3-Part Webinar Series: Interpretation of Study Findings
Part III: Predictive Value and Diagnosis

Questions Asked: 12 September 2024

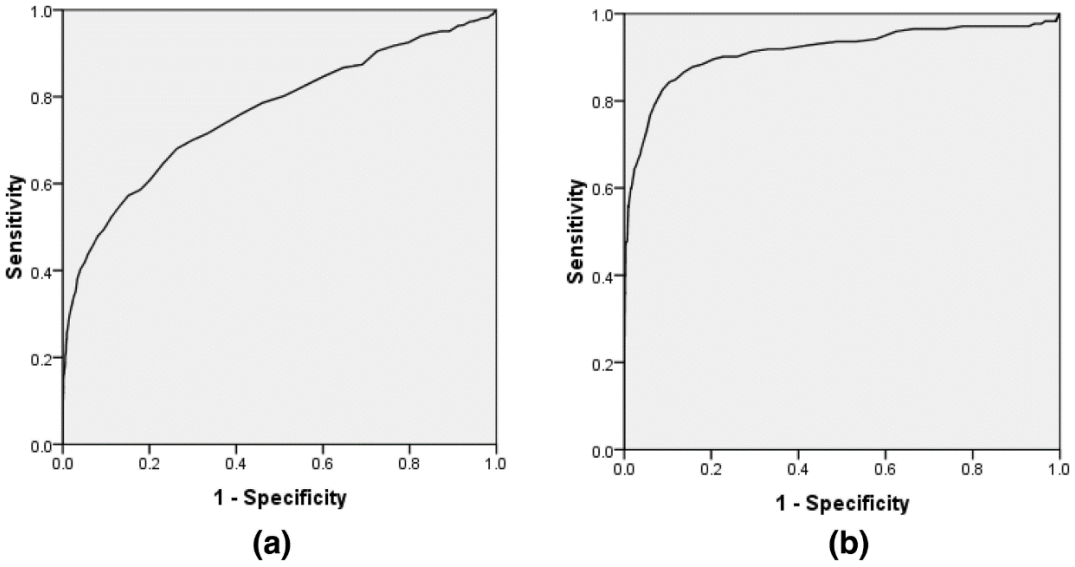
1. I understood the explanation of the calculation of the sensitivity of the tests explained here. I would like to know, in the case of a disease that does not use a test for diagnosis, such as tetanus and other diseases, how I will find out its sensitivity and specificity by means of a case definition.

   Sensitivity and specificity are properties of the test and not affected by disease preavalence. The spatula test for tetanus has a sensitivity of 94% and a specificity of 100%. The spatula test is a simple bedside test that can help diagnose tetanus by touching the back of the throat with a tongue blade or spatula. A positive result is a reflex spasm of the jaw muscles, while a negative result is a gag reflex. If tetanus is present, patients develop a reflex spasm of the masseters and bite the spatula (ie, a positive test result). In 400 patients, this test had a sensitivity of 94% and a specificity of 100%.

2. How would we interpret sensitivity, specificity, and PPV if the screening test gives continuous or ordinal data? For e.g., the RBS is divided into normal, impaired, or disease.

   The sensitivity of FPG to diagnose pre-diabetes or diabetes is 43.8% when the cut off is 5.6 mmol/L with a specificity of 94.2%. The sensitivity to identify diabetes mellitus is 80.8% with a specificity of 92.1% at the same cut off value.

ROC curve for FPG in screening (a) for pre-diabetes/diabetes; (b) for diabetes



3. How can a researcher apply Predictive values and Sensitivity tests to Surveillance Systems Evaluation (SSE)? For instance, if I am carrying out Rabies SSE or Malaria SSE in an endemic community.

Good questions and SSE can be considered pariculalry regarding the prevlence of disease.

