Assessing Diagnostic Articles: Likelihood Ratios

Evidence Based Medicine:
Pedi 101, Part 1
Section of Emergency Medicine
Baylor College of Medicine
Houston, Texas
The patient encounter

Formulating the clinical question

Searching the evidence

Appraising the evidence

Drawing conclusions that impact on practice

Uncertainty in diagnosis or therapy, controversies

Patient Intervention Comparison Outcome

Hierarchy of evidence
Pre-appraised resources

SAEM. Evidence Based Medicine Online Course 2005
Review the PICO question

Patient: In children with fever and petechiae

Intervention: -

Comparison (if relevant): does well-appearing vs not well-appearing

Outcome: predict bacteremia?
PICO questions can be categorized:

- Etiology
- Diagnosis
- Therapy
- Prognosis
Clinical query

- Where do we look for answers?
- Possible resources:
  - www.cochrane.org
  - http://ebm.bmjjournals.com
  - www.library.tmc.edu
  - Up to Date
Hierarchy of Evidence

Meta-analysis of RCTs
systematic review of RCTs

Individual RCT

Observational studies
patient-important outcomes

Basic research
test tube, animal, human physiology

Clinical experience

Critical Appraisal: Diagnosis

- **Validity**
  - Will the study reflect the truth?
  - Rapid review: Do they give a search strategy and assess quality?

- **Importance**
  - Are the effects big enough to matter?
  - Rapid review: How precise is the answer?

- **Applicability**
  - Is it useful here and now?
  - Rapid review: Are the costs similar? Is the benefit worth the cost?
Defining risk

- Pre-test and post-test probabilities
- Likelihood ratios
- Sensitivity and specificity of a test
Pre-test probability

- Defined as the prevalence
- The probability of a disease before any testing results
- The assumptions we function with
Case

- 7 year old with sore throat, tonsillar hypertrophy, cervical lymphadenopathy, and absence of coryza.

Given minimal but appreciable risks from therapy with Penicillin, would you treat if...

- the probability of disease were 70%?
- the probability of disease were 98%?
A diagnostic test (rapid strep), can change your probability of disease.

This is a post-test probability.
Post-test probability

- Probability of having a condition after the test result is available
- The reason a test is obtained is to increase or decrease the probability of disease that existed prior to the test
Case

- In the example, the pre-test probability was 70%, let’s assume the post-test probability with a positive rapid strep is now 98%. Now would you treat?

In essence, we are interested in how a diagnostic test alters the likelihood of a disease.

Likelihood ratios.
Understanding likelihood ratios...

what does it mean to the clinician?
Sensitivity:

- The proportion of patients with the disorder under study who have a positive result.
- The probability that given the disease is present, an abnormal test result indicates presence of disease.

Sensitivity

\[ \text{Sensitivity} = \frac{\text{TP}}{\text{TP} + \text{FN}} \]

<table>
<thead>
<tr>
<th></th>
<th>Disease Present</th>
<th>Disease Absent</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Test Positive</strong></td>
<td>True Positive</td>
<td>False Positive</td>
</tr>
<tr>
<td><strong>Test Negative</strong></td>
<td>False Negative</td>
<td>True Negative</td>
</tr>
</tbody>
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Specificity:

- The proportion of patients who do not have the target disorder and whose test results are negative.
- The conditional probability that given the disease is absent, a normal test result excludes the disease.

Specificity

\[ \text{Specificity} = \frac{TN}{FP+TN} \]

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Determining post-test probability

- Calculate
- Or do it the simple way with a nomogram!

Adapted from Comprehensive Case Studies: ACEP, EBM Listserve 2003
Relationship between odds and probability

To use LR: convert between odds and probability

\[
\text{Odds} = \frac{\text{Probability}}{1 - \text{Probability}}
\]

\[
\text{Probability} = \frac{\text{Odds}}{\text{Odds} + 1}
\]
What if we don’t know the likelihood ratio?
The LR for a positive test result is the ratio of true positive results to false positive results.

A helpful test will have a large LR positive.

\[
LR(\text{positive}) = \frac{\text{sensitivity}}{1 - \text{specificity}}
\]
Likelihood ratio negative

The LR for a negative test result is the ratio of false negative results to true negative results.

A helpful test will have a small LR negative.

\[ LR(\text{negative}) = \frac{1 - \text{sensitivity}}{\text{specificity}} \]
The nomogram


Adapted from Comprehensive Case Studies: ACEP, EBM Listserve 2003
The nomogram!

For our child with pharyngitis: assume the rapid strep used in the unit carries a LR+ of 25.
For our rapid strep (Q-test)

- Given a sensitivity of 94.2% and a specificity of 96.3%:

\[
LR(\text{positive}) = \frac{\text{sensitivity}}{1 - \text{specificity}}
\]

\[
LR(\text{positive}) = \frac{.942}{1-.963} = 25
\]
The nomogram!

For our child with pharyngitis: the rapid strep used in the unit really does carry a LR+ of 25.
Summary

- Related EBM to practice
- PICO questions
- Queries
- Diagnosis studies
  - Pre and post test probabilities
  - Likelihood ratios
Optional case exercise

- 2 1/2 year old girl is brought in by mother
- Fever to 103°F
- You remember a SBI lecture and wonder about the etiology of fever as it relates to UTI
- PICO: In children with fever without a focus, what is the prevalence of UTI?
- Query: [www.library.tmc.edu](http://www.library.tmc.edu)
Diagnosis

- 9% of children 0-36 months with fever in the ED have a UTI
- Urine dipstick used to measure leukocyte esterase and bacterial nitrates.
- Sensitivity and specificity are: Sensitivity = 0.40 & Specificity = 0.98
- Is a urine dipstick going to change your decision-making?

Adapted from Comprehensive Case Studies: ACEP, EBM Listserve 2003
Calculating LR:

- **Pre-test probability is 9%**

Adapted from Comprehensive Case Studies: ACEP, EBM Listserv 2003
Diagnosis

Sensitivity = 0.40
Specificity = 0.98

- LR+ = Sens / (1 - Spec) = 0.4 / 0.02 = 20
- LR- = (1 - Sens) / Spec = 0.6 / 0.98 = 0.61

- Pretest odds of disease = 0.09 / 0.91 = 0.1
- Bayes' theorem: 0.1 x 20 = 2 = Post test odds of a UTI.
- Post test probability = 2 / 3 = 0.67

Adapted from Comprehensive Case Studies: ACEP, EBM Listserv 2003
Using the Fagan nomogram

Adapted from Comprehensive Case Studies: ACEP, EBM Listserv 2003
Diagnosis

- This means that the patient is very likely (67%) to have a UTI.
- Similarly for a negative test:
  - LR- = (1 - Sens) / Spec = 0.6 / 0.98 = 0.61
  - Bayes' theorem: 0.1 x 0.61 = 0.06,
  - Post test odds = 0.06
- If test is negative, still 6% chance of UTI.

Adapted from Comprehensive Case Studies: ACEP, EBM Listserv 2003
Summary

- Related EBM to practice
- PICO questions
- Queries
- Diagnosis studies
  - Pre and post test probabilities
  - Likelihood ratio: how many times more likely is the test to be positive when the disease is there than when the test is positive but the disease is absent
Questions?
Credits

- Society for Academic Emergency Medicine: Evidence Based Medicine Course 2005
- JAMA. User’s Guides to the Medical Literature 2002
- Katz D. Clinical epidemiology and evidence based medicine 2001 Sage Publications