Adjustment of sensitivity and specificity of clinical diagnostic test using Bayesian analysis

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Abstract:

The Bayesian approach is a statistical analysis technique that integrates field-collected data and expert opinion into probability model. There is a direct link between Bayesian statistics and diagnostic tests daily used by clinicians. This link is Bay's theorem for calculating the positive or negative predictive values of a diagnostic test. To this end, we have tried to apply this approach for the analysis of the data relating to the diagnostic test concerning raised blood pressure (HTA).

Keywords: diagnostic test, sensitivity, specificity, Bay's theorem, prevalence.

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1. Introduction :

Research uses statistics that are absolutely ubiquitous. Nowadays, few articles of this kind can do without the use of estimations, confidence intervals, or statistical tests. Biomedical All these results are obtained with different techniques, all of which are part of frequentist statistics. There are also alternative statistical methods called Bayesian methods based on the Bayes theorem.

The Bayesian approach is gaining renewed interest, notably thanks to the improvement of certain calculation techniques and the appearance of appropriate software, it dominates in biostatistics publications and responds in epidemiology. Bayes' theorem is well known to clinicians who use it in diagnostic tests. The aim of this work is to show the interest of Bayesian statistics in the context of biomedical research in general, based on the link between diagnostic tests and Bayesian reasoning.

1. Materials and method:

1.1 The Bayesian approach:

In statistics, there are two main philosophical approaches. The first is called the frequentist approach or classic approach. The frequentist approach to statistical data considers the parameter as a fixed but unknown constant. However, the alternative approach is called the Bayesian approach, it consists of treating the unknown parameter of the proposed model as a random variable and associates it with a probability distribution, called prior distribution. For a Bayesian statistician, this distribution represents all the information available on the parameter and the inaccuracies associated with it, in a practical context, it also includes all the opinions of experts. In contrast, the data are considered fixed. The data combined with this prior information will be used to specify a new probability density called posteriori distribution. These results are the consequences of Bayes' theorem.

1.2 Bayes theorem:

Bayesian theory was born from Bayes 'theorem, reverend Thomas Bayes' (1802-1761) eponymous theorem, which posthumously published his formula in the Philosophical Transactions (1763) in the (Essay Towards Solving a Problem in the Doctrine of Chances) of the Royal Society of London. Bayes' theorem, also called Laplace's inverse probability theorem, which rediscovered it independently of Bayes, is based on conditional probabilities.

A general description of the inversion of probabilities is given by Bayes' theorem: If A and E are events such that P (E) ≠ 0, P (A | E) and P (E | A) are connected by:

$$\boldsymbol{P(A|E) = \frac{P(E|A)P(A)}{P(E|A)P(A) + P(E|\bar{A})P(\bar{A})} = \frac{P(E|A)P(A)}{P(E)}}$$

This theorem is also an updating principle, because it describes the update of the likelihood of A: P (A) to P (A | E), once E has been observed. Bayes (1763) gives a continuous version of these results, namely, for a random variable θ, called parameter of model and data X, of conditional distributions P (x | θ) and a marginal distribution P (θ) which measures the prior probability , the conditional distribution of θ knowing x is the posterior probability:

$$\boldsymbol{P(x) = \int P(x|\theta)P(\theta)d\theta}$$

$$\boldsymbol{P(\theta|x) = \frac{P(x|\theta)P(\theta)}{P(x)} = \frac{P(x|\theta)P(\theta)}{\int P(x|\theta)P(\theta)d\theta}}$$

Which is the formal complete expression of Bayes' theorem for a continuous random variable. We can therefore simplify the previous expression and note the theorem as follows:

$$\boldsymbol{P(\theta|x) \propto P(x|\theta)P(\theta)}$$

In statistical terms, the Bayes theorem updates the information on θ by extracting the information contained in the observation X.

1.3Diagnostic test:

A diagnostic test is a tool for determining whether or not a patient has a disease as part of a decision aid. This test provides a qualitative result, positive or negative. When developing a diagnostic test, two "sick" and "non-sick" groups are built. The presence of the disease is established using a gold standard test, so we are interested in the following characters:

- S: have the disease
- NS: do not have the disease
- T +: positive test
- T-: negative test

By crossing the results, we obtain a table to evaluate the qualities of this diagnostic test.

Table Nº 01: Contingency table showing the results of a diagnostic test.

	Desease	Non-desease	Total
Test positif	True positive (TP)	False positive (FP)	P
Test negative	True négative (TN)	False négative (FN)	N
Total	TP+TN	FP+FN	

Source :TALBI Fatiha**.**

- P: number of positive tests
- N: number of negative tests

- TP + TN: total number of patients submitted a test
- FP + FN: total of non-patients submitted a test.

