The True and False Negatives of Screening

My March editorial\(^1\) focused on the financial costs associated with a commonly performed ophthalmic screening procedure—routine dilated fundus examination. This month's editorial is something of a sequel.

The performance of a screening test is usually expressed in terms of its sensitivity and specificity. The sensitivity is the proportion of diseased or abnormal patients that are identified by the test, and often referred to as the true positive rate. Conversely, the specificity is the proportion of normal or healthy patients that are correctly classified by the test, and often referred to as the true negative rate. The false positive rate—the proportion of healthy individuals classified as abnormal by the test—is simply 1 minus the specificity.

Elmore et al.\(^2\) recently reported the 10-year risk of false positive screening mammograms and clinical breast examinations. Over a period of 10 years, nearly one-third of the women screened had at least one false positive mammogram or clinical breast examination. The study received much attention from the news media. In particular, there was a good deal of discussion of the psychological burden that can be placed on a woman by a positive result and the economic costs of supplementary clinical tests prompted by a positive screening result (estimated to be one-third of the costs of the screening program).

It is important to note that the screening tests evaluated by Elmore and coworkers\(^3\) do not have excessively poor specificity. The reported false positive rates for mammography and clinical breast examination were 6.5% and 3.7%, respectively. These translate to specificities of 93.5% and 96.3%, which compare very favorably to many of our established and emerging ophthalmic screening procedures.\(^3\) Many of our clinical tests, such as automated perimeters, adopt a specificity of 95%, i.e., the clinician is alerted when a patient's score or results lie outside the range that would be found in 95% of an age-matched population.

As common sense predicts, repeated administration of any screening test will result in an ever-increasing risk of the patient giving a positive test result. As Adrian Hill put it, "a normal patient is merely one who has not been tested enough." Elmore and colleagues\(^4\) estimate the cumulative risk of having at least one false positive after 10 screenings was 49.1% for mammograms (= 1 - 0.935\(^{10}\)).

An aspect of screening that is frequently overlooked is that even in the presence of a positive test, the patient is most likely normal. The probability of disease being present given a positive test result can be estimated using Bayes' theorem and depends not only on the sensitivity and specificity of the screening test, but also on the prevalence of the disease in the population being screened.\(^4\) Let us consider a screening test with a sensitivity of 95% and a specificity of 95%. Let us also assume an underlying disease prevalence of 0.5% in the population being screened. This is similar to the prevalence of glaucoma in an ophthalmic population undergoing a regular visual field screening program. For these sensitivity, specificity, and prevalence values, the probability of the disease being present in an individual who gives a positive test result is only 8.72% or 1 in 11. For a test with a sensitivity and specificity of 99%, the equivalent probability would still be only 1 in 3.

In summary, practitioners should not assume that a positive screening test result means that the patient has the disease in question. I have recollections of patients being condemned to twice yearly full-threshold visual field examinations on the basis of one borderline field screening or because one clinician judged a disc to be suspicious. A patient who gives a positive on a screening test should still be regarded as normal until confirmed by a repeat or a more extensive test battery.

I believe that responsible clinicians factor in all of this information when discussing test results with a patient. Informing the patient that, even though they have tested positive, the probability that they have the disease is small may allay much of the stigma and anxiety that can surround positive screening test results.

REFERENCES


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