Introduction to Evidence-based Medicine
October 7, 2002

Objectives

Define Evidence-based Medicine
Describe the complementary relationship of Evidence-based Medicine to pathophysiological reasoning
Define the following test characteristics: sensitivity, specificity, positive predictive value, negative predictive value
Define and describe Bayes’ theorem

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 patient

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   Textbooks out-of-date
   Experts may be wrong
   Continuing medical education ineffective
Variability in practice pattern
Discrepancies between best evidence and practice

What knowledge is required to guide 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 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)

Two Questions

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

EBM and POM

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. For example, a 60 year-old man referred to a cardiologist with a history of exertional retrosternal chest discomfort that is relieved by 5 to 15 minutes of rest has a 94% probability of having angiographically documented coronary artery disease. A 30 year-old woman with sharp left-sided pain that is constant has less than 1% chance of having coronary artery 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.
Bayes Theorem states the relationship between prevalence and predictive value:
*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>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Test positive</strong></td>
<td>True positive</td>
<td>False positive</td>
</tr>
<tr>
<td></td>
<td>A</td>
<td>B</td>
</tr>
<tr>
<td><strong>Test negative</strong></td>
<td>False negative</td>
<td>True negative</td>
</tr>
<tr>
<td></td>
<td>C</td>
<td>D</td>
</tr>
</tbody>
</table>

**Total # with Condition**  **Total # without condition**

- **Predictive value**
  - PPV = \( \frac{A}{A+B} \)
  - NPV = \( \frac{D}{C+D} \)