

Teaching Information Mastery: The Case of Baby Jeff and the Importance of Bayes' Theorem

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The sensitivity and specificity of diagnostic tests seem to be difficult concepts for many physicians who are used to viewing laboratory results, physical examination findings, pathology results, and other diagnostic test results as definitive findings that are beyond challenge. Even more difficult are concepts like pretest probability and the predictive values of tests. In fact, we have noticed that the eyes of listeners often glaze over when these topics are discussed.

Nonetheless, physicians and medical trainees must learn that everything written on a lab report in black and white is not necessarily, well, black and white. To do this we need to convey the importance of Bayes' Theorem.

Simply put, Bayes' Theorem states that, as the likelihood of a disease decreases (ie, as the pretest probability of disease decreases), so does the likelihood that a positive test result will signify that a disease is really present. In other words, in primary care, where disease prevalence is generally low, tests results that are positive do not always mean that a disease is present.

To communicate the importance of these concepts to clinical prac-

tice, we use the following case to illustrate the effects of not heeding Bayes' theorem. It is a real-life example that has drama, suspense, and reality mixed together in a way that has had a pronounced effect on many of the learners who have heard us describe it. The details are as they happened, although the names have been changed.

The Case Example

A recent graduate of our family practice residency program (both of us were at Harrisburg Hospital when it occurred) noticed a poster in the hospital's newborn nursery. The poster announcement stated that all male newborns would be screened for muscular dystrophy using a heel stick blood test for creatinine phosphokinase (CPK). Being unaware of this new screening test, the physician asked the nurses about the study. The nurses knew nothing, but referred the physician to the neonatologist in charge of the study for further information. The neonatologist presented our family physician with the test characteristics of the CPK determination as a screening test for muscular dystrophy, and they seemed astounding: a sensitivity of 100% and a specificity of 99.98%. The neonatologist was unaware of the positive and negative predictive values for the test but assured our physician that they were very high given these superlative test characteristics.

Our graduate, knowing the value of predictive values (but not being sure about how to calculate them),

approached one of us. The incidence of muscular dystrophy at birth ranges from 1 in 3,500¹ to 1 in 15,000² male births. Using a conservative and easy estimate to calculate incidence—1 in 5,000 males—we calculated the predictive values and were quite surprised at their results, which we will discuss further.

Now the plot starts to thicken. At the same time, the wife of a current third-year resident in our program delivered a full-term male infant—their first child after a long period of infertility. They named their son Jeff, the resident's name. As you may have guessed by now, Baby Jeff had an abnormal CPK test. Unknown to us at the time, Daddy Doctor Jeff had contacted the same neonatologist with the same question we had, albeit with a much more personal stake: "What is the chance that my son has muscular dystrophy?" The neonatologist didn't say that it was 100% likely but told Dad and Mom that it was highly probable, and they needed to start preparing themselves for the inevitable task of caring for a child with muscular dystrophy. Mother and son were sent home with the infant son carrying a presumptive diagnosis of muscular dystrophy.

This news was, of course, devastating. Mom and Dad, Grandma and Grandpa, aunts and uncles, and the rest of the extended family all went from the peak of excitement after the news of this wonderful birth to a feeling of great despair, knowing with near certainty that

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Baby Jeff was destined to die slowly at an early age from a relentless and unforgiving neurological disease. For the first week of his life, Mom cried almost constantly, and Dad wished that he hadn't made this child his namesake. A few weeks later, the infant finally underwent an invasive gastrocnemius muscle biopsy, which, fortunately, was negative.

So what is the answer to the first important question, "What was the probability that Baby Jeff had muscular dystrophy at the time he was sent home?" Figure 1 shows the

method we use for showing the calculations to learners, using the information from this example. We use large numbers to remind learners that this is a screening test with implications for the entire population and also to avoid calculations using decimals.

In a sample of 100,000 male newborn babies, 20 will have muscular dystrophy (1 in 5,000, or a .02% prevalence). Using a sensitivity of 100%, we can complete boxes A and B in Figure 1. The test will correctly detect all 20 afflicted infants. This leaves 99,980 males

without muscular dystrophy. The specificity can be used to complete boxes C and D. Of the males without muscular dystrophy, 99,960 will test negative (99,980 x .9998), leaving 20 males who will test falsely positive for muscular dystrophy.