1.4 **Intrinsic characteristics of a diagnostic test:**

In practice, there are few clinical signs or tests that can be interpreted in a univocal way, some patients have a positive sign or test, without suffering from the desired disease, on the contrary, although carrying the desired disease, do not present a clinical sign or presenting a negative test. Thus, the clinician must be able to have the characteristics of a test allowing him to interpret the results and apply them on his patient, these are the qualifiers of sensitivity and specificity.

- **sensibility:**

The sensitivity of a test is determined on a population of patients known to have disease D because it has undergone a baseline test. It is defined by the proportion of patients who have the desired disease and whose test is positive, in other words by the proportion of patients with disease D that the test detects correctly (true positives). In contrast, the proportions of patients with D disease that the test did not identify are false negative results. Apply these definitions on the board:

$$\text{sensibility} \quad (\boldsymbol{Se}) = \frac{\boldsymbol{VP}}{\boldsymbol{TP+FN}}$$

The sensitivity (Se) is also the probability of having a positive test when one is ill, that one notes P (P | M).

- **specificity:**

The specificity of a test is determined on a population of patients, which is known to have no disease, because it has undergone a reference test. It is defined by the proportion (%) of patients who do not have the desired disease D and whose test is negative, in other words by the proportion of patients who are not carriers of the disease D that the test correctly determines (true negatives) . In contrast, the proportion of non-disease-positive patients is false positive. Also apply these definitions in Table 1:

$$\text{Specificity } (\boldsymbol{Sp}) = \frac{\boldsymbol{VN}}{\boldsymbol{TN+FP}}$$

The sensitivity (Sp) is also the probability of having a negative test when one is not sick, that one notes P (N | ND).

- **Limits of sensitivity and specificity:**

Sensitivity and specificity describe the characteristics of a diagnostic test and are derived from a population of patients known to be carriers or non-carriers of the disease D. Or, in practice, the clinician is confronted with the result of the test but do not know if the patient actually has the desired disease or not. He must therefore know, if the test is positive, what is the probability that the patient is actually carrier of the disease M; and if the test is negative, what is the probability that the patient is not a carrier of the disease M. This information is given by the notions of positive predictive value and negative predictive value of a test.

1.5Establishment of the posterior probability:

There are two methods to establish the posterior probability of the disease, both using the same notions of sensitivity, specificity, and prior probability, one is based on predictive values, and the other uses likelihood.

From the result of a diagnostic test, it is therefore sought to determine the sick / non-sick status. Before applying the test to the patient, the doctor does not know whether or not he has the disease, he only knows that the probability that he has the disease is not zero, even if it is often very low. The probability that the patient has the disease before the test can be estimated by the prevalence of the disease in the general population, noted by Pre (D). This prevalence constitutes a prior knowledge existing before the carrying out of the diagnostic test and in the absence of other clinical information on the patient. This is the best estimate of risk for the subject being sick .

This is where the theorem of Reverend Bayes comes in, which makes it possible to determine the posterior probability of a disease as a function of the result of the test, based only on the prior probability values (prevalence), sensitivity and specificity of the test.

Table Nº 02: Contingency table showing the results of a diagnostic test as probabilities

	Desease	Non-dessease	Total
Test positif T^+	P(P|D).Pre(D)	P(P|ND).Pre(ND)	P
Test négatif T^-	P(N|D).Pre(D)	P(N|ND).Pre(ND)	N
Total	Pre(D)	Pre(ND)	

Source :TALBI Fatiha**.**

According to Bayes' theorem, if the test is positive, the posterior probability of having a disease P(D| P) is called the positive predictive value (PPV) of a test. It is given by the following report:

$$\boldsymbol{P(D|P) = \frac{P(P|D).Pre(D)}{P(P|D).Pre(D) + P(P|ND).Pre(ND)}}$$

Similarly, if the test is negative, the posterior probability of not having a disease P(ND| N) is called the negative predictive value (NPV) of a test. It is given by the following report:

$$\boldsymbol{P(ND|N) = \frac{P(N|ND).Pre(ND)}{P(N|D).Pre(D) + P(N|ND).Pre(ND)}}$$

The PPV therefore combines prior information (the prevalence of the disease) and the test results (the test is positive). Similarly, the NPV combines prior information (the prevalence of not having the disease) and the test result (the test is negative). In summary, we update the information on the situation of patients with the Bayes theorem.

Another way of expressing posterior probability is likelihood ratios (LR). The LR of a test combines its sensitivity and specificity into a single factor.

If the test is positive: : $\boldsymbol{LR^+ = \frac{Se}{1-Sp}}$

if the test is negative : $\boldsymbol{LR^{-}} = \frac{\boldsymbol{1-Se}}{\boldsymbol{Sp}}$

2. **Results and Analysis:**

Raised blood pressure (HTA) is a cardiovascular pathology defined by high blood pressure. HTA can be acute or chronic, with or without signs of severity. It is commonly referred to as high blood pressure for systolic blood pressure greater than 140 millimeters of mercury (mmHg) and diastolic blood pressure greater than 90 mmHg.

