Evidence-Based Practice:

Articles of Diagnosis

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Pediatrics
Duke University Health System
Why conduct diagnostic tests?
Diagnostic Tests
Learning Objectives:

1. Define pre-test and post-test probabilities and their impact on the diagnostic process.

2. Describe action thresholds in the context of the diagnostic process.

3. Derive likelihood ratios from a published article and apply to a clinical scenario.
Evidence-based Medicine Cycle

THE PATIENT

ASSESS

ASK

ACQUIRE

APPLY

APPRAISE

The 5 A’s
You are an ED physician (or parent/aunt/uncle/neighbor) and you’ve just evaluated a 16yoM brought in by his parents for evaluation of **abdominal pain** which began yesterday. It’s gradually worsening.

Pain began 36hrs ago and is located near his belly button. He developed a fever (101.2F) 12 hours ago and feels nauseated with loss of appetite. No trauma. He’s vomited twice (no blood or bile) and had 1 loose stool today. Says abd hurts when he’s walking. Previously healthy w/o abd surgery.

**Physical exam:**
- No fever, normal vital signs. Appears ill and moves w/o discomfort.
- Lungs are clear
- Normal bowel sounds, tender everywhere including right lower area
- Rest of exam is unremarkable.

**WBC 14,000**
- 60% neutrophils
- Urine normal
HOW LIKELY IS IT THAT HE HAS ACUTE APPENDICITIS
Bryant,
NEJM, 302: 411
WHAT IS YOUR BEST ESTIMATE (PROBABILITY) THAT HE HAS ACUTE APPENDICITIS?
Pre-test Probability

An estimate of how likely it is that a patient has a specific disease before any additional testing is done.

Where does this come from?

| Clinical judgment from H&P / tests | Prevalence of disorder in your population | Clinical manifestations of disease articles | Differential diagnosis articles | Clinical prediction rules |
Fagan Nomogram

Mark Pre-Test Probability
Annotate with ✓
### Pediatric Appendicitis Risk Calculator (pARC)

<table>
<thead>
<tr>
<th>Sex</th>
<th>Female</th>
<th>Male</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Age</th>
<th>&lt; 3&lt;sup&gt;rd&lt;/sup&gt; yrs</th>
<th>3-7 yrs</th>
<th>8-13 yrs</th>
<th>&gt;13 yrs</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Duration of pain, hrs</th>
<th>&lt;24</th>
<th>24 to &lt;48</th>
<th>48 to 96</th>
<th>&gt;96</th>
<th>Unknown (defaults to &lt;24 hrs)</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>WBC</th>
<th>$14 \times 10^3$ cells/μL</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Neutrophil</th>
<th>Enter a value for neutrophil if it is available; otherwise, leave it as blank</th>
</tr>
</thead>
<tbody>
<tr>
<td>Value</td>
<td>60 %</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Presence of pain with walking</th>
<th>No</th>
<th>Yes</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Maximal tenderness in RLQ</th>
<th>No</th>
<th>Yes</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Abdominal guarding</th>
<th>No</th>
<th>Yes</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>History of migration of pain to RLQ</th>
<th>No</th>
<th>Yes</th>
</tr>
</thead>
</table>

### pARC Score (ED)

32%

### Risk group

Moderate risk
How certain do you need to be that your patient has appendicitis to call the surgeon and recommend this child go to the OR?

50% (Write this down) 100%
Treatment threshold

How certain you’d like to be of a diagnosis before proceeding with treatment

Depends on:
- Prognosis of the disease under consideration
- Effectiveness, safety, availability of treatment(s)
- Safety and costs of next test(s)
How low would your suspicion of acute appendicitis need to be in order to send him home?

0%  (Write this down)  50%
3 Observation threshold

How certain you’d like to be that a patient does NOT have a diagnosis before you would not pursue further testing

Depends on:

• Prognosis of the disease under consideration
• Effectiveness and availability of treatment
• Test accuracy, safety, acceptability to the patient
Mark Thresholds
Treatment with ♥
Observation with X
Diagnostic Tests Spur Action

Zone of Action

0% Threshold

LR

Zone of Uncertainty

LR

100% Threshold

Observation

Zone of Action

Probability below Obs threshold: no testing warranted

Probability between Obs and treatment threshold: further testing required

Probability above treatment threshold; testing completed; treatment commences
PROBABILITY OF SPECIFIC DIAGNOSIS
BACTERIAL PNEUMONIA
LEUKEMIA

Diagnosis UNCERTAIN
BACTERIAL PNEUMONIA

Healthy 20yo
Multiple antibiotic allergies
BACTERIAL PNEUMONIA

Frail 78yo
History of severe COPD
BACTERIAL PNEUMONIA

55yo, current smoker
“Two family members recently died of PNA and I’m afraid I have it too– and I’m not leaving until you tell me for sure if I have it or not...”
Likelihood Ratio