Positive predictive values (PPVs) can vary considerably between countries. For example, Ethiopia had the lowest PPVs for both the histidine-rich protein II (HRP2) and parasite lactate dehydrogenase (pLDH) assays, while Guinea had the highest PPVs for both assays.

Negative predictive values (NPVs) are generally high across countries, with values above 90% for both the HRP2 and pLDH assays. However, the NPV for the pLDH-based test can drop significantly as transmission intensity increases.

Rapid diagnostic tests (RDTs) can be used in surveillance systems to help detect and manage outbreaks, and to monitor for potential biothreats. RDTs can help identify cases early, which can lead to earlier vaccination and treatment, and increased ICU capacity. RDT and PCR sensitivity increase as parasite density increases. For example, one study found that RDT sensitivity was lowest in samples with a parasite density below 100 parasites/µL. Polymerase chain reaction (PCR) is a DNA-based method that can be used to detect malaria parasites in a blood sample. Highly sensitive and specific, can detect mixed infections, and can identify species of malarial parasites. Results can take time to be available, and it's not optimized for routine diagnostics in clinical settings. Most useful for confirming the species of malarial parasite after an initial diagnosis, and for epidemiological studies. PCR is more sensitive than traditional microscopy methods, especially in cases of low parasitemia. It can also be used to detect mixed infections, and to identify the species of malarial parasite. However, PCR results can take time to be available, and the time lag between sample collection and result dissemination can limit its usefulness in clinical settings.

In areas with limited resources, such as rural areas, PCR may not be practical as a diagnostic method. However, PCR is becoming more important for epidemiological studies as the world works toward eliminating malaria

4. Does it make sense to repeat a negative test where disease prevalence is very high?

Great, but complicated question- A high negative predictive value (NPV) for a second screening test means that the test is effective at identifying patients who do not have the disease:

Predictive values are based on the test's sensitivity and specificity, as well as the prevalence of the disease in the population being tested. When the prevalence of a disease is low, the PPV

will be low, even if the test has high sensitivity and specificity. In these cases, a large number of people with positive test results will actually be found to not have the disease.

- ***A test's NPV is the percentage of patients with a negative test result who do not have the disease. A high NPV, close to 100%, indicates that the test is performing well.***
- ***Factors that affect NPV - A test's NPV is affected by the prevalence of the disease in the population, and usually changes in the opposite direction to the positive predictive value (PPV).***

So the repeat of a screening test for a first negative test – that has a high PPV and relative lower NPV would NOT provide additional value. A case in point – COVID testing – even though an individual has two negative tests but symptoms present – because of the NPV issues – the recommendation is to treat as a positive case.

There is some indication that positive antibody tests should be repeated to ensure their accuracy. Opinions vary with some thinking this is a waste of resources and no reimbursement for doing a second test and some believing that there really won't be any effect on treatment.

An example of repeat test with PPV - Test A has an Se of 95% and Sp of 90% and Test B has an Se of 80% and Sp of 95%, and the prevalence of disease is 1.0%.In this scenario, you are retesting with Test B all the positives seen from Test A, which means the prevalence of disease in that repeat population is actually the PVpos yielded by Test A, i.e. 2 passes in calculating predictive value, the first with the starting prevalence of 1.0% and the 2nd with the resulting PVpos as the prevalence for apply Test B.

Prevalence	First Test PVpos	Repeat Test PVpos
20%	70%	97%
10%	51%	94%
4%	28%	86%
2%	16%	75%
1%	8.7%	61%

So, if New York had a disease prevalence of 20% and California at 2%, the testing strategy for the situation in New York (20%) should be different from the strategy for California (2%). Repeat testing will be necessary in California, but not in NY.

5. What are the practical implications of testing among a population with a low prevalence for a disease when we use a high sensitivity and high specificity test? Do we have to accept that some people 'will fall through the cracks' and their disease will not be detected? I am a bit conflicted about the ethics of this.

