

# Evidence Based Medicine in Nuclear Medicine Practice; Part I: Introduction, Asking Answerable Questions and Searching for the Best Evidence

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## ABSTRACT

Evidence Based Medicine (EBM) is a new approach to patient management which incorporates best evidence with the clinical expertise of the health care providers. Although this approach has had a rapid growth in many clinical disciplines, its applications in radiology and nuclear medicine has not been addressed sufficiently. In this review EBM is briefly explained and the first two steps of the evidence based practice are described.

**Key words:** Evidence based medicine, Nuclear medicine

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## INTRODUCTION

Evidence Based Medicine (EBM) is defined as systematic search, critical appraisal, and finally using the best evidence for clinical practice (1, 2). This task is proved to be time-consuming by the traditional approaches. EBM incorporates the most valid evidence in the body of literature with the clinical expertise of the health care providers. Although this approach has been applied in several different clinical settings,

in specialties like radiology and nuclear medicine it has not been fully developed (3, 4). In this review, the concept of EBM and its application in nuclear medicine is explained in details. It should be noted that most of the discussed issues are almost completely applicable to radiology discipline and might also be useful for radiologists.

In EBM practice, we use standard methods for searching, evaluating the validity of the data, and effect size of the found evidence (2). These standard methods make the results of EBM practice reproducible. This is the main difference between EBM practice and the traditional one. Several steps have been proposed for EBM practice (2, 5-6). These steps are shown in Table 1. In this review and the 2<sup>nd</sup> part, the four steps mentioned above have been summarized with the main focus on the diagnostic studies, which constitute the major body of nuclear medicine practice.

**Table 1.** Four steps of Evidence Based Medicine (EBM) practice.

<i>Step I:</i> Asking an answerable question
<i>Step II:</i> Searching for the best evidence
<i>Step III:</i> Critical appraisal of the evidence
<i>Step IV:</i> Applying evidence to an individual patient

### STEP 1: ASKING AN ANSWERABLE QUESTION

This step is the main part of EBM practice. Asking answerable question is defined as taking clinical data and converting them into a format to be applied in the next steps of EBM practice (7). To perform this task, we should divide our clinical question into several distinct sections. 1) Specific group the patient belongs to. 2) The test we want to apply for the diagnosis of the disease. 3) The test with which we would like to compare the test in part 2 (usually the gold standard). 4) The intended outcome. "PICO" is the acronym for this 4-part question: "P" for patient, "I" for intervention, "C" for comparison and "O" for outcome. This format for questioning is extremely helpful for searching the available literature for the

best evidence. The final question is usually expressed in a single sentence. The major parts of this sentence can be underlined for more convenience in the future searches.

#### **Example 1:**

Assume that you are a Nuclear Medicine specialist. You have a 20 year old female patient with hyperthyroidism due to toxic hot nodule. You want to know whether iodine therapy or surgery is the best option for treatment of this patient. The answerable question for this scenario is shown in Table 2.

#### **Example 2:**

Assume that you are a Nuclear Medicine specialist and the pneumatologist of your hospital want to know if you can help for differentiation between active from inactive tuberculosis in an adult patient with the history of treated pulmonary tuberculosis 6 months ago, since the result of the sputum culture takes several weeks to be ready. The pneumatologist wants to know if <sup>99m</sup>Tc-sestamibi can be helpful or not. The answerable question for this scenario is shown in Table 3.

### STEP 2. SEARCHING FOR THE BEST EVIDENCE.

In the growing world of internet and computer science, finding the best evidence is becoming more and more difficult and time consuming. This is the main obstacle for finding the best evidence in the published medical literature. Ely et al. reported that family physicians asked an average of 3.2 questions for every 10 patients seen in an ambulatory clinic, but only pursued answers to 36% of those questions (8). In another study by Ely et al. inadequate time for search is introduced as one of the main reasons for not using the best evidence in daily practice (9). If we want to use the best available evidence, we should be equipped with a good strategy for searching the literature.

**Table 2.** Answerable question for the clinical scenario of example 1.

<b>Patient or Problem</b>	A 20 year old patient with toxic thyroid nodule
<b>Intervention</b>	Iodine therapy
<b>Comparison</b>	Surgery
<b>Outcome</b>	Safe treatment of hyperthyroidism
<b>Question</b>	In a 20 year old patient with toxic thyroid nodule, how effective and safe is iodine therapy for treatment of hyperthyroidism compared to surgery?

**Table 3.** Answerable question for the clinical scenario of example 2.

<b>Patient or Problem</b>	Adult patient with the history of treated pulmonary tuberculosis.
<b>Intervention</b>	<sup>99m</sup> Tc-sestamibi scintigraphy
<b>Comparison</b>	Sputum culture
<b>Outcome</b>	Differentiation of active from inactive pulmonary tuberculosis.
<b>Question</b>	In an adult patient with the history of treated pulmonary tuberculosis, how sensitive is <sup>99m</sup> Tc-sestamibi scintigraphy for differentiation of active from inactive pulmonary tuberculosis?

