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What clinician should know on sensitivity, specificity and predictive value?

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Predictive value relies on prevalence of disease in the population. Prevalence is a measure of disease burden for the specific time point or during a specified time period not to confuse with incidence which is the rate of new cases or event during specified time period of population at risk. As prevalence increases, PPV also increases while NPV decreases. In contrast, Se and Sp are independent of prevalence. Se and Sp can be influenced by differences in disease characteristic such as clinical severity, laboratory value cut-offs and etc. Receiver operating characteristic (ROC) curve displays graphically the trade-off between Se and Sp and its useful in assigning the best cut-offs for the best Se and Sp levels.

Clinically relevant parameter for screening test is NPV while confirmatory test is PPV. Any confirmatory test is often mandatory not to produce any false positive result – they should be as specific as possible. Usually, what patient interested to know is what is the probability they would have the disease if the test is positive, this is what PPV can offer.

So, let us start with definition first.

Sensitivity (Se) is a probability of a positive test result given the presence of disease can be written as :
P (positive test | disease present)

Specificity (Sp): probability of a negative result given the absent of disease which can be written as :
P (negative test| absent disease)

Positive predictive value (PPV): probability of the present disease given a positive test result which can be written as :
P (disease present| positive test)

Negative predictive value (NPV) : probability of the disease absent given a negative test result which can be written as :
P (disease absent|negative test)

Notation (|) means given an event already happened

Figure 1

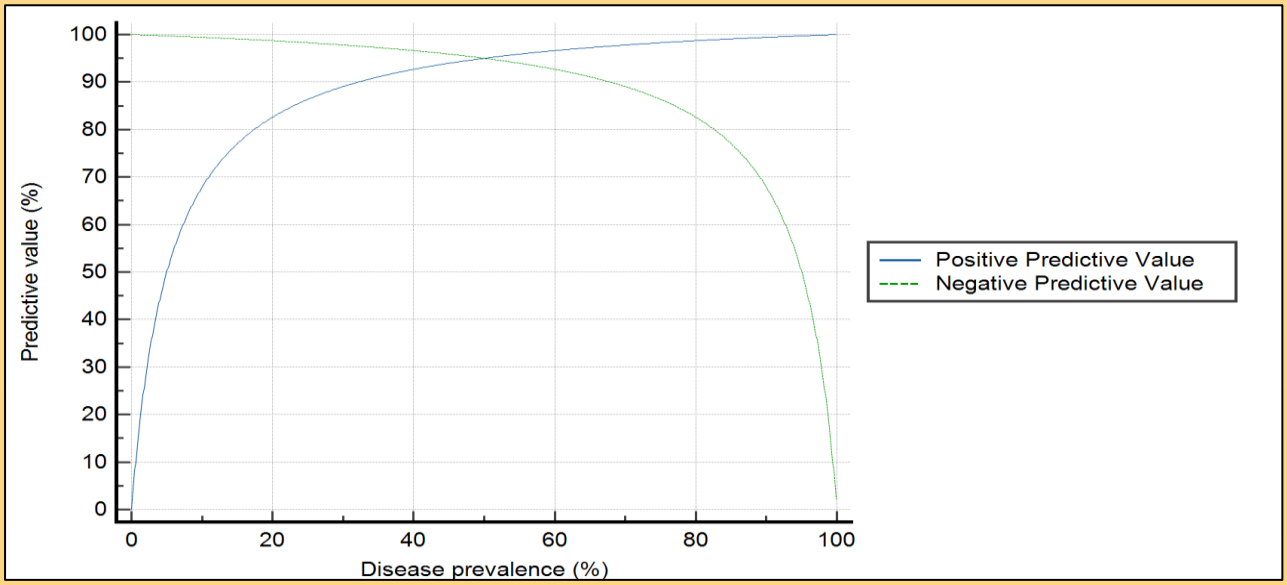

Figure 1 illustrates the effect of disease prevalence when both sensitivity and specificity are fixed at 95%. PPV and NPV are directly related to the prevalence of the disease in a population. The higher the disease prevalence, the higher the value of PPV. When the disease prevalence is low, PPV will still be low while NPV increases.

