

Section 1

Reviews

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ADVICES ON SEARCH AND CRITICAL APPRAISAL OF BIOMEDICAL LITERATURE PART I, GENERAL WORKFLOW

Both physician-scientists and practicing physicians regularly experience the need to browse, select, and critically appraise the current biomedical literature. There have been many useful reviews on each of the aforementioned topics. Still, having a unified and coherent workflow, feasible to fit into a busy clinical routine, would surely be appreciated by physicians. In addition, many of the aforementioned reviews have been written to target the audience in developed countries. In contrast, particularities of the access to the literature in developing countries (or economies in transition) have been addressed less frequently. Finally, new computational approaches, including machine translation and automated text mining, are rapidly emerging. These are indeed worthy addressing as the initiatives that could provide a great help to practicing physicians for rapid, yet comprehensive literature appraisals.

The present review aims to provide physicians with the workflow and methodological recommendation on browsing, selecting, and critical appraisal of the biomedical literature, with the specific focus on patient- and disease-oriented publications. The review further aims to overcome the aforementioned limitations of the previously published literature on this subject.

Key words: physician-scientist; physician; biomedical literature; critical appraisal; workflow; electronic databases; machine translation; data mining; algorithm.

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Introduction

The current time has been described as the Information Age (or Digital Age or Computer Age) [1]. This term implies that information, or rather the ability to extract and process information, is the key to success in modern society. In line with this, medicine has been undergoing a dramatic shift in both training and practicing aspects. While textbooks and monographs are still used by medical students, trainees and practicing physicians, there is an increasing need to consult the original information sources. The main driver behind this change is the desire to build one's own perspective on a particular aspect of a human disease. This is typically done by accessing online materials, such as biomedical publications or government documents.

The Information Age is coinciding with the introduction of genomic, transcriptomic and other “omics” technologies into clinical medicine, and with increased digitization of medicine. The latter advancements and changes fuel the expectations from patients, medical community, and the regulator that diagnostic and therapeutic procedures will soon be very individualized. The ability to “zoom in” on an individual patient is underlying the most recent clinical paradigm called Precision Medicine. As a consequence of

this paradigm, we have been witnessing a major transformation of the medical practice. In fact, the scale of this transformation is comparable to what had followed the introduction of the concept of evidence-based medicine.

The evidence-based medicine concept has been introduced about three decades ago [2]. Fundamental to this concept is the need for standardized assessment of the strength of clinical evidence, which is reviewed according to the so-called Evidence Pyramid (Figure 1).

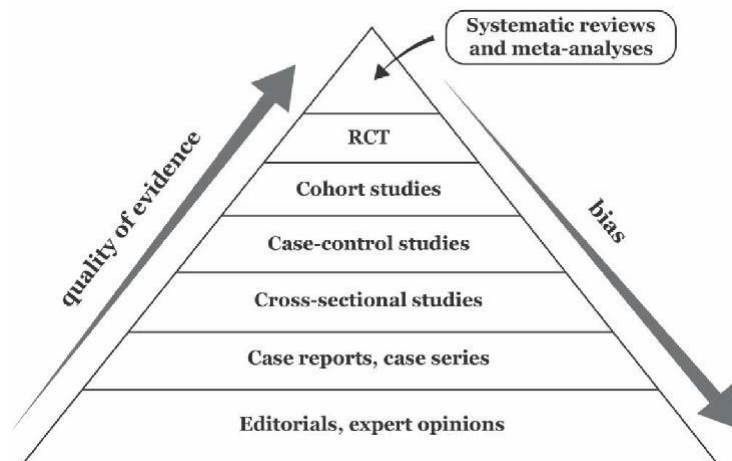


Figure 1 – Evidence Pyramid

Stemming from this are the expert panel guidelines. Said guidelines are used as the basis for the most current clinical decisions.

Since the introduction of the Evidence Pyramid, the way we deal with the patient- and disease-re-lated information has been developed further. For instance, new tools for extracting information about

patients have recently become available. In particular, we are now better able to regard the patient perspectives, such as quality of life, approach to the underlying disease, motivation and other critical factors by conducting qualitative studies (interviews, focus group discussions, observations [3, 4]; (Figure 2).

