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COMMENTARY

The ecosystem of evidence cannot thrive without efficiency of knowledge generation, synthesis, and translation

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Abstract

Evidence-based medicine (EBM) has experienced numerous advances since its inception over 2 decades ago. Yet a persistent gulf remains between how medicine is actually practiced and the goal of providing care based on best available research evidence integrated with patient perspective and clinical expertise. A primary source of challenge for EBM is induced by inefficiencies in the generation, synthesis, and translation of evidence. During the 8th International Conference for Evidence-based Healthcare Teachers and Developers, GIMBE Foundation presented an innovative approach by defining an ecosystem of evidence. Based on the features of a natural ecosystem, the ecosystem of evidence is influenced by living organisms: stakeholders replete with competition and collaboration among and between them, as well as their conflicts of interest; the environment: social, cultural, economic, and/or political contexts; and nonliving components: scientific evidence, influenced by the rules, standards, and frameworks associated with evidence generation, synthesis, and translation. This article provides an analysis of the strengths and weaknesses of this ecosystem with a focus on nonliving components, specifically evidence generation, synthesis, and translation. Specific suggestions are outlined for building a stable and resilient ecosystem of evidence.

Keywords: Evidence-based medicine; Knowledge translation; Evidence synthesis; Biomedical research; Research design; Ecosystem

1. Introduction

Evidence-based medicine (EBM) has experienced numerous advances [1] since its inception more than 25 years ago [2]. Yet a persistent gulf remains between the goal of providing care based on best available research evidence integrated with patient perspective and clinical expertise and how medicine is actually practiced. Critics raise concerns that EBM tends to focus on benefits while ignoring adverse events, that it reports average results and thus disregards the wide variability in individual risks and responsiveness, that it neglects the patient-doctor relationship and clinical judgment, that it leads to a sort of reductionism, and that it is vulnerable to distortion by corruption and conflicts of interest (COI) [3]. As John Ioannidis argues, ‘‘EBM is paying the price of its success: having become more widely recognized, it is manipulated and misused to support subverted or perverted agendas that are hijacking its reputation value’’ [3].

Fortunately, the scientific community has progressively shifted the debate from generic and unjustified criticisms to real issues that affect evidence generation, synthesis, and translation into clinical practice and health care delivery [4,5]. A lively debate on EBM and its myriad strengths and threats was published in a series of articles in this journal in April 2017 [3,6–10]. We posit that the true problem is not the crisis of EBM per se, as suggested by its detractors, but rather inefficiencies in the generation, synthesis, and translation of evidence. For example, in some cases, there is significant waste due to the proliferation of duplicative systematic reviews (SRs) and clinical practice guidelines (CPGs). In other cases, there are gray areas of clinical practice where evidence is lacking, insufficient, fragmented, or conflicting. In the latter case, it is impossible to make recommendations, for or against many health care interventions. Moreover, inefficient translation of evidence leads to gaps between research and clinical practice. These gaps produce suboptimal health outcomes and waste due to the overuse [11] and underuse [12] of drugs, devices, diagnostic tests, and other health care interventions.

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What is new?

What this adds to what was known?

- Evidence-based medicine is assessed through the lens of an ecosystem made up of living organisms, the environment, and non-living components.
- Strengths and weaknesses of the non-living components of this ecosystem (scientific evidence generation, synthesis, and translation) are identified.

What is the implication and what should change now?

- Evidence Generation: Enhance efforts to increase value and reduce waste in medical research.
- Evidence Synthesis: International cooperation is needed to improve quality and reduce duplication of systematic reviews and clinical practice guidelines.
- Evidence Translation: Strategies are needed to implement and monitor advances in knowledge translation, shared decision-making, and patient adherence.
- In the ecosystem of evidence, the evidence synthesis must always inform generation of new evidence, and evidence translation must inform both generation and synthesis of evidence.

During the 8th International Conference for Evidence-based Healthcare Teachers and Developers (Box 1), GIMBE Foundation (Gruppo Italiano per la Medicina Basata Sulle Evidenze, an Italian Evidence-Based Medicine Group) presented its innovative approach to the ecosystem of evidence, based on the definition of a natural ecosystem: a community of living organisms in conjunction with the nonliving components of their environment (air, water, mineral, soil), interacting as a system.

