Evidence-based diagnosis: I. Diagnosis and probabilities

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Diagnosis research

Diagnosis research is far less advanced than pharmaceutical research. New pharmaceuticals are subjected to phases I, II, III, and IV studies. On the other hand new diagnostic modalities are not subjected to similar studies before entering the market. Thus one should be extremely careful before rushing to use a new diagnostic modality or technique.

Cross-sectional independent blind comparison with a gold-standard is the method of choice in assessing new diagnostic modalities. Before accepting the results of such studies in practice one should thoroughly assess them for their validity, relevance, and results using a specific sheet for appraising articles about diagnosis. The procedure of critical appraisal is not the scope of this article but of a next one.

The Process of diagnosis

Diagnosis is the process of using history, physical examination, and investigations to identify the disease responsible for the patient’s complaint. This process ends up with a decision that varies between starting treatment, asking for more investigations, or to ignore the condition completely. These decisions are taken based on the probabilities of the presence or absence of various diseases and disorders which are usually calculated at a subconscious level.

The probability of the presence of any disease or disorder ranges between 0% and 100%. In practice, we examine our patients and define the possible causes of their complaints to end up with an estimated probability for each possible cause that falls somewhere between these two limits (0 - 100%).

For each disorder there are two important thresholds of probabilities; one is called the “test threshold” and the other is called the “treatment threshold” (1) (Figure 1).

According to the estimated disease probability we follow one of three strategies:

a. If our estimation falls below the testing threshold, further testing or starting treatment are not warranted.

b. If our estimation falls somewhere between the testing and treatment thresholds, further testing is required.

c. If our estimation falls above the treatment threshold we start treatment.

To make the above concept clearer let us suppose that while you were working in the emergency department you have been asked to examine a pregnant young lady in the emergency
Pretest probability falls between test and treatment thresholds

Test is performed

Test –ve Posttest probability is less than pretest one

Test +ve Posttest probability is more than pretest one

Diagnostic tests and probabilities

Diagnosis is a guessing game or in more scientific terms it is the art of estimating the probability of the presence or absence of a certain disease or disorder in a particular patient.

It is important for clinicians to look at diagnostic tests, not as tools that confirm or exclude the presence or absence of the disease, but as tools that help them to change their patient’s “pretest probability” of having a particular disease to a “posttest probability” of having it. The majority of diagnostic tests we use are not 100% conclusive in ruling in or out of the disease.

Figure 2. Effect of test result on disease probability
There is always a possibility of either false positive or false negative results. Thus a positive test result does not mean that the disease is present 100% as well as a negative test result does not mean that it is absent 100%.

To elaborate more on the concept of pretest and posttest probabilities let us go back to the thresholds concept; if the probability of a certain disorder falls between the test and treatment thresholds; further testing is warranted and we would call the estimated probability in this situation “the pretest probability of the disorder”. After the test we will end up with a new probability according to the test result that is called the “the posttest probability of the disorder”. This new probability will be less than the pretest probability if the test result was negative and will be more than it if the test result was positive (figure 2).

But again, after the test, our decision to treat, test or ignore, follow the same procedure mentioned above once more. If the new probability “the posttest one” falls above the treatment threshold, we will start treatment and if it falls below the test threshold we will ignore this diagnosis, while if it falls between the two thresholds we need to do more tests (more investigations) to reach a better conclusion.

Back to our example of bleeding with pregnancy an ultrasound examination detecting a live fetus will increase the probability of threatened abortion from a pretest probability of 80% to a posttest probability of 99% and will decrease the probability of missed abortion from a pretest probability of 19% to a posttest probability of 0% and will not affect the probability of associated gynecological lesion that would stay at 1%.

What decides the pretest probability of a disease?

The probability of a patient to have a particular disease depends on many factors the most important of which are 1) the prevalence of the disease in the community, 2) the absence or presence of risk factors, 3) symptoms, and 4) signs. This process of estimating the probability of the presence of a certain disease is based mainly on the doctor’s experience, intuition and wise judgment. While protocols are available for treatment, diagnosis is the area where physicians’ experience counts as research is still primitive to give estimates of the various probabilities of a given disease in absence or presence of various risk factors, symptoms and signs. However, for some disorders clinical prediction rules and scoring systems have been developed to help clinicians estimate a probability of occurrence of specific disorders. Research in this area should be encouraged.

What decides the test threshold?

The test threshold is the probability below which the physician decides that a certain diagnosis warrants no further consideration. It depends mainly on 1) the seriousness of the diagnosis, 2) the safety of the test, and 3) the implications of the test on the management of the condition. In mild diseases, one sets his testing threshold high while in serious diseases one sets his testing threshold very low. In a patient with premenopausal bleeding, you will not risk missing a diagnosis of endometrial carcinoma if its probability is as low as 1% but you will not bother testing for an impaired estrogen to progesterone ratio even if its probability was much higher than this. In invasive tests that have serious side effects, as chorionic villous sampling for the diagnosis of chromosomal anomalies, we tend to push the test threshold higher and if the test will give us a diagnosis that has no effect on our treatment, as testing for ovum fertilizability, we might also push the test threshold higher.

What decides the treatment threshold?

The treatment threshold is the probability above which the physician decides to start treatment. It depends mainly on 1) the seriousness of the condition, 2) the safety and affordability of the treatment, and 3) the safety of the tests required to confirm the diagnosis. In the hypoglycemic coma example we set our treatment threshold very low because the condition is life threatening and the treatment is safe and affordable. While in the missed abortion example we push the treatment threshold for termination of pregnancy very high.
so that we don’t loose a viable pregnancy before being 100% sure. In some invasive and serious tests we will be inclined to avoid doing the test, thus, we tend to push our treatment threshold lower down.

**What decides the posttest probability?**

The posttest probability of the presence of the disease is the most important measure we look for after performing the test. It depends mainly on the 1) pretest probability and 2) the “likelihood ratio” of the preformed test. I have highlighted how to calculate the pretest probability and will elaborate on the likelihood ratio, which is the single most important measure of a test, in a coming article.

**Key points:**

Diagnosis research is far less advanced than therapeutic research. Thus, diagnosis is the area where the doctor’s experience makes most of the difference.

Diagnosis aims at estimating a set of probabilities of the disorders that might be responsible for the patient’s complaint. According to the estimated probability we, ignore the diagnosis, ask for investigations, or start treatment. This decision is based on two important thresholds known as test and treatment thresholds.

The majority of diagnostic tests are not conclusive in ruling in or out of the disease but they help us re-evaluate our estimated pretest probability to a posttest one. This posttest probability depends on the pretest one as well as the likelihood ratio of the performed test.

**REFERENCES**