## The Evolving Nature of Evidence-Based Medicine: The Past Present and Future

During the last three decades, the concept of Evidence-Based Medicine (EBM) has caused great interest among healthcare professionals (1). In essence, Evidence Based Medicine (EBM) is "the conscientious, explicit and sensible use of current best practice in making decisions about the care of individual patients" (2). The components of EBM include the use of evidence, clinical judgement and patient preference. In practice, EBM represents integration of clinical expertise, patient's values and best available evidence in process of decision making related to patients health care (3). Clinical judgement is especially vital in the evidencebased approach to care because the evidence found may not be relevant to a specific patient (4). Medical knowledge grows every day, so that previously accepted facts rapidly become obsolete due to the explosion of scientific information (5).

The forces which had kept the EBM movement alive and ongoing were altered significantly during the coronavirus (Covid)-19 pandemic (6). The sudden pandemic exposed discrepancy between the demand and availability of scientific evidence (7). Deaths of thousands of people including physicians and other health-care workers (while offering Covid-19 care) across the globe shook the confidence of the physicians towards the practice of EBM. Journals started publishing in a hurry, spewing incomplete and at times misleading scientific articles about Covid-19, leaving the physicians in a dilemma about the evidence (8). In the circumstances, the practitioner of EBM has had to turn helplessly to non-documentary evidences to treat Covid-19 patients.

Like the proverbial coin, however, EBM has its two sides, too. There are a number of limitations and criticisms of EBM (9,10). Research produced by EBM, such as from Randomized Controlled Trials (RCTs), may not be relevant for all treatment situations (11). Research tends to focus on specific populations, but individual persons can vary substantially from population norms. Because certain population segments have been historically under-researched (due to reasons such as race, gender, age, and comorbid diseases), evidence from RCTs may not be generalizable to those populations (12).

Thus, EBM applies to groups of people, but this should not preclude clinicians from using their personal experience in deciding how to treat each patient (13). As the medical adage goes, "Knowledge gained from clinical research does not directly answer the primary clinical question of what is best for the patient at hand"EBM should not discount the value of clinical experience (14).

In order to progress EBM, the success of future clinical trials requires a fundamental transformation in how trials are designed, conducted, monitored, adapted, reported and regulated to generate the best evidence (15). The status quo model is unsustainable. Instead, preventive, personalized, patient-participatory medicine is needed, and paradigm shifts are required to get there via sustainable growth. The Covid-19 pandemic created an opportunity to observe how routine clinical care and clinical trials can work synergistically to generate evidence (16). While the Covid-19 pandemic exposed inherent systemic limitations of the clinical trial landscape, it also spurred some positive changes, including new trial designs and a shift towards a more patient-centric and intuitive evidence-generation system of evidence-based medicine (17).

Clearly, one of the key lessons of the Covid -19 pandemic has been that current paradigms must be continuously challenged by emerging technologies and by all stakeholders, encompassing the new generations of scientists, physicians, the pharmaceutical industry, regulatory authorities and, most importantly, patients. In principle, the next generation of EBM will be guided by advances in wearable technologies, data science and machine learning, which have begun to transform EBM, offering a tantalizing glimpse into a future of next-generation 'deep medicine' (18).

The last 30 years have witnessed breathtaking, unparalleled advancements in scientific research from a better understanding of the pathophysiology of basic disease processes and unraveling of the cellular machinery at atomic resolution to developing therapies that alter the course and outcome of diseases in all areas of medicine. Moreover, exponential gains in genomics, immunology, proteomics, metabolomics, gut microbiomes, epigenetics and virology in parallel with big data science, computational biology and Artificial Intelligence (AI) have propelled these advances (19). In addition, the dawn of CRISPR-Cas9 technologies has opened a tantalizing array of opportunities in personalized medicine. However, despite the tantalizing array of stunning advances in basic science and technology, clinical translations in major areas of medicine remains lagging (20). An organic, participatory and all-inclusive evolution of EBM provides a promising avenue of synthesizing and applying cutting-edge healthcare to the individual patient (21,22).

In conclusion, EBM is conscious, specific, reasonable use of modern, best evidences in making

decisions about treatment of individual patients. It is not a medical cook-book with recipes, but its good application brings cost-effective and better health care. Its real purpose is to help the doctor make use of the best available evidence doctor to choose for his patient the best possible solution, with the purpose of achieving assured optimum healthcare outcomes in every aspect.

EBM is of great utility in helping avoid major mistakes in the course of treatment, in that way raising the quality of healthcare service delivery. In a wider context, EBM can literally help save the lives of patients. EBM requires new knowledge from the physician. Practically, that means mastery of the English language and computer savvy, which provides access to medical databases, the ability to search medical literature and the opportunity to acquire and hone the basic skills in the interpretation of epidemiological and statistical results. Once the physician masters the search technique and the use of EBM, he/she gets a mighty "ally" in their daily noble work. Since each physician must, in one way or another, seek valid information, we can say that the proper use of EBM saves the doctor's time and raises their level as well as the quality of provided medical services. Ultimately, it also increases satisfaction of the health professionals, contributing to satisfaction, which is the secret sauce of a never-ending positive cycle of continuous service delivery improvement.

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