KEY CONCEPTS SERIES

Bayes' rule in diagnosis

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Abstract

Establishing an accurate diagnosis is crucial in everyday clinical practice. It forms the starting point for clinical decision-making, for instance regarding treatment options or further testing. In this context, clinicians have to deal with probabilities (instead of certainties) that are often hard to quantify. During the diagnostic process, clinicians move from the probability of disease before testing (prior or pretest probability) to the probability of disease after testing (posterior or posttest probability) based on the results of one or more diagnostic tests. This reasoning in probabilities is reflected by a statistical theorem that has an important application in diagnosis: Bayes' rule. A basic understanding of the use of Bayes' rule in diagnosis is pivotal for clinicians. This rule shows how both the prior probability (also called prevalence) and the measurement properties of diagnostic tests (sensitivity and specificity) are crucial determinants of the posterior probability of disease (predictive value), on the basis of which clinical decisions are made. This article provides a simple explanation of the interpretation and use of Bayes' rule in diagnosis. © 2020 The Author(s). Published by Elsevier Inc. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

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1. Introduction

The diagnostic process in clinical practice [1−3] is based on probabilities and, consequentially, filled with uncertainty. During the process of establishing a diagnosis, the probability of the disease of interest is continuously shifting, either upward or downward, depending on the specific information gathered during the diagnostic process. Important pieces of information for diagnosing a certain disease are the results of one or more diagnostic tests. The main goal of diagnostic testing is to rule in or rule out the presence of a disease with a sufficient level of certainty.

Generally speaking, the better the diagnostic test, the more certainty about the diagnosis after the test. Common properties of the quality of diagnostic tests include sensitivity and specificity. Sensitivity refers to the probability of a true-positive test result in someone with the disease, whereas specificity refers to the probability of a true-negative test result in someone without the disease. In everyday practice, however, the presence or absence of disease obviously is not known at the moment of testing—otherwise, why test? Instead, one has to rely on the predictive value of a positive or negative test result to estimate the probability that the disease is present or absent, respectively.

The purpose of diagnostic testing is to move from the probability of disease before the diagnostic test (prior probability) to the probability after the diagnostic test based on the test result (posterior probability). It is very hard to objectify these probability shifts as part of the diagnostic reasoning by which clinicians gain more certainty about a diagnosis. Actually, clinicians often tend to overestimate the predictive value of a diagnostic test result when not appropriately considering the prior disease probability [4]. This is where a famous statistical theorem can help: Bayes' rule [5]. One of the uses of Bayes' rule is quantifying the diagnostic process of updating prior into posterior probabilities [6].

2. Definition

Bayes' rule represents the probabilistic nature of diagnostic reasoning in the form of a mathematical equation. This equation expresses the relationship between probabilities operating during the diagnostic process, showing that the most

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important determinants of the posterior probability of disease are the prior probability and the test properties. Bayes' rule is often presented using the language of diagnostic testing [7], including posterior probabilities (predictive values), sensitivity (Sn) and specificity (Sp), and prior probabilities (often called prevalence; Prev). In many textbooks, equations for Bayes' rule are typically depicted as follows:

Positive predictive value (PPV) =

$$\frac{\text{Sn} \times \text{Prev}}{\text{Sn} \times \text{Prev} + (1 - \text{Sp}) \times (1 - \text{Prev})}$$

Negative predictive value (NPV) =

$$\frac{\text{Sp} \times (1 - \text{Prev})}{(1 - \text{Sn}) \times \text{Prev} + \text{Sp} \times (1 - \text{Prev})}$$

These equations may look obscure at first sight, but are actually easy to understand when considering probabilities rather than frequencies in a diagnostic contingency table (Table 1).

Using Table 1, it can be seen that Bayes' rule for the positive predictive value (PPV) and negative predictive value (NPV) simply represents an alternative expression of the traditional formulas for these posterior probabilities; PPV = P(D+|T+) = A/(A+B) and NPV = P(D−|T−) = D/(C+D). Other predictive values can also be derived with ease. For instance, the probability of disease after a negative test result (1-NPV) is often relevant in clinical practice because it estimates the chance of a false-negative diagnosis. Table 1 shows that 1-NPV = P(D+|T−) = C/(C+D) = [(1-Sn) × Prev] / [(1-Sn) × Prev + Sp × (1-Prev)].

3. Practical illustration

Suppose a clinician wants to use a diagnostic test to estimate the presence or absence of a pulmonary embolism (PE) in someone suspected of PE (prior probability is estimated to be 50%). The clinician can choose between two different tests [8]: D-dimer with 97% sensitivity and 41% specificity or compression ultrasound (CUS) with 49% sensitivity and 96% specificity. For ruling out PE, the negative predictive value is of interest. Which test is most useful

for that purpose? Bayes' rule provides the answer. NPV D-dimer = [0.41 × (1-0.50)] / [(1-0.97) × 0.50 + 0.41 × (1-0.50)] = 0.93 and NPV CUS = [0.96 × (1-0.50)] / [(1-0.49) × 0.50 + 0.96 × (1-0.50)] = 0.65.

D-dimer testing clearly outperforms CUS for ruling out PE. This is mainly due to D-dimer's high sensitivity, which thereby has the strongest influence on the negative predictive value because of the low chance of false-negative results. Based on a negative D-dimer test, one has gained 43% (0.93−0.50) more certainty regarding the absence of PE, compared with only 15% (0.65−0.50) for CUS. In contrast, however, CUS is better than D-dimer for ruling in PE in someone with a 50% prior probability. Bayes' rule shows this; the PPV for D-dimer is 0.62, and the PPV for CUS is 0.92.

