What should urologists know about evidence-based medicine?

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ABSTRACT

Objectives: This article outlines the basic principles of evidence-based medicine (EBM) and provides urologists with some tools to further explore, understand, and work with EBM.

Materials and Methods: A narrative review was conducted illustrating several aspects of EBM.

Results: Based on the definition of EBM, the aspects of evidence are clarified and a systematic approach is presented for integrating the evidence with individual patient values and circumstances. Next, sources for finding the best evidence are described and misconceptions about EBM are corrected. Finally, the current state of EBM in urology is discussed.

Conclusions: It is clear that EBM will have an increasing relevance for urologists. Therefore, it is essential that all urologists have an understanding of the fundamental principles of EBM.

Keywords: Evidence-based medicine, integrating evidence in to clinical practice, urology

INTRODUCTION

Evidence-based medicine (EBM) was introduced in the early 1990s, originally as a new educational method. The practice of EBM means integrating individual clinical expertise with the best available external evidence from clinical research. To do so, it is essential that the external evidence is derived from reliable resources that meet the highest quality standards. Many medical specialties have embraced EBM and have urged researchers to report their data using criteria that allow the highest level of evidence to be applied. Urology is a rather late adopter of EBM and it was not until early this century that urologists became aware of the EBM concept. This article will outline the basic principles of EBM and provide urologists with some tools to further explore, understand, and work with EBM.

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DEFINITION OF EVIDENCE-BASED MEDICINE

The most widely used definition of EBM is the one that was introduced by David Sackett, an internist at McMaster University in Canada. He stated that evidence-based medicine is "the conscientious, explicit, and judicious use of the current best evidence in making decisions about the care of individual patients."[1] In other words, EBM applies to clinical decisions about individual patients. The "conscientious, explicit, and judicious use" refers to the translation that each individual clinician needs to make from best available evidence to the individual circumstances of the patient. To do this, clinical expertise is required to evaluate the clinical condition of the patient and to judge his individual needs and preferences. "The best available external evidence" means clinically valid and relevant research. This evidence can originate from basic sciences or especially from patient-centered clinical research.

Ideally, doctors use both individual clinical expertise and the best available external evidence and neither one is enough in itself. Even the most excellent external evidence may be inapplicable to or inappropriate for individual patients or local settings and resources. The balanced application of evidence is considered the central point of practicing EBM.

What is evidence?

According to the principles of EBM, the best available evidence should be used in clinical decision-making. The term "best evidence" refers to the hierarchy of evidence that was proposed
by Sackett and colleagues. According to this hierarchy, large randomized trials stand at the top, providing the highest level of evidence (LoE), whereas the lowest level of evidence, that is, opinion, stands at the bottom [Figure 1]. RCTs are most likely to provide unbiased evidence, provided that the RCTs are of high quality and the results are not heterogeneous. High quality refers to the execution and reporting of RCTs based on criteria defined by the Consolidated Standards of Reporting Trials (CONSORT) group. The CONSORT statement presents an evidence-based, minimum set of recommendations for reporting RCTs. It offers a standard for authors to prepare reports of trial findings, facilitating their complete and transparent reporting, and aiding their critical appraisal and interpretation. The CONSORT Statement comprises a 22-item checklist and a flow diagram, along with some brief descriptive text. The checklist items focus on reporting how the trial was designed, analyzed, and interpreted; the flow diagram displays the progress of all participants through the trial. An extension to the CONSORT Statement was developed for RCTs of Non-Pharmacologic Treatment interventions (CONSORT NPT). The CONSORT NPT checklist takes into consideration specific issues when assessing NPT, such as difficulties of blinding, the complexity of the intervention, and the influence of care providers’ expertise and of the centers’ volume of care on treatment effect [Table 1].

Unfortunately, not all clinical questions can be appropriately addressed in RCTs. Especially in the urologic literature, randomized trials or systematic reviews are rarely available. As a result, it is possible that the best available evidence comes from a lower level of the hierarchical rating system and the clinical decision must be made on weaker evidence. In the absence of meta-analyses, individual high-quality RCTs or well-designed observational studies with sufficiently large and consistent sizes of effect are the next best choices to inform clinical decision-making. Even case series may contribute important evidence, depending on the question being asked. It should be emphasized that RCTs provide LoE 1 in treatment trials but are not feasible in harm studies or etiology studies, as the following example shows. It is well known that smoking can cause bladder cancer, however, no one would conduct an RCT exposing patients to the effects of smoking versus not smoking on developing bladder cancer.