This study uses the Bayesian approach on a population of 50 people, to provide an estimate of the true prevalence of hypertension in this population. The diagnostic test was performed using a manual (stethoscope) or automatic blood pressure monitor where the measurement was confirmed at three medical consultations.

Table N° 03: Results of the HTA test, and calculation of the sensitivity and specificity of the test

	Presence of HTA	Absence of HTA	Total
Test positive	22	3	25
Test negative	14	11	25
Total	36	14	50

Source :TALBI Fatiha.

Se=66.7% ; 1-Se= 33.3% and Sp=82.4% ; 1-Sp=17.6%

The doctor applies the test to a patient and gets the positive result, so what is the probability that the patient is really sick? To solve this problem, additional information is needed: the prevalence of HTA (the prior probability that the patient has HTA), two cases are given in the table, concerning the diagnosis of HTA positive in a woman 70 years old: Pre (D) = 85%; and a young man of 30 years or Pre (D) = 30%. Applying Bays theorem the posterior probabilities are:

Table N° (04): Calculation of predictive values (prior prevalence of HTA: 85%)

Statistic	Value	Confidence Interval 95%
PPV	93%	84% - 99%
NPV	38%	19% - 57%

Source :TALBI Fatiha.

Table N° 05: Calculation of predictive values (prior prevalence of HTA:30%)

Statistic	Value	Confidence Interval 95%
PPV	29%	12% - 47%
NPV	95%	88% - 99%

Source :TALBI Fatiha.

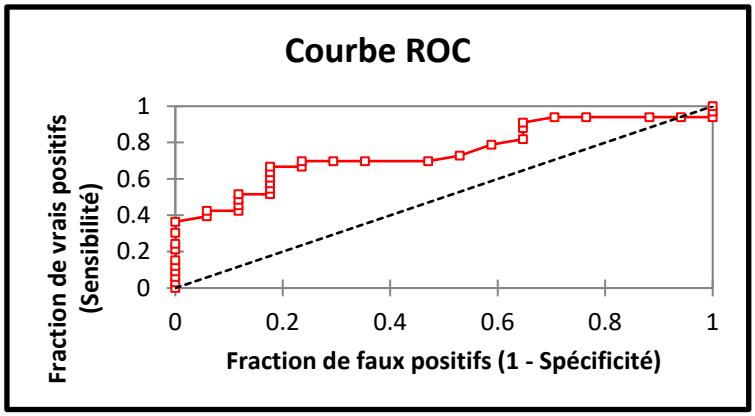
According to the results of the tables, the probability that the woman of 70 suffers from HTA if the test is positive is 93%, and if the result of the test is negative, the probability that this woman suffers from this disease is 62% (100-38)%. For the young man of 30, the probability of having an HTA if the test is positive is 61%, and if

the result of the test is negative, the probability of this young person suffering from this disease is 15%. (100-85)%.

Let's see how a variation in the prevalence of HTA changes the predictive values. If the prior probability of HTA is very high (85%), its posterior probability will remain high despite a negative test (62%). Conversely, if the prior probability of the disease is low (30%), its posterior probability will not necessarily increase significantly clinically, even if the test returns positive (29%). This illustrates the importance, before performing a test, of determining the prior probability of the disease in a particular patient and of anticipating what will become its posterior probability as a function of the test result.

In general, the results of a diagnostic test are shown using the Receiver Operating Characteristic (ROC) curve:

Fig N° 01: ROC Curve Using XLSTAT Software



The sign where the ideal exam would be one that would have a sensitivity of 100% and a specificity of 100% and therefore predictive values, too, of 100%. Unfortunately, it has not yet been found, in practice it is necessary to make a compromise between sensitivity and specificity that vary in opposite directions. If we privilege the sensitivity of an examination, it will often be not very specific and reciprocally.

3. Discussion:

A test is only useful if the posterior probability that it provides leads to a change in the attitude that would have been taken as a function of the prior clinical probability. Indeed, for each disease, there is a probability threshold beyond which the investigations are stopped and a treatment started, and a probability threshold below which the examinations are stopped and the diagnosis discarded.

The anticipation of the clinical prior probability, if the examinations are carried out, thus makes it possible to judge their impact on the care of a patient. In our analysis, the studied test leads us to two possible strategies:

- keep the diagnostic of HTA and treat (or follow) the patient;
- consider the diagnostic as unlikely and seek further investigations to arrive at a definitive conclusion (absence versus presence of the disease sought).

4. Conclusion:

In summary, Bayesian statistics showed its simplicity of interpretation of a procedure traditionally used in medicine, that of diagnostic tests.

Most often, the diagnostic test compares two integers only: presence or absence of the disease. But it is quite possible to imagine diagnostic situations where one has to compare more than two hypotheses or apply more than one diagnostic test to arrive at a decision. The principle of the Bayesian approach can always apply perfectly.

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