

sensitivity, specificity, positive and negative predictive values of combined tests

Define $X: \{\text{not infected, infected}\} \rightarrow \{0, 1\}$ by $X(\text{not infected}) = 0$ and $X(\text{infected}) = 1$.

Define T a sample space that describes the sequence of two tests for which T_1 is the first test (Test 1) and T_2 is the second test (Test 2). Then we have $T_1, T_2: \{\text{negative, positive}\} \rightarrow \{0, 1\}$ by $T_1, T_2(\text{negative}) = 0$ and $T_1, T_2(\text{positive}) = 1$.

Define sensitivity $p = P(T = 1|X = 1)$

Define specificity $q = P(T = 0|X = 0)$

Let p_1, q_1 denote the sensitivity and specificity of Test 1.

Let p_2, q_2 denote the sensitivity and specificity of Test 2.

Let p_T, q_T denote the sensitivity and specificity of the combined tests.

Let π denotes the prevalence.

Assume that there is no change of infection status throughout the period we consider and also assume that results of individual tests T_1, T_2 are independent.

Overall, we have considered 3 different scenarios as follows.

Section 1: Calculating sensitivity and specificity of combined tests

Scenario 1

If Test 1 is positive, define T as positive. If Test 1 is negative, repeat Test 2 after 3 days. If Test 2 is positive, define T as positive. Otherwise T is negative.

In this scenario,

$$P(T_1 = 1|X = 1) = p_1, P(T_1 = 0|X = 0) = q_1$$

$$P(T_2 = 1|X = 1) = p_2, P(T_2 = 0|X = 0) = q_2$$

By definition, the sensitivity of combined tests in this case is

$$\begin{aligned} p_T &= P(T \text{ positive}|X = 1) \\ &= 1 - P(T \text{ negative}|X = 1) \\ &= 1 - P(T_1 = 0, T_2 = 0|X = 1) \\ &= 1 - P(T_1 = 0|X = 1)P(T_2 = 0|X = 1) \text{ (since the result of } T_1, T_2 \text{ are independent)} \\ &= 1 - (1 - p_1)(1 - p_2) \\ &= p_1 + p_2(1 - p_1) \end{aligned}$$

And the specificity of combined test in this case is

$$\begin{aligned} q_T &= P(T \text{ negative}|X = 0) \\ &= P(T_1 = 0, T_2 = 0|X = 0) \\ &= P(T_1 = 0|X = 0)P(T_2 = 0|X = 0) \text{ (since the result of } T_1, T_2 \text{ are independent)} \\ &= q_1 q_2 \end{aligned}$$

Note that if Test 1 and Test 2 are the same kind of tests,

$$P(T_1 = 1|X = 1) = P(T_2 = 1|X = 1) = p_1$$

$$P(T_1 = 0|X = 0) = P(T_2 = 0|X = 0) = q_1$$

Therefore, simply replace p_2, q_2 with p_1, q_1 respectively

We have the sensitivity of combined tests in this case is

$$p_T = 2p_1 - p_1^2$$

And the specificity of combined test in this case is

$$q_T = q_1^2$$

Scenario 2

If Test 1 is negative, T is negative. If Test 1 is positive, repeat after three days. If Test 2 is negative, T is negative, otherwise T is positive.

Note that in this scenario, Test 1 must be the golden standard PCR test. Since it has the general high performance in sensitivity than other kinds of tests, only then we can define this scenario as if the first test is negative, the result is negative.