***Medical knowledge resources***

The medical knowledge resources can be divided into a hierarchy of journals and databases. At the bottom of this hierarchy are primary or original journals which most

of us are familiar with. These journals publish the original articles regarding different issues. Journal of Nuclear Medicine, Iranian Journal of Nuclear Medicine, etc. are among these journals. The articles of these journals are indexed in

different databases such as Pubmed (10), SCOPUS (11), and many others. Iranian medical literature is indexed in the invaluable database of Iranmedex. A very especial option of this database is the links to the full texts of the indexed articles (12).

The next level of medical resources contains secondary journals. The secondary journals systematically search for the best evidence in the primary journals and publish the most relevant articles. Evidence based journals are a type of secondary journals which critically appraise the articles they mention. An example of these journals is Evidence Based Mental Health Journal (13). Unfortunately, there are no such journals regarding Nuclear Medicine literature.

The next level of medical resources constitutes the journals which publish review articles and systematic reviews. Seminars in Nuclear Medicine is one of these journals. We should be aware that review articles-although very useful- are the opinions of individuals on a topic and can be very misleading since there is no standard method for writing them. On the contrary, systematic reviews and meta-analyses are objective reviews which are more reliable than the review articles. The main characteristics of narrative review articles, systematic reviews, and meta-analyses are depicted in Table 4. Although articles in this level are indexed in databases such as Medline and SCOPUS, the main database for systematic reviews and high quality Randomised Controlled Trials (RCT) is the Cochrane Library (14). The TRIP database

(15) is another example for databases in this level.

The Cochrane Library has three major parts which make it very useful to find the most relevant evidence with highest quality. The first major part of the Cochrane Library is Cochrane Database of Systematic Reviews (CDSR). This part provides the highest quality systematic reviews and meta-analyses which are prepared by collaborative review groups. The methodologies for preparing these systematic reviews are clearly defined. CDSR is the gold standard for systematic reviews. The second part of the Cochrane Library is Database of Abstracts of Reviews of Effects (DARE). This part provides the other systematic reviews and meta-analyses which have been published in other resources and journals. The quality of these systematic reviews is not as high as the Cochrane reviews are. It is better to appraise these systematic reviews critically with a standard method before using them as an EBM resource. The last section of the Cochrane Library is Cochrane Central Register of Controlled Trials (CENTRAL). This is an international collection of Randomised Controlled Trials (RCT) from various sources. It also includes reports published in other sources not currently listed in Pubmed or related databases. The three parts mentioned above are most efficient for treatment or intervention clinical questions.

**Table 4.** Characteristics of narrative review articles, systematic reviews, and meta-analyses.

Narrative review articles	Systematic reviews	Meta-analyses
Methods to collect and interpret data are subjective	Methods to collect and interpret data are objective	Quantitative. Otherwise the same as systematic review.
Not appraisable	Appraisable	
Replication impossible	Easily replicable	

Although there are many other medical resources which provide the best available evidence, currently a few of them address the issues of radiology and nuclear medicine. For the questions regarding interventions and treatment, usually the Cochrane Library should be searched for any systematic review or RCT. If this search does not yield any useful article, Pubmed (and other resources) are recommended. However, when the clinical question is of diagnostic nature (as it is the case for the major parts of Nuclear Medicine practice) the Pubmed is recommended (16). In the rest of this article, the Pubmed database and searching strategies in this database are explained.

#### *How to search in Pubmed*

Pubmed is a bibliographic database which catalogues a huge amount of articles related to medicine and allied sciences. Almost all physicians are familiar with this database and use it as the main resource for their research (17).

There are many ways to search efficiently in Pubmed. Using Medical Subject Headings (MeSH) terms and limiting the search results to a specific selection are among them. These strategies are usually time-consuming. Explaining these strategies is beyond the scope of this article. A detailed discussion on this topic can be found elsewhere (7, 18).

For clinical questions regarding diagnosis, which most of the Nuclear Medicine practice is dealing with, the “Clinical Queries” option of the Pubmed is recommended (16). To access this part in the web site, click the Pubmed queries link on the left pane of the screen (Figure 1.) The PubMed Clinical Queries web page is shown in Figure 2.

As discussed before, for each clinical scenario, a “PICO” question should be formulated. It is recommended to underline the most important terms in the “PICO” question, number the order of importance,

and consider alternate spelling, synonyms, and truncations. Boolean operators are very useful for combining the separate parts of the “PICO” question. These operators should be in upper case. When “AND” is used, both terms would be present in the result of the search and for “OR”, the search would have either terms. The general structure for PICO-based search is shown in Table 5.

