MAT^2
MATerials MATemàtics
Volum 2021, treball no. 6, 5 pp. ISSN: 1887-1097
Publicació electrònica de divulgació del Departament de Matemàtiques
de la Universitat Autònoma de Barcelona
www.mat.uab.cat/web/matmat

PCR tests with high sensitivity and specificity are truly trustworthy under high prevalence or medical prescription

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A well known and frequently cited example that mathematicians use to motivate the importance of Bayes Theorem is connected to the interpretation of sensitivity and specificity of medical tests [5, 9]. The sensitivity is the probability of a positive result given that you are sick, and the specificity is the probability of a negative result given that you are not sick. A test is usually considered good if it has high sensitivity and high specificity. The argument suggest that, in spite of enjoying such good specifications, a good medical test does not guarantee that, having a positive test, one has a high probability of being sick.

In particular, we can apply the argument to PCR tests. Assume, for example, that such a test has sensitivity equal to 97.2% and specificity equal to 98.6%. These are, to our knowledge, the most optimistic published values for these parameters. They mean that the probability of a positive test when you are infected is 0.972 and the probability of a negative test when you are not infected is 0.986. Thus, the probabilities of a true positive and a true negative are high. Does this mean that, if you get a positive test, to be infected has a high probability? And what about the probability of being sane if the test was negative? Obviously, Bayes Theorem plays a role in answering these questions. For our argument, we assume that both sensibility and specificity are smaller than 100%, which is the case for the majority of medical tests and, in particular, is a true assumption for PCR tests. Under this assumption, if the prevalence of the disease is small, the probability of a true positive test may be unexpectedly small. Prevalence is the probability of being infected. It is usually a small value. For example, we can well assume that a prevalence of 2% is high for Covid-19. Then

$$\begin{aligned} P(\text{infec}|\text{pos}) &= \frac{P(\text{pos}|\text{infec})P(\text{infec})}{P(\text{pos}|\text{infec})P(\text{infec}) + P(\text{pos}|\text{not infec})P(\text{not infec})} \\ &= \frac{0.972 \cdot 0.02}{0.972 \cdot 0.02 + (1 - 0.986) \cdot 0.98} = \frac{0.01944}{0.03316} \\ &= 0.58624849. \end{aligned}$$

Obviously, a probability of 58.62% of being infected after a positive test seems to be surprisingly small. Does this mean, then, that PCRs are not trustworthy? No. With the same data, the probability of a true negative is really high:

$$\begin{aligned} P(\text{not infec}|\text{neg}) &= \frac{P(\text{neg}|\text{not infec})P(\text{not infec})}{P(\text{neg}|\text{not infec})P(\text{not infec}) + P(\text{neg}|\text{infec})P(\text{infec})} \\ &= \frac{0.986 \cdot 0.98}{0.986 \cdot 0.98 + (1 - 0.972) \cdot 0.02} = \frac{0.96628}{0.96684} \\ &= 0.99942079. \end{aligned}$$

This means that, with these data, a negative test is truly trustworthy.

Moreover, the argument does not take into account that the prevalence could be large. Indeed, prevalence of Covid-19 is still unknown and may be bigger than 2%. Assume, for a moment, a prevalence of 30%. Then the same computation of the probability of a true positive gives a quite different result:

$$\begin{aligned} P(\text{infected}|\text{positive}) &= \frac{0.972 \cdot 0.3}{0.972 \cdot 0.3 + (1 - 0.986) \cdot 0.7} = \frac{0.2916}{0.3014} \\ &= 0.96748507. \end{aligned}$$

In such a case, the probability is almost equal to the sensitivity of the test (it would be equal if the specificity is of 100%) and seems to be really trustworthy.

Of course, one can guess that a prevalence of 30% is, for the majority of diseases, a very high value whose assumption is not realistic. But the computations above also hide an important factor: people who take a medical test are not randomly selected from the population. They usually have a medical prescription based either in their symptoms or —for an infectious disease as Covid-19— the fact that they are close contacts to infected people. In both cases, the prevalence of the chosen subject dramatically increases, to the point that assuming a 20% or a 30% of prevalence for them is a very realistic assumption. Thus, the conclusion is clear: PCR test with high sensitivity and specificity are truly trustworthy, when administrated under medical prescription. Moreover, a complete massive test will have many false positives, while the use of massive test in zones where prevalence is high, will facilitate the detection and isolation of asymptomatic infected people.

The argument, with no comments about prevalence, frequently appears in many introductory books to Probability Theory [2, 3] and, more frequently, in books [5, 9] and articles [4, 6, 8] devoted to vulgarization of mathematics but also in some research papers [7]. I made the experiment of writing "Uses of Bayes Theorem" at Google's search engine and found that this example is discussed —again with no special attention to the role of prevalence in the computations— in several of the first tenth websites sorted by the system. One of them is a letter published at Scientific American in 2016 [4], and the same topic also appears as part of another two papers in the same journal in 2012 [6] and 2006 [8].

As Scientific Director of a collection of books [10] devoted to explain the importance of mathematics in the new era of big data and artificial intelligence, which implies an explanation of its role in the development of many applications in science and technology —including topics as diverse as social networks, collaborative filters, political decisions, network science, big data, electoral systems, chatbots, digital communications, robotics, mathematical models of pandemics, personalized medicine, digital privacy, etc.— I have had to review many books where Bayes Theorem is used and, in several of them, I found that the authors presented the argument above with no references to prevalence. In every case I suggested to the authors that a mention to prevalence was necessary, because otherwise the argument could be confusing. When I did this the n-th time, I mentioned the case to a friend, who is a working physician, looking for his empathy. To my surprise, my friend —who is a clever person and a very good experienced physician that works at a respected hospital— needed to check every computation and, after that, he still said that there was something missing, since his experience told him that a positive result in a medical test (and, in particular, this was so with PCR test) usually means that the person is already infected, and he also believed that prevalences are never that high [1]. It was only after this conversation that, with the help of a good coffee, I became aware that a hidden factor in the argument, and one that I had never read anywhere, is the fact that, when you take a PCR test is because you have some symptoms or you are a close contact to some infected person, and this information of course has a main effect on your prevalence. This is again the result of applying a Bayesian conception of probability: the information we have about an experiment is usually helpful to change our priors. I consider that not including the role of prevalence in the argument, and not pointing up the fact that medical test are not usually taken on arbitrarily chosen people but on people who have some symptoms, may cause confusion. A person who has read Paulos's article [6] may well decide not to take a PCR test prescribed by his physician, alluding that the result is like to toss a coin!

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Publicat el 2 de desembre de 2021