If Test 1 and Test 2 are different tests, we have $P(T_1 = 1|X = 1) = p_1$, $P(T_1 = 0|X = 0) = q_1$

$P(T_2 = 1|X = 1) = p_2$, $P(T_2 = 0|X = 0) = q_2$

The sensitivity of combined tests in this case is

$$\begin{aligned} p_T &= P(T \text{ positive}|X = 1) \\ &= P(T_1 = 1, T_2 = 1|X = 1) \\ &= P(T_1 = 1|X = 1)P(T_2 = 1|X = 1) \text{ (since the result of } T_1, T_2 \text{ are independent)} \\ &= p_1p_2 \end{aligned}$$

And the specificity of combined test in this case is

$$\begin{aligned} q_T &= P(T \text{ negative}|X = 0) \\ &= 1 - P(T \text{ positive}|X = 0) \\ &= 1 - P(T_1 = 1, T_2 = 1|X = 0) \\ &= 1 - P(T_1 = 1|X = 0)P(T_2 = 1|X = 0) \text{ (since the result of } T_1, T_2 \text{ are independent)} \\ &= 1 - (1 - q_1)(1 - q_2) \\ &= q_1 + q_2(1 - q_1) \end{aligned}$$

If Test 1 and Test 2 are the same kind of tests, simply replace p_2, q_2 with p_1, q_1 respectively

$P(T_1 = 1|X = 1) = P(T_2 = 1|X = 1) = p_1$

$P(T_1 = 0|X = 0) = P(T_2 = 0|X = 0) = q_1$

The sensitivity of combined tests in this case is

$$p_T = p_1^2$$

And the specificity of combined test in this case is

$$q_T = 2q_1 - q_1^2$$

Section 2: Calculating positive and negative predictive values of both individual and combined test

Individual tests:

By definition, positive predictive values (PPV) is given the test result is positive, what is the probability that the person has the disease.

$$\begin{aligned}
 PPV &= P(X = 1|T = 1) \\
 &= \frac{P(X = 1)P(T = 1|X = 1)}{P(T = 1)} \\
 &= \frac{P(X = 1)P(T = 1|X = 1)}{P(X = 0)P(T = 1|X = 0) + P(X = 1)P(T = 1|X = 1)} \text{ (By Law of Total Probability)} \\
 &= \frac{\pi p}{\pi p + (1 - \pi)(1 - q)}
 \end{aligned}$$

By definition, negative predictive values (NPV) is given the test result is negative, what is the probability that the person does not have the disease.

$$\begin{aligned}
 NPV &= P(X = 0|T = 0) \\
 &= \frac{P(X = 0)P(T = 0|X = 0)}{P(T = 0)} \\
 &= \frac{P(X = 0)P(T = 0|X = 0)}{P(X = 0)P(T = 0|X = 0) + P(X = 1)P(T = 0|X = 1)} \text{ (By Law of Total Probability)} \\
 &= \frac{(1 - \pi)q}{(1 - \pi)q + \pi(1 - p)}
 \end{aligned}$$

Combined tests:

Scenario 1(same as above)

By Law of Total Probability, we have

$$\begin{aligned}
 P(T_1 = 0) &= P(X = 0)P(T_1 = 0|X = 0) + P(X = 1)P(T_1 = 0|X = 1) \\
 &= (1 - \pi)q_1 + \pi(1 - p_1) \\
 P(T_1 = 1) &= P(X = 0)P(T_1 = 1|X = 0) + P(X = 1)P(T_1 = 1|X = 1) \\
 &= (1 - \pi)(1 - q_1) + \pi p_1 \\
 P(T_2 = 0) &= P(X = 0)P(T_2 = 0|X = 0) + P(X = 1)P(T_2 = 0|X = 1) \\
 &= (1 - \pi)q_2 + \pi(1 - p_2) \\
 P(T_2 = 1) &= P(X = 0)P(T_2 = 1|X = 0) + P(X = 1)P(T_2 = 1|X = 1) \\
 &= (1 - \pi)(1 - q_2) + \pi p_2
 \end{aligned}$$

