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PRACTICE

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Explaining laboratory test results to patients: what the clinician needs to know

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Better understanding by patients of why tests are performed and what the results mean increases satisfaction with care.[1-4] Patients increasingly have direct access to their test results through online portals. Although patients may discuss test results with family and friends or seek information on the internet,[5] the responsibility for explaining test results lies with clinicians. Discussions must take into account the patient's literacy and numeracy level, and clinicians should explain clearly what the results mean and how they influence treatment choices.

Why are tests performed?

It is crucial to understand why a test was done to understand the meaning of its result. The following are common reasons for testing:

- Diagnosis: to confirm (or exclude) a specific diagnosis when suggestive symptoms or signs are present—for example, measurement of glycated haemoglobin in a patient with thirst and suspected type 2 diabetes
- Monitoring: to monitor response to treatment (for example, prostate specific antigen in prostate cancer) or disease progression (estimated glomerular filtration rate in chronic kidney disease)
- Risk stratification: to help assess disease risk and the need for preventive therapy—for example, lipid measurement to help quantify cardiovascular disease risk
- Screening: undertaken in asymptomatic people to assess the risk of occult disease and the need for further confirmatory tests—for example, colorectal cancer screening by faecal occult blood testing or neonatal screening for inborn errors of metabolism.

Reference intervals

"My sodium level is slightly low at 131 mmol/L: is there something wrong?" (Box 1)

A reference interval usually includes 95% of the test results obtained from a presumed healthy population (fig 1A⇓).[6] For many tests the reference distribution is "normal" or has a Gaussian distribution around the population mean; for other tests it may be skewed to the right or to the left around a population median.[6] Quoted reference intervals may not take into account important factors such as the influence of sex, age, and ethnicity. By definition 2.5% of healthy people (one in 40) will have results just outside either end of the reference interval. The chance of a test result in a healthy person falling outside the reference interval is 5% when a single test is performed but increases to 64% when 20 tests (such as a full blood count, urea and electrolytes, and liver function tests) are performed. This may lead to unnecessary further investigation and overtesting; follow-up of such minor abnormalities in an otherwise well patient may not be indicated. It is useful for patients to know that reference intervals have limitations, and that if many tests are performed it is not surprising that the occasional result falls slightly outside the reference interval.

For many tests the reference interval depends on the analytical method used so only the reference interval provided by the testing laboratory should be used, not those used by other laboratories or from internet sources or comparisons with friends and family. Although initiatives are under way to harmonise reference intervals between laboratories in the United Kingdom, differences still exist for some commonly requested tests (sometimes for good scientific reasons).[7]

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The bottom line

- Minor test abnormalities in well people may have no clinical relevance. By definition, 5% of healthy people will have test results that fall just outside the 95% healthy population reference interval
- Consider the possibility of false positives and negatives: the predictive value of tests varies with different disease prevalence in different settings; if the index of suspicion is high, further tests may be warranted even if the result is negative
- Outside of formal screening programmes, speculative screening tests in well asymptomatic people have little value and may result in over investigation and unnecessary treatment

Box 1: "My sodium level is slightly low at around 131 mmol/L: is there something wrong?"

Although most healthy people have a sodium value between 133 mmol/L and 146 mmol/L, one in every 40 healthy people will have a reading just below this range. Because you are otherwise well and the level has not changed, it is unlikely to be important.

The predictive value of tests

"My coeliac disease blood test result is negative: does this mean I have nothing to worry about? (Box 2)

Because test results in health and disease usually overlap (fig 1B⇓), the results of an individual test may not always differentiate healthy people from those with disease. The positive predictive value (PPV) of a test is the probability that a patient with a positive test result has the disease, whereas the negative predictive value (NPV) is the probability that a patient with a negative test result does not have the disease. There is always a trade off between PPV and NPV, which will change with the particular cut off used to differentiate between the healthy and disease groups. A cut off chosen to maximise PPV will increase the number of false negatives; a cut off chosen to maximise NPV will do so at the cost of more false positives. No tests have both 100% sensitivity and 100% specificity. All test results must be interpreted in the context of the patient's clinical features, and if the index of suspicion is high further investigation may be warranted even if the test result is negative.