Some scientific journals (eg, British Journal of Urology International) now provide a level of evidence with every published article. The main objective for these journals is to place a study into context for the reader, implying that a higher LoE should be more convincing for readers seeking to answer a clinical question. In urology reports, references to LoE have been largely limited to footnotes in clinical practice guidelines, for example, as published by the National Institute for Clinical Excellence, the BAUS or the European Urological Association.

Integrating individual patient values and circumstances with the evidence

To apply EBM to clinical patient care requires a systematic approach. The “evidence cycle” as described by Sackett et al provides a guideline to approaching clinical problems in a systematic manner using evidence-based medicine. The evidence cycle consists of 6 distinct steps represented by the letter “A”: Assess, Ask, Acquire, Appraise, Apply, and Assess.

1. Assess: The physician needs to understand the patient’s problem and to determine the full context of patient characteristics, demographics, and differential diagnosis to be able to formulate a clear research question.
2. Ask: Compose a clear research question for the patient’s problem. The patient-oriented clinical question (PICO) is a very useful tool to achieve this [Table 2].
3. Acquire: The third step is to retrieve the evidence from literature databases. A search strategy with appropriate MeSH terms/subheadings is essential. Librarians can help if the PICO is well designed; they can also help focus the question or even develop it further to assist in finding the most appropriate articles.
4. Appraise: The fourth step is to determine whether the evidence retrieved is useful and to assess the quality of RCTs using an RCT validation score, for example, the CLEAR NPT [Table 1]. Another option is to use the key validity questions as advocated by Guyatt et al. Although originally designed to evaluate RCTs,
parts of these guidelines are also applicable to other study designs, as they evaluate possible methodological safeguards. For example, even in case series, outcome assessment could be done by an independent outcome assessor.

**Primary guides**

- Was the assignment of patients to treatments randomized?
- Were all patients who entered the trial properly accounted for and attributed at its conclusion?
The final step is to evaluate one’s own—

**Secondary guides**

- Were the patients, health workers, and study personnel “blind” to the treatment?
- Were the groups similar at the start of the trial (in non-RCTs)?
- Aside from the experimental intervention, were the groups treated equally?

We recommend to read the original articles on how to use this guide. In addition, we suggest a guide to prevent readers from being misled by articles reporting the results of intervention studies as described in detail below.

5. **Apply**: The fifth step is to apply the evidence retrieved to the patient under investigation. The evidence found must be fit into the patient’s context of complaints, characteristics, demographics, and desires. For example, cultural differences may influence the decision whether or not to use the evidence found. Treatment of a patient can never be based on evidence alone. The available evidence must always be put into the context of the specific clinical circumstances and the patient’s values and preferences.

6. **Assess**: The final step is to evaluate one’s own performance in executing these steps and seek ways to improve future performance.

Using this approach, it is essential to formulate a good clinical question once the patient’s problem is clear. The clinical questions that may arise from a patient’s scenario can be divided into so-called foreground questions and background questions. Foreground questions query knowledge needed for specific clinical decision-making, for example, questions may be relating to diagnosis, prognosis, or cost-effectiveness. Background questions relate to the pathophysiology of a disease and query knowledge that is usually obtained early during training.

In daily practice, urologists will mainly face foreground type questions, which is why these stand at the center of the EBM process.

For example, a man aged 52 years may present in an outpatient clinic with colic pain caused by a 9 mm stone in the lower pole of the right kidney, reporting no fever and with serum creatinine within normal limits.

A background question that may arise from this scenario would concern the factors that promote the formation of renal calculi. Foreground questions on the other hand would be about how best to treat a patient with a 9 mm stone in the lower pole of the right kidney, how best to establish the diagnosis of kidney stone what is the natural history of a patient with 9 mm kidney stone or which management strategy would offer the optimal balance of therapeutic effectiveness and costs.

A useful tool to formulate a good and answerable clinical question is the so-called PICO format, which stands for Patient, Intervention, Comparison, Outcome [Box 2]. The question should be structured in such a way that it will guide the subsequent literature search to the best available evidence. Formulating a clinical question requires not only information about the clinical scenario (eg, adult male with kidney stone), but also knowledge of applicable therapeutic measures, such as intervention and comparison [eg, Extracorporeal Shockwave Lithotripsy (ESWL), Ureteroscopy (URS), and Percutaneous surgery (PNL)], and the outcome of interest (eg, stone-free rate). In addition, the PICO format suggests specifying, which study design is likely to yield the highest level of evidence. For questions of therapeutic effectiveness, for instance, this would be a systematic review with a meta-analysis of several RCTs with low heterogeneity.