The ecosystem of evidence is influenced by

- Living organisms: stakeholders replete with competition and collaboration among and between them, as well as their COIs (Fig. 1).
- The environment: social, cultural, economic, and/or political contexts.
- Nonliving component: scientific evidence, influenced by the rules, standards, and frameworks associated with evidence generation, synthesis, and translation (Fig. 2).

GIMBE Foundation has analyzed the strengths and weaknesses of the generation, synthesis, and translation of evidence and has formulated suggestions to build a stable and resilient ecosystem of evidence.

Box 1 History of EBHC conference

Since 2001, the GIMBE Foundation has been organizing the International Conference of Evidence-based Health Care (EBHC) Teachers & Developers in Italy, with its now-long tradition firmly rooted in Sicily. After having held the first conferences in Altavilla Milicia (2001) and in Palermo (2003), the event has since 2005 been held in Taormina, where the 8th EBHC conference took place on 25−28 October 2017. Since its inception, the conference aims to promote exchange and the development of international networks to improve tools, techniques, and educational pathways and to implement and teach EBHC. The conference includes plenary sessions held by international experts, oral presentations selected from among the hundreds submitted by professionals worldwide, and interactive workshops, poster sessions, and working groups. Over the years, the more than 800 individuals representing all health professions and disciplines from around the world have come to Sicily to discuss and share their experiences of teaching and implementing EBHC. Delegates include researchers, clinicians, decision-makers, administrators, students, and representatives of influential scientific societies. The EBHC Conference has also produced the "Sicily Statement" [13], a pivotal consensus article that represents an international standard for evidence-based practice (EBP), and its further extension on EBP learning assessment tools [14].

The 9th edition of the EBHC International Conference will be held in Taormina on 6th-9th November 2019: www.ebhc.org.

2. Strengths and weaknesses

2.1. Evidence generation

Strengths in evidence generation are driven by global efforts to improve research efficiency, reproducibility, and transparency and to reduce research waste [15]. Efficiency is being addressed by groups like the REduce research Waste And Reward Diligence (REWARD) Alliance [16] that provides a platform for sharing methods and resources to improve value and reduce waste in biomedical and clinical research. The REWARD Alliance's work is complemented by the James Lind Alliance Priority Setting Partnership [17] that identifies high priority areas of research to meet the needs of patients and clinicians. The Evidence-Based Research Network [18] also fosters efficiency by promoting best practices in the production, updating, and dissemination of SRs and by emphasizing that no new primary research should be conducted without prior SR of existing evidence.

Fig. 1. Health care and health research stakeholders.

Fig. 2. Generation, synthesis, and translation of evidence.

Reproducibility of research has been enhanced by common reporting standards. Particularly, valuable resources in this domain include the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) reporting guidelines [19], the Preferred Reporting Items for Systematic Reviews and Meta-Analysis for Protocols (PRISMA-P) [20] guidelines, and the statement by The Academy of Medical Sciences committing to a global effort to improve reproducibility and reliability of biomedical research [21]. The Enhancing the QUAlity and Transparency of health Research network [22] provides an invaluable and extensive repository of research reporting guidelines for researchers to access.

Transparency of research has been enhanced by efforts to promote clinical trial registration and data sharing. Clinical trial registration not only facilitates transparency, it also reduces publication and reporting bias. Such registration has gained recognition as an essential practice through initiatives such as AllTrials [23], the World Health Organization's (WHO) International Clinical Trials Registry Platform [24], and statement on public disclosure of clinical trial results [25] and the International Committee of Medical Journal Editors (ICMJE) requirement, as a condition of consideration for publication, that trials are registered in a public trials registry [26]. The ICMJE has also led efforts to promote data sharing by researchers [27]. Current policy for member journals requires that clinical trials enrolling participants after January 1, 2019 include a data sharing plan in their trial registration.