Major methods of qualitative research	Explanation
Ethnography / Participant observation	Descriptive collection of data in their natural context
Interview / Unstructured interview	A “free-flowing” discussion
Interview / Semi-structured interview	A mixture of some predetermined questions and some spontaneous, “free-flowing” questions
Interview / In-depth interview	Interview aiming at detailed collection of personal memories, experiences, histories, perspectives, and opinions
Focus group	Unstructured group interview aiming at gathering behaviours, social norms, and interactions of participants in a group

Figure 2 – Qualitative studies

Electronic health-related data	Explanation
Electronic medical record	Digital equivalent of a medical chart that usually stays with one healthcare provider
Electronic health record	Also a digital equivalent of a medical chart; is meant to travel with the patient or to be shared between healthcare providers
Personal health record	An electronic collection of one's health record; is meant to be owned and managed by the patient

Figure 3 – Electronic health-related data

This valuable tool has yet to find its ranking within the aforementioned Evidence Pyramid.

Our ability to extract information has further been improved by the introduction of electronic health-related data. This digital tool has already evolved into splitting into several branches: Electronic Medical Records, Electronic Health Records, and Personal Health Records (Figure 3). The mining of these data also provides valuable patient-related information. Similar to qualitative studies, there is no consensus yet where electronic health data mining will fit into the aforementioned Evidence-Based Pyramid.

Given the multitude of information sources and the large volume of the current biomedical information, expert panels may not be able to update their recommendation in sync with the needs of clinical medicine. Thereby, practicing physicians will have to be able to find and assess the clinical literature on their own (that is, independently of the expert panels). This concerns both the physicians who are actively engaged in research (the so-called “physician-scientists”) and physicians with predominantly clinical activities.

Furthermore, the very implementation of Precision Medicine may depend on the physicians’ ability to make informed decisions about individual patients, especially when regarding rare diseases or rare forms of common diseases. Thereby the skill to retrieve, assess, and appraise biomedical information is expected to become increasingly relevant for physicians.

There are many useful and comprehensive reviews on how physicians can access biomedical information. However, not so many of these reviews address the particular needs of physicians in developing countries and economies in transition.

These particular needs, from the author’s point of view, are the following.

First, reviews describing comprehensive literature searches (that is, how to conduct “systematic reviews”) often assume that the reader has a full and comprehensive access to biomedical literature. However, even in developed countries this may not always be the case. For example, physicians employed outside of major academic centres habitually have only a limited access to biomedical literature. Furthermore, access to biomedical literature is even scarcer in low- and middle-income countries [5, 6].

Second, current biomedical literature is increasingly published in English, even by the journals published outside of the USA, Canada, UK, the European Union, Australia and New Zealand. Depending on the underlying language proficiency, physicians, whose native language is not English, may experience substantial problems with comprehending the literature. Especially the English medical terminology, abbreviations, and scientific units may be confusing for a non-native speaker. We believe that this justifies an adaptation of the systematic review recommendations to permit the readership from non-English speaking countries to fully enjoy the benefits of international electronic literature databases. The latter are typically run in English language.

Given the aforementioned particularities, the present review will be the first one of the review series, which will collectively aim to address the following objectives.

First, these reviews will provide the reader from a low- or middle-income with an easily understandable workflow of how to work with biomedical literature. The focus will be made specifically on the patient-and disease-related literature. Second, these reviews will aim to adapt the recommendations on systematic literature review and literature appraisal, such that these recommendations can be utilized by

physicians in low- and middle-income countries. Finally, the newest computational advances, such

as utilization of machine translation, will also be discussed.