ONE specific test result

DISEASE

NO DISEASE
Likelihood Ratio – for a POSITIVE test

SAME test result

DZ

No

DZ
Likelihood Ratio – for a NEGATIVE test

SAME test result

DZ

No

DZ
**Disease**
STREP THROAT

**Test**
RAPID STREP

**LR+**
Proportion of patients with a **POSITIVE** rapid strep who **HAVE** strep throat

Proportion of patients with a **POSITIVE** rapid strep who **DO NOT HAVE** strep throat

**LR-**
Proportion of patients with a **NEGATIVE** rapid strep who **HAVE** strep throat

Proportion of patients with a **NEGATIVE** rapid strep who **DO NOT HAVE** strep throat
Disease: Appendicitis

Test: WBC > 15

LR+:
- Proportion of patients with a WBC > 15 who HAVE appendicitis
- Proportion of patients with a WBC > 15 who DO NOT HAVE appendicitis

LR-:
- Proportion of patients with a WBC ≤ 15 who HAVE appendicitis
- Proportion of patients with a WBC ≤ 15 who DO NOT HAVE appendicitis
Disease: Pulmonary Embolism
Test: Low Prob VQ

LR_{LowProbVQ}

Proportion of patients with a Low Prob VQ who HAVE a pulmonary embolism

Proportion of patients with a Low Prob VQ who DO NOT HAVE a pulmonary embolism
A ratio is a ratio is a ratio is a _________?

LR = 1
LR > 1
LR < 1
LR = 1
No impact on likelihood of disease

Increasing impact

LR = 0.01
LESS Likely

LR = 0.05
LESS Likely

LR = 0.1
LESS Likely

LR = 0.2
LESS Likely

LR = 0.5
MORE Likely

LR = 1
No impact on likelihood of disease

LR = 10
MORE Likely

LR = 50
MORE Likely

LR = 100
MORE Likely

Increasing impact
LR = 1
NO CHANGE

Increasing impact
LR = 0.2
LESS Likely
LR = 0.1
LESS Likely
LR = 0.05
LESS Likely
LR = 0.01
LESS Likely
LR = 5
MORE Likely
LR = 10
MORE Likely
LR = 50
MORE Likely
LR = 100
MORE Likely

LR = < 0.1
VERY Useful
LR = 0.1-10
MAY BE Useful
LR = > 10
VERY Useful
## Common LRs

<table>
<thead>
<tr>
<th>Test and cutoff</th>
<th>Value</th>
<th>Likelihood Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Rapid nucleic acid amplification</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Influenza</td>
<td>+</td>
<td>18.4</td>
</tr>
<tr>
<td></td>
<td>-</td>
<td>0.08</td>
</tr>
<tr>
<td><strong>Forced expiratory time for COPD</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>9 sec</td>
<td>4.8</td>
</tr>
<tr>
<td></td>
<td>6-9 sec</td>
<td>2.7</td>
</tr>
<tr>
<td></td>
<td>&lt; 6 sec</td>
<td>0.45</td>
</tr>
<tr>
<td><strong>Ferritin for iron-def anemia</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>&lt; 15</td>
<td>55 (35-84)</td>
</tr>
<tr>
<td></td>
<td>35-45</td>
<td>1.8 (1.5-2.2)</td>
</tr>
<tr>
<td></td>
<td>45-100</td>
<td>0.5 (0.48-0.60)</td>
</tr>
</tbody>
</table>
THE RATIONAL CLINICAL EXAMINATION

EVIDENCE-BASED CLINICAL DIAGNOSIS

David L. Simel, MD, MHS • Drummond Rennie, MD
Back in the zone of uncertainty...

Is there a test that can help us?
You are an ED physician (or parent/aunt/uncle/neighbor) and you’ve just evaluated a 16yoM brought in by his parents for evaluation of abdominal pain which began yesterday. It’s gradually worsening.

It’s 1am: you know ultrasound is first-line for diagnostic imaging for appendicitis in children. Radiology is slammed with many studies to do - it’ll be at least an hour or 2 wait - you don’t want to subject this child to a CT first-line.

You have done many ultrasounds, including of the abdomen looking for appendicitis. You are considering putting the probe on this patient’s belly yourself....
Study Architect

1. Type of study design?

2. In what clinical setting(s) would you recruit patients?

3. Which patients would you recruit (be specific)?

4. What is your plan for evaluating the accuracy of ultrasound?
Study Architect
Risk of Bias Assessment for a Diagnostic Test Article

1. Representative group of patients with this disease?

2. Uniform comparison to reference standard?

3. Blinding of those interpreting new test and reference standard?
Prospective Cohort

Exposure present

Exposure absent

Outcome - Yes

Outcome - No
Your sessions with the medical librarians pay off!