Weaknesses in evidence generation include research funders' low adherence to REWARD recommendations [28], a lack of evidence on the best ways to engage patients in research [29], and excessive fragmentation and bureaucracy in the regulation and management of research [30]. Furthermore, despite validated tools for assessing risk of bias, too many trials still use inadequate methods [31] and reproducibility of research is still low [32]. There are also too many primary studies without SRs of available evidence [33]. The Center for Evidence-Based Medicine Outcome Monitoring Project [34] has demonstrated high frequency of post hoc outcomes switching in SRs. In addition, TrialsTracker [35] built by the Evidence-Based Medicine Data Lab reveals an alarmingly high rate of under-reporting of clinical trials. All of these are issues that need to be resolved. There are also too many reporting guidelines, their impact is unknown [36], and there is still too little reporting that systematically sets research results in the context of previous trials [37].

2.2. Evidence synthesis

SRs and CPGs are the most common evidence syntheses in the research evidence ecosystem.

2.2.1. Systematic reviews

Strengths in the area of SRs include development of the hierarchy of evidence, from the traditional EBM pyramid to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach, currently endorsed or used by more than 100 organizations around the world [38]. Other strengths include the availability of Cochrane Collaboration guides and handbooks to standardize and improve the methodology of SRs [39], the PRISMA reporting guidelines [40] and their extensions, and the GRADE methods in Cochrane reviews [41]. Weaknesses of SRs include the widespread "publish or perish" virus, resulting in an epidemic production of useless, incomplete, outdated, methodologically flawed SRs [42]. Other weaknesses are the slow growth of Cochrane reviews and protocols [43] and that the impact factor of Cochrane Database of Systematic Reviews has remained substantially

unchanged [44]. Finally, there is also the fact that the Database of Abstracts of Reviews of Effects, a repository of high-quality SRs, has not been updated since March 2015 [45] due to funding limitations.

2.2.2. Clinical practice guidelines

Among the strengths of CPGs is the increasing development and global leadership of the Guidelines International Network (G-I-N), which comprises over 100 organizations involved in developing and implementing CPGs [46]. Other strengths are the use of the international standards for producing and appraising CPGs developed by G-I-N [47], the Appraisal of Guidelines for Research Evaluation Enterprise (AGREE) [48], and the Institute of Medicine [49]. G-I-N has also developed standards for COI disclosure and management [50]. GRADE standards have provided a common method for formulating CPG recommendations [51], and reporting standards are now available for CPG developers including the AGREE reporting checklist [52], the Reporting Items for practice Guidelines in HealThcare Statement [53], and the Checklist for the Reporting of Updated Guidelines [54].

Weaknesses of CPGs include the fact that there are too many on the same disease/condition and many are of low quality or outdated [47–49]. CPG recommendations are also at risk of being influenced by COIs. Usability can be limited by the fact that CPGs do not take into account multimorbidity [55], and recommendations are often limited in scope due to insufficient evidence. Finally, there is no central CPG database searchable according to quality criteria.

2.3. Evidence translation

Evidence translation refers to the integration of evidence into clinical practice. A strength of evidence translation is the existence of robust frameworks that illustrate the process of integrating evidence into practice including critical determinants, methods, and tools for knowledge translation (KT). The ''pipeline'' framework developed by Paul Glasziou and Brian Haynes illustrates the process of how clinicians become aware of evidence, accept it, address its applicability, and apply it [56]. The pipeline framework also addresses the need for patients to agree with and adhere to recommendations for ultimate success. The Knowledge-to-Action framework [57] outlines methods to identify the best available evidence to address an organizational problem and the steps required for integration into the organization's workflow. Users are encouraged to adapt evidence to their local context, assess barriers and facilitators to its implementation, measure and evaluate change in organizational processes and outcomes, and monitor and react to efforts for sustained knowledge use. Among the many frameworks for KT, the Consolidated Framework for Implementation Research provides a comprehensive method for assessing barriers and facilitators to implementing evidence at the organizational level [58].