The above example alo addresses this issue. First, your concern with this issue is to be applauded. It is an important concern. All really depends on the disease of interest and the prevalence – and the concern about false positives and false negatives. And your asseseesment if it is acceptable for that some people 'will fall through the cracks' and their disease will not be detected.

6. What is the best solution for the disease prevalence in the population issue regarding the PPV? Are there any alternatives for PPV?

   Positive predictive value (PPV) and prevalence are both statistical measures that are related to the likelihood of a patient having a disease after a test. Positive predictive value (PPV) is the probability that a patient with a positive test result actually has the disease. PPV is calculated by dividing the number of true positives by the total number of people who tested positive.

   Prevalence is the proportion of a population that has a disease or condition at a specific time. Prevalence affects PPV, and the two move in opposite directions:. As prevalence increases, so does PPV. This is because the proportion of true positives to false positives increases. As prevalence decreases, so does PPV. This is because the proportion of true positives to false positives decreases.

   Not an alternative but to increase the positive predictive value of a screening test, a program could target the screening test to those at high risk of developing the disease, based on considerations such as demographic factors, medical history or occupation.

7. What factors may affect sensitivity and specificity?

   Sensitivity refers to a test's ability to designate an individual with disease as positive. A highly sensitive test means that there are few false negative results, and thus fewer cases of disease are missed. The specificity of a test is its ability to designate an individual who does not have a disease as negative. Maximization of the sum of sensitivity and specificity is formally equivalent to minimization of the sum of false negative and false positive misclassification likelihoods.

   Sensitivity and specificity are specific to a diagnostic test. So the affecting factots would be those affecting the quality, accuracy and validity of the test.

8. How do we measure blood pressure variability (BPV) efficiently? Since taking multiple BP may not be feasible, how can we address this? Is there any device to handle this?

   The term BPV encompasses a wide range of BP variations, occurring over seconds or minutes (very short-term BPV), along 24 hours (short-term BPV, usually assessed by ambulatory BP monitoring), and between days (mid-term or day-to-day BPV, assessed with home BP monitoring). Different methods to estimate BPV have in fact been proposed during the last years; among them, the most commonly applied is the average real variability (ARV), which is the average of the absolute differences between consecutive BP readings.

BPV can be measured using a variety of indices, including 1] Standard deviation (SD) A common metric that reflects the dispersion of BP measures around the mean BP; 2] Coefficient of variation (CV) - Calculated by dividing the SD by the mean BP, this metric reduces the correlation with mean BP.

BPV is a major predictor of heart attack and stroke. Patients with blood pressure that varies significantly from one doctor's visit to the next may be at greater risk of cardiovascular events.

BPV can be assessed using ambulatory blood pressure monitoring (ABPM). However, the accuracy of devices used to measure BP can be questionable due to the lack of a standardized validation protocol.

9. Can secondary hypertension contribute to undiagnosed hypertension or vice versa?

   Secondary hypertension: A condition where high blood pressure is caused by another condition, such as sleep apnea, migraine medications, or thyroid problems. Secondary hypertension is common, affecting about 10% of people with high blood pressure. Undiagnosed hypertension: A condition where someone has high blood pressure but doesn't know it.

   So a person could have secondary hypertension and be unaware. Likewsie – a person could aware they have hypertension BUT unaware it is secondary hypertension Thus proper diagnosis is key for all.

10. This is for Prof. Whelton. We found the prevalence of undiagnosed high blood pressure among prisoners in two prison settings among those less than 45 years old. The majority of those with high blood pressure were those who abused substances before incarceration and had high salt intake. Could such findings pass your litmus test?

    Yes --- of potential interest. A reviewer would likely probe the selection process. Specifically, were those enrolled in the study a representative sample of the two prisons? Were those two prisons representative of all prisons in your country? Do the results have potential implications for all prisoners, worldwide, or are they limited to the country/region studied. If the latter, the paper may have greater relevance/interest for journals that are targeted to readership in your country/region. Good luck. Paul