**Table 5.** The general structure of a PICO-based search.

(Patient OR synonym 1 OR ...)
AND
(Intervention OR synonym 1 OR ...)
AND
(Comparison OR synonym 1 OR ...)
AND
(Outcome OR synonym 1 OR ...)

For the PICO question of example 2 mentioned above, we can search with the following terms:

Adult AND (MIBI OR sestamibi) AND sputum culture AND (active pulmonary tuberculosis)

Each part of the above-mentioned terms corresponds to the PICO parts of the PICO-based question mentioned in Table 3.

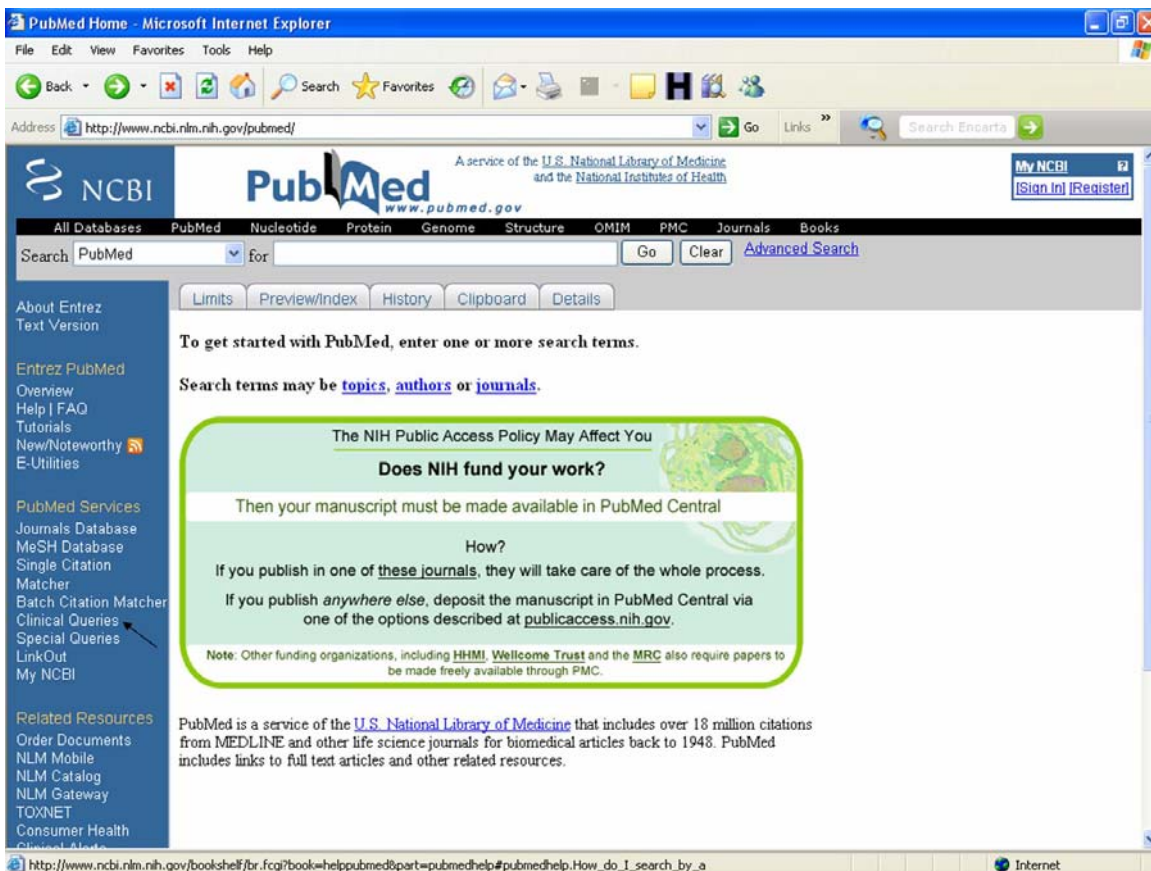
For the PICO question of example 1, the search terms would be as follows:

(Female OR Young female) AND (Iodine therapy OR Radioactive iodine) AND

surgery AND (Toxic thyroid nodule OR Toxic thyroid adenoma)

In the Pubmed Clinical Queries, you can choose the category and scope of your search. The category defines the type of the clinical question you are searching for, such as etiology, treatment, diagnosis, etc. The scope is the spectrum of the search you want

to conduct. Usually the narrow search yields less but more relevant results and the broad search yields more but less relevant results. For the PICO question of example 2 with the “diagnosis” and “broad” checked under the category and scope, the search yielded 2 articles.



**Figure 1.** Pubmed Web page. The clinical queries link is shown by a black arrow on the left side of the screen.

Usually this kind of search is the fastest and the most efficient when having a PICO question of diagnosis nature (7). This is also true when etiology and prognosis type of questions is considered. For the intervention and treatment questions, searching for systematic reviews in The Cochrane Library is the most efficient way. Pubmed Clinical

Queries also provide an option to limit your search to systematic reviews.