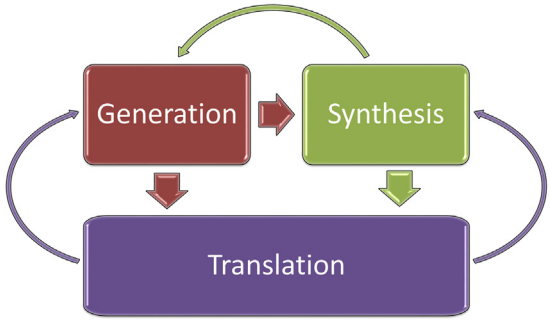

Fig. 3. The ecosystem of evidence: the multidirectional approach.

Weaknesses for evidence translation are primarily related to the fact that implementation science, the study of methods to promote integration of EBPs into health care settings, is a young science. Evidence for evidence translation is currently highly context-specific, making generalization difficult. Furthermore, implementation science principles are not yet included in most academic curricula. What we do know is that professional behaviors can be heavily influenced by habit and COIs, that information systems are fragmented and not well connected and that patients and the general public still lack awareness of the effectiveness, appropriateness, and safety of health care interventions [56,57].

3. The way forward

There are many paths that can be taken to strengthen EBM. We believe that the priorities outlined below are most urgent and offer the best potential for creating a robust and sustainable evidence ecosystem.

3.1. Evidence generation

Many issues must be addressed and strategies implemented to increase value and reduce waste in biomedical research. For example, development of reporting guidelines is often not sufficiently robust [59], and we need vigorous efforts to expand the use and impact of reporting guidelines [60]. Furthermore, both the WHO statement and ICMJE policies concerning clinical trials must be extended to registering observational studies. Strategies to reduce the fragmentation of regulatory policies must also be identified and implemented, and more opportunities to increase the reproducibility of biomedical research must be leveraged. Fewer publications and more high-quality evidence could be fostered by changing the standards by which biomedical research is assessed for funding and impact and by increasing the efficiency of basic research [61,62]. Finally, a better balance is needed between basic, translational, clinical, and health services research [33].

3.2. Evidence synthesis

In terms of evidence synthesis, improved SRs depend on international policies that converge SR development toward Cochrane reviews. A new ICMJE Statement is also needed that includes mandatory registration on the PROSPERO International Prospective Register of Systematic Reviews [63] for publication and that encourages the publication of short versions of Cochrane reviews in affiliated ICMJE journals. Finally, a centralized database for non-Cochrane, high-quality SRs is essential.

The necessary improvement of CPGs depends on international cooperation to avoid CPG duplication and the proliferation of low-quality CPGs. In addition, universal application of G-I-N standards would result in improved management of COIs. CPGs also require better strategies to account for multimorbidity in their recommendations. Furthermore, a central CPG database is needed that allows searches according to quality criteria (e.g., AGREE II, G-I-N, IOM). Finally, CPG usability would improve if recommendations were integrated into clinical decision support systems.

3.3. Evidence translation

To improve the translation of evidence into clinical practice and health care delivery, more high-quality evidence is needed regarding KT, shared decision-making, and patient adherence. In addition, standards are needed to define KT priorities at the local level as are standards for adapting CPGs to the local setting. Performance measures that assess effectiveness of KT efforts must be valid and reliable. Furthermore, outcome measures, as well as performance measures and reward systems must be aligned across layers of organizational structure (professional → team → health care organization → health care system). The general public's, and especially patients', health literacy must also be improved; knowledge of the effectiveness, appropriateness, and safety of health care interventions will help to align patient expectations with best practices in medicine and public health care systems.

Finally, in the ecosystem of evidence, the flow must no longer be unidirectional but multidirectional (Fig. 3); evidence synthesis must always inform generation of new evidence, and evidence translation must inform both generation and synthesis of evidence. The time has come for public and private payers to stop financing health interventions of unproven efficacy and to increase funds for comparative effectiveness research.

4. Conclusion

The current state of the EBM ecosystem for evidence generation, synthesis, and translation has areas that are thriving and others that are at risk. Recognition of these strengths and weaknesses and paths forward to a more robust system allows health care and public institutions to focus on real problems facing EBM rather than those purported by universal critics. Much progress has been made over the past 25 years and much more is needed to deliver the ultimate promise of EBM for patients and the public.

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