It is advisable to keep the PICO question as simple as possible. For example, based on the clinical scenario mentioned above, of a good clinical question using the PICO formula would be: In a (male) patient with a 9 mm kidney stone (P), how does treatment with ESWL (I) compared with PNL (C) with regard to stone-free rates (O) in RCTs. Based on such a clear and relevant research question, a directed search of the literature databases can be performed.

**Sources of evidence**

Nowadays doctors are flooded by information from various sources. Medical journals, congresses, textbooks, and the internet provide a daily stream of useful and not so useful information. For clinicians it is important to direct all this information in an efficient way. Searching for evidence can either be done directly, for instance by entering relevant search words into a database, such as Medline, or by consulting databases that provide preappraised evidence, the most well known being those within the Cochrane Collaboration.

Furthermore, there is an increasing number of dedicated journals, such as Clinical Evidence, Evidence-based Healthcare, Evidence-based Cardiovascular Medicine, Evidence-based Obstetrics and Gynecology, Cancer Treatment reviews—Evidence based Oncology, so on, that can provide doctors with evidence-based information. Last but not least, guidelines also constitute a convenient source of evidence. They can be found using the National Guidelines Clearing House website, which is an open access public resource [Appendix 1]. Each of these resources is discussed briefly below.
urology. Using search engines such as PubMed® or OVID®, clinicians can identify relevant studies from the National Library of Medicine [Appendix 1]. The drawback to primary literature sources, however, is the need to identify high-quality studies from a multitude of investigations on a particular topic. To prevent too many irrelevant hits, the “clinical queries” feature in PubMed can be used for evaluated search strategies. This feature has built-in filters to help the visitor find randomized trials and to identify relevant systematic reviews. Relevant studies would be retrieved, and then critically appraised for their validity, impact, and applicability. To remain up-to-date, one can also register for a free e-mail service to receive all new trials in a specific search area on a daily, weekly, or monthly basis. These strategies can dramatically reduce the time required to identify high-quality research.

Pre-appraised evidence

Pre-appraised resources include the Cochrane library, ACP Journal Club, Evidence-Based Medicine, Up to Date, and Bandolier [Appendix 1]. These resources have conducted the searches, summarized the results and provided “user-friendly” summaries and bottom-line conclusions. The most renowned is probably the Cochrane database of Systematic Reviews. This database provides SRs on various topics in medicine, focusing almost entirely on RCTs. In this database, several urological issues can be found, such as early versus deferred androgen suppression in the treatment of advanced prostate cancer, immunotherapy for advanced renal cell cancer, prostate cancer screening, and quinolone antibiotics for uncomplicated cystitis in women.

Guidelines

Guidelines have an important role in EBM and there are several guidelines available for urologists. The AUA and EAU, for example, provide guidelines addressing the most common urological problems, which can be very useful in clinical decision-making [Appendix 1]. These guidelines usually represent the consensus among a panel of experts, who ideally applied a formal and critical appraisal process to assess the quality of the available evidence for a given clinical question, and who subsequently graded the strength of the recommendation. While guidelines are used by many urologists, it is important to note that they also have certain drawbacks. Firstly, not all guidelines are based on the EBM approach. Secondly, guidelines are generic and mainly applicable to an idealized index patient with certain clinical characteristics. Thirdly, guidelines are not available for all topics. Moreover, there often is a considerable time lag between the publication of the latest clinical studies and their incorporation into professional guidelines. Also, guidelines by different organizations can come to different conclusions, even when reviewing the same evidence. This is by the considerable variations of guidelines that address PSA-based prostate cancer screening. These differences can largely be explained by the differences in methodology used to formulate recommendations.

Misconceptions about EBM?

Based on the definitions of EBM and its basic principles it is possible to clarify several misconceptions about EBM. A common misconception is that physicians cannot practice EBM on clinical issues that have not been investigated in RCTs, since the absence of RCTs implies that no evidence exists on that particular clinical issue. According to the definition of EBM, however, decisions should be based on the best available evidence. If no RCT exists, one has to solve the case based on lower grade evidence leading to a weaker recommendation.