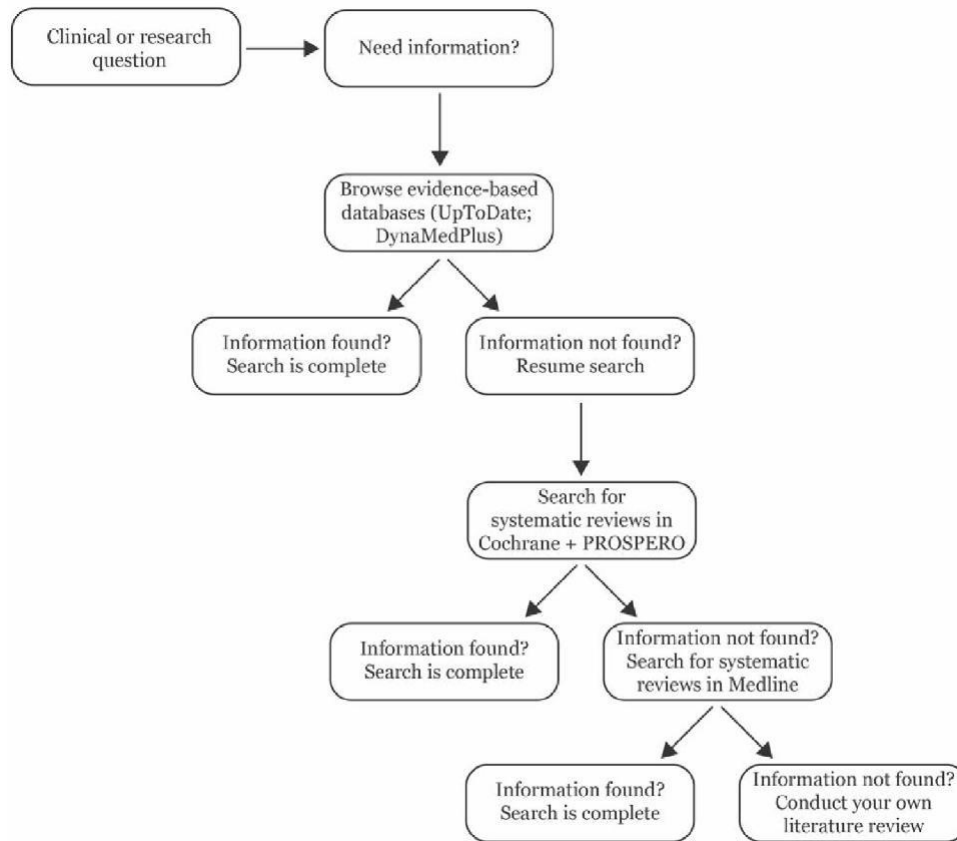


Figure 4 – Suggested workflow

General workflow: electronic databases on evidence-based medicine

To gain insights into a particular clinical topic, the author of this review usually starts with consulting the available clinical literature (Figure 4). In particular, the electronic databases on evidence-based medicine or the latest review papers provide the desired insights (Figure 4).

With regard to electronic databases on evidence-based medicine, the author of this report has a preference for beginning with consulting the UpToDate database (Figure 4). This is a US-based electronic database of evidence-based medicine (www.uptodate.com), covering a multitude of clinical topics. These topics are written and up-dated on a regular basis by expert groups. Importantly, UpToDate habitually indicates when (a) the literature search has been renewed and (b) when the UpToDate topic of interest has been revised. This permits the reader to make an individual in-

formed decision as to whether further literature searches would be necessary. Specifically, if the topic of interest has been recently updated, and all clinical questions have been covered, then there may not be a need for further literature searches (Figure 4).

The use of the UpToDate database requires subscription, which includes the use of a phone app. An individual user needs to pay a subscription fee for access to this database. Alternatively, his or her university or hospital can purchase a collective licence. For users from certain regions (often referred to as “resource -limited settings”), the UpToDate database offers topics pertinent to Global Health (<https://www.uptodate.com/home/uptodate-resource-limited-settings>). In addition, various discounts are given to countries in acute need (such as, following a natural disaster) [7]. Furthermore, subscription options may be different between different countries, so it is worth checking the coun-

try-specific pricing for subscription (<https://www.uptodate.com/home/uptodate-around-world>).

A regular use of the UpToDate database by practicing physicians improves the level of provided clinical care [8]. This highlights the high level of clinical recommendations provided in this evidence-medicine clinical database. Furthermore, the use of UpToDate (that is, if the medical topic of interest is available) is faster than getting the same information using a biomedical search engine PubMed [9].