Furthermore, the performance of the test depends on the prevalence of the disease in the population tested: for a given cut off, as disease prevalence falls the PPV will also fall (the number of false positives will increase). Tests that perform well in a specialist hospital setting where the prevalence of a particular disease is high may be less useful in primary care where disease prevalence may be lower:

Faecal elastase is commonly measured to assess exocrine pancreatic function; it has a reported sensitivity and specificity of 75% and 95%, respectively. In a hospital patient cohort in which the prevalence of chronic pancreatitis was 8.5%, a positive test result had a predictive value for exocrine pancreatic insufficiency of 58%.[8] However, the prevalence of exocrine pancreatic insufficiency is much lower in primary care. If the test is applied to a population with a disease prevalence of 0.1% the positive predictive value falls to 1.2%.

Monitoring and variability in test results

"My cholesterol was 5.7 mmol/L. I improved my diet but now it has gone up to 6.1 mmol/L: why?" (Box 3)

All numerical test results vary over time even without a change in the patient's clinical status.[9] This variability comprises three elements:

- Pre-analytical variability: for example, time of sampling, fasting and hydration status, exercise, delay in sample centrifugation
- Analytical variability: which arises from random error (imprecision) in measurement in the laboratory
- Biological variability: random fluctuation around a homeostatic set point. For tests that are affected by cyclical rhythms, such as gonadotrophins and sex hormones in women and testosterone in men, this may be great. However, even more stable tests fluctuate—for example, about 6% variation for total cholesterol and 5% for creatinine.

All these factors can combine to produce relatively large day to day variability in test results.[9 10] This is an important consideration when test results are used to monitor disease progression or response to treatment.

Taking into account these three components of variability, for a cholesterol level of 6.1 mmol/L, the "true" result is likely to be within the range 5.4-6.8 mmol/L, and for a level of 5.7 mmol/L it is likely to be within the range 5.0-6.4 mmol/L. Because of the overlap between these two ranges, the difference in the results may simply reflect expected variability rather than any increase in cholesterol concentration.[10]

Tests for risk stratification

"My cholesterol is high so why am I not being offered treatment?" (Box 4)

Testing can be used for risk stratification and making decisions about preventive treatment. A good example is cardiovascular risk prediction where serum cholesterol on its own is a relatively poor predictor of risk. However, combined with other information such as age, sex, comorbidities, and family history in a risk calculator such as QRISK2 (www.Qrisk.org) it provides a more robust measure of absolute cardiovascular risk that can help to decide whether to offer lipid lowering therapy.[11] Two patients may therefore have the same cholesterol concentration but different cardiovascular risk, with one being offered lipid lowering therapy and the other not. Representation of risk by pictographs is well understood by patients (fig 2⇓).[12]

Screening tests

"Can I get some cancer blood tests done as part of my health check?" (Box 5)

Screening tests assess the risk of disease in asymptomatic people, with subsequent tests needed to confirm the presence of disease. Examples include neonatal screening for inborn errors of metabolism and faecal occult blood testing in colorectal cancer screening programmes. The premise is that early detection of disease in asymptomatic people improves outcomes and that false positive results do not create a burden. This is not always the case, and the limitations of screening tests need to

Box 2: "My coeliac disease blood test result is negative: does this mean I have nothing to worry about?"

The negative test result makes coeliac disease unlikely but does not completely rule it out. However because of your symptoms, I would like to discuss with the gastroenterology specialist whether further investigation for coeliac disease is needed.

Box 3: My cholesterol was 5.7 mmol/L. I improved my diet but now it has gone up to 6.1 mmol/L: why?'

Cholesterol levels vary from day to day depending on such factors as body rhythms, fluid intake, and season of the year. A small change in cholesterol like this is probably due to this natural variation rather than a true rise in value.

Box 4: "My cholesterol is high so why am I not being offered treatment?"

Only people at higher risk of heart disease benefit from cholesterol lowering tablets. Although your cholesterol level is increased, we calculated that your risk of heart disease over the next 10 years is low because you are otherwise healthy, don't smoke, and have normal blood pressure. The benefit from a cholesterol lowering tablet at this stage is likely to be low and such tablets may also have side effects.

be carefully explained. For example, although some tumour markers have a role in monitoring known cancer, they have limited value as a screening test in apparently healthy people.[13] They generally lack sufficient sensitivity (will miss some tumours) and specificity (will give false positive results). The lack of specificity may lead to inappropriate further investigation and possibly unnecessary treatment (because the natural course of some cancers is poorly understood).