Now that we have the table completed, the positive predictive value of the test can be calculated. Half the positive tests are true positives, and half the positive tests are false positives—20 each—making the predictive value of a positive test only 50%! Stated differently, the chance that Baby Jeff really has

Figure 1

An Outline of How to Use the Case to Illustrate How Predictive Values Are Calculated and Their Importance

Step One—Set up a 2X2 table using a hypothetical cohort and the known prevalence.

		Muscular Dystrophy	
		+	-
CPK test	+	a	b
	-	c	d
		20	99,980

Standard 2X2 table using a hypothetical cohort of 1000,000 infants. Since the prevalence of disease is .2% (1 in 5,000), 20 boys will have muscular dystrophy, and 99,980 will not.

Step Two—Fill in the four boxes using sensitivity and specificity.

		Muscular Dystrophy	
		+	-
CPK test	+	20	20
	-	0	99,960
		20	99,980

Since the sensitivity of the CPK test is 100%, all 20 patients with muscular dystrophy will have a positive CPK test (box a—true positives). There will be no false negative results (box c).

Since the specificity of the CPK test is 99.98%, one can calculate how many patients without muscular dystrophy will have a negative test. The answer is 99,980 x 99.98%=99,960, which goes into box d (true negatives). The remaining 20 infants have a positive CPK test but do not have muscular dystrophy (box b—false positives).

Step Three—Calculate positive and negative predictive value from the newly constructed table.

		Muscular Dystrophy	
		+	-
CPK	+	20	20
	-	0	99,960
		20	99,980

One can now see that, of the patients with a positive CPK test, only 20 (50%) actually have muscular dystrophy. The other 20 (50%) do not. These predictive values can be calculated as follows:

Positive predictive value = $a/(a+b) = 50\%$

Negative predictive value = $d/(c+d) = 100\%$

Therefore, the likelihood of a positive test result representing true disease is 50%!

CPK—creatinine phosphokinase

muscular dystrophy, even with a positive test, is only 50%. This can be calculated from the table with the formula $A/(A+B)=.50$.

Thus, while sensitivity and specificity are useful when determining the ability of a diagnostic test to predict the absence or presence of a target disorder, they don't tell us the usefulness of the test for identifying the proportion of patients with positive test results who have the disorder. In this case, they don't tell us the probability that Baby Jeff truly has muscular dystrophy. Only the positive predictive value answers this question.

What are the major points that make this story a teaching tool? Even almost-perfect tests can still have less than acceptable positive predictive values if the prevalence of the disease being tested is low, as it often is in primary care settings. The low predictive value of tests applies not just to rare diseases like muscular dystrophy but also to more-common disorders like breast cancer. For example, for every 100,000 women ages 40 to 50 years undergoing breast cancer screening

with mammography, 6,035 mammograms will be abnormal, of which 5,998 will be falsely positive, leaving only 36 positive tests that represent true cancers.³

Finally, we must not forget that it is imperative that diagnostic tests not be performed unless the disease being detected can be either managed or cured (ie, that the patient or family will benefit as a result of early detection of the disease). This point is going to become increasingly important with the explosion in genetic testing that is about to occur as a result of the human genome mapping project. We were unable to find any research demonstrating improved outcomes from early detection of muscular dystrophy.

Conclusions

This dramatic example of Baby Jeff can be used to illustrate to learners the importance of Bayes' theorem in the real world of clinical practice. It points out the real dangers in using diagnostic tests, even those that on first appearance look extremely useful, without con-

sidering the harm that can be caused by unnecessary or inaccurate testing. It also illustrates the sharp distinction between the clinical usefulness of predictive values as compared with the test characteristics of sensitivity and specificity. Family physicians must understand these concepts and take responsibility, as the physician in this example did, for the health of their patients at all levels of care and protect them from well-intentioned but misinformed policies.

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