

2.6.A Testing Thresholds for Strep Throat

Let's return to Clinical Scenario #1 from Chapter 1, in which we had a graduate student with sore throat, fever, pus on the tonsils and tender lymph nodes.

Assume:

- i. The drug cost of a course of penicillin V (500 mg 3 times a day) to treat acute Group A streptococcal throat infection (“strep throat”) is about \$12 (www.GoodRx.com, with a coupon), and the expected cost in patient inconvenience, risk of adverse or allergic reactions, and contribution to antibiotic resistance is another \$48. So, the total expected treatment cost is \$60.
- ii. Treating someone who really has strep throat (and not some other pharyngitis) decreases symptom severity, length of illness, transmission to others and the (already minute) risk of rheumatic fever. The value of this averages about \$150, but since the cost of treatment is \$60, the net benefit of treating someone with strep throat is \$90. This can also be viewed as the net cost of failing to treat someone with strep throat. Penicillin will not help the patient if the sore throat is caused by something other than Group A strep.
 - a) Draw a graph like figure 2.2, labeling the axes, lines and intercepts. Although you can check your answer at www.ebd2.net, draw the graph by hand.

6a. The graph looks just like Figure 2.2 except that C = \$60 and B = \$90 and the x-axis is the probability of strep throat.

- b) At what probability of strep throat should you treat with penicillin? Show the point on the graph and the equation to derive it; you can check your answer at ebd2.net

6b. $C/(C + B) = \$60/(\$60 + \$90) = 0.4$. It's where the lines cross on the graph.

- c) According to UpToDate (7/11/18) the sensitivity of a rapid strep test is 77-92% and specificity is 88-99%. If a rapid strep test were 85% sensitive and 95% specific, for what range of prior probabilities would it have the potential to affect management? (Ignore the cost of the test.) Do this calculation using likelihood ratios, then draw a line for “free rapid strep testing” on the graph.

6c. The lower limit for testing, below which even if a (free) rapid strep test were positive we would not treat, depends on the LR+. The $LR+ = \text{Sensitivity}/(1 - \text{specificity}) = .85/.05 = 17$. Since the treatment threshold is $P = 40\%$, the post test odds at which we would treat = 40:60, or 2:3. So we divide these post-test odds by the LR+ to get the No Treat-Test threshold odds:

Pretest odds = post-test odds/LR = $(2/3)/17 = 2/51$

So the pre-test probability below we would not test and not treat (using the shortcut that if odds are a:b, probability = $a/(b+a) = 2/(51+2) = 2/53 = .038$

Similarly, to get the post test odds above which we would treat without testing (Test-Treat threshold odds), we use LR^- . $LR^- = (1-sensitivity)/specificity = .15/95 = 0.158$. So we divide the post-test odds of 2:3 by LR^- to get:

$$(2/3)/0.158 = 4.22.$$

So the post test probability = $4.22/(1+4.22) = 4.22/5.22 = 0.81$.

- d) Now assume that a perfect rapid strep test for Group A streptococcal throat infection has been developed. The test causes negligible discomfort and results are available nearly instantaneously, but the test costs \$40. When does it make sense to use this test? Draw a line for testing on the graph and explain.

6d. The most that a perfect test can save you in misclassification costs is the expected cost at the treatment threshold, when you are most uncertain about what to do. This is $0.4(\$90) = 0.6(\$60) = \$36$, so with these values of C and B it is *never* worth doing a \$40 rapid strep test, even if the test is perfect. The test line is higher than the intersection of the No Treat and Treat lines, so not treating or treating empirically will always be a lower cost option than testing.

- e) UpToDate recommends using the Centor criteria to estimate the pretest probability of strep throat to assist in the decision to do a rapid strep test in patients with a sore throat. The criteria are: 1) tonsillar exudates (pus on the tonsils); 2) tender anterior cervical (front of the neck) lymph nodes; 3) Fever and 4) absence of cough. The authors recommend forgoing testing for patients with ≤ 2 criteria (probability of strep $\leq 21\%$) and testing for 3 criteria (probability of strep 38%) or 4 criteria (probability of strep 57%). Use the regret graph calculator at www.ebd2.net to find a cost T for the rapid strep test that would be consistent with the UpToDate recommendation.

6e. The numbers work out if the rapid strep tests costs about \$15. If it costs much more than that, then we would treat without testing for patients with 4 Centor criteria. If it costs much less than that, we should also do the test in patients with 2 Centor criteria.

- f) Perhaps when you read the stem of this question you were surprised at how much we inflated the cost C of treatment, to about 5 times the actual medication cost. Experiment with the regret graph calculator and see how much you can reduce C while still having the calculator provide results consistent with the UpToDate recommendations.