In an earlier paper (1), we pointed out that the prescribed Bayesian method is not employed for diagnosis in practice due to two features of this method which are likely to cause diagnostic errors in practice. These two features are (a) interpretation of a prior probability as subjective prior degree of belief in a disease and (b) inference (diagnosis) of a disease from a posterior probability generated by combining a prior probability and a likelihood ratio (LR) for attest result. These two features are absent, we noted, in the method that is actually employed in practice (1), which consists of formulating a suspected disease as a hypothesis without any prior probability attached to it and inferring a disease from a highly informative test result (LR greater than 10) alone. This method is employed because it is highly accurate in diagnosing a disease in patients with varying prior probabilities. The overall diagnostic accuracy of this method in practice has been found to be 85 to 90 percent (2). We shall characterize and describe this method in detail in this paper.

We propose the method employed for diagnosis in practice is identical to the frequentist confidence method developed by the distinguished Polish-American statistician, Jerzy Neyman (3), in first half of the twentieth century as an objective method of statistical inference in opposition to the subjective Bayesian method. In this method, a probability is interpreted as a frequency, which is determined by observation in a random sample, that is then attached to a procedure by which a parameter (disease) is inferred (4). In the Bayesian method, on the other hand, a probability is interpreted as a subjective degree of belief from which a parameter (disease) is inferred. The prior probability of a parameter does not play any role in inference by the confidence method, while it plays a key role in the Bayesian method, as a posterior probability from which a parameter is inferred is generated from a prior probability. We shall now discuss how and why the method of diagnosis in practice is identical to the confidence method, illustrating our discussion with example of diagnosis of acute myocardial infarction (MI) in practice.

It is well-known from experience that we suspect acute MI in a series of different patients with varying presentations and therefore with varying prior probabilities over a period of time. Thus we may suspect it in a 65 year old man with highly characteristic chest pain (high prior probability) as well as in a 40 year old woman with highly uncharacteristic chest pain (low prior probability) (5). We do not know in advance the prior probability of acute MI in the next patient in whom we suspect it and the prior probability in one patient is independent of prior probability in another patient in whom we suspect it. Therefore, we suggest, this prior probability can be looked upon as being a random variable (6) and the series of these patients as a random series. All the various series in which different physicians in different places suspect acute MI in patients with varying prior probabilities can be looked upon, we suggest, as random series as well. All these various random series can be looked upon, we suggest, as random samples that are drawn from a population of patients with varying prior probabilities in whom acute MI is suspected. Nature appears to function as a perfect gambling machine, as Barnard (7) pointed out in another context, in sending us patients with varying prior probabilities in whom we suspect acute MI

It is customary in practice to perform an EKG in every patient in whom acute MI is suspected to evaluate it. In one random series of these patients, the frequency of acute MI in presence of acute ST elevation EKG changes, which have a likelihood ratio (LR) of 13, is observed to be 86+/-2 percent with confidence level of 95 percent (8). This indicates that the sampling distribution of this frequency in 95 percent other random samples shall be between 84 and 88 percent by the Central Limit Theorem (9). This means that if 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 series in which the frequency of acute MI in presence of this test result is between 84 and 88 percent. This enables us to infer (diagnose) acute MI, we suggest, with a high degree of confidence (95 percent) in the high accuracy (84 to 88 percent) of this inference in this patient. The limits, 84 and 88 percent of the confidence interval 84-88 percent function, as Cox (10) points out, as a measuring technique in this patient, which is calibrated like other measuring instruments, indirectly by the hypothetical consequences of its repeated use.

We note the prior probability of acute MI in a patient in whom we suspect it does not play any role in inference of acute MI from acute ST elevation EKG changes in the confidence method. This indicates that this inference is made in every patient suspected of having acute MI in whom acute ST elevation EKG changes are observed, regardless of prior probability of acute MI. This is precisely what is done in practice. Thus this inference is made in practice in the 65 year old man as well as in the 40 year old woman (5) mentioned above, if acute ST elevation EKG changes are observed in both patients. The confidence method of inferring acute MI has many other highly desirable features as follows:

(1) The confidence inference of acute MI from acute ST elevation EKG changes is highly reliable as its high accuracy of around 86 percent is known from observation in a random sample. Furthermore, this inference is consistent with our experience of finding it be accurate in 8 to 9 out of 10 patients (around 86 percent) in whom acute MI is suspected.
(2) It is objective as it is made from a highly informative test result (LR greater than 10) which anyone can observe. For example, no one is likely to argue with diagnosis of acute MI from acute ST elevation EKG changes in a patient in whom acute MI is suspected or of pulmonary embolism from positive chest CT angiogram in a patient in whom it is suspected.
(3) An accurate estimate of prior probability of acute MI is not required in this method, as it plays no role in inference which makes it easy and straightforward.
(4) This confidence inference is highly plausible as the test result, acute ST elevation EKG changes, from which it is made, represents acute myocardial injury, which is a key feature of acute MI. Similarly, the confidence diagnosis of pulmonary embolism from positive chest CT angiogram is highly plausible as this test result represents partial or total obstruction of a pulmonary arterial vessel, which is a key feature of pulmonary embolism.
(5) The confidence inference of acute MI from acute ST elevation EKG changes in a patient in whom acute MI is suspected, is made with the same high degree of confidence in its high accuracy all over the world including USA (11), Europe (11),, India (12) and Africa (13). This is made possible by the random nature of series of patients in whom acute MI is suspected in these

different places so that the frequency of acute MI in presence of acute ST elevation EKG changes is between 84 and 88 percent in all these series.

(6) As noted earlier, this confidence inference is made in every patient in whom acute ST elevation EKG changes are observed, regardless of prior probability of acute MI. This facilitates highly accurate diagnosis of acute MI in all patients with varying prior probabilities in practice.

(7) This confidence inference is done in a dichotomous manner (acute MI present or not) as observing acute ST elevation EKG changes is similar to passing a test in the confidence method. If this test result is observed, the patient passes a test, so to speak, and acute MI is inferred to be present. This method of inference is straightforward compared to the Bayesian method, in which we never know how high the posterior probability of acute MI needs to be for us to infer it in a patient.

Thus the confidence method is employed in practice as it helps achieve the goal in diagnosis in practice of diagnosing acute MI with a high degree of accuracy in patients with varying prior probabilities. This high accuracy is achieved by attaching a probability to a procedure from which the disease is inferred, instead of attaching it to a disease as is done in the Bayesian method. Thus probability, in the form of a high frequency of around 86 percent is attached to the procedure of inferring acute MI from acute ST elevation EKG changes.

We find any disease which has a test capable of generating a highly informative result (LR greater than 10) (14) is diagnosed in practice by the confidence method. Thus 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 practice in any patient regardless of prior probability of disease. A disease which does not have such a test is diagnosed, we believe, from combination of two or three test results whose combined value is greater than 10, but this matter needs to be investigated further.

The availability of a test capable of generating a highly informative result with LR greater than 10 plays a crucially important role in achieving high diagnostic accuracy in the confidence method. This is best appreciated by the example of pulmonary embolism whose diagnosis in patients with varying prior probabilities became highly accurate only after availability of perfusion lung scan (18) and chest CT angiogram (15), which are capable of generating highly informative results.

The notion of prior probability plays an entirely different role, in our view, in the confidence method than it does in the Bayesian method. In the confidence method, a prior probability, derived from a prevalence, represents the chance of a disease being present in a patient. It only role in diagnosis in practice, we suggest, is in a non-urgent diagnostic situation where it helps prioritize testing of various disease in a differential diagnosis. The disease with the highest prior probability is tested first as it has the greatest chance of being present.

We wish to emphasize, our account of the method of diagnosis in practice in this paper is descriptive and not prescriptive. We have merely described how experienced physicians actually diagnose in practice. We find it remarkable that the method they have developed to deal with the challenge of diagnosing a disease accurately in different patients with varying prior probabilities is identical to the confidence method of statistical inference developed independently in the first half of the twentieth century. There is no overarching principle, such as that of coherence in the Bayesian method, which is employed in developing this method. This method has been developed purely with the goal of achieving high diagnostic accuracy. What has aided development of this method, we believe, is the random nature of series of patients in which a disease is suspected.

The recognition that the method employed for diagnosis by experienced physicians in practice is the confidence method has important implications, we believe, for teaching diagnosis to medical students. There is no need, for example, to teach them to estimate a prior probability accurately, as it does not play any role in inference in the confidence method.

In conclusion, we have argued in this paper that it is the frequentist confidence method, which is employed for diagnosis in practice due to its high diagnostic accuracy in patients with varying prior probabilities. This method is easy to use, highly reliable, highly accurate, and leads to a diagnosis which is objective and consistent with our experience. The employment of this method in practice also explains why a suspected disease such as acute MI, for example, is diagnosed from a test result such as acute ST elevation EKG changes in a similar manner all over the world.

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