**Sensitivity, specificity and other statistics**

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**calculated for diagnostic and prognostic tests**

**David M. Thompson**

**2x2 table relating dichotomous test results to a dichotomous outcome like a disease**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  | True state,  sometimes validated by "gold standard” | |  |
|  |  | Outcome present (+) | Outcome absent (-) |  |
| Test  Result | positive test  (+) | TP | FP | total who test  positive |
| negative test  (-) | FN | TN | total who test negative |
|  |  | total with condition | total without condition | total |

**Prevalence** = (TP+FN)/ total, the proportion who truly have the condition.

**Important conditional probabilities:**

***Sensitivity and specificity.*** We assume that these are stable properties of a test and are unrelated to disease prevalence. We should examine this assumption carefully for many tests.

Sensitivity = TP/(TP+FN)

the probability that someone with the condition will test positive.

Specificity = TN/(TN+FP)

The probability that someone without the condition will test negative.

***Predictive Values.*** These depend on the prevalence of the condition in the population to which the test is applied.

Predictive Value Positive (PV+) = TP/(TP+FP)

The probability that someone with a positive test truly has the condition.

Predictive Value Negative (PV-) = TN/(TN+FN)

the probability that someone with a negative test truly does not have the condition.

**Spin and Snout: a mnemonic for clinical decision-making**

SPIN: use a SPecific test to rule IN or confirm a clinical hypothesis. Because highly specific tests generate very few false positives, a positive test is likely to be a true positive.

SNOUT: use a SeNsitive test to rule OUT or discard a clinical hypothesis. Because highly sensitive tests generate very few false negatives, a negative test is likely to be a true negative.

**Likelihood Ratios for dichotomous tests**

Let D represent disease,

so that D+ represents the true presence of disease

and D- represents the true absence of disease.

Let T represent a results of a dichotomous test,

so that T+ represents a positive test

and T- represents a negative test.

Sensitivity (Sn) = p(T+|D+)

1-Sensitivity (1-Sn) = p(T-|D+)

Specificity (Sp) = p(T-|D-)

1-specificity (1-Sp) = p(T+|D-)

Therefore, Sn/(1-Sp) =

This is the LR+, the “likelihood ratio” associated with a positive test.

The LR+ compares the probability of obtaining a positive test when the disease is truly present with the probability of obtaining a positive test when the disease is truly absent.

In parallel, the LR- is the likelihood ratio associated with a negative test.

LR- =

The LR- compares the probability of obtaining a negative test when disease is truly present with the probability of obtaining a negative test if the disease is truly absent.

**Likelihood ratios link prior (pre-test) and posterior (post-test) odds of a diagnosis**

LR \* prior odds of a disease = posterior odds of a disease

Multiplying a test’s likelihood ratio (from, for example, a published estimate) with the pretest odds that one has a disease (an estimate of which can come from clinical knowledge) produces an estimate of the “posterior” or *post-test odds* that the person has the disease.

For example,

Assume that, prior to performing a test, we believe the odds a person has a disease is 0.25. An odds of 0.25 maps to a probability of or 0.33.

Assume that we obtain a positive result on a clinical test whose published Sn (0.8) and Sp (0.9). Such a test has an LR+ of () = 8.

So, given a positive test, the post-test odds of disease are 0.25\*8 or 2. These post-test odds of 2 equate to a probability of 2/(2+1) or 0.67. In this example, a positive test increased the estimated probability of disease from a pre-test value of 0.33 to a post-test estimate of 0.67.

**The LR+ links prior (pre-test) and posterior (post-test) odds of disease when a test is positive**

Here’s the algebra that justifies the calculation we performed above. The clinician’s pre-test estimate of the probability of disease is p(D+). The equivalent pretest odds is then p(D+)/ p(D-).

Given a positive test, the product of the likelihood ratio LR+ and the pretest odds is:

p(T+|D+) p(D+) p(T+∩D+)

=\*

\*\*

p(T+|D-) p(D-) p(T+∩D-)

Dividing the expression’s numerator and denominator by the probability of a positive test, p(T+)

p(T+∩D+) / p(T+) p(D+|T+)

=\*

p(T+∩D-) / p(T+) p(D-|T+)

produces an expression that we recognize as the post-test odds of disease. Note that the odds are *conditional* on having obtained a positive test result.

**The LR- links prior (pre-test) and posterior (post-test) odds of disease when a test is negative**

How, in this example, would a negative test alter one’s suspicion of a diagnosis or disease? The same test with Sn of 0.8, Sp of 0.9, and LR+ of 4, will have an LR- =

Multiplying the LR- by the pre-test odds of disease yields an estimate of the posterior odds of disease.

