Cancer screening

Karol Sikora

Abstract

Cancer screening is a source of much debate. At the interface between public health, specialist care, economics and policy, it creates tensions between professional groups, politicians, the media and the public. A screening test may be cheap, but applying it to a population (with rigorous quality control and effective processing of patients with abnormal results) creates a huge workload and therefore cost. Screening can also have profound psychological effects on individuals. People with false-positive results require investigation and yet are usually found eventually not to have cancer. Unless screening can be shown to reduce mortality from a specific cancer, the resources used are better spent on improving care, and this has led to disparities in screening recommendations between countries. Advances in our understanding of the genetic basis of cancer are likely to provide both new approaches to cancer risk assessment and new challenges for developing screening strategies, by risk banding populations based on polymorphisms in low-penetrance cancer risk genes. The American Cancer Society reviews its guidelines for cancer screening annually. These represent a global gold standard that is difficult to emulate in most healthcare economies.

Keywords breast; cancer detection; cervical cancer; colon; prostate

What's new?

- Patient choice is increasingly used when the overall benefits of screening are uncertain (e.g. mammography in 40—50 year-olds, prostate-specific antigen for prostate cancer)
- Partial automation of image analysis will reduce the expense of cytology and radiograph analysis
- Low-penetrance cancer risk genes are being discovered for several common cancers and will allow effective risk banding of populations
- New imaging technology with lower radiation risk is becoming available to assess patients with equivocal screen-detected abnormalities
- New private-sector providers of health and genetic screening are emerging and will reduce costs and increase consumerism in this area

Definitions

Cancer screening is defined as the systematic application of a test to individuals who have not sought medical attention because of symptoms. It may be opportunistic (offered to patients consulting their doctor for another reason) or population-based (covering a predefined age range, with elaborate call and recall systems). The risk of dying from a cancer always increases with its degree of spread or stage. The aim of screening is to detect cancer in its early, asymptomatic phase. The problem is that many screening tests are relatively crude, and cancers may have metastasized before they are detected by the screen.

- Sensitivity varies between tests. A 100% sensitive test detects all cancers in the screened population. The most rigorous means of calculating sensitivity is to determine the proportion of expected cancers not presenting as interval cases between screens. Good cancer registration is essential when making this calculation.
- Specificity is the proportion of negative results produced by a test in individuals without neoplasia. A 100% specific test gives no false-positive results. Investigation of patients without cancer is a major factor in the cost of screening.

Karol Sikora *PhD FRCP FRCPE FRCR FFPM is Professor of Cancer Medicine at Hammersmith Hospital, London, and Medical Director of Cancer Partners, UK. He was seconded to be Chief of the WHO Cancer Programme. Conflict of interests: none declared.*

Advantages and disadvantages of screening

The advantages and disadvantages of screening (Table 1) must be considered carefully, and vary between cancers and tests. The three main problems in assessing the benefit of any screening test for cancer are lead-time bias, length bias and selection bias, all of which impair the effectiveness of screening as a method of reducing cancer mortality.

- Lead-time bias advances the diagnosis but does not prolong survival, as occurs when the disease has already metastasized though the primary tumour is still small. Patients die at the same time they would have died if the disease had not been detected early.
- Length bias results in diagnosis of less aggressive tumours. Rapidly growing cancers with a poorer prognosis present in the screening interval, reducing the value of the screening process.
- Selection bias occurs even in the best-organized healthcare systems.

Advantages and disadvantages of screening

Advantages	Disadvantages
• Better outcome	• Longer morbidity if prognosis is unaltered
• Less radical therapy needed	• Over-treatment of borderline abnormalities
• Reassurance for those with negative results	• False reassurance for those with false-negative results
• Psychological benefit to population	• Unnecessary investigation of false-positive results
• Attractive to politicians	• Risks of screening test and investigations
• Savings because therapy is less complex	• Resource costs of screening system

Table 1

Worried but healthy individuals (who would present with cancer symptoms early) comply with screening programmes obsessionally, whereas less well-educated and socially disadvantaged individuals do not.[1] In the UK NHS breast cancer screening programme, compliance varies between communities depending on relative deprivation, ethnic mix and degree of social exclusion.