If the broad search retrieved too many results, you can use the limit tab on the top of the result screen to limit your search or alternatively the narrow search can be chosen. Detailed explanation can be found elsewhere in the literature (18).

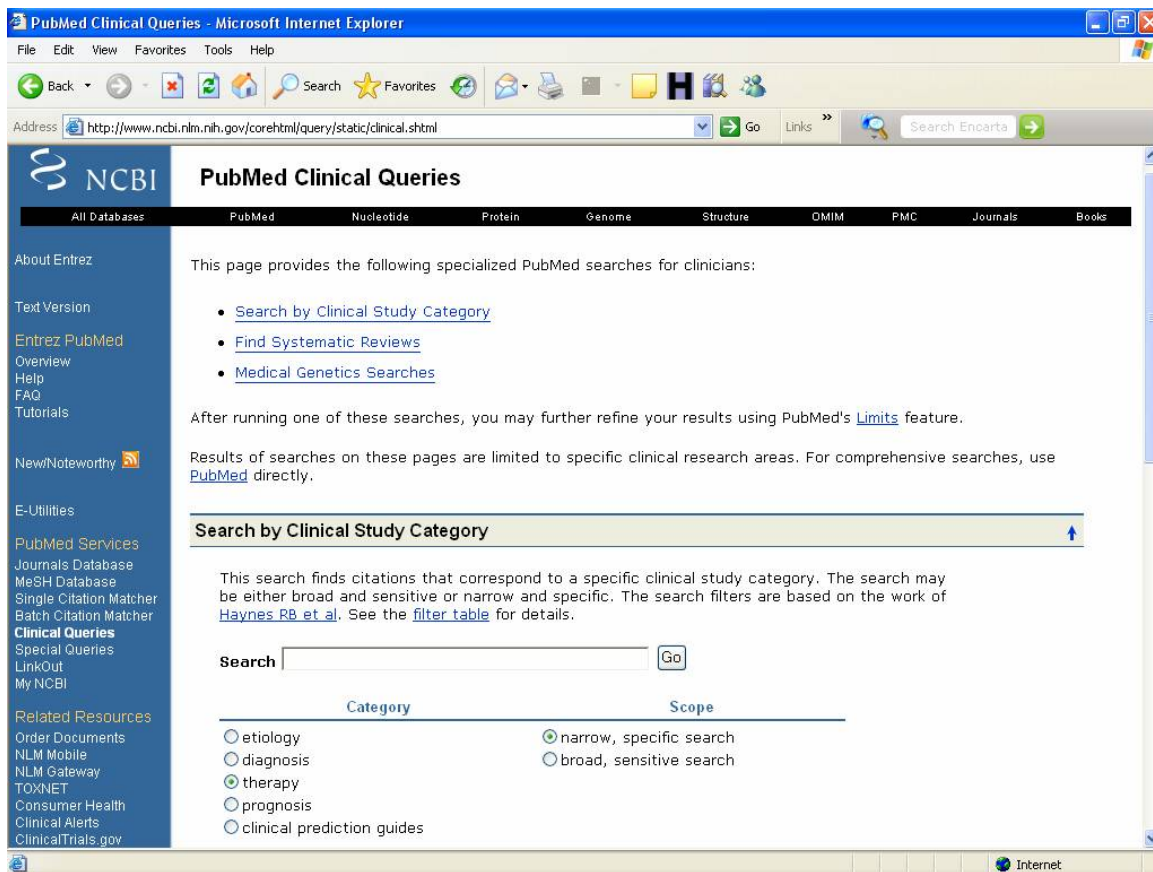


Figure 2. PubMed Clinical Queries Web page.

### *Full-text articles: how to get them*

Many Nuclear Medicine journals are freely available online. Iranian Journal of Nuclear Medicine, Hellenic Journal of Nuclear Medicine, Nuclear Medicine Review, Nuklearmedizin, Annals of Nuclear Medicine (not the recent issues), Journal of Nuclear Medicine (not the recent issues), and Journal of Nuclear Medicine Technology (not the recent issues) are among these freely accessible journals. For those physicians who have university Athens system subscription, most of the other journals are also freely available. This is also true for the Cochrane Library and its systematic reviews. As mentioned above links to full texts of many Iranian articles

can be found in Iranmedex website, although this site is not itself free.

### **FINAL WORD**

After completion of the search, the highest quality articles should be selected. Many of the published articles are not of high quality and do not meet the evidence based standards. Unfortunately, this is the case for most of the clinical questions in Nuclear Medicine discipline. Appraising the retrieved articles is the next step of EBM practice. For this task, one should be familiar with the levels of evidence. This important topic will be discussed fully in the next article of this series.

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