Predictive Values, Sensitivity and Specificity in Clinical Virology

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Infectious Diseases and Microbiology

2009

Reality

- Diagnostic tests are never perfect. False positive and false negative results occur.

- How much of a problem these false results may cause depends on the **clinical** context in which a test is used.

Reality

Truth

	Disease present	Disease absent
Positive test	True positive	False positive
Negative test	False negative	True negative

Sensitivity and Specificity

- **Sensitivity** = ability of a test to detect a true positive.

- Sensitivity = $\dfrac{\text{True positive}}{\text{True positive + false negative}}$

- **Specificity** = ability of a test to exclude a true negative.

- Specificity = $\dfrac{\text{True negative}}{\text{True negative + false positive}}$

Sensitivity and Specificity

- Sensitivity and specificity are characteristics of the test, while predictive values depend of the disease prevalence in the population being tested.

- Often sensitivity and specificity of a test are inversely related.

Predictive Values

- Predictive values are of importance when a positive result does not automatically mean the presence of disease.

- Unlike sensitivity and specificity, predictive value varies with the prevalence of the disease within the population.

- Even with a highly specific test, if the disease is uncommon among those tested, a large proportion of the positive results will be false positives and the positive predictive value will be low.

Predictive Values

- **Positive predictive value** = proportion of positive test that are true positives and represent the presence of disease.
- **PPV** = $\dfrac{\text{true positive}}{\text{true positives + false positives}}$

- **Negative predictive value** = proportion of negative test that are true negatives and represent the absence of disease.
- **NPV** = $\dfrac{\text{true negative}}{\text{true negative + false negative}}$

A test with 90% sensitivity and specificity and a disease with 10% prevalence

	Patients with disease	Patients without disease	All patients
Positive Test	90	90	180
Negative Test	10	810	820
TOTAL	100	900	1000

PPV = 90 / (90 + 90) = 90 / 180 = 50%

NPV = 810 / (810 + 10) = 810 / 820 = 98.7%

So 50 % of positive results will be false +ves

A test with 90% sensitivity and specificity and a disease with 1% prevalence

	Patients with disease	Patients without disease	All patients
Positive Test	9	99	108
Negative Test	1	891	892
TOTAL	10	990	1000

PPV = 9 / (9 + 99) = 9 / 108 = 8.3%

NPV = 891 / (891 + 1) = 891 / 892 = 99.9%

So 91 % of positive results will be false +ves

PPV and NPV for test with 90% sensitivity and specificity.

Prevalence	PPV	NPV
1%	8%	>99%
10%	50%	99%
20%	69%	97%
50%	90%	90%

Positive predictive value (PPV)

- If the test is applied when the proportion of people who truly have the disease is high then the PPV improve.

- Conversely, a very sensitive test (even one which is very specific) will have a large number of false positives if the prevalence of disease is low.
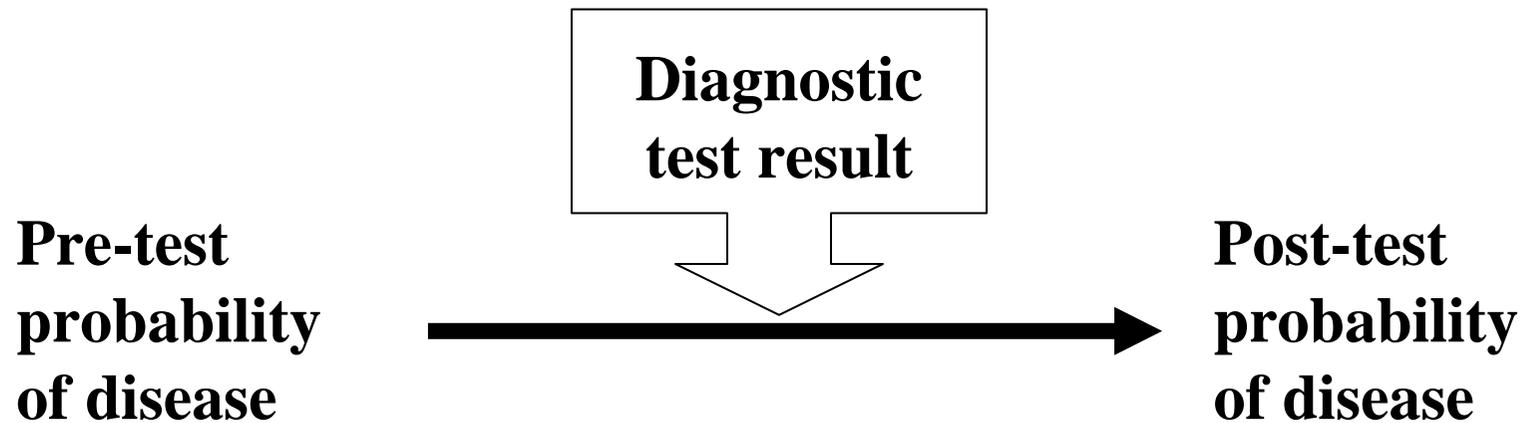
Summary

- Sensitivity and specificity are intrinsic attributes of the test being evaluated (given similar patient and specimen characteristics), and are independent of the prevalence of disease in the population being tested

- Positive and negative predictive values are highly dependent on the population prevalence of the disease

Likelihood ratios

- The degree to which a test result modifies your pre-test probability of disease is expressed by the "likelihood ratio" (Bayes Theorem)

Positive likelihood ratio

- The **positive likelihood ratio** is the chance of a positive test result in people *with* the disease, divided by the chance of a positive test result in people *without* the disease

Negative likelihood ratio

- This is the chance of a negative test result in people *with* the disease, divided by the chance of a negative test result in people *without* the disease

Intuitive Assessments

- Yes! But even experienced clinicians may disagree on the interpretation of a diagnostic test result

- This reasoning "makes explicit" the reasons for such disagreement:
  - Differing estimates of pre-test probability?
  - Differing estimates of test performance?
  - Differing willingness to tolerate uncertainty?

Sensitivity and Specificity

- Selecting the optimal balance of sensitivity and specificity depends on the purpose for which the test is going to be used.

- A screening test should be highly sensitive and a confirmatory test should be highly specific.

Sensitivity and Specificity

- In practice a test is either used for sensitivity or specificity.

- What is the test for?
- Test with high **sensitivity** are used to **RULE OUT** those without the disease

- Tests with high **specificity** are used to **RULE IN** those with the disease.

Series testing

- You can use the post-test probability of one test as the pre-test probability of the next test – Testing in Series

- Diagnostic tests performed in series or sequence allows for orderly progression up or down the probability tree until you are happy with the diagnostic decision.

- The specificity is increased but the sensitivity falls.

Parallel testing

- Often a battery of tests is requested at the same time – testing in parallel.

- Sensitivity is increased because a diagnosis is made when there is positive in either test.

- The result will be a high number of false positives because the specificity is reduced.

Series or Parallel

	Sens	Spec
A	0.8	0.6
B	0.9	0.9
A and B (series)	0.72	0.96
A or B (parallel)	0.98	0.54

Sensitivity Bias

- Diagnostic tests are often studied in populations different from those to whom they are applied. If the study population is very "sick" the sensitivity may be higher than when the test is applied to a more "general" population, particularly when there is diagnostic uncertainty.

Specificity Bias

- Specificity may be higher in a "healthy" population (low probability). When used in patients who are "sicker" (and for whom there is more diagnostic uncertainty) more false positive results are likely – specificity bias.

Thank you

Questions

Finally a word from your virologist – (sample) size is important !!