Developing a screening programme

Rational decision-making about cancer screening requires a detailed analysis of factors that may vary between populations.

- The cancer should be common and its natural history properly understood. This enables a realistic prediction of the proposed test's likely value.
- The test should be effective (high sensitivity and specificity) and acceptable to the population. Cervical smears are difficult to perform in many Islamic countries, where women prefer not to undergo vaginal examination, and the take-up rate for colonoscopy is low in asymptomatic individuals because it is uncomfortable and sometimes unpleasant.
- The healthcare system must be able to cope with patients who produce positive results and require investigation. This may be a particular problem at the start of a population-based study.
- Ultimately, screening must improve the survival rate in a randomized controlled setting.

The natural history of many cancers (including incidence and mortality) may change over time for reasons that are poorly understood.[2] In Europe, the incidence of stomach cancer has decreased dramatically over the last few decades, whereas breast cancer deaths reached a peak in the UK in 1989 and have decreased slightly each year since.

Outside pressures: lobby groups often exercise political pressure to implement screening programmes (even when the effectiveness of the programme is undemonstrated) and manufacturers of equipment or suppliers of reagents may exercise commercial pressure. In fee-for-service-based provider systems, there is a huge financial inducement for doctors to screen and investigate, because doing nothing earns no money. The launch of the NHS breast screening service by the UK Government in 1989 was viewed by many as a pre-election vote-winning exercise rather than a rational public health intervention, and there are now similar pressures to introduce prostate cancer screening, though uncertainty remains about the management of men with slightly elevated prostate-specific antigen (PSA: see below).[3]

Guidelines: many groups (e.g. governmental, medical charities, health-maintenance organizations, professional bodies) have produced guidelines on cancer screening. These guidelines vary widely between countries, reflecting bias in interpretation of evidence and cultural values in the practice of medicine; for example, annual PSA testing and digital rectal examination in men over 50 years of age are recommended by the American Cancer Society (ACS), but are not advocated in most other countries. The USA carries out more cancer screening on those populations that can afford it either through insurance or direct payment than any other country. Table 2 compares the current ACS guidelines to those of the UK Department of Health.

Developing countries: the incidence of a particular cancer in a particular country and the economics of screening must be considered carefully — the cost of the technology required must correspond with the gain. Low-cost, direct-inspection techniques for oral and cervical cancer by non-professional health workers seem attractive for achieving tumour down-staging and hence better survival results, but the overall effectiveness of cervicoscopy programmes in India and China has been surprisingly poor. It remains to be seen whether intravital staining with acetic acid can enhance the specificity at little extra cost.[4]

A major cost in instituting any screening procedure is informing the public and then developing the logistics, often under difficult geographical conditions. Cultural barriers may be insurmountable without better education, particularly of girls, who as mothers will become responsible for family health. Low-technology tests have low specificities; as a result, hard-pressed secondary care facilities are inundated with patients with non-life-threatening abnormalities. Detailed field assessment, preferably in a randomized setting, is essential before firm recommendations can be made, but political factors often interfere with this process. The well-meaning charitable donation of second-hand mammography units to some African countries has led to haphazard introduction of breast screening in populations in which the incidence of breast cancer is low and where there are few resources to deal with abnormal results.

Assessing the benefits of screening programmes

The ultimate measure of success in a screening programme is a demonstrable reduction in mortality in the screened population. However, this needs large numbers of individuals, and at least 10 years' assessment for most of the common cancers.

Comparison of American Cancer Society and UK Department of Health guidelines in 2010 for common cancers

	USA	UK
Breast	40+	53—70 (changing to 47—73)
	Yearly mammogram	3-yearly mammogram
Colon	50+	60+
	Yearly FOBT	One-off FOBT
	5-yearly sigmoidoscopy	
Prostate	50+	50+
	Yearly PSA	Patient choice
Lung	None	None
Cervix	18—70	25—50
	2-yearly smear	3-yearly smear
		50+
		5-yearly smear

FOBT, faecal occult blood testing; PSA, prostate-specific antigen.

Table 2