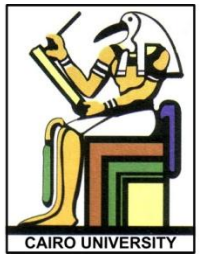


ADVANCED TOPICS IN BIOMEDICAL ENGINEERING

Lecture 1 - 2012

Prof. Yasser Mostafa Kadah

Evidence-Based Medicine (EBM)

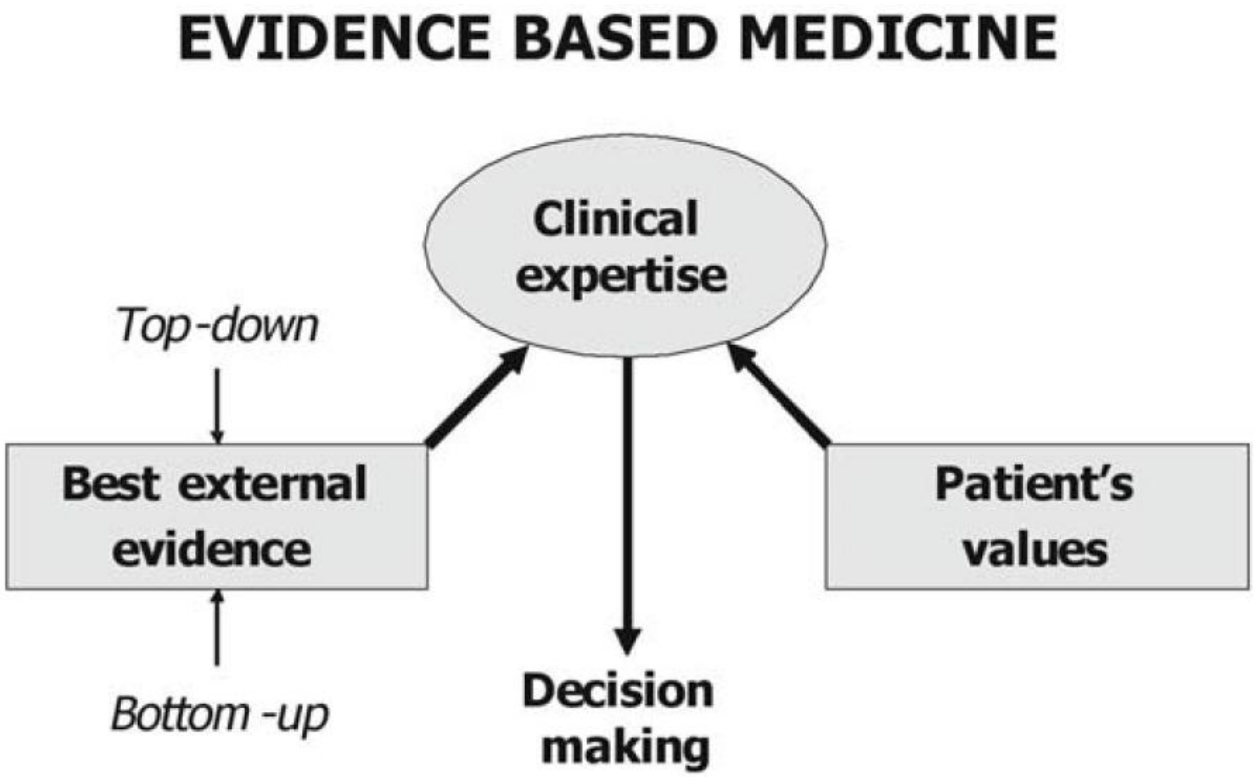
- Clinical practice should be based on the critical evaluation of the results obtained from medical scientific research
- This notion of a clinical practice based on the results (the evidence) given by the research has engendered the discipline of evidence-based medicine (EBM)
  - Also referred to as evidence-based healthcare or evidence-based practice
- In this context the term *evidence* is more closely associated with the concepts of proof, demonstration, or testability than simply with visibility or clarity
- In fact, the general meaning of the new discipline suggests a clinical practice no longer based on bequeathed knowledge, on opinions, impressions, and perceptions, but on demonstrable proofs

Evidence-Based Medicine (EBM)

- Definitions of EBM:
  - "The systematic application of the best evidence to evaluate the available options and decision making in clinical management and policy settings"
  - "Integrating clinical expertise with the best available external clinical evidence from research"
- EBM is the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients
- EBM is the use of mathematical estimates of the risk, of benefit and harm, derived from high-quality research on population samples, to inform clinical decision making in the diagnosis, investigation or management of individual patients

