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Guidelines in dermatology—*Quo vadis*?: Facts and controversies

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Abstract Since their introduction in 1980s, medical guidelines have become a milestone in the modern medical practice and science. Being a key feature of modern evidence-based medicine, guidelines offer the opportunity for unification and standardization of diagnostic procedures, their use guarantees the equal access of patients to medical service, and they represent a scaffold for inexperienced physicians. The implementation of guidelines also can serve as a basis in malpractice issues and can contribute to the formation of national and international health care policies. In past decades, the process of development, update, and practical application of clinical guidelines has been seriously improved; however, certain limitations still exist, namely cost-effectiveness issues, editorial independence, applicability, accessibility, and external validity. This contribution discusses the advantages and the drawbacks in the use and the development of medical guidelines, emphasizing future perspectives and challenges in the development of clinical guidelines.

> *Every science touches art at some points, every art has its scientific side, the worst man of science is he who is never an artist, and the worst artist is he who is never a man of science.*[1]
> –Armand Trousseau, Lectures on Clinical Medicine delivered at the Hotel-Dieu, Paris, 1868

Introduction

Medicine has been accepted as the art and the science of healing, since its early origins, dating back to ancient Greece, as witnessed in a text by Alcmaeon of Croton (ca. 500 bc).[2] Today, in the era of technical progress and evidence-based medicine (EBM), we follow the constant development and publishing of a great number of guidelines for diagnosis and management in medicine. The question of whether the "art of medicine" is compatible with the adoption of ubiquitous guides to practice medicine gains more actuality today than ever before.

Medical guideline: what is it?

There is no uniform definition of what clinical guidelines are. One definition says "guidelines" is a term referred to as

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(1) rules or instructions given by an official organization telling you how to do something or (2) something that can be used to help make a decision or form an opinion.[3] A guideline in clinical medicine is the "systematically developed statements to assist both practitioner and patient decisions in specific circumstances"[4] or "systematically developed statements that aim to help physicians and patients reach the best health care decisions."[5] Hence, the major role of incorporating guidelines into practice is to improve the quality of medical care and to implement scientifically supported evidence in real-life settings. Medical guidelines originated in the early 1980s.[6] Initially, the idea for their implementation was to raise the cost-effectiveness of medical treatments.

Different types of medical guidelines exist. Depending on the issuing authority, guidelines can be a domain of specialty organization (eg, surgery, gastroenterology, and dermatology), scientific and branch societies (eg, British Association of Dermatologists), task forces (eg, U.S. Preventive Services *Task Force*), and international organizations (eg, World Health Organization, European Dermatological Forum).

Interdisciplinary issues require collaboration for unification of the criteria for diagnosis and management. An example was the creation of an internationally recognized consensus on the classification and therapy of urticaria by the joint project of the European Academy of Allergology and Clinical Immunology, European Union-funded Network of Excellence, Global Allergy and Asthma European Network (GA^{2}LEN), and approved by the European Dermatological Forum and the European Union of Medical Specialists.[7,8]

Depending on the focus, guidelines can also cover diagnostic procedures, therapeutic strategies, and laboratory practice in a defined scope, disease, or condition. Another point for the use of clinical guides is their accessibility. A number of databases are available online and in print, for example, the "EBM Guidelines," with the incorporation of the text of the Cochrane Database of Systematic Reviews.[9]

In the field of dermatology, the increasing number of guidelines is obvious. A March 2009 PubMed search that included the terms "guidelines," and "dermatology" retrieved more than 1000 hits.[10] An advanced search in the "EBM guidelines" database resulted in 535 primary hits for skin diseases and procedures in dermatology. Thus, one may pose the questions on how easy and practical it is to use clinical guidelines, exactly which guides one should use, and where to find them.

Guidelines in dermatology: advantages

Medicine has revealed different faces throughout its development, from early empiricism through the knowledge of the "nature of the disease and cure" of the Greeks, to the medicine of the great authorities in the Middle Ages, and now the ongoing development of EBM.[2] In the beginning of the 21st century, diagnosis and treatment are being based on research-derived evidence rather than on clinical skills and experience alone. Medical guidelines that are based on randomized clinical trials and systemic reviews, the major tools of EBM, are a powerful implement in the hands of the clinician.

Guidelines are a milestone in modern medical science. They represent a scaffold for the unification and standardization of medical treatments and procedures for diagnosis. Although not a guarantee, an institutional guideline enhances the possibility—and the right—of patients to have equal access to health care, the latter being a mandatory clause in the constitutions of most countries.

