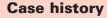# The trouble with testing: Screening

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Case history

Richard is a 42 year old executive, presenting for his annual check. He is a patient who takes great interest in his health. Richard's ribs were fractured in a motor vehicle accident five years ago. He takes no medications, does not smoke and drinks only occasionally. His weight is normal (height 182 cm, weight 78 kg*) and he keeps fit with guidance from his personal trainer.

Richard would like to have last year's tests repeated (routine biochemistry, haematology, thyroid function and lipids).

Question 1

Assuming Richard has no underlying disease, how likely is it that all tests will be within normal range?
A. likely (>70%)
B. moderate (closer to 50/50)
C. unlikely (<30%).

Question 2

Assuming a 'full screen' includes 30 independent tests, how likely is it that the results of one or more tests will be outside the normal range?

Question 3

Should you discuss the likelihood of Richard having a positive result before ordering the tests?

Question 4

If one or more of the tests is abnormal, how should you and he react?

Feedback

Answer 1

Answer C: unlikely (<30%). Generally, the normal or reference range quoted by laboratories includes 95% of a healthy population, ie. 5% of healthy people will have abnormal results (2.5% a low result, 2.5% a high result). The likelihood of a false-positive result increases with the number of tests performed (see below).

Answer 2

For each test there is a 95% chance of Richard's result being normal (normal range includes 95% of the normal population), but a 5% chance of it being inappropriately reported as abnormal. For two tests, the chance of both being normal is (0.95x0.95). For 30 tests, the chance of all results being normal is $(0.95)^{30}=0.21$. Therefore, the chance of

* Body mass index (BMI) = weight (kg)÷height^2 (m^2)=78÷1.82^2=23.5 kg/m^2. Healthy BMI 20–25, overweight 25–30, obese >30.

one or more tests being abnormal is 1.0–0.21=0.79 (ie. ~80%). As noted, the more tests that are performed, the higher the likelihood of a false-positive result.

Answer 3

Given the likelihood of one or more abnormal results, you should discuss with Richard his options if one or more of the results are abnormal (see below). It is usually easier to agree on a sensible course of action before ordering tests than after, when 'worried well' patients may wish to follow up abnormal results with further investigations, which in turn, may result in more false-positive results. As investigations become more sophisticated and sensitive, the likelihood of detecting 'incidentalomas' increases. You may find yourself arranging invasive investigations for an 'incidentaloma' that has no clinical significance and may have better remained undiscovered.

Ideally, we would not screen 'worried well' patients. Instead, we would 'case find', using specific tests for a specific suspected diagnosis in a high risk individual.

Answer 4

In general, it is always best to confirm a major, unexpected abnormality. The only way to positively confirm an incorrect result is to repeat the collection and analysis. If confirmed, look for patterns consistent with likely diseases. For example, an isolated increase in alkaline phosphatase in an older person could suggest Paget disease; whereas increased alkaline phosphatase combined with increased gamma-glutamyl transpeptidase, hyperuricaemia and macrocytosis, could be the result of high alcohol intake in another patient.

If an abnormal test is confirmed but no pattern or cause identified, the 'tincture of time test' will help you decide. The abnormality may disappear if caused by a transient problem such as a viral infection, remain at a clinically insignificant level, or may prompt further investigation because of the severity of the abnormality or its progression.

Laboratory or imaging colleagues can often provide useful advice, but you and they should be clear about the implications of positive and negative results before you investigate further.

Conflict of interest: none declared. AFP

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