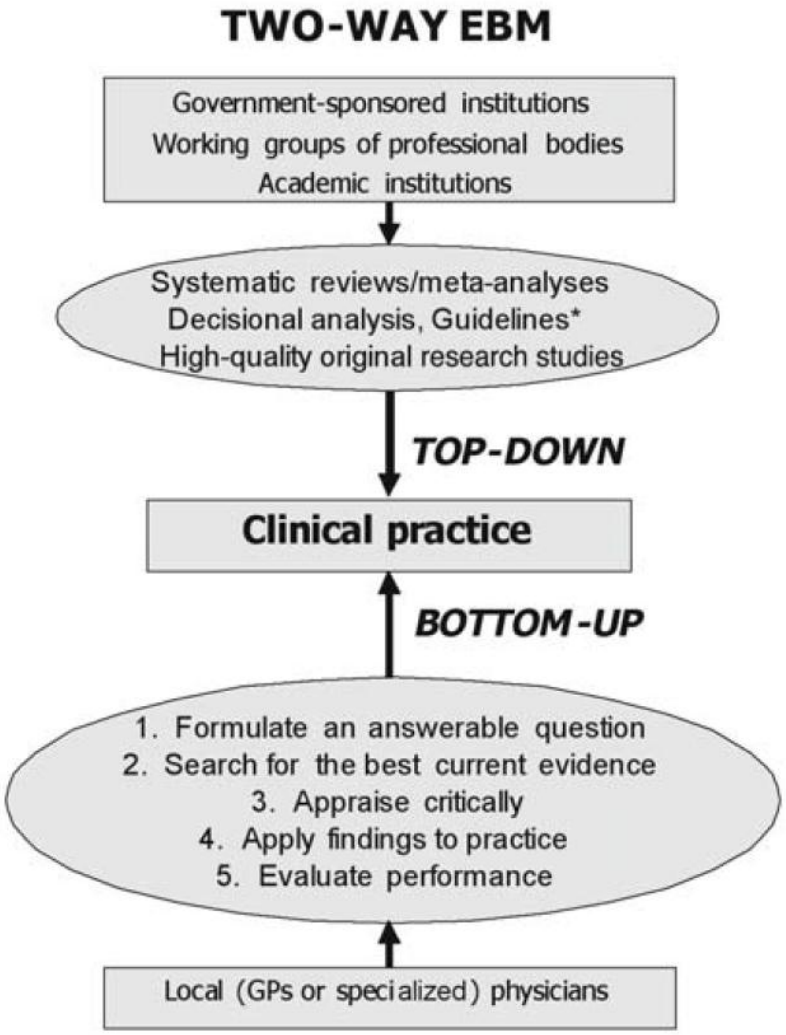
Evidence-Based Medicine (EBM)

- EBM is not only the combination of current best available external evidence and individual clinical expertise. A third factor must be included in EBM: *patient's values and choice*



Evidence-Based Medicine (EBM)

- Two approaches:
  - Top-Down
  - Bottom-Up
- General EBM aim: *"to maximize the quality and quantity of life for the individual patient"*



EBM Limitations

- Judged as unproven
- Very time-consuming (and therefore expensive),
- Narrowing the research agenda and patients' options,
- Threatening professional autonomy and clinical freedom
- Large clinical areas – radiology being one of them – have not been sufficiently explored by studies according to EBM criteria
  - Real patients can be totally different from those described in literature
  - Makes clinical trials not directly applicable

Evidence-Based Radiology (EBR)

- Delayed diffusion of EBM in radiology
  - Only appeared in the literature starting in 1996
- Only around 30% of what constitutes 'imaging knowledge' is substantiated by reliable scientific inquiry (Medina and Blackmore, 2006)
- Other authors estimate that less than 10% of standard imaging procedures is supported by sufficient randomized controlled trials, meta-analyses or systematic reviews
- Comparison between two diagnostic imaging modalities is markedly different from the well-known comparison between two treatments, typically between a new drug and a placebo or standard care
  - Thus, the classic design of the randomized controlled trial is not the standard for radiologic studies.

Particular Traits of Radiology

- Technical expertise
  - Evaluation of the diagnostic performance of imaging modalities must be based on a deep insight of the technologies used for image generation and postprocessing
  - Technical expertise has to be combined with clinical expertise in judging when and how the best available external evidence can be applied in clinical practice
    - This aspect is just as important as “clinical expertise”
  - Example: consequences of ignoring a technical detail such as slice thickness in evaluating the diagnostic performance of MRI: using a 3-mm instead of a 5-mm thickness, the diagnostic performance for detection of choledocholithiasis changed from 0.57 sensitivity and 1.0 specificity to 0.92 sensitivity and 0.97 specificity

Particular Traits of Radiology

- Reproducibility
  - We need to perform studies on the reproducibility of the results of imaging modalities (intraobserver, interobserver, and interstudy variability), an emerging research area which requires dedicated study design and statistical methods (e.g. Cohen k statistics and Bland-Altman analysis)
  - In fact, if a test shows poor reproducibility, it will never provide good diagnostic performance, i.e. sensitivity and specificity. Good reproducibility is a necessary (but not sufficient) condition for a test to be useful