Apart from UpToDate, other evidence-based clinical databases are available, including DynaMedPlus (<http://www.dynamed.com/home/>), Medscape (<https://www.medscape.com/>), or ClinicalKey (<https://www.clinicalkey.com>). Among these alternative databases, the author's individual preference is DynaMedPlus (Figure 4). This database is maintained by EBSCO Health. While it features fewer clinical topics than UpToDate (respectively, ~3,300 vs. >10,000), the use of DynaMedPlus offers, in the author's view, three distinct advantages.

First, the information presented in DynaMedPlus is concise and provided in "bulleted" chapters and subchapters. Thereby, it is easier for a busy clinician to quickly find the topic of interest.

Second, DynaMedPlus provides ICD codes, which is another useful feature in a clinical practice.

Third, this database permits subscribing to regular electronic updates. Importantly, DynaMedPlus, similar to UpToDate, is available as a mobile version.

If the topic of interest is not available in the UpToDate, or DynaMedPlus or other databases, or the topic of interest has not been updated recently, the next steps can be undertaken.

General workflow: identification of available or prospective systematic reviews

The author habitually looks for a systematic review (Figure 4). Systematic reviews, which aim at both clinicians and expert panels, are the overviews written with the goal of critical and comprehensive synthesis of the literature. They are written according to specific guidelines [10, 11] to increase accuracy and consistency.

To identify systematic reviews on the topic of interest, the author conducts searches in databases of systematic reviews (Figure 4).

Cochrane Library (<https://www.cochranelibrary.com/>) is one such database. It comprises systematic reviews conducted by the standards agreed upon by the contributors of the Cochrane Library, which is considered by many as the highest standard among systematic reviews. Cochrane Library

is run by a UK-based charity organization called Cochrane Collaboration, whose main goal is to promote evidence-based medicine. The access to the Cochrane Library is per subscription, although users from certain countries are eligible for a free access. Furthermore, a yearly subscription is not needed to access individual systematic reviews. In particular, a user can purchase only specific re-views.

As mentioned above, the advantage of Cochrane Library is that it requests the contributors to follow a specific pre-determined template for systematic reviews. Therefore, there is a great consistency in the review format, which makes it easier for the reader to absorb the information. The Cochrane Library is fully searchable, and one can use combinations of keywords and specific terminology called Medical Subject Heading (MeSH), combined for higher precision using Boolean logic operators "AND", "OR", or "NOT". The searches can also be refined by adding the information on authors or titles of the publications. Alternatively, Cochrane Library can be browsed for clinical topics (e.g., "gastroenterology" or "rheumatoid arthritis").

Importantly, Cochrane Library provides information when a systematic review has last been updated. Thereby a reader can see for himself/herself whether the information in Cochrane Library is up-to-date, accurately reflecting the newest developments on the topic of interest.

It is possible that a systematic review on the topic of interest would not be available in both UpToDate / DynaMedPlus and Cochrane Library. If this is the case, it makes sense to conduct own review of biomedical literature.

Systematic reviews are time-consuming and are usually conducted by team of investigators. It is possible that one such systematic review is being worked upon. To verify this, the author checks for prospective systematic reviews, which are underway on the topic of interest. A typical way how to find such prospective reviews is through searching of a register of prospective systematic reviews (Figure 4).

One such register, called PROSPERO, is managed by the University of York, United Kingdom (<https://www.crd.york.ac.uk/prospéro/#aboutpage>). This particular register is fully searchable, and the access to the registered protocols is free. These protocols are done for both ongoing and prospective systematic reviews. The protocols habitually indicate the proposed date when a systematic review is to be finalized. It is important to keep in

mind, however, that there is always some lag time between completion of a systematic review and the publication date. Therefore, an immediate availability of a particular systematic review following its completion should not be expected. If the desired information is not available in the aforementioned

electronic databases on evidence-based medicine or in databases of systematic reviews, the author then conducts a scoping review of biomedical literature. The essential steps of conducting a scoping review will be described in the next review of this review series.

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