Introduction to Evidence-based Medicine  
September 17, 2004

Objectives

Define Evidence-based Medicine
Describe the complementary relationship of Evidence-based Medicine to inductive reasoning
Understand the need for developing strategies for managing medical evidence
Define Baye’s theorem, and be able to apply it in a qualitative manner

Evidence-based medicine is the integration of best research evidence with clinical expertise and patient values.

Best research evidence includes basic science evidence, but focus is on Patient-centered clinical research: diagnosis, prognosis, therapy trials

Clinical expertise: Use own clinical skills and past experience to rapidly Identify each patient’s unique health state, diagnosis, individual risks and Benefits of potential interventions, and personal values and expectations.

Unique preferences, concerns, expectations, each patient brings to a clinical Encounter, and which must be integrated into clinical decisions if they are to Serve patients

Why evidence-based medicine?

Significant need for valid, up-to-date information about diagnosis, prognosis, therapy, prevention.
Traditional sources of information inadequate
Textbooks out-of-date
Continuing medical education ineffective
Variability in practice pattern
Discrepancies between best evidence and practice

Evidence-based medicine and inductive, pathophysiologic reasoning are complementary, but can, at times, lead to what initially appears to be contradictory “truths”

Must have some understanding of pathophysiology of disease before diseases can be more accurately diagnosed or better treated.

Disease oriented evidence –What is the pathophysiology of this disease? Physiologic derangement X appears to be causally related to disease Y. What is the mechanism of action of drug A?
If drug A affects X, and X is related to disease Y, drug A should therefore have a beneficial effect on disease Y. Based on our understanding of the disease, we think our treatment will work.

Patient oriented evidence – We did an experiment, and drug A is harmful for patients with disease Y. We know our treatment is harmful.

Maybe our understanding of disease X or the effects of drug Y is incomplete, thus leading to further laboratory and clinical investigations.

**Practicing evidence-based medicine requires:**
- Managing medical information
- Application of best available research evidence in clinical-decision making

**Managing Medical Information**
- Biomedical knowledge is increasing rapidly
- Much of what you learn as a medical student will quickly become outdated.
- Two broad strategies:
  - “Hunting” and “Foraging”

**Hunting for information**
- Ask the right (clinical) question – a practice “learning objective”
- Search for information
- Evaluate its relevance
- Evaluate its validity
- Apply the information to patient care

**Foraging – “Keeping Up”**
- “Stay abreast of the literature, and go to CME conferences”
- Newer methods – “push technology”
  - “Bulletin boards”

**Application of knowledge in clinical practice**

**Current paradigm**
- Unsystematic observations from clinical practice can be used to build and maintain knowledge about patient prognosis, accuracy of diagnostic tests, and efficacy of treatment.
- Study and understanding of basic mechanisms of disease and pathophysiologic principles is sufficient guide for clinical practice.
Content expertise and clinical experience are a sufficient base upon which to generate valid guidelines for clinical practice

New paradigm

- Clinical experience and development of clinical instincts are crucial and necessary, particularly for diagnosis of disease.
- Understanding basic mechanisms of disease are necessary but insufficient guides for clinical practice.
- This understanding (basic mechanisms of disease) necessary to determine whether the results of a clinical study can be applied to your patient.
- This understanding necessary in the many instances when there is insufficient or conflicting trial data to guide patient management
- Understanding certain rules of evidence is necessary to correctly evaluate literature on causation, prognosis, use of diagnostic tests, and effectiveness of treatment.
  (Clinical epidemiology course next year)
- Understanding of the patient (concerns, beliefs, desires, lifestyle, financial constraints, family) necessary to proper application of evidence

Two Questions

“What is the evidence (derived from clinical epidemiologic investigations) that this is so?”
“Does it apply to my patient?”

Applying EBM to diagnosis – Understanding Bayes Theorem

Bayes Theorem states the relationship between the results of a diagnostic test and prevalence (the frequency that a disease occurs in a population)

The predictive value of a given diagnostic test is related to its pre-test prevalence in the population.

The history and physical are a diagnostic test.

The clinical exam (history and physical) has similar properties as other diagnostic tests, such as x-rays or measurement of blood values, in determining the absence or presence and extent of disease. Some of these properties include accuracy (how close is the result to the true situation) and reliability (if determined again, how likely will the same data be found). In many conditions, the history and physical are very accurate at confirming or excluding the presence of disease.