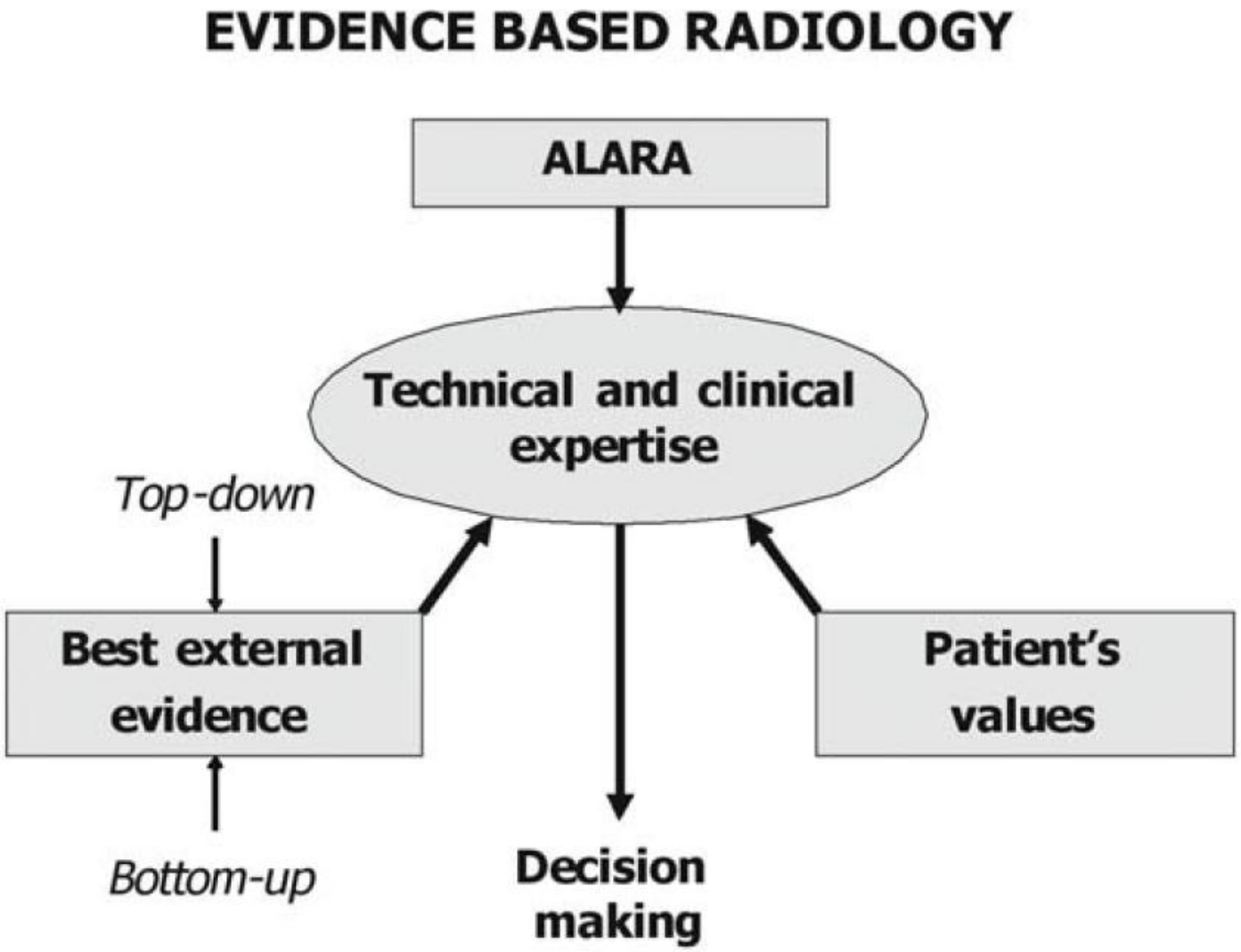
Particular Traits of Radiology

- High speed of technologic evolution
  - Increasing availability of multiple options in diagnostic imaging should be taken into consideration along with their continuous and sometimes unexpected technologic development and sophistication
  - Thus, the high speed of technologic evolution has created not only the need to study theory and practical applications of new tools, but also to repeatedly start with studies on technical performance, reproducibility, and diagnostic performance.
  - The faster the advances in technical development, the more difficult it is to do the job in time.
  - This development is often much more rapid than the time required for performing clinical studies for the basic evaluation of diagnostic performance.
    - From this viewpoint, we are always too late with our assessment studies.