However the use of tumour markers in patients with symptoms of disease may be more useful—for example, CA-125 measurement combined with ultrasound can be help make a diagnosis in women with symptoms suggestive of ovarian cancer.[14]

Conclusion

It is important to explain test results and put them in the context of the patient's overall condition. A better understanding of test results may improve patient satisfaction with their care.

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Box 5: "Can I get some cancer blood tests done as part of my health check?"

You have no features that make me worried about cancer. Cancer blood tests are not useful here as they are not very good at picking up cancer; they also give a lot of false positive readings that need further complex tests to sort out and can sometimes lead to unnecessary treatment and anxiety. They are mainly used for following up patients with known cancer. A better approach for picking up cancer is to come back to see me promptly if you have any worrying symptoms.

How patients contributed to this article

The concept for this article came from discussions between the authors and many patients in outpatient clinics and other settings on how best to communicate laboratory test results. The specific vignettes were discussed with individual patients.

Figures

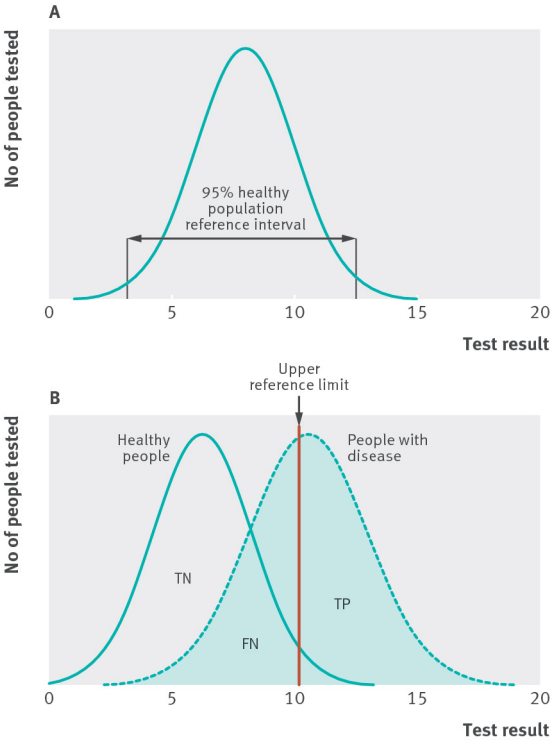

Fig 1 (A) Distribution of test results in a healthy population with a 95% reference interval. (B) Distribution of test results in a healthy population and a population with disease illustrating a large overlap. Using a cut off (in this case the upper limit of the healthy population reference interval) the following may be defined: true positives (TP), true negatives (TN), false positives (FP), and false negatives (FN)

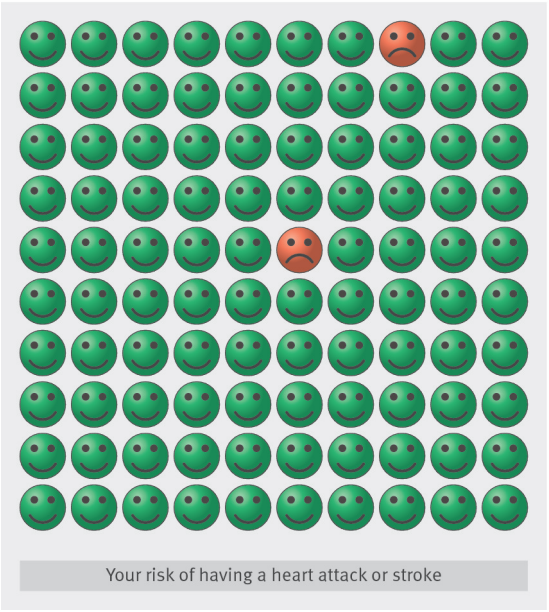

Fig 2 Pictographs of the risk of having a heart attack or stroke within the next 10 years