Consequently, EBM is not cookbook medicine as another popular misconception would have it. Urologists, like all trained doctors, are the experts in combining clinical features, patient preferences, and available evidence from the urological literature. Therefore, urologists make the decision, not the literature. The six As described above illustrate this process. Clinical expertise is key in developing answerable questions, finding suitable literature, appraising manuscripts, and combining this knowledge with patient preferences and local clinical settings. Thus, EBM starts with the patient and ends with the patient. A third misconception is that EBM practitioners should be statisticians. Indeed, some basic knowledge on statistical concepts is helpful. However, understanding study methodology and finding sources of bias during critical appraisal are most important.

Evidence-based urology

Unfortunately, evidence-based medicine is not yet widely used in urology. Most published studies in the urological journals have a low level of evidence and, as a consequence, a low grade of recommendation, as in other surgical fields. The vast majority of publications consists of single-center case-series. A study conducted by Bowraski et al evaluated the LoE in four major urology journals in 2000 and 2005 using the CEBM rating system. When combining level I and II evidence, they found that 16% and 15% of studies in 2000 and 2005, respectively, provided a high LoE. A critical assessment of the quality of reporting of RCTs in the urology literature conducted by Scales et al revealed that less than half of the RCTs adequately described the study method.

In recent years, however, some progress has been made. In the urology literature today there is more attention to the concepts of EBM. Especially the work of the American urologist Dahm and his coworkers introduced a broad awareness of the basic principles of EBM urology. An International Evidence-based Urology Working Group has been established and is reporting on all kinds of topics regarding EBM in the urology literature. The editors of some leading urology journals have recognized that EBM is essential for their readers resulting in a series of publications about the concepts of EBM in their
Appendix 1: Selection of electronic databases for guidelines, pre-appraised and primary evidence

| Source                          | Web address                                      | Description                                                                                      |
|--------------------------------|---------------------------------------------------|-------------------------------------------------------------------------------------------------|
| Cochrane Library               | http://www.cochrane.org/reviews/index.htm         | High-quality systematic reviews, which cover a complete topic; limited coverage, time lag, can be difficult to use. |
| ACP Journal Club               | http://www.acpjnc.org/                            | Structured abstracts of high-quality studies that meet validity criteria; limited coverage.       |
| Bandolier                      | http://www.jr2.ox.ac.uk/bandolier/                | Performs monthly systematic search of Medline and Cochrane Library for meta-analysis and systematic reviews which are then presented in a summarized format. |
| Clinical Evidence              | http://www.clinicalevidence.com                   | On-line textbook that provides evidence-based reviews of select topics many of which are relevant to the practice of urology. |
| Turning Research into          | http://www.tripdatabase.com                       | Practice (TRIP) Meta-search engine of Internet research, including evidence-based resources, guidelines, online textbooks, and Medline. |
| National Guidelines Clearing House | http://www.guideline.gov                      | Comprehensive database of evidence-based clinical practice guidelines and related documents from a variety of different agencies |
| American Urological Association (AUA) | http://auanet.org/guidelines                   | Rapidly expanding depository of clinical guidelines published by the AUA. Recent additions (2005) address the management of erectile dysfunction and staghorn calculi. |
| European Urological Association (EAU) | http://www.uroweb.org                        | Practice guidelines covering a wide range of urological topics published by the EAU. |
| National Cancer Center Network | http://www.ncn.org                               | Provides treatment guidelines for prostate, kidney, testis, and urothelial cancer, as well as screening guidelines for prostate cancer. |
| Medline search engine date Difficult to quality | http://www.ncbi.nlm.nih.gov/entrez            | One of the most well known, public for (primary) publications; up to search effectively, limited ability for filtering. |

Adapted from Scales et al.[12]

Efforts are being made to publish an LoE rating with every published article, offering readers a guide for placing the right degree of confidence in its results and conclusions.[24] In addition, it might be expected that such a provision would increase awareness of this important concept and would ultimately raise the LoE that urology reports provide.

To spread the understanding of EBM among urologists even further, workshops are being organized for the members of the AUA. Furthermore, there are several online resources that can help urologist to expand their knowledge on EBM [Appendix 2].

CONCLUSION

The practice of EBM means integrating individual clinical expertise with the best available external evidence. Since the introduction of EBM over 20 years ago, the concept has been broadly embraced and increasingly implemented in daily decision-making, both in medical specialties and more recently in surgical specialties. In urology EBM is still in its infancy. However, it is clear that EBM will have an increasing role for urologists and that an understanding of its underlying principles is
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highly relevant to their clinical practices. Therefore, it is essential that all urologists have an understanding of the fundamental principles of EBM.

Key message: EBM will have an increasing importance for urologists and understanding its underlying principles is highly relevant to our clinical practices.

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