Providing High Value Cost-Conscious Care:

Biostatistical Concepts You Need to Know

http://hvc.acponline.org/
Learning Objectives

• Understand that a working knowledge of basic statistical concepts is essential to practicing high-value care

• Discuss how statistical measures are used in making effective and efficient decisions about diagnosis and treatment

• Review important statistical tools for diagnosis: sensitivity & specificity, predictive values, and likelihood ratios

• Review important statistical tools for treatment: risk ratios, absolute and relative measures, and numbers needed
Statistics in Diagnosis

- Diagnostic decision making - sequential process of reducing uncertainty regarding a patient’s diagnosis

- Start with *pretest probability of disease* estimate
  - how likely it is that the patient actually has a specific disease as the cause of his or her symptoms

- Diagnostic testing
  - to gather additional information to help us decide whether it is more or less likely that the patient has that disease

- Testing continues until we reach a threshold (a *posttest probability of disease*)

- Statistical measures
  - help us understand how effective a particular test may be in process
Pretest Probability

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

• Derived from -
  - Known prevalence of disease in population with characteristics of patient
  - Probability rules
  - Experience

• Clinical presentation influences our pretest probability of disease
Patient Presentation - Mr. D

- 41 yo man with antero-lateral chest pain x 2 d:
  - Originally sharp in nature and now a dull ache; non-radiating
  - Duration is 10 - 30 seconds; without change in position
  - At times it is associated with exertion but can occur at rest
  - He does have occasional heartburn but this feels different
  - He reports some shortness of breath with symptoms but no diaphoresis, nausea or vomiting

- Cardiac risk factors:
  - 10 pack-year tobacco use history; not currently smoking
  - No family history of early MI or sudden cardiac death
  - Most recent LDL 83 and HDL 37
Patient Presentation - Mr. D

Questions:

- Estimate this patient’s pretest probability for ischemic heart disease as a cause of his symptoms (low, medium or high)?
- Would you evaluate this patient further for ischemic heart disease?
- If so, what would be your next diagnostic test, and why?
Expressions of Probability

Range of subjective probability estimates assigned to each expression by 16 physicians

<table>
<thead>
<tr>
<th>Expression Used</th>
<th>0.0</th>
<th>0.05</th>
<th>0.1</th>
<th>0.2</th>
<th>0.3</th>
<th>0.4</th>
<th>0.5</th>
<th>0.6</th>
<th>0.7</th>
<th>0.8</th>
<th>0.9</th>
<th>0.95</th>
<th>1.0</th>
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<tbody>
<tr>
<td>‘sometimes’</td>
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“The wide variation observed in the subjective probabilities is apparently due to consistently different interpretations of expressions by individual physicians.”

Bryant & Norman, NEJM 1980;302(7):411
Diagnostic Testing

• Being able to select appropriate diagnostic tests in a specific patient is critical to practicing high-value care
  • Evaluation should not be the same for every patient
  • Not all patients require or benefit from testing
  • Tests vary in their ability to detect or exclude disease, and testing will be more or less effective in different patients depending on their risk of disease and clinical presentation
  • Testing characteristics help us to understand value of test
Test Characteristics: Sensitivity and Specificity

- They describe the ability of a test to discriminate between those who truly have a disease and those who do not by comparing the results of that test to a ‘gold standard’
- They do not change when applied to different patient populations

**Sensitivity** is the ability of a test to detect disease if it is truly present

**Specificity** is the ability of a test to exclude disease if it is truly absent

- Reciprocal relationship
Disease Prevalence: Positive and Negative Predictive Values

- Predictive values are a means of accounting for the variable prevalence of disease when we apply that test to a specific group.

- **Positive predictive value** is the probability that a patient (in a specific population) with a positive test actually has disease.

- **Negative predictive value** is the probability that a patient (in a specific population) with a negative test does not have disease.
The Power of a Test to Change Your Mind: Likelihood Ratios

- **Likelihood ratios combine the sensitivity and specificity of a test with pretest probability of disease in a specific patient**, avoiding the need to perform statistical calculations based on test characteristics and prevalence data.

- They provide a sense of how ‘powerful’ a test is in influencing our pretest probability of disease.

- Likelihood ratios may be positive (LR(+)), which are used when assessing for the presence of disease when a test result is positive, and negative (LR(-)), which are used when excluding disease with a negative test result.

- Likelihood ratios may also be calculated sequentially with serial testing, if needed.
Likelihood Ratios

Using likelihood ratios:

1. Use the estimated pretest probability of disease as an anchor on the left side of the graph

2. Draw a straight line through the known likelihood ratio (either (+) or (-))

3. Where this line intersects the graph on the right represents the posttest probability of disease
Likelihood Ratios

- A likelihood ratio of 1 indicates that the test has no influence on the pretest probability; a likelihood ratio >1 increases the pretest probability, while a likelihood ratio of <1 decreases the pretest probability.

- In general:
  - A LR(+) of 10 increases the pretest probability by ~45%
  - A LR(+) of 5 increases the pretest probability by ~30%
  - A LR(+) of 2 increases the pretest probability by ~15%
  - A LR(-) of 0.5 decreases the pretest probability by ~15%
  - A LR(-) of 0.2 decreases the pretest probability by ~30%
  - A LR(-) of 0.1 decreases the pretest probability by ~45%

- Even if specific LR calculations are not performed for a patient, simply knowing the LR of a test helps in making testing decisions.
Patient Presentation - Mrs. T

- 32 yo woman - 2 day history dull, aching, left-sided CP.
  - First noted after exercise
  - Constant since onset, worse with positional changes
  - No associated nausea, vomiting, diaphoresis, lightheadedness
  - Some shortness of breath
  - Improved with acetaminophen
- Physically active, exercises regularly, no smoking history
- Father died of heart attack age 55
- Past medical history:
  - Unremarkable PMH, no active conditions, lipids 2 years ago - LDL 122, HDL 42
  - BP 122/70; hr 60; BMI 25
  - Her cardiac and general physical examinations are normal, resting EKG normal
Mrs. T

- What is your estimate of her pre-test probability?
- Based on this estimate, would you perform additional testing?
- How might cardiac stress testing influence your pretest probability?