Poor definition or imprecise standard of procedures, or both, may result in divergent research conclusions and incompatibilities in treatment practices, as has been shown for the control of severe or difficult-to-treat asthma.[11] Hence, there is a growing demand for standardization not only for medical terms and definitions but also for diagnostic and therapeutic procedures. In addition, application of guidelines can be beneficial for the quantitative risk assessment in human observational studies.[12]

One of the biggest advantages of guidelines is the prevention of potential diagnostic and therapeutic mistakes, especially at the hands of young specialists. At the beginning of their clinical practice, physicians often allow mistakes to slip in due to their limited experience. A guidelines-based practice is a chance to diminish errors. Guidelines are a framework for inexperienced and unqualified physicians, but a guideline can never replace the authority of medical education and clinical practice. Clinical guidelines are increasingly used in patient management.[6]

A lot of progress has undoubtedly been achieved since guidelines were first introduced in medical practice. They have been developed after a strictly established set of principles and procedures.[13] Thus, peer reviewed and reliable information is reaching the everyday medical practitioner. One can use guidelines only if fundamental knowledge and practical experience are present as preexisting conditions.

The development of guidelines gives physicians the opportunity to discover and implement scientific knowledge in their routine clinical practice, thus guaranteeing their patients have open access to medical achievements. Guideline-driven results can increase the confidence of practicing dermatologist in sharing their experience with other qualified specialists with different economic and medical backgrounds in other countries. This often provides opportunities of learning and sharing gold standard scientific and practical medical standards, thus improving patient care.

The development of guidelines offers a basis for a dialog and consensus of opinions among dermatologists from different countries. In this way, physicians are able to share personal experiences working with patients from different nationalities and genetic backgrounds. This improves the chances for understanding the essence of diseases. Elaboration of guidelines is a ground for professionals from different

specialties to share their knowledge and points of view in particular problem-solving discussions. As a wide-ranging specialty, dermatology frequently faces multidisciplinary problems, the solving of which requires collaboration of different specialties; for example, sexually transmitted infections frequently need the shared expertise of gynecologists, urologists, and dermatologists.

Medical guidelines are easily accessible and ready to use. After the computerized primary care guidelines included in the *Physician's Desk Reference and Database* were introduced in Finland in 1989,[14] a survey amongst the practicing physicians revealed that each user made from 1 to 10 searches daily, with the average time elapsed of 4.9 minutes to find and read an article. Physicians found the requested information in nearly 90% of the cases, and, in particular, dermatology was the most popular field of interest.[14,15] In addition, patients are reassured when a physician refers to a database in search of the treatment options for their condition.[15]

Clinical practice guidelines (CPG) are often used as a reference in malpractice judicial issues.[16,17] CPG are generally developed by medical societies, and their primary intention is to raise the effectiveness of a defined procedure or treatment and improve the outcome. Sticking to the scientifically based and evidenced standards is intended to protect the medical practitioner and the patient from malpractice. Physicians should be aware of the legal use of CPG because, for instance, some guidelines include a disclaimer that they are not intended and devised for the arena of the malpractice court.[17]

The implementation of guidelines into dermatologic practice allows national health care policymakers to plan drug policy to prevent, or at least reduce, the occurrence of multi-drug-resistant bacterial disorders and to perform research on local resistance of different bacterial strains after antibiotic therapy.

CPG are generally advisory but not compulsory. They should not be accepted as a dogma but should be practically applied in the context of basic knowledge of biology and medicine.[18] The enhanced communications in medical research as well as the dynamic development of new methods in medical practice justify the incorporation of clinical guidelines in routine practice. For this reason, clinical guides require constant updating to incorporate the current best evidence in making decisions about the care of individual patients. This concept is in unison with the famous first aphorism of Hippocrates, "Life is short, the art is long."[19]

Guidelines in dermatology: limitations

The process of development, update, and practical application of clinical guidelines has been seriously improved in recent decades; however, certain limitations still exist, namely cost-effectiveness issues, editorial independence, applicability, accessibility, and external validity.[4,20]

Having witnessed and lived in the restrictive regime of socialism, we can understand the restrictions created by frames and guidelines in any scope of life. At that time, we had forbidden and restrained fields and spheres; for example, we can still remember the underestimation of Gregor Mendel's laws in genetics as being considered based on an unsubstantiated scientific theory.

Being a framework for diagnostic and therapeutic approaches, clinical guidelines confine the application of new medications, treatment regimens, and the introduction of alternatives to the classical treatments constituting medical guidelines. An example in dermatology is the implementation in practice of sulfones as anti-inflammatory and antineutrophilic agents. In their 70-year history, sulfones were initially applied as antibacterial agents.[21] Today they are successfully used in a variety of dermatoses mainly characterized by accentuated neutrophil and eosinophil accumulation. Turning back to art, one may wonder if the great artists would have created their masterpieces if they were following guidelines.

CPGs reflect the effect of clinical research on health care, and hence, encompass the limitations of EBM itself. Very few clinical trials with negative results are published, and until the regulatory authorities find ways to ensure the public has availability to all trials with both positive and negative results, the optimal use of EBM would be questionable. In addition, basic and clinical research findings are integrated in CPGs, with a significant delay and many omissions.

