Introduction

Diagnosis can be looked upon, we suggest, as a process of inference in which the starting point is a patient with symptoms and the conclusion is an assessment of the disease causing illness in this patient. The goal in diagnosis, as is well-known, is to assess this disease accurately so that it can be treated and prognosticated correctly. It follows, the method employed for diagnosis in practice shall be a method which achieves very high diagnostic accuracy. In this paper, we shall discuss what this method is.

The Bayesian method of diagnosis

The Bayesian method appears to have been prescribed for diagnosis due to its coherence defined in terms of not losing a bet placed on a Bayesian inference (diagnosis) (1,2). In this method, a disease is inferred (diagnosed) from its posterior probability, interpreted as a final subjective degree of belief which is generated by combining a prior probability as prior degree of belief and likelihood ratio (LR) of a test result (3). Our interest as practicing physicians is in knowing if the Bayesian method leads to an accurate diagnosis of a disease, that is, if it corresponds to the actual occurrence of the disease in a patient. We shall examine this issue by looking at diagnosis performed by the Bayesian method in a real patient.

Bayesian diagnosis in a real patient

We run into a problem here for we cannot find any published report of diagnosis that has been performed by the Bayesian method in a real patient. For example, in all published diagnostic exercises in real patients such as in clinical-pathologic conferences (CPCs) and clinical problem solving exercises (4,5), a prior probability is not interpreted as prior degree of belief and nor is a disease diagnosed from a posterior probability interpreted as final degree of belief, clearly indicating the Bayesian method has not been employed for diagnosis. The closest we come to finding such a patient is in a clinical problem solving exercise (6) in which information about a real patient is provided from which a Bayesian diagnosis could be made, but is not made. We shall now discuss this patient.

The patient is a healthy 40 year old woman with no cardiac risk factor who presents with highly uncharacteristic chest pain in whom acute myocardial infarction (MI) is suspected, whose prior probability is estimated to be 7 percent from its prevalence. If the Bayesian method were to be employed for diagnosis in this patient, this very low prior probability would be interpreted as very strong prior degree of belief against acute MI in this patient. It is not clear to us from the standpoint of a practicing physician what purpose is served by this interpretation in making an accurate diagnosis in this patient. If anything, this interpretation may lead to a diagnostic error by ruling out acute MI without any testing. In any case, this Bayesian interpretation does not appear to have been made in this patient and a test, an EKG is performed to evaluate suspected acute MI. A highly informative result, acute ST elevation EKG changes with likelihood ratio (LR) of 13 for acute MI (7) is observed. In the Bayesian method, the prior probability of 7 percent would be combined with the LR of 13 to generate a posterior probability of 50 percent (Appendix 1), which would be interpreted as equivocal final degree of belief from which acute MI would be inferred to be indeterminate in this patient.

The confidence method of diagnosis

But the discussing physician in this exercise does not make this Bayesian diagnosis. Instead, he diagnoses acute MI conclusively and accurately from the test result, acute ST elevation EKG changes, alone which he interprets as very strong evidence for it. This interpretation is based, we suggest, on his knowledge and experience that this test result diagnoses acute MI accurately with the high frequency of 86 percent (in 8 to 9 out of 10 patients) in a random series of patients with varying prior probabilities of acute MI (8). This method of diagnosis, as we have discussed in detail elsewhere (9), is the frequentist confidence method, which is the other major method of statistical inference (other than the Bayesian method) (10).

We note the prior probability of acute MI does not play any role in inference of acute MI by the confidence method in this patient. We find that acute MI is diagnosed from acute ST elevation EKG changes in any patient in whom it is suspected anywhere in practice with a high degree of confidence in the high accuracy (86 percent) of this diagnosis regardless of its prior probability (11,12,13). We suggest prior probability of a disease, which is estimated from its prevalence, is interpreted in practice as chance of a disease being present in a patient and not as a prior degree of belief in it. Its only role in diagnosis in practice, in our view, is to prioritize 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 highest chance of being present. This role of prior probability does not come into play in the above 40 year old woman as the suspected disease is acute MI, which is potentially life-threatening and needs to be tested first despite its very low prior probability.

