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Medicine for Managers

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Cancer – How close is Universal Detection?

The word 'cancer' can make the skin creep. Treatment has improved but our success rates are not as good as other countries like Canada and Australia. Success depends on early diagnosis and effective and rapid treatment. Diagnosis is often delayed. Perhaps, in twenty years or less, we might go to a medical facility for a simple blood test to identify perhaps dozens of malignant tumours before they cause symptoms. Far fetched? Probably not.

The prospect of a multi-cancer detection system is very exciting and could represent a major advance in medical care. However, there is a way to go before it is made available to the population in general because there are problems with any diagnostic test which need to be overcome or at least managed.

1. Does it work? If there are abnormalities which can be detected, does the test do it reliably, or does it result in false negatives which cause reassurance which is misplaced?
2. Does the test result in false positives, generating unnecessary fear and distress?
3. Does testing of this sort make the worried well even more worried?
4. Will it be available at a cost which will make it feasible for routine Health Service use or will it be at a cost which only the well-to-do can afford privately?

Cancer itself has been recognised for 5,000 years. The ancient Egyptians described its sinister nature and evidence of it has been found in preserved mummies.

Hippocrates provided the word carcinoma to describe an inexorable lesion with finger-like projections, which he thought was crab-like.

The Roman physician Celsus translated the term as ***bracchia cancri*** (arms of a crab), which was shorted to cancer.

The Greek physician Galen used the term ***oncos***, the Greek word for swelling, from which the modern word oncology is derived.

For a thousand years, cancer was thought to be due to excess of what Hippocrates called ***black bile,*** from which the word melancholy is derived

With the development of post-mortems in the fifteenth century and later, they became more common.

Spread via lymph channels was suspected by 16th and 17th Century physicians and ***John Hunter*** (1728-93) postulated a mechanism.

In the nineteenth century a number of eminent physicians put forward a range of observations and theories about the disease, its origins, its spread and its inexorable progress.

X-rays, discovered in the 1890s, became used and the first case of radiation related cancer was identified in a technician who had been over-exposed.

Through the first half of the twentieth Century, physicians and researchers experimented and produced tumours in laboratory animals. Factors causing cancer began to be identified.

Papanicolaou discovered that malignant cells were shed from the cervix of a woman with cervical cancer, and the Pap-test or ***cervical smear*** was the result.

In the 1930s, the association between asbestos and lung cancer and, five years later, between smoking and lung cancer, were established.

Chemotherapy was first developed in the 1940s and ***methotrexate*** was identified as a treatment for childhood leukaemia. The relationship of hormones to cancer was also elucidated.

Mammography was developed in the 1960s and during the 1970s, a host of developments occurred including ultrasound and MRI and the knowledge of the disease and its treatment burgeoned.

Oncogenes were discovered. These genes cause cells to grow out of control. ***Tumour Suppressor Genes*** were also found to repair DNA, regulate cell-division and provide cellular obsolescence

In the 1990s, ***BRCA1*** and ***BRCA2*** genes, associated with the development of breast cancer, were identified.

The understanding of cancer has expanded enormously over the last thirty years. Identification and diagnosis, and management is considerably better. But there is still a long way to go preventively and therapeutically before cancer can be consigned to the history books.

There are already several multi-cancer early detection approved tests, marketed directly to consumers and undergoing tests in the NHS.

They involve a single blood test to detect markers of cancer in the blood before the individual develops any symptoms.

A recent study using predictor tests was published in July 2023. Of 5,461 people in the study, 323 were found to have test changes suggestive of cancer, 244 of who subsequently received a cancer diagnosis.

This was a positive response of just over 75%.

The accuracy of a negative predicted value was 97.5%. Unsurprisingly, the test was more accurate in older people and in those with more advanced cancer.

A Galleri test, which is available in the USA, is undergoing a clinical trial in the NHS involving 140,000 volunteers.

A recent article in the Lancet did express concerns about the rates of detection of cancer in its early stages, the level of false-positive results and the inaccuracy of identifying the site

of a suspected cancer. Another concern is that there is little significant evidence to support whether such tests actually prolong life. In the USA, a Galleri test may cost about $950.

Such tests raise a range of ethical, clinical and economic challenges for a cash-strapped NHS. If the tests become more available in the UK, then the management of a patient who receives a positive test (positive signal) could be very difficult.

Questions will include:

- Whether the cost of testing patients with a positive signal but without any definite symptoms, which will cost thousands of pounds, can be justified in a Health Service under pressure given the incidence of false positives?
- Should such tests be funded by the NHS or should they be chargeable?

With regard to negative tests, and particularly tests subsequently shown to be false negatives, how should they be managed?

With both false positive and false negative tests, an 'acceptable figure' for both will be essential because patients who proceed to such tests will have to agree to undergo them on the understanding that false results may occur one in **X** times and so there is a percentage risk that the result will be wrong either way.

If funded by the NHS, how often should they be available? Ten yearly? Five Yearly? Yearly?

Of course, if the result of such cancer tests is the achievement of consistently earlier diagnosis, then to be able to treat patients in a more timely fashion will reduce cancer costs and be more likely to achieve a cure. At present, delays in diagnosis result in the NHS spending fortunes on anti-cancer drugs, often required repeatedly and often in combination with surgery and radiotherapy.

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Earlier diagnosis, quicker treatment and increased success rates would be a huge achievement.

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The latest year for available data is 2019, when the top ten causes of cancer death in the UK were:

1.	Breast	56,987
2.	Prostate	55,068
3.	Lung	48,706
4.	Bowel	44,706
5.	Melanoma	17,845
6.	Non-Hodgkin's Lymphoma	13,979
7.	Head and Neck	13,049
8.	Kidney	12,050
9.	Pancreas	11,031
10.	Bladder	10,515

In that year 387,820 new cancer diagnoses were reported overall, consisting of 200,386 male and 187,434 women. The figures had risen by 5.8% in the two years since 2017.

In 2019 there were 166,502 cancer deaths recorded, of which 88,688 were in men and 77,814 were in women.

Clearly, as testing is refined, as there is quicker follow-up, both of patients with symptoms and those identified in post testing positive cases, and as there is better, quicker diagnosis and successful treatment, inroads will be achieved into the numbers of cancer deaths.

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