An applied bibliometric study revealed a median age of 8 years for articles cited in 15 clinical guidelines developed in the United Kingdom. Most of the reports were published by authors living in the United States of America (36%) or the United Kingdom (25%), which was 2.5 times more than expected given that about 10% of all biomedical outputs were published in the United Kingdom.[22] The same study also found that clinical guidelines do not cite basic research papers. Another commentary in the *British Medical Journal* said that after decades of experience,

> Clinical guidelines are rarely based solely on research evidence. In most cases they also incorporate the consensus views of experts. Despite recognition of the need for rigor in developing a consensus, current approaches often lack sufficient transparency, fail to make clear what influence the level of resources in the health system has, lack sufficient reliability, and will never achieve comprehensive and timely coverage of the whole range of health care.[23]

Therefore, a new approach is suggested that makes the goals, reasons for disagreement, and degree of consensus explicit.[23]

A recent contribution in *The New England Journal of Medicine* said that many clinical guidelines in the United

States of America are influenced by the pharmaceutical industry and special interest groups:

> At present, the financial ties between guidelines panels and industry are extensive. A survey of 685 disclosure statements by authors of guidelines concerning medications found that 35% declared a potential financial conflict of interest… Guidelines have… been questioned when pharmaceutical and medical-device companies with a financial stake in the outcome provide substantial funding for their development and implementation.[24]

We are still far from elucidating and implementing an optimal approach for the creation of clinical guidelines that will guarantee lack of influences, editorial independence, and explicitly-centered public health interest.

Internationally adopted medical guidelines and consensuses are not always applicable locally due to ethnic, social, geographic, and economic factors. Dermatology patients often resort to complementary and alternative medicine (CAM) for their conditions.[25] Among patients with allergic contact dermatitis who responded to a questionnaire-based survey, 40% used CAM and 29% had visited an alternative practitioner.[25] Medicine, being a conservative discipline, hardly accepts alternatives to "classically approved" practices. Does it mean, then, that CAM cannot find place in the treatment process parallel to conventional therapies?

A country's legislative policies and requirements of local authorities can hinder the application of internationally applied guidelines (eg, the registration policies for biologics and thalidomide). The major hindrance in the implementation of guidance on a local level is the discrepancy in the organization of the health care systems in different countries. In these cases, the major principle of the World Health Organization, "think globally, act locally," is valid. National strategies and recommendations should be consistent with the requirements of local authorities and other socioeconomic factors. On the other hand, financial interests from industry and third parties can potentially influence (1) the fields of study interests (testing new formulations instead of prevention surveys), (2) publishing bias (negative and confirmatory results), and (3) reimbursement policies.

An important issue is "off-label" prescribing, which refers to therapeutic options for rare conditions or specific populations and not the improper or illegal use of a drug, and its applicability in the era of CPGs.[26] Mycophenolate mofetil was approved for the treatment of psoriasis in 1970s, and later its usage was discontinued due to the concern of carcinogenesis.[27] Despite that, dermatologists have used the medication successfully to treat a number of diseases, mainly among the autoimmune blistering disorders and connective tissue disorders. Thalidomide is another drug undergoing a Renaissance in its dermatologic applications.

Dermatology is a specialty with more than 4000 clinical entities and syndromes; thus, the role of evidence-based CPGs for rare conditions is questionable. First, the "nostrum" in dermatology is to coin the diagnosis, and second, there are many conditions for which the lack of available scientific evidence is obvious. Can the access to guides replace medical education? Hardly could anyone answer positively. And this is not the major purport of clinical guidelines. Clinical guidelines are not a "cookbook" in medical practice. Medical education and training is the mandatory base for further development of skills and knowledge, in accordance with the concept of continuing medical education. Therefore guidelines can be accepted as an auxiliary tool instead of being the "conducting baton" in the hands of the physician.

Conclusions

Who will drive progress in medicine? Obviously, not the ones who strictly stick to the guidelines. This poses some dilemmas: What will medicine be like for the ones who follow the established guidance? How will it look to those who do not attaching unreservedly to guidelines. What will be the share of the latter? Will there be young investigators in the group of those who stand against the routine?

The development and the practical application of clinical guidelines is a dynamic process. The main challenges in this process are the need for constant update and refinement of guides, harmonization conformable to local health care policies, and avoidance of subjectivity in interpretation of the available scientific evidence. The future perspectives in the field of medical guidelines development can be summarized as follows:

- Constant updates are needed to increase the efficacy and keep the guidelines current with the accumulated evidence.[28] The Cochrane Systematic Reviews are a reliable ground for guideline development because authors are expected to actualize their reviews annually.
- The guideline should include information on the cost of the defined treatment as well as a comparison to alternative methods and preventive strategies.[4]
- The development of methods for monitoring guideline use in health care is needed to increase feedback on how really effective is the use of guidelines in medical practice.[29]
- The individualized approach to each patient is the next step in the development of the medical science, mirrored by the principles of personalized medicine: medical treatment tailored to an individual's phenotypic, clinical, genetic, and molecular information.[30] Hence, medical guidelines will have to be adapted to this new concept.

Clinical guidelines should not be accepted as a frame with insurmountable boundaries. Instead, they should be regarded as aids to, not substitutes for, clinical judgment and should represent the base of the scaffold on which the future development of the "art and science of medicine" would be built.

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