Four (related) test characteristics help describe the accuracy of the clinical exam: Sensitivity, specificity, negative predictive value and positive predictive value.
Sensitivity – The proportion of patients with a disease who have an abnormal test result. 
Synonyms – true positive (TP) rate, Positivity in Disease (PiD)

Specificity - The proportion of patients without the disease who have a normal test result. 
Synonyms -- true negative (TN) rate, Negativity in Health (NiH)

Clinical Question: Does this patient have alcohol dependency or abuse?

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>GGT</td>
<td>54%</td>
<td>76%</td>
</tr>
<tr>
<td>Liver function tests</td>
<td>37%</td>
<td>81%</td>
</tr>
<tr>
<td>“Yes” to 1 or more of 4 CAGE questions</td>
<td>85%</td>
<td>81%</td>
</tr>
<tr>
<td>“Yes” to 3 or more of 4 CAGE questions</td>
<td>51%</td>
<td>99.7%</td>
</tr>
</tbody>
</table>

Tests that are highly sensitive are better at “ruling out” or excluding a disorder if the test result is negative.

Tests that are highly specific are better at “ruling in” or diagnosing a disorder if the test result is positive. For example, a patient who answers 3 or more of the 4 CAGE questions very likely suffers from alcohol dependency or abuse.

Sensitivity and specificity are guides for determining which test to choose

Positive predictive value (PPV) – Proportion of patients with a positive test result who have the target disorder.

Negative predictive value (NPV) – Proportion of patients with a negative test result who do not have the target disorder.

Most clinicians find the predictive values to intuitively make more sense, and to be more clinically useful. Predictive values are useful in interpreting the results of a test – is this condition present or absent in this patient? However, to determine predictive values, the probability of disease in a population must be known. This probability, or rate, of disease is referred to as prevalence.
Returning to Bayes theorem:

*The predictive value of a given diagnostic test is related to its pre-test prevalence in the population.*

A 2 x 2 table can be used to determine predictive values, if sensitivity (Se), specificity (Sp), and prevalence (P) are known.

<table>
<thead>
<tr>
<th></th>
<th>Condition present</th>
<th>Condition absent</th>
<th>Predictive value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Test positive</strong></td>
<td>True positive</td>
<td>False positive</td>
<td>PPV = A/(A+B)</td>
</tr>
<tr>
<td></td>
<td>A</td>
<td>B</td>
<td></td>
</tr>
<tr>
<td><strong>Test negative</strong></td>
<td>C</td>
<td>D</td>
<td>NPV = D/(C+D)</td>
</tr>
<tr>
<td></td>
<td>False negative</td>
<td>True negative</td>
<td></td>
</tr>
</tbody>
</table>

Qualitatively, what this means is that:

For a rare disease, a positive test does not mean that a patient has a disease.

For a common disease, a negative test does mean that the patient has a disease.

As a further example, let’s examine the use of mammography in the 40 y/o woman discussed in small group this week:

Sensitivity of mammogram (for identification of breast cancer) = 0.9
Specificity of mammogram = 0.94
Prevalence = 0.0004
For 100,000 women

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<tbody>
<tr>
<td><strong>Test positive</strong></td>
<td>True positive</td>
<td>False positive</td>
<td>PPV = A/(A+B)</td>
</tr>
<tr>
<td></td>
<td>36</td>
<td>5998</td>
<td>.005</td>
</tr>
<tr>
<td><strong>Test negative</strong></td>
<td>4</td>
<td>93962</td>
<td>NPV = D/(C+D)</td>
</tr>
<tr>
<td></td>
<td>False negative</td>
<td>True negative</td>
<td>.99</td>
</tr>
</tbody>
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The large majority of women with an abnormal screening mammogram do not have breast cancer!
Summary

Evidence-based medicine requires you to combine knowledge of pathophysiology, experimental evidence about patient outcomes, your own clinical expertise with knowledge of the patient to care for the patient.

Knowledge is expanding rapidly, we will need to help you develop good hunting and foraging skills so you can keep up after you graduate from medical school.

A history and physical can be a diagnostic test – the likelihood that the answer to a question or something you find on an exam is important or not is related to how common a condition is in the population.