Evaluation of Acute Appendicitis by Pediatric Emergency Physician Sonography

Adam B. Sivitz, MD*; Stephanie G. Cohen, MD; Cena Tejani, MD

*Corresponding Author. E-mail: asivitz@barnabashealth.org.

<table>
<thead>
<tr>
<th>Reference Standard Test</th>
<th>Test</th>
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<tbody>
<tr>
<td><strong>+</strong></td>
<td><strong>+</strong></td>
</tr>
<tr>
<td>True Positive</td>
<td>False Positive</td>
</tr>
<tr>
<td>False Negative</td>
<td>True Negative</td>
</tr>
<tr>
<td><strong>-</strong></td>
<td><strong>-</strong></td>
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</tbody>
</table>

"Truth"
Sensitivity

Of all patients with disease, the proportion who test positive

<table>
<thead>
<tr>
<th>Disease</th>
<th></th>
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<tbody>
<tr>
<td><strong>+</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>+</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>-</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- **True Positive**
- **False Positive**
- **False Negative**
- **True Negative**

True Positive = True Positive + False Negative
Specificity

Of all patients without disease, the proportion who test negative

<table>
<thead>
<tr>
<th>Disease</th>
<th>Test</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td>True Positive</td>
<td>- False Positive</td>
</tr>
<tr>
<td>-</td>
<td>False Negative</td>
<td>True Negative</td>
</tr>
</tbody>
</table>

True Negative + False Positive
Positive Likelihood Ratio

The proportion of patients with disease who test POSITIVE — COMPARED TO — the proportion of patients without disease who test POSITIVE

True Positive
True Positive + False Negative

÷

False Positive
False Positive + True Negative

Test

Disease

+True Positive + False Negative

False Positive

-False Negative + True Negative

Test

+True Positive

False Positive

-False Negative

True Negative
Negative Likelihood Ratio

The proportion of patients with disease who test NEGATIVE – COMPARED TO –
the proportion of patients without disease who test NEGATIVE

\[
\text{False Negative} = \frac{\text{True Positive}}{\text{True Positive} + \text{False Negative}}
\]

\[
\text{True Negative} = \frac{\text{True Negative}}{\text{True Negative} + \text{False Positive}}
\]
Sensitivity
Specificity

Likelihood Ratios
<table>
<thead>
<tr>
<th>Appendicitis</th>
<th>+</th>
<th>-</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Equivocal</td>
<td>U/S</td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>85</td>
<td>179</td>
</tr>
</tbody>
</table>
**LR+** Proportion of patients with appendicitis who have a positive US compared to the proportion of patients without appendicitis who have a positive US.

<table>
<thead>
<tr>
<th>Appendicitis</th>
<th>+</th>
<th>-</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td>72</td>
<td>13</td>
</tr>
<tr>
<td>U/S Equivocal</td>
<td>8</td>
<td>67</td>
</tr>
<tr>
<td>-</td>
<td>5</td>
<td>99</td>
</tr>
</tbody>
</table>

\[
\text{LR}_+ = \frac{72}{85} = 12
\]
**LR-**: Proportion of patients with appendicitis who have a negative US compared to the proportion of patients without appendicitis who have a negative US.

<table>
<thead>
<tr>
<th>U/S</th>
<th>Appendicitis</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>+</td>
<td>72</td>
<td>13</td>
</tr>
<tr>
<td></td>
<td><strong>8</strong></td>
<td><strong>67</strong></td>
</tr>
<tr>
<td>-</td>
<td>5</td>
<td>99</td>
</tr>
</tbody>
</table>

\[
\text{LR}_- = \frac{\frac{5}{85}}{\frac{99}{179}} = 0.11
\]
**LR_{Equiv}:** Proportion of patients with appendicitis who have an equivocal US compared to the proportion of patients without appendicitis who have an equivocal US.

<table>
<thead>
<tr>
<th></th>
<th>+</th>
<th>-</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td>72</td>
<td>13</td>
<td>85</td>
</tr>
<tr>
<td>-</td>
<td>8</td>
<td>67</td>
<td>75</td>
</tr>
<tr>
<td>Total</td>
<td>80</td>
<td>80</td>
<td>160</td>
</tr>
</tbody>
</table>

LR_{Equiv} = \frac{8/85}{67/179} = 0.25
Back to the patient...
Ultrasound Positive
Ultrasound
Negative
$LR_{\text{Equiv}} = 0.25$
Ultrasound
Equivocal
Fagan Nomogram

MedCalc

Post-test Probability (LR)  

Pre-test probability: 30%
Likelihood Ratio: 6.8
Post-test probability: 74.5%
Likelihood Ratios

Integrate sens & spec

Affect real-time decision-making

May be used for tests with more than 2 possible results
Teaching Strategies

Centered session on patient case
Ultrasound

Concepts over calculations

Article choice

Learners did work - application