We will go through an example on how to calculate Se and Sp using 2x2table. Se and Sp can be calculated using 2x2 table directly provided we have true positive (TP), true negative (TN), false positive (FP) and false negative (FN) result.

	RT-PCR Covid-19/ Disease status		Total results
Rapid Ag Test X	Positive	Negative	
Positive	52 (TP)	2 (FP)	54
Negative	5 (FN)	185 (TN)	190
Total Results	57 (Se)	187 (Sp)	244

Sensitivity (Se): Test positive (TP) / Disease present (TP + FN) = 52/52+5= 0.912
Specificity (Sp): Test Negative (TN)/ Disease absent (TN+ FP) = 185/185+2 =0.98

Differ with PPV and NPV, we need to take account on prevalence in the calculation. Here, we will calculate PPV and NPV using two different prevalence values.

i) Prevalence from 2x2 table :
= 57 (total number of positive cases) / 244 (total population at risk) =0.23

ii) Let say the **prevalence COVID-19 in Malaysia**:
= 56989 (total number Covid-19 in Malaysia) / 33119118 (Total Malaysia population) = 0.0017

PPV: P (disease present| positive test)
NPV: P (disease absent|negative test)

Using the Bayes' theorem and after taking into consideration the prevalence using multiplication and reciprocal rule, the PPV and NPV can be appropriated and expressed as below:

$$PPV = \frac{\text{Prevalence} \times \text{Sensitivity}}{(\text{Sensitivity} \times \text{Prevalence}) + (1\text{-specificity}) \times (1\text{- prevalence})}$$

$$NPV = \frac{\text{Specificity}(1\text{- Prevalence})}{(\text{Specificity})\ (1\text{- prevalence}) + (1\text{-sensitivity}) \times \text{Prevalence}}$$

i) Using prevalence by 2x2 table :

PPV = (0.23 x 0.912)/((0.23x 0.912) + (1-0.98).(1-0.23))= 0.93
(Thus, the chance the patient has COVID-19 given a positive test is 93%)

NPV = (1-0.23)(0.98) / ((0.98)(1-0.23) + (1-0.912)(0.23)) = 0.97

ii) Using prevalence of Covid-19 in Malaysia :

PPV = (0.0017 x 0.912)/((0.0017x 0.912) + (1-0.98).(1-0.0017))= 0.072
(Thus, the chance the patient has COVID-19 given a positive test is 7.2%)

NPV = (1-0.0017)(0.98) / ((0.98)(1-0.0017) + (1-0.912)(0.0017)) = 0.99

Bayes' theorem is stated as below:
P (B|A) = P(A and B) / P (A)

There are two most important rule in understanding of conditional probability.

1. Reciprocal rule
P (Event A |Event B) ≠ P (Event B| Event A)
= Which means sensitivity is not equal to PPV.

2. Multiplication rule
P (Event A and Event B) = P (A) x P (B| A)

We have shown mathematically that predictive values are determined by the Se and Sp of a test as well as the prevalence of a disease in the population. In contrast, Se and Sp are independently affected by prevalence. Given this mathematical property, the measures of Se and Sp can be used and computed across different populations with difference prevalence rate with the assumption that the disease characteristics such as clinical severity or laboratory cut-offs does not differ much depending on the measures and extent of a disease.

For clinicians, sensitivity and specificity may still be useful to rule conditions (i.e illnesses) in or out during the course of a patient's differential diagnosis. On the other hand, predictive values are more clinically useful and intuitive. For a patient to be 'predicted' (diagnosed) as negative confidently, a highly sensitive diagnostic test is required in a low disease prevalent population. Although it is desirable to have tests with high sensitivity and specificity, the values for those two metrics should not be relied on making decisions about individual people in screening situations. PPV and NPV is more appropriate to indicate the likelihood that a test can successfully identify whether people do or do not have the target condition/disease base on the result.

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