ABSTRACT

In this paper, we examine the process of diagnosis in practice and find the method employed for it is not the prescribed Bayesian method as a prior probability is not interpreted as a prior degree of belief and a disease is not diagnosed from a posterior probability in practice. The Bayesian method is not employed as it fails to diagnose a given disease accurately in different patients with varying prior probabilities.

We find the method that is employed in practice is the frequentist confidence method in which a prior probability is not interpreted as a prior degree of belief or evidence and a disease is diagnosed from a highly informative test result in every patient, regardless of its prior probability, with a high degree of accuracy.

The recognition that the method employed for diagnosis in practice is not the Bayesian but the confidence method has important implications for teaching diagnosis to medical students.

INTRODUCTION

The goal in diagnosis in practice, as is well-known, is to determine a disease causing illness accurately in a patient with symptoms so that it can be treated and prognosticated correctly. It follows, the method which is employed for diagnosis in practice is such that it achieves high diagnostic accuracy. In this paper, we shall examine the method employed for diagnosis in a real patient discussed in a clinical problem solving exercise, to find out what this method is.

The patient is a healthy 40 year old woman with no cardiac risk factors who presents with highly uncharacteristic chest pain (1). The disease, acute myocardial infarction (MI) is suspected from this presentation and formulated as a hypothesis, that is, as a plausible cause of illness in this patient. It is evaluated by performing a test, an EKG, which reveals acute ST elevation EKG changes. This test result with likelihood ratio (LR) of 13 (2) is interpreted as being highly informative and considered strong evidence from which acute MI is conclusively and accurately diagnosed in this patient.

It is clear the method employed for diagnosis in this patient is not the prescribed Bayesian method for two reasons; (a) the prior probability of acute MI of 7 percent which is derived from its prevalence in a population is not interpreted as strong prior degree of belief against acute MI (b) acute MI is not diagnosed to be indeterminate from the posterior probability of acute MI of 50 percent (Appendix 1), which is generated by combining the prior probability of 7 percent and LR of 13. The method employed for diagnosis in this patient, we propose, is the frequentist confidence method, which is the other main method of statistical inference (other than the Bayesian method).

In the confidence method, a prior probability is not interpreted as a prior degree of belief or evidence for or against a suspected disease, which is merely a hypothesis regardless of its prior probability (3) as is seen in this patient. The hypothesis is evaluated by a test and if a highly informative result (LR greater than 10) (4), such as acute ST elevation EKG changes, is observed, the disease hypothesis is considered to have passed a highly demanding test from which the disease (acute MI) is conclusively diagnosed in a given patient. This diagnosis is believed to be highly accurate based on the high frequency of around 86 percent of its accuracy in other patients (5).

We note that prior probability of acute MI does not play any role in diagnosis of acute MI from acute ST elevation EKG changes in the confidence method. Therefore this diagnosis is made conclusively with a high degree of accuracy in this method in any patient in whom acute MI is suspected, regardless of its prior probability. This is precisely what we find is done in practice. We find that any disease which has a test capable of generating a result with LR greater than 10 is diagnosed in practice in a similar manner by the confidence method. For example, pulmonary embolism is diagnosed from positive chest CT angiogram, LR 20 (6) and deep vein thrombosis from positive venous ultrasound study, LR 16 (7) in any patient regardless of prior probability of disease in practice. A disease which does not have such a test is diagnosed in practice, we suggest, from two or three test results whose combined LR is greater than 10, but this, we believe, needs to be studied further.

THE CONFIDENCE METHOD OF DIAGNOSIS

We shall now discuss why the confidence method is employed for diagnosis in practice. It is well-known that any disease, acute MI for example, occurs in different patients with varying presentations and therefore with varying prior probabilities that range from high to low. For example, it occurs in an elderly man with highly characteristic chest pain (high prior probability) as well as in a young woman with highly uncharacteristic chest pain such as the young woman mentioned above (low prior probability). Therefore experienced physicians suspect acute MI in a patient in whom its prior probability is high as well as in one in whom it is low. In a series of such patients the prior probability in one patient is obviously independent of its prior probability in another patient and we do not know in advance the prior probability in the next patient in whom we shall suspect acute MI. Therefore, this prior probability can be looked upon, we believe, as being a random variable (8) and the series as being a random sample which is drawn from a population of patients with varying prior probabilities in whom acute MI is suspected.

