teacher Education Pedagogy*. Hershey, Pa: IGI-GLOB-AL.com., ©2019.
8. Jenicek M. *Fallacy-Free Reasoning in Medicine. Improving Communication and Decision Making in Research and Practice*. Chicago, IL: American Medical Association, 2009.
9. Toulmin SE. *The Uses of Argument*. Cambridge: Cambridge University Press, 1958 (Updated edition 2003).
10. Toulmin S, Rieke R, Janik A. *An Introduction to Reasoning*. 2nd Edition. New York: Collier Macmillan, 1984.
11. Jenicek M. *Teaching critical thinking in medicine. A journey back to the future*. In: Facione NC, Facione PA: *Critical Thinking and Clinical Reasoning in the Health Sciences. An International Multidisciplinary Teaching Anthology*. Millbrae, Ca: The California Academic Press, 2008.
12. Jenicek M. *How to read, understand, and write 'Discussion' sections in medical articles. An exercise in critical thinking*. *Med Sci Monit*. 2006; 12: SR28-SR36.
13. Jenicek M. *Writing a 'Discussion section in a medical article: An exercise in critical thinking and argumentation*. Chapter 27, pp. 457-465 in: *Biomedical Research. From Ideation to Publication*. Edited by G. Jagadeesh, S. Murthy, YK Gupta and A Prakash. New Delhi / Philadelphia / Baltimore / New York / London / Buenos Aires / Hong Kong / Sydney / Tokyo: Wolters Kluwer Health/ Lippincott / Williams &Wilkins, 2010.
14. Jenicek M. *Do we need another discipline in medicine? From epidemiology and evidence-based medicine to cognitive medicine and medical thinking?* *J Eval Clin Pract*. 2015; 21: 1028-34.
15. Ebell MH, Siwek J, Weiss BD, Woolf SH, Susman J, Ewigman B et al. *Strength of Recommendation Taxonomy (SORT): A Patient-Centered Approach to Grading Evidence in the Medical Literature*. *American Family Physician*, 2004; 69: 548-556.
16. Smith FG, Tong JE, Smith JE. *Evidence-based medicine. Continuing Education in Anesthesia Critical Care & Pain*. 2006; 6: 148-151.
17. Baker A, Young K, Potter J, Madan I. *Reviews of grading systems for evidence-based guidelines produced by medical specialties*. *Clin Med*. 2010; 104: 358-63.
18. Burns PB, Rohrich RJ, Chung KC. *The Levels of Evidence and their*

- Role in Evidence-Based Medicine. *PlastReconstr Surg*. 2011; 128: 305-310.
19. Hill AB. The environment and disease: association or causation? *Proc Roy Soc Med*. 1965; 58: 295-300.
 20. Schunemann H, Hill S, Guyatt G, Akl EA, Faruque A. The GRADE approach and Bradford Hill's criteria for causation. *J Epidemiol Community Health* 2010.
 21. GRADE Handbook. Introduction to GRADE Handbook. Handbook for grading the quality of evidence and the strength of recommendations using the GRADE approach. Edited by H. Schünemann, J. Brozek, G. Guyatt and A. Oxman. 55p. at www.gdtgrande.org/app/handbook/handbook.html, last retrieved Sep 19, 2019.
 22. Guyatt GH, Oxman AD, Vist GE et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *Br Med J*. 2008; 336: 924-6.
 23. Guyatt GH, Oxman AD, Schünemann HJ, Tugwell P, Knottnerus A. GRADE guidelines: A new series of articles in the *Journal of Clinical Epidemiology*. *J Clin Epidemiol*. 2011; 64: 380-382.
 24. Moberg J, Oxman A, Rosenbaum S, Schünemann HJ, Guyatt G, Flottorp S, Glention C, Lewin S, Morelli A, Rada G, Alonso-Coello for the GRADE Working Group. The GRADE evidence to decision (EtD) framework for health system and public health decisions. *Health Res Policy Syst*. 2018; 16: 45.
 25. Neumann I, Alonso-Coello P, Vandvik PO et al. Do clinicians want recommendations? A multicenter study comparing evidence summaries with or without GRADE recommendations. *J Clin Epidemiol*. 2018; 99: 33-40.
 26. Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, Schünemann HJ, GRADE Working Group. GRADE; an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ*. 2008; 336: 924-926.
 27. Emparanza JI, Cabello JB, Burls AJE. Does evidence-based practice improve patient outcomes? An analysis of a natural experiment in a Spanish hospital. *J Eval Clin Pract*, 2015; 21: 1059-1065.
 28. Wikipedia, the free encyclopedia. Precision medicine. 5p. retrieved from 2019.
 29. Handbook of Philosophy of Science. Volume 16. Philosophy of Medicine. Edited by Fred Gifford. General preface by Dov Gabbay, Paul Thagard and John Woods. Amsterdam: Elsevier and North Holland, 2011.
 30. Peters S, Black M. Evidence-Based Horsemanship. Shelbyville, Ky, 40065: Wasteland Press, 2012 (2018).
 31. Jenicek M. How to Think in Medicine. Reasoning, Decision Making, and Communication in Health Sciences and Professions. Abingdon and New York: Routledge (Taylor @ Francis Group/Productivity Press), 2018.
 32. Dixon RA, Munro JF, Silcox PB. The Evidence-Based Medicine Workbook. Critical appraisal for clinical problem solving. Oxford (UK): Butterworth Heinemann, 1997.
 33. Sackett DL, Scott Richardson W, Rosenberg W, Haynes RB. Evidence-based medicine. How to Practice & Teach EBM. New York and Edinburgh: Churchill Livingstone, 1997 (Second edition 2000). Users' Guides to the Medical Literature. A Manual for Evidence-Based Clinical Practice. 3rd Edition. Edited by G. Guyatt, D. Rennie, M.O. Meade and D.J. Cook. New York and Chicago: McGraw Hill Education / JAMAevidence, 2015. Previous editions 2002 and 2008.
 34. Straus SE, Richardson WS, Glasziou P, Haynes RB. Evidence-Based Medicine. How to Practice and Teach EBM. 3rd Edition. Edinburgh and London: Elsevier/Churchill Livingstone, 2005. Previous editions 1997 and 2000.
 35. Brownson RC, Baker EA, Leet TL, Gillespie KN. Evidence-Based Public Health. Oxford and New York: Oxford University Press, 2003.
 36. A Dictionary of Epidemiology. Fourth Edition. Edited by JM Last (with Associate Editors, RA Spasoff, SS Harris and M. Thuriaux, Linguistic and lexicographic consultant JB Anderson). Oxford and New York: Oxford University Press, 2001.