The positive predictive values for combined test is

$$\begin{aligned}
 PPV_T &= P(X = 1|T \text{ is positive}) \\
 &= P(X = 1|T_1 = 1 \text{ Or } T_1 = 0, T_2 = 1) \\
 &= \frac{P(X = 1 \cap T_1 = 1) + P(X = 1 \cap T_1 = 0, T_2 = 1)}{P(T_1 = 1) + P(T_1 = 0, T_2 = 1)} \text{ (event } T_1 = 0, T_1 = 1 \text{ form a partition of sample space)} \\
 &= \frac{P(T_1 = 1)P(X = 1|T_1 = 1) + P(T_1 = 0, T_2 = 1)P(X = 1|T_1 = 0, T_2 = 1)}{P(T_1 = 1) + P(T_1 = 0, T_2 = 1)} \text{ (by Bayesian Theorem)} \\
 &= \frac{P(X = 1)P(T_1 = 1|X = 1) + P(X = 1)P(T_1 = 0, T_2 = 1|X = 1)}{P(T_1 = 1) + P(T_1 = 0)P(T_2 = 1)} \text{ (by Conditional Probability)} \\
 &= \frac{\pi p_1 + \pi p_2(1 - p_1)}{(1 - \pi)(1 - q_1) + \pi p_1 + ((1 - \pi)q_1 + \pi(1 - p_1))((1 - \pi)(1 - q_2) + \pi p_2)}
 \end{aligned}$$

The negative predictive values for combined test is

$$\begin{aligned}
(*)NPV_T &= P(X = 0|T \text{ is negative}) \\
&= P(X = 0|T_1 = 0, T_2 = 0) \\
&= \frac{P(X = 0)P(T_1 = 0, T_2 = 0|X = 0)}{P(T_1 = 0, T_2 = 0)} \text{ (by Bayesian Theorem)} \\
&= \frac{P(X = 0)P(T_1 = 0|X = 0)P(T_2 = 0|X = 0)}{P(T_1 = 0)P(T_2 = 0)} \text{ (by Conditional Probability)} \\
&= \frac{(1 - \pi)q_1q_2}{((1 - \pi)q_1 + \pi(1 - p_1))((1 - \pi)q_2 + \pi(1 - p_2))}
\end{aligned}$$

Note that if Test 1 and Test 2 are the same kind of tests,

$$\begin{aligned}
P(T_1 = 0) &= P(T_2 = 0) = P(X = 0)P(T_1 = 0|X = 0) + P(X = 1)P(T_1 = 0|X = 1) \\
&= (1 - \pi)q_1 + \pi(1 - p_1) \\
P(T_1 = 1) &= P(T_2 = 1) = P(X = 0)P(T_1 = 1|X = 0) + P(X = 1)P(T_1 = 1|X = 1) \\
&= (1 - \pi)(1 - q_1) + \pi p_1
\end{aligned}$$

in this scenario.

By simply replacing $P(T_2 = 1)$ and $P(T_2 = 0)$ with $P(T_1 = 1)$ and $P(T_1 = 0)$ and p_2, q_2 with p_1, q_1 respectively, we have the positive predictive values for combined test is

$$PPV_T = \frac{\pi p_1(2 - p_1)}{((1 - \pi)(1 - q_1) + \pi p_1)((1 - \pi)q_1 + \pi(1 - p_1) + 1)}$$

And the negative predictive values for combined test is

$$(*)NPV_T = \frac{(1 - \pi)q_1^2}{((1 - \pi)q_1 + \pi(1 - p_1))^2}$$

Scenario 2(same as above)

By Law of Total Probability, we have

$$\begin{aligned}
P(T_1 = 0) &= P(X = 0)P(T_1 = 0|X = 0) + P(X = 1)P(T_1 = 0|X = 1) \\
&= (1 - \pi)q_1 + \pi(1 - p_1) \\
P(T_1 = 1) &= P(X = 0)P(T_1 = 1|X = 0) + P(X = 1)P(T_1 = 1|X = 1) \\
&= (1 - \pi)(1 - q_1) + \pi p_1 \\
P(T_2 = 0) &= P(X = 0)P(T_2 = 0|X = 0) + P(X = 1)P(T_2 = 0|X = 1) \\
&= (1 - \pi)q_2 + \pi(1 - p_2) \\
P(T_2 = 1) &= P(X = 0)P(T_2 = 1|X = 0) + P(X = 1)P(T_2 = 1|X = 1) \\
&= (1 - \pi)(1 - q_2) + \pi p_2
\end{aligned}$$