0.22 \* 0.25 = 0.055

The algebra is very similar to that demonstrated earlier:

LR- \* pre-test odds of disease = post-test odds of disease, conditional on having obtained a negative test result

p(T-|D+) p(D+) p(T-∩D+) p(T-∩D+) / p(T-) p(D+|T-)

=\*

=\*

=\*

\*\*

p(T-|D-) p(D-) p(T-∩D-) p(T-∩D-) / p(T-) p(D-|T-)

The posterior odds of disease, 0.055, is equivalent to a probability of disease of , or around 0.052 or 0.053. A negative test has “moved” the clinical assessment of disease probability from a pre-test value of 0.33 to a post-test value of 0.05.

**Thresholds that guide the decision to test, or to treat**

|  |  |  |
| --- | --- | --- |
| No treat , No test | Test, then treat based on test results | Treat, No test |

No treat - test threshold Test-treat threshold

When the odds (or probability) of disease are above the test-treat threshold, *even a negative test* won’t produce a posterior odds of disease sufficiently large to convince you against treatment. Again, testing is pointless in this case, and you will proceed with treatment.

When the odds (or probability) of disease are below the no treat-test threshold, they are so small that *even a positive test* won’t produce a posterior odds of disease sufficiently high to convince you to test. In that case, testing is pointless, as is treatment.

We can regard the two thresholds as special values for the *prior odds*, the odds of disease estimated before testing. Testing is indicated if the prior odds of disease are between these two thresholds.

We can calculate these two threshold values by using the relationships:

LR+ \* prior odds of disease = posterior odds of disease given a positive test

LR- \* prior odds of disease = posterior odds of disease given a negative test

**The no treat-test threshold**

Given the expected performance (Sn and Sp) of the test we plan to use, at what minimal threshold for the prior odds can we hope to “break even” between the costs and benefits of further testing if we obtain a positive test?

The first of the relationships applies to this question.

LR+ \* prior odds of disease = posterior odds of disease given a positive test

We regard the “treatment threshold odds” as posterior odds.

We regard the no treat-test threshold odds as the prior odds of disease.

Then, the odds for the no treat-test threshold =

This is the value for the prior odds below which we could not hope to balance benefits and costs, even if a positive test modified our view of the disease odds. We would refrain from testing, understanding that even a positive test would not cause us to act.

However, if we judge the pre-test odds of disease to be greater than this threshold, we would proceed with testing.

**The test-treat threshold**

Given the expected performance (Sn and Sp) of the test we plan to use, at what maximal threshold for the prior odds can we be assured of “breaking even” between costs and benefits of treatment, *even if we obtain a negative test*?

The second the relationship applies to this question.

LR- \* prior odds of disease = posterior odds of disease given a negative test

We regard the “treatment threshold odds” as posterior odds.

We regard the test-treat threshold odds as the prior odds of disease.

Then the odds for the test-treat threshold are

Given our test’s expected performance, this is the value for the prior odds above which we know that benefits outweigh costs, even if a negative test result modified our view of these odds. If we judge the pre-test odds to be this high, we would refrain from testing, understanding that even a negative test would not dissuade us from treating.

If we judge the pre-test odds of disease to be lower than this threshold, we would proceed with further testing.

**Bayes theorem unifies conditional probabilities like Sensitivity and PV+**

Sensitivity and PV+ share, by their definitions, the number of true positives that is contained in “cell a” of the table below. Bayes theorem builds on this commonality to find a way to express PV+ in terms of sensitivity, specificity and prevalence.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | | Disease status | | |
| Disease | No disease | Total |
| Test Result | Positive | A | B | A + B |
| Negative | C | D | C + D |
| Total | A + C | B + D | N = A + B + C + D |

Step 1:

Sn = a/(a+c)

PV+ = a/(a+b)

We can define a and b in terms of Sn and Sp,

then define PV+ in terms of Sn and Sp**.**

Step 2:

Sn = a/(a+c),

so a=Sn\*(a+c)

Sp= d/(b+d),

so 1-Sp=b/(b+d),

and b=(1-Sp)\*(b+d)

Step 3:

PV+ = a/(a+b)

Substituting the expressions defined above for cells a and b:

PV+ = Sn(a+c) / [Sn(a+c)+(1-Sp)(b+d)]

Dividing the numerator and denominator by the total n

PV+ = [Sn(a+c)/n] / [Sn(a+c)/n + (1-Sp)(b+d)/n]

=

We can regard the PV+ as a post-test probability (PostTP), the probability of an outcome given the result of a test.

If sampling is cross-sectional, we can substitute for the prevalence a “pre-test probability” (preTP), a judgment about the probability of the outcome BEFORE administering the test. Then:

PV+ = PostTP =

Specificity and the predictive value negative (PV- ) similarly share cell d, which enumerates the number of true negatives. Therefore, similar algebra permits expression of the (PV-), the probability that a patient whose test is negative does NOT have the disease, in terms of specificity and prevalence.

PV- **= -**

**References**

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