It is customary in practice to perform an EKG in any patient in whom acute MI is suspected. In one random sample of such patients, the frequency of acute MI in presence of acute ST elevation EKG changes has been observed to be 86+/-2 percent with confidence level 95 percent (5). This means that the sampling distribution of this frequency in other random samples drawn from the population will be between 84 and 88 percent in 95 percent of these samples by the Central Limit Theorem (9). Therefore when we observe acute ST elevation EKG changes in a patient in whom we suspect acute MI, we are 95 percent confident this patient has been drawn from a random sample in which the frequency of accurate diagnosis of acute MI in presence of acute ST elevation EKG changes is 84 to 88 percent. This enables us to diagnose acute MI in this patient (such as the 40 year old woman) with a high degree of confidence (95 percent) that this diagnosis is highly accurate (84 to 88 percent). In making this diagnosis, the limits 84 and 88 percent of the confidence interval, 84 to 88 percent, function, as Cox points out (10), as a measuring technique in this patient. This measuring

technique is calibrated like other measuring instruments indirectly by the hypothetical consequences of its repeated use.

We note that a series of patients with varying prior probabilities in whom acute MI is suspected anywhere in the world can be looked upon as being a random sample that is drawn from the population of such patients. This suggests that if acute ST elevation EKG changes are observed in one of these patients, acute MI will be diagnosed with a high degree of confidence (95 percent) in the high accuracy (84 to 88 percent) of this diagnosis. This is precisely what we find how acute MI is diagnosed from acute ST elevation EKG changes everywhere in the world, whether in USA or Europe (11) or in India (12) or in Africa (13).

As the confidence diagnosis of acute MI from acute ST elevation EKG changes in a given patient is made from the performance of this test result in leading to an accurate diagnosis in 84 to 88 percent (8 to 9 out of 10) other patients, this diagnosis in a given patient is highly reliable due to its high accuracy.

We have identified the confidence method as the method employed for diagnosis in practice by a careful analysis of the goal and process of diagnosis in practice. This method is employed, we find, because it helps achieve the goal of diagnosing a disease in patients with varying prior probabilities with a high degree of accuracy. We did not find any evidence for employment of the prescribed Bayesian method for diagnosis in our analysis of the process of diagnosis in practice. For example, we did not find a prior probability interpreted as prior degree of belief or a disease to be diagnosed from its posterior probability in any of the published diagnostic exercises in a real patient such as clinical-pathologic conferences (CPCs) or clinical problem solving exercises (14,15).

THE BAYESIAN METHOD OF DIAGNOSIS

We shall now discuss why the Bayesian method has been prescribed for diagnosed and why it is not employed for diagnosis in practice. It was prescribed for diagnosis, looked upon as a form of inference, in the early 1960s on grounds of its coherence based on a betting argument (16). It was argued that if a bet is made on a Bayesian inference from a posterior probability with odds based on the

posterior probability, then a Dutch book, which is a series of bets that ensures betting loss, cannot be created against the inferring agent. A Bayesian inference is thus considered coherent, as a Dutch book in betting cannot be created with it. What is of interest in this prescription, from the point of view of diagnosis, is that there is no mention of diagnostic accuracy in it, which is of primary concern to practicing physicians. This does not seem to us to be a minor slip, but due to the very nature of the Bayesian method. For an eminent Bayesian statistician, Dennis Lindley has stated, "The Bayesian theory is about coherence, not about right or wrong" (17).

SHORTCOMINGS OF THE BAYESIAN METHOD

We shall now examine the consequences if the Bayesian method were to be employed for diagnosis in practice, for example, in the 40 year old woman mentioned above. In the Bayesian method, the very low prior probability of acute MI of 7 percent would be interpreted as very strong prior degree of belief against it which may lead to this disease not being suspected or tested leading to a serious diagnostic error. The Bayesian method thus appears to encourage diagnostic errors due to failure to suspect a disease with an atypical presentation (low prior probability), which have been reported in several studies (18,19).

The Bayesian diagnosis of acute MI being indeterminate from the posterior probability of 50 percent in this patient is equivalent to a bet placed on it with odds of 1 to 1 and is thus coherent justifying the use of the prescribed Bayesian method. But it is not made in practice, as it is inconsistent with our experience of the 84 to 88 accuracy of diagnosis of acute MI in patients with acute ST elevation EKG changes. In addition, in the Bayesian method, a totally worthless test result with LR of 1 may play a role in a Bayesian diagnosis as we show in the following example. Let us suppose, a 65 year old man with multiple cardiac risk factors presents with highly characteristic chest pain in whom the prior probability of acute MI is estimated to be 85 percent. An EKG, performed to evaluate this disease reveals non-specific T wave EKG changes with LR of 1 in this patient.. The posterior probability of acute MI of 85 percent, generated by combining the prior probability of 85 percent and LR of 1 (Appendix 2) will be interpreted as strong

total degree of belief from which acute MI would be diagnosed with a high degree of certainty in the Bayesian method. We doubt however if this Bayesian diagnosis would be made in practice in a patient with the totally worthless test result, non-specific T wave EKG changes with LR of 1.