We find that any disease, which has a test capable of generating a highly informative result with LR greater than 10 (14) is diagnosed in practice with a high degree of confidence in the high accuracy (85 percent or greater) of this diagnosis regardless of its prior probability by the confidence method in any patient in whom this disease is suspected. For example, pulmonary embolism is diagnosed from positive chest CT angiogram, LR 20 (15); deep vein thrombosis from positive venous ultrasound study, LR 16 (16); and covid-19 disease from positive covid-19 PCR test, LR 14 (17) in any patient in whom the respective disease is suspected, regardless of prior probability of the disease. A disease, which does not have such a test is diagnosed, we suggest, from a combination of two or three test results whose combined LR is greater than 10, but this, we believe, needs to be investigated further.

In practice, we do not diagnose a disease in a Bayesian manner from a high posterior probability if an observed test result for it is non-informative. For example, acute MI is not diagnosed from a high posterior probability of, say, 85 percent in a 65 year old man with multiple cardiac risk factors presenting with highly characteristic chest pain (with prior probability of acute MI of, let us assume, 85 percent) in whom the non-informative test result, non-specific T wave EKG changes with LR of 1 (Appendix 2) is observed, even though this diagnosis would be justified by the Bayesian method.

Main challenge to achieving high diagnostic accuracy in practice

We believe, the greatest challenge to achieving high diagnostic accuracy in practice is posed by the wide variation in presentations and therefore in prior probabilities of a given disease in different patients. For example, as we mentioned above, acute MI may present in the above 40 year old woman in whom its prior probability is very low as well as in the above 65 year old man in whom its prior probability is very high. What is required for diagnosis in practice is a method which is highly reliable in diagnosing a disease accurately regardless of its prior probability. The Bayesian method is not such a method, primarily because a prior probability is interpreted as a prior degree of belief in this method. As we discussed above, this interpretation may lead to a diagnostic error by ruling out a disease with an atypical presentation (low prior probability). In addition, the Bayesian step of combining a prior probability and a LR to generate a posterior probability from which a disease is inferred leads to a situation in which a highly informative test result such as acute ST elevation EKG changes in a patient with a low prior probability such as in the 40 year old woman above, becomes ineffective and a non-informative test result such as non-specific T wave EKG changes becomes effective in a patient with a high prior probability such as in the above 65 year old man. Due to these issues, the Bayesian method is not employed for diagnosis in practice as we discussed above.

Meeting this challenge by the confidence method

The challenge posed by the varying prior probabilities of a disease in different patients is met, we believe, by employing the confidence method for diagnosis in practice. The two features of this method which are instrumental in dealing with this challenge are as follows:

(a) Every disease that is suspected from a presentation is formulated as a hypothesis only, without any prior probability attached to it so that it does not have any prior degree of belief or prior evidence for or against it. This feature enables every disease to be tested, regardless of its prior probability and diagnosed accurately if it is present. It is this feature which is mainly responsible, we believe, for a disease with a low prior probability to be diagnosed accurately on a routine basis in published diagnostic exercises in real patients.

(b) A diagnostic hypothesis is verified to be correct (or not) by a highly informative test result (with LR greater than 10) regardless of its prior probability if a test capable of generating such a result is available. The impact of availability of such a test is best appreciated, we believe, in the case of pulmonary embolism, whose diagnosis became highly accurate in patients with varying prior probabilities after availability of perfusion lung scan and chest CT angiogram, which are capable of generating results with LR greater than 10.

Confidence method as hypothesis testing

It is to be noted, a diagnostic hypothesis in the confidence method in every patient has only two states, either it is correct or it is not correct. The assessment about the state of a hypothesis is made by testing; if a highly informative test result with LR greater than 10, is observed, the hypothesis passes a test, so to speak, and it is assessed to be correct. Thus a diagnostic hypothesis of acute MI is assessed to be correct if acute ST elevation EKG changes, LR 13 are observed or the diagnostic hypothesis of pulmonary embolism is assessed to be correct if positive chest CT angiogram, LR 20 is observed. A LR level greater than 10 for a test result to diagnose a disease definitively appears to have been chosen, it seems to us, to ensure an accurate diagnosis of a disease in 85 percent or more patients with varying prior probabilities.