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>LR</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECG Stress</td>
<td>68%</td>
<td>77%</td>
<td>LR pos – 2.9</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>LR neg – 0.42</td>
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<tr>
<td>Echo Stress</td>
<td>85%</td>
<td>77%</td>
<td>LR pos – 3.7</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>LR neg – 0.19</td>
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<tr>
<td>Nuclear Med Stress</td>
<td>88%</td>
<td>74%</td>
<td>LR pos – 3.4</td>
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<tr>
<td></td>
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<td>LR neg – 0.16</td>
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</table>
Statistics in Treatment

• High-value therapeutic decision making requires understanding the effectiveness of different treatment options, and balancing potential benefits with both medical and financial costs

• Methods for assessing treatment interventions include:
  • Risk Ratios
  • Absolute measures
  • Relative measures
  • Numbers needed
Assessing Treatment Interventions: Risk Ratios and Odds Ratios

• Ratios are often referred to by the nature of the outcome being evaluated - risk or hazard, or benefit

• Risk ratios compare the occurrence of an outcome or the odds of an outcome due to a treatment intervention in a group of patients compared to a control group

• Odds ratios are a different statistical method but are interpreted similarly; relative risks are used for randomized, controlled trials and cohort studies, while odds ratios are used for case-control studies

• When events in the intervention group are significantly less frequent than in the control group, the relative risk or odds ratio (and their confidence intervals) will be less than 1; if the converse holds true, they will be greater than 1
Assessing Treatment Interventions: Absolute Measures

- Absolute measures describe the absolute changes in risk or benefit in a treatment group compared to a control group.
- These measures are usually named by the outcome being evaluated:
  - Absolute risk reduction (ARR)
  - Absolute risk increase (ARI)
  - Absolute benefit increase (ABI)
- Absolute measures are used to calculate the numbers needed.
Assessing Treatment Interventions: Relative Measures

- Relative measures define the proportional changes in risk or benefit in a treatment group compared to a control group.

- These measures are also named by the outcome being evaluated:
  - Relative risk reduction (RRR)
  - Relative risk increase (RRI)
  - Relative benefit increase (RBI)

- Relative measures may overstate the clinical importance of a treatment effect, particularly if the occurrence of a disease is low; for example, a 50% reduction in a disease that affects 1% of the population may not be as clinically important as a similar reduction in a disease that is seen in 30% of people.
Assessing Treatment Interventions: Numbers Needed

• Numbers needed are an estimate of the number of patients in which an intervention must be applied to generate one occurrence of the outcome

• The outcome of interest may be a benefit of treatment (number needed to treat - NNT) or potential harm (number needed to harm - NNH)

• The lower the number needed, the greater the magnitude of the intervention’s effect - a NNT of 3 means that 3 patients would need to be treated with the intervention to see a benefit

• NNT and NNH are often calculated for the same intervention, making balancing risks and benefits easier
Patient Presentation - Mrs. T

Available evidence for aspirin treatment to prevent ischemic CAD:

<table>
<thead>
<tr>
<th>Event</th>
<th>Aspirin (%/y)</th>
<th>Control (%/y)</th>
<th>Risk Ratio</th>
<th>Absolute Risk</th>
<th>Relative Risk Reduction</th>
<th>Numbers Needed</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary Prevention</strong></td>
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<tr>
<td>Non-Fatal MI</td>
<td>0.21</td>
<td>0.25</td>
<td>0.84</td>
<td>0.04% Reduction</td>
<td>16% Reduction</td>
<td>NNT = 2,500</td>
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<tr>
<td>Major Extracranial Bleed</td>
<td>0.11</td>
<td>0.08</td>
<td>1.37</td>
<td>0.03% Increase</td>
<td>37.5% Increase</td>
<td>NNH = 3,333</td>
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<tr>
<td><strong>Secondary Prevention</strong></td>
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<tr>
<td>Non-Fatal MI</td>
<td>1.60</td>
<td>2.30</td>
<td>0.69</td>
<td>0.7% Reduction</td>
<td>30% Reduction</td>
<td>NNT = 143</td>
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<tr>
<td>Major Extracranial Bleed</td>
<td>0.25</td>
<td>0.06</td>
<td>2.69</td>
<td>0.19% Increase</td>
<td>3% Increase</td>
<td>NNH = 526</td>
</tr>
</tbody>
</table>
Patient Presentation - Mrs. T

- Statistical information presented in these different ways helps in understanding the potential risks, benefits, and magnitude of effect for a specific treatment.

- However, this information does not tell you what to do with a specific patient in whom the benefit/risk ratio must be determined on an individual basis.

- Additional statistical data may also be available for specific groups of patients with differing risk factors that may reflect a different benefit/risk ratio.

- However, this information may inform clinical and shared decision making.

- How would you discuss this with Mrs. T?
Summary

START:

• Calculating pre-test probability before ordering a diagnostic test or treatment

• Using biostatistical methods to decide whether testing/treatment will improve patient outcomes

STOP:

• Routinely evaluating patients with “one size fits all” diagnostic testing

• Making testing/treatment recommendations without understanding if and how they will help the patient
References