More importantly, irrespective of the test properties (sensitivity and specificity), Bayes' rule also shows that if prior probabilities change, so do different posterior probabilities. Understanding this is crucial when performing diagnostic tests. Bayes' rule demonstrates how prior probabilities influence posterior probabilities [6,7,9]. In general, if prior probabilities increase, the positive predictive value increases, whereas the negative predictive value decreases. The reverse is true for decreasing prior probabilities. This has very important implications for diagnostic testing in clinical practice. For example, a negative D-dimer test rules out PE in low-prevalence settings (e.g., 1-NPV is 1% if prior probability is 10%), but is less useful in high-prevalence settings (e.g., 1-NPV is 15% if prior probability is 70%; see appendix). Furthermore, Bayes' rule also provides insight into how multiple tests could be combined as a strategy for establishing a diagnosis (e.g., in the form of diagnostic algorithms or clinical prediction rules) [1].

4. Pointers

Altogether, insight into the use of Bayes' rule in diagnosis is relevant for understanding the interplay between the prior probability of disease and diagnostic test

Table 1. The diagnostic contingency table

	Disease present (D+)	Disease absent (D−)	
Test positive (T+)	Probability of true positive (A) P(T+|D+) × P(D+) = Sn × Prev	Probability of false positive (B) P(T+|D−) × P(D−) = (1-Sp) × (1-Prev)	Probability of positive test result (A+B) = P(T+)
Test negative (T−)	Probability of false negative (C) P(T−|D+) × P(D+) = (1-Sn) × Prev	Probability of true negative (D) P(T−|D−) × P(D−) = Sp × (1-Prev)	Probability of negative test result (C+D) = P(T−)
	Prior probability of presence of disease (A+C) = P(D+) = Prev	Prior probability of absence of disease (B+D) = P(D−) = (1-Prev)	Total probability (A+B+C+D) = 100%

P, probability. Unconditional probabilities (e.g., P(D+) = probability that the disease is present before the test is applied) and conditional probabilities (e.g., P(T+|D+) = probability of a positive test given that the disease is present, that is, probability of a positive test among those with the disease) are shown.

properties in determining the posterior probability of disease. It is useful for the following:

- quantifying changes in disease probabilities based on diagnostic test results;
- interpreting pretest to posttest gains in diagnostic certainty about the disease;
- choosing between diagnostic tests depending on whether the purpose of testing is to rule in or rule out the disease;
- clarifying that predictive values are *strongly* dependent on the prior probability of disease, which should always be taken into account when interpreting diagnostic test results.

Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jclinepi.2020.12.021.

References

[1] Knottnerus JA, Buntinx F. The evidence base of clinical diagnosis : theory and methods of diagnostic research. 2nd ed. Oxford ; Hoboken, NJ: Wiley-Blackwell Pub./BMJ Books. xiii; 2009:302.

[2] Newman TB, Kohn MA. Evidence-based diagnosis. Cambridge ; New York: Cambridge University Press. xiii; 2009:295.

[3] Celentano DD, Szklo M. Assessing the validity and reliability of diagnostic and screening tests. In: Gordis Epidemiology. Elsevier; 2019:94−122.
Useful textbooks on theoretical concepts and principles related to clinical or medical diagnosis.

[4] Manrai AK, Bhatia G, Strymish J, Kohane IS, Jain SH. Medicine's uncomfortable relationship with math: calculating positive predictive value. JAMA Intern Med 2014;174(6):991−3.

[5] Efron B. Mathematics. Bayes' theorem in the 21st century. Science 2013;340:1177−8.

[6] Westbury CF. Bayes' rule for clinicians: an introduction. Front Psychol 2010;1:192.

[7] Khamis HJ. An application of Bayes rule to diagnostic-test evaluation. J Diagn Med Sonogr 1990;6(4):212−8.

[8] Patel P, Patel P, Bhatt M, Braun C, Begum H, Wiercioch W, et al. Systematic review and meta-analysis of test accuracy for the diagnosis of suspected pulmonary embolism. Blood Adv 2020;4(18):4296−311.

[9] Weatherall M. Information provided by diagnostic and screening tests: improving probabilities. Postgrad Med J 2018;94(1110):230−5.

Further Reading

[1] Knottnerus JA, Buntinx F. The evidence base of clinical diagnosis : theory and methods of diagnostic research. 2nd ed. Oxford ; Hoboken, NJ: Wiley-Blackwell Pub./BMJ Books. xiii; 2009:302.

[2] Newman TB, Kohn MA. Evidence-based diagnosis. Cambridge ; New York: Cambridge University Press. xiii; 2009:295.

[3] Celentano DD, Szklo M. Assessing the validity and reliability of diagnostic and screening tests. In: Gordis Epidemiology. Elsevier; 2019:94−122.

[4] Manrai AK, Bhatia G, Strymish J, Kohane IS, Jain SH. Medicine's uncomfortable relationship with math: calculating positive predictive value. JAMA Intern Med 2014;174(6):991−3.
Short report on results of research showing (strong) overestimation of positive predictive value in a low-prevalence setting (low prior probability).

[6] Westbury CF. Bayes' rule for clinicians: an introduction. Front Psychol 2010;1:192.
Comprehensive explanation of conditional probabilities, Bayes' rule, and implications for diagnostic testing.

[7] Khamis HJ. An application of Bayes rule to diagnostic-test evaluation. J Diagn Med Sonogr 1990;6(4):212−8.
An intuitive explanation of the formulas relating sensitivity, specificity and prevalence to predictive values according to Bayes' rule.

[9] Weatherall M. Information provided by diagnostic and screening tests: improving probabilities. Postgrad Med J 2018;94(1110):230−5.
Explanation of Bayes' rule in diagnostic testing extended to the use of likelihood ratios and disease odds instead of probabilities.