The positive predictive values for combined test is

$$\begin{aligned}
(*)PPV_T &= P(X = 1|T \text{ is positive}) \\
&= P(X = 1|T_1 = 1, T_2 = 1) \\
&= \frac{P(X = 1)P(T_1 = 1, T_2 = 1|X = 1)}{P(T_1 = 1, T_2 = 1)} \text{ (by Bayesian Theorem)} \\
&= \frac{P(X = 1)P(T_1 = 1|X = 1)P(T_2 = 1|X = 1)}{P(T_1 = 1)P(T_2 = 1)} \text{ (by Conditional Probability)} \\
&= \frac{\pi p_1 p_2}{((1 - \pi)(1 - q_1) + \pi p_1)((1 - \pi)(1 - q_2) + \pi p_2)}
\end{aligned}$$

And the negative predictive values for combined test is

$$\begin{aligned}
NPV_T &= P(X = 0 | T \text{ is negative}) \\
&= P(X = 0 | T_1 = 0 \text{ Or } T_1 = 1, T_2 = 0) \\
&= \frac{P(X = 0 \cap T_1 = 0) + P(X = 0 \cap T_1 = 1, T_2 = 0)}{P(T_1 = 0) + P(T_1 = 1, T_2 = 0)} \text{ (event } T_1 = 0, T_1 = 1 \text{ form a partition of sample space)} \\
&= \frac{P(T_1 = 0)P(X = 0 | T_1 = 0) + P(T_1 = 1, T_2 = 0)P(X = 0 | T_1 = 1, T_2 = 0)}{P(T_1 = 0) + P(T_1 = 1, T_2 = 0)} \text{ (by Bayesian Theorem)} \\
&= \frac{P(X = 0)P(T_1 = 0 | X = 0) + P(X = 0)P(T_1 = 1, T_2 = 0 | X = 0)}{P(T_1 = 0) + P(T_1 = 1)P(T_2 = 0)} \text{ (by Conditional Probability)} \\
&= \frac{(1 - \pi)(q_1 + q_2 - q_1q_2)}{(1 - \pi)q_1 + \pi(1 - p_1) + ((1 - \pi)(1 - q_1) + \pi p_1)((1 - \pi)q_2 + \pi(1 - p_2))}
\end{aligned}$$

Note that if Test 1 and Test 2 are the same kind of tests,

$$\begin{aligned}
P(T_1 = 0) &= P(T_2 = 0) = P(X = 0)P(T_1 = 0 | X = 0) + P(X = 1)P(T_1 = 0 | X = 1) \\
&= (1 - \pi)q_2 + \pi(1 - p_2) \\
P(T_1 = 1) &= P(T_2 = 1) = P(X = 0)P(T_1 = 1 | X = 0) + P(X = 1)P(T_1 = 1 | X = 1) \\
&= (1 - \pi)(1 - q_2) + \pi p_2
\end{aligned}$$

in this scenario.

By simply replacing $P(T_2 = 1)$ and $P(T_2 = 0)$ with $P(T_1 = 1)$ and $P(T_1 = 0)$ and p_2, q_2 with p_1, q_1 respectively, we have the positive predictive values for combined test is

$$(*)PPV_T = \frac{\pi p_1^2}{((1 - \pi)(1 - q_1) + \pi p_1)^2}$$

The negative predictive values for combined test is

$$NPV_T = \frac{1 - \pi q_1(2 - q_1)}{((1 - \pi)q_1 + \pi(1 - p_1))((1 - \pi)(1 - q_1) + \pi p_1 + 1)}$$