It appears to us the Bayesian method was prescribed for diagnosis solely on the basis of its coherence without a careful analysis of the goal and process of diagnosis in practice. Such an analysis would have revealed that any given disease occurs in different patients with varying prior probabilities with our goal being achievement of high diagnostic accuracy in every patient regardless of prior probability of a disease and not achieving coherence. This goal of diagnostic accuracy cannot be achieved in principle by the Bayesian method in which a prior probability is interpreted as a degree of belief. This feature of the Bayesian method is likely to lead to a diagnostic error in the case of a disease with an atypical presentation as we have discussed above. In addition the diagnostic accuracy of a Bayesian diagnosis is unknown. For example, we do not know the diagnostic accuracy of the Bayesian diagnosis of acute MI in a hundred patients with varying prior probabilities who have acute ST elevation EKG changes. In the absence of knowledge of this diagnostic accuracy, the Bayesian diagnosis of acute MI in a patient with acute ST elevation EKG changes is not reliable and thus not made in practice.

ADVANTAGES OF THE CONFIDENCE METHOD

We would like to emphasize that the confidence method, unlike the Bayesian method, has not been prescribed but has been developed for use in diagnosis in practice by experienced physicians to achieve the goal of high diagnostic accuracy of a disease in different patients with varying prior probabilities. The features of the confidence method which help achieve this goal are as follows:

(a) A prior probability is not attached to a suspected disease as a hypothesis so that it does not have a degree of belief or prior evidence for or against it. This allows every suspected disease to be tested and diagnosed accurately regardless of its prior probability. This is seen in every published diagnostic exercise in a real patient such as a CPC or a clinical problem solving exercise

in which a disease with a low prior probability is routinely diagnosed accurately due to this feature. In the confidence method, a prior probability derived from a prevalence is interpreted, we suggest, as chance of a disease in a patient. Its only role in diagnosis is in prioritizing testing of various diseases in a differential diagnosis in a non-urgent diagnostic situation. The disease with the highest prior probability is tested first as it has the greatest chance of being present.

(b) The employment of a highly informative test result (LR greater than 10) to diagnose a disease conclusively with a high degree of accuracy in any patient regardless of its prior probability if the disease has a test capable of generating such a result. The impact of such a test on diagnostic accuracy is seen best in the case of pulmonary embolism whose diagnosis became highly accurate with availability of perfusion lung scan and chest CT angiogram which are capable of generating highly informative results.

(c) The high reliability of a confidence diagnosis in a given patient as it is based on its high observed accuracy (around 85 percent or greater) in other patients.

(d) The random nature of a series of patients in which the accuracy of a confidence diagnosis is observed. This makes this accuracy applicable to confidence diagnosis of a disease in any patient in whom it is suspected anywhere in the world.

TEACHING DIAGNOSIS

The recognition that the confidence and not the Bayesian method is the correct method which is employed by experienced physicians in practice to achieve high diagnostic accuracy has important implications, we believe, for teaching diagnosis to medical students and novice physicians as follows:

(1) The accurate estimation of prior probability of a suspected disease is not important as it does not play any role in a confidence diagnosis. Its approximate estimation is sufficient as its only role is in prioritizing testing of various suspected diseases.

(2) Greater emphasis on teaching about wide variation in presentations (prior probabilities) of a given disease in different patients. An effective way would be by providing them virtual experience of this feature by having them review presentations of 50 to 100 consecutive patients with a certain disease (acute MI for example) seen at a medical center as we have pointed out (20).
(3) Making them aware that a disease is diagnosed conclusively from observation of a highly informative test result (LR greater than 10) with a high degree of accuracy (around 85 percent or greater) regardless of its prior probability if such a test is available. Teaching them about tests for various diseases which are capable of generating such results.

CONCLUSION

In conclusion, we have examined the method employed for diagnosis in practice and found it not to be the prescribed Bayesian method as this method fails to diagnose a given disease accurately in patients with varying prior probabilities. Instead, the method employed for diagnosis in practice, we found, is the confidence method in which a disease is diagnosed from a highly informative test result in different patients with varying prior probabilities with a high degree of accuracy. The recognition that the method employed for diagnosis in practice is the confidence method has important implications for teaching diagnosis to medical students.

Appendix 1

Prior probability of 7 percent = Prior odds of 1/13

In odds form of Bayes' theorem,

Posterior odds = Prior odds x Likelihood ratio

Therefore,

Posterior odds = 1/13 x 13 = 1/1 = Posterior probability of 50 percent.

Appendix 2

Prior probability of 85 percent = Prior odds of 85/15

In odds form of Bayes' theorem,

Posterior odds = Prior odds x Likelihood ratio

Therefore,

Posterior odds = 85/15 x 1 = Posterior probability of 85 percent.

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