High reliability of the confidence method

A great advantage of the confidence method is that diagnosis of a disease by this method in a given patient is highly reliable as it is validated by our experience. As we mentioned above, the diagnosis of acute MI from acute ST elevation EKG changes in the above 40 year old woman is validated by our experience of finding this diagnosis to be accurate in 8 to 9 out 10 (86 percent) patients in whom acute MI is suspected, regardless of prior probabilities of acute MI. It is to be noted, the experience which we bring to bear on a given patient is gained from a series of patients with varying prior probabilities. This is unavoidable, as the patients in whom we suspect acute MI over a period of time form a random series (9). We believe the fact that this experience is gained from a series of patients with varying prior probabilities is not of any practical consequence, as acute MI is the same disease with the same pathophysiology, as far as we know, in all patients regardless of its prior probability. A major shortcoming of the Bayesian method, in our view, is that a Bayesian diagnosis is not validated by our experience. For example, we do not have any experience to validate the Bayesian diagnosis of acute MI being indeterminate from the posterior probability of 50 percent in the 40 year old woman discussed above.

Evolution of the confidence method of diagnosis

The use of the confidence method, in which a suspected disease is a hypothesis without any prior probability attached to it and in which a hypothesis is inferred to be correct from a highly informative test result (LR greater than 10), for diagnosis in practice has evolved, we believe, to meet the challenge of diagnosing a disease accurately in patients with varying prior probabilities. The uniformity everywhere in diagnosis of a suspected disease is facilitated by the random nature of the series of patients with varying prior probabilities in which the disease is suspected, as we have discussed elsewhere (18).

Imposition of the Bayesian method

By contrast, the Bayesian method has been imposed on diagnosis from the outside, as it were, without an analysis of the goal or process of diagnosis. It has been prescribed due to its coherence in which practicing physicians have no interest, we believe, as the Bayesian method does not lead to diagnostic accuracy. Achieving diagnostic accuracy with the Bayesian method may not be possible, for an eminent Bayesian statistician, Dennis Lindley (19), has noted, “The Bayesian theory is about coherence, not about right or wrong”. In any case, we do not find any evidence either from published literature or from personal experience that the Bayesian method is employed for diagnosis in practice. The noted clinical investigator, Alvan Feinstein (20), commented as well in 1977, “I know of no clinical setting or institution in which the Bayesian diagnostic methods are being regularly used for practical diagnostic purposes in a routine or specialized manner".

Probability applied to a procedure in the confidence method

It is hard to understand the attraction of the Bayesian method which explains its continued prescription despite it not being employed for diagnosis in practice due to its tendency to cause diagnostic errors as we discussed above. We speculate, this may be due to a belief that a disease can only be diagnosed from probability of a disease as diagnosis is inherently uncertain and probability represents uncertainty. But probability is employed in the frequentist confidence method as well, but in a different manner. In the frequentist confidence method, a probability is attached not to a disease but to a procedure (10) for inferring a disease with high accuracy in a given patient. For example, the probability of inferring acute MI from acute ST elevation EKG changes is high in the form of the high frequency of 86 percent with which this test result infers acute MI accurately in a random series of patients with varying prior probabilities, in whom acute MI is suspected. The confidence method is highly accurate, as the overall diagnostic accuracy with its use in practice is 85 to 90 percent (21).

Conclusion

In this paper, we have put forward arguments in favor of the confidence method being the method that is employed for diagnosis in practice due to its high accuracy in diagnosing a disease in patients with varying prior probabilities. We thus have a differential diagnosis of sort between the prescribed Bayesian method and our claim about the confidence method being the method employed for diagnosis in practice. This can be looked upon as being similar to a differential diagnosis between two or more diseases being the cause of illness in a patient during diagnosis. And just as we settle the issue regarding differential diagnosis during diagnosis by testing, we suggest, settling the issue regarding differential diagnosis about method of diagnosis by experimental studies.

We believe, it is important to reach agreement about the method that is employed for diagnosis in practice as it has important implications for teaching diagnosis to medical students. For example, if we agree that this method is the confidence method, then we see no need to teach students to estimate prior probability of a disease accurately as it plays no role in diagnosis in this method. The focus in teaching this method would be on teaching about the wide range of presentations of a disease in different patients so that a disease is suspected even when its presentation is atypical and on teaching about highly informative test results which enable a disease to be diagnosed accurately.

Appendix 1

Prior probability of 7 percent = Prior odds of 7/93

In odds form of Bayes' theorem,

Prior odds x Likelihood ratio = Posterior odds

Therefore,

7/93 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,

Prior odds x Likelihood ratio = Posterior odds

Therefore,

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

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