Particular Traits of Radiology

- A balance must be struck between apparent (e.g. diagnostic) benefit and real benefit to the patient
  - Qualitative leap in radiologic research is now expected: from the demonstration of the increasing ability to see more and better, to the demonstration of a significant change in treatment planning or, at best, a significant gain in patient health and/or quality of life – the patient outcome
- "As low as reasonably achievable" (ALARA) principle
  - Considered as embedded in radiologic "technical and clinical expertise"
  - Regarded as "*fourth dimension*" of EBR, due to the increasing relevance of radioprotection issues in radiologic thinking and practice

Evidence Based Radiology (EBR)



Health Technology Assessment (HTA) in Radiology

- HTA in EBM and EBR
  - How is the evidence produced?
  - Which methods should be used to demonstrate the value of a diagnostic imaging technology?
- HTA should answer the following four fundamental questions:
  - Does it work?
  - For whom?
  - At what cost?
  - How does it compare with alternatives?

HTA

- Efficacy
  - Reflects the performance of medical technology under ideal conditions,
- Effectiveness
  - Evaluates the same performance under ordinary conditions
- Efficiency
  - measures the cost-effectiveness
- To evaluate the impact of the results of studies, i.e. the level at which the HTA was performed, we need a hierarchy of values
  - Such a hierarchy has been proposed for diagnostic tests and also accepted for diagnostic imaging modalities

HTA: The Six-Level Scale

Level	Parameters under investigation
6. Societal impact	Cost-benefit and cost-effectiveness analysis from a social perspective
5. Patient outcomes	Fraction of patients improved with the test compared with fraction improved without the test; difference in morbidity between the patients with the test and those without the test; gain in quality-adjusted life years (QALYs) obtained by the patients with the test compared with those without the test
4. Therapeutic impact	Fraction of patients for whom the test is judged useful for treatment planning or for whom the treatment planning is modified on the basis of the information supplied by the test
3. Diagnostic impact	Fraction of patients for whom the test is judged useful for reaching the diagnosis or for whom the diagnosis is substantially modified after the test; positive and negative likelihood ratios
2. Diagnostic performance	Sensitivity, specificity, accuracy, positive predictive value, negative predictive value and receiver operator characteristic (ROC) analysis; intraobserver, interobserver and interstudy reproducibility
1. Technical performance	Gray scale range; modulation transfer function change; sharpness; spatial resolution, in-plane (line pairs per mm, pixel size) and through-the-plane (slice thickness), integrated in voxel size; signal-to-noise ratio; contrast resolution (contrast-to-noise ratio); time resolution (images/sec) etc

HTA: The Six-Level Scale

- This hierarchical order is a one-way logical chain.
  - A positive effect at any level generally implies a positive effect at all preceding levels but not vice versa
  - While a new diagnostic technology with a positive impact on patient outcome probably has a better technical performance, higher diagnostic accuracy, etc. compared with the standard technology, *there is no certainty that a radiologic test with a higher diagnostic accuracy results in a better patient outcome*
- New equipment or a new imaging procedure should have extensive HTA assessment before it is adopted in routine practice
  - Shortage of coherent and consistent scientific evidence in the radiology literature!
  - Example: lack of evidence in well-established Cranial CT for head injuries

Reasons for Shortage of High Level Radiological Studies

- Radiology was judged as the most rapidly evolving specialty in medicine
  - Level 5 and 6 studies entail long performance times, huge economic costs, a high degree of organization and management for longitudinal data gathering on patient outcomes, and often require a randomized study design (by way of example, the average time for 59 studies in radiation oncology up to publication of the results reviewed in 2005 was about 11 years)
  - Two essential needs: full cooperation with clinicians who manage the patient before and after a diagnostic examination, and methodological and statistical expertise regarding randomized controlled trials
- Two alternatives to clinical trials and meta-analyses exist
  - They are the so called “pragmatic” studies and “decision analysis”

Alternatives to Clinical Trials

- A *pragmatic* study proposes the concurrent development, assessment, and implementation of new diagnostic technologies
  - this seems to demonstrate the potential for responding to the dual demand of the increasing pace of technologic development in radiology and the need to attain higher levels of radiologic studies, thus in a single approach obtaining data on diagnostic confidence, effect on therapy planning, patient outcome measures and cost-effectiveness analysis
- *Decision analysis*, based on deductive reasoning, tries to overcome the limited external validity associated with clinical trials
  - Different diagnostic or therapeutic alternatives are visually represented by means of a decision tree and dedicated statistical methods are used (e.g. Markov model, Monte Carlo simulation)

Assignments

- Report on the available mammography databases
  - Describe the image characteristics in each (resolution, number of bits, source, etc.)
  - Describe the available pathologies in these databases and how to find them in the images
  - Download sample images from each and write a simple program to read and display them on the software of your choice