From our perspective as practicing physicians, chance plays a role in the process of diagnosis in practice at three places as follows:

(a) Initially, when we encounter a patient with symptoms. It is purely a matter of chance whether this patient has a typical presentation with high prior probability of a disease or whether he or she has an atypical presentation with low prior probability of a disease. For example, this patient could be a 65 year old man with multiple cardiac risk factors presenting with highly characteristic chest pain which is typical for acute myocardial infarction (MI) with high prior probability of acute MI. Or this patient could be a 40 year old healthy woman with no cardiac risk factor presenting with highly uncharacteristic chest pain (1) which is atypical for acute MI with low prior probability of acute MI.
(b) Once we have encountered a given patient such as the 65 year old man or the 40 year old woman, it is a matter of chance, which is measured by prior probability of a disease derived from its prevalence, whether this patient has this disease or not. For example, the chance of acute MI in the above 65 year old man is high while it is low in the above 40 year old woman.
(c) After we perform a test for a suspected disease, such as an EKG for suspected acute MI in the above two patients, we make an assessment about the chance of the disease being present after observing the test result.

We shall now discuss how chance in these three places impacts the process of diagnosis in practice.

(1) When we encounter a given patient with a certain presentation, which is due to chance as noted above, we have no idea why this patient has presented with this particular and not some other presentation. All we know is that this presentation poses a problem which we seek to resolve by diagnosing the disease causing illness in this patient. The importance of a presentation being due to chance is that a series of patients with varying presentations and therefore with varying prior probabilities in which we suspect a given disease over a period of time is a random series everywhere

where this disease is suspected (2). This makes diagnosis of a disease, for example, of acute MI uniform everywhere it is suspected as we have discussed in detail elsewhere (2).

(2) When we encounter a patient in whom the prior probability of a disease, for example, of acute MI is high, such as in the above 65 year old man, we know the chance of acute MI in this patient is high, but this does not help us in assessing if this particular patient has or does not have acute MI. Similarly in the above 40 year old woman in whom the prior probability of acute MI is low, we know the chance of acute MI in this patient is low, but this does not help us in assessing if acute MI is present or not in this particular patient. Our goal in practice, as is well-known, is to diagnose acute MI accurately in both these patients if it is present. Therefore the strategy we adopt in pursuing this goal is to simply assume acute MI is present in both these patients and formulate it as a hypothesis. As a hypothesis, this assumption may or may not be correct. We wish to emphasize there is no prior probability attached to this hypothesis so that there is no prior degree of belief or prior evidence for or against acute MI in either patient. We find this strategy to be adopted in all published diagnostic exercises in real patients such as clinical-pathologic conferences (CPCs) and clinical problem solving exercises in which a suspected disease is formulated as a hypothesis only without any prior probability attached to it (3,4). We view this strategy as a key factor in achieving high accuracy in diagnosis of a disease in patients with varying prior probabilities in practice.

(3) A test, an EKG, is performed to evaluate if the hypothesis of acute MI is correct in the 65 year old man as well as in the 40 year old woman. If the highly informative test result, acute ST elevation EKG changes with likelihood ratio (LR) of 13 is observed in both patients, the hypothesis of acute MI is inferred to be correct and acute MI diagnosed in both patients with a high degree of confidence (95 percent) in the high accuracy (86 percent) of this inference (5). This diagnosis is made in any patient anywhere in the world in whom acute MI is suspected and acute ST elevation EKG changes observed, regardless of prior probability of acute MI, as we have discussed in detail elsewhere (6,7,8). This diagnosis is made by

the frequentist confidence method of statistical inference which we have described in detail elsewhere (9). With this method, the chance of accurate diagnosis of acute MI in a patient is very high at 86 percent, that is, in 8 to 9 out of 10 patients in any patient in whom acute MI is suspected (5).

We find that that any disease which has a test capable of generating a result with LR greater than 10 is diagnosed in practice by the confidence method (10) in a manner similar to that of acute MI. For example, pulmonary embolism is diagnosed from positive chest CT angiogram, LR 20 (11); deep vein thrombosis from positive venous ultrasound study, LR 16 (12); and covid-19 disease from positive covid-19 PCR test, LR 14 (13). A disease which does not have such a test is diagnosed in practice, we believe, from a combination of two or three test results, whose combined LR is greater than 10, but this needs to be investigated further. The confidence method is employed for diagnosis in practice, we believe, to meet the challenge of diagnosing a disease with a high degree of accuracy in patients with varying prior probabilities (varying chance). This challenge is met successfully for the most part, as the overall diagnostic accuracy in practice is 85 to 90 percent (14)

We find the Bayesian method, which has been prescribed as the normatively correct method (15), has no engagement with issues raised by the element of chance during diagnosis. Thus this method does not take into account the valuable real world finding that a series of patients in which we suspect a given disease is a random series due to chance. Due to neglect of this finding, the Bayesian method fails to explain why the diagnosis of acute MI from acute ST elevation EKG changes is more or less uniform all over the world. Furthermore by interpreting the low prior probability of acute MI in the 40 year old woman as a strong prior degree of belief against acute MI, instead of interpreting it as low chance of this disease in this patient, this method increases the risk of not suspecting or testing this disease leading to a diagnostic error. Then the Bayesian diagnosis in this patient of acute MI being indeterminate from a posterior probability of 50 percent generated by combining a prior probability of 7 percent and LR of 13 for acute ST elevation EKG changes (1) (Appendix) is at odds with our experience in practice of this diagnosis being accurate in 8 to 9 out of 10 (86 percent) patients (5). In the clinical problem solving exercise in which this real patient was presented, the discussing physician diagnosed acute MI conclusively and accurately from acute ST elevation EKG changes alone (1), we believe, by the confidence method. It does not appear to be widely appreciated, it seems to us, that the Bayesian method has been prescribed due to its coherence based on a betting argument and not due to its diagnostic accuracy (16,17,18).

We have argued in this paper that the element of chance in the process of diagnosis plays a key role in shaping the method employed for diagnosis in practice to achieve high accuracy in diagnosis of a disease in patients with varying prior probabilities. This method consists of suspecting a disease from a presentation and formulating it as a hypothesis without attaching any prior probability to it. The hypothesis is evaluated by performing a test and inferring it to be correct if a highly informative result with LR greater than 10 is observed with a high degree of accuracy everywhere in the world where this disease is suspected. This geographic uniformity in diagnosis is achieved due to the random nature, because of chance, of the series of patients with varying prior probabilities in which a disease is suspected. This method of hypothesis generation and verification is the frequentist confidence method, which is the other (other than the Bayesian method) major method of statistical inference (19).

Appendix

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 13 = 1/1 = Posterior probability of 50 percent

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