

SCREENING FOR COLORECTAL CANCER – BENEFIT OR BURDEN?

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Australia is currently in the process of undertaking pilot studies to evaluate the probable efficacy of a national mass screening programme to reduce colorectal cancer mortality. Adelaide (South Australia), Melbourne (Victoria) and Mackay (Queensland) have been chosen as the sites for the \$7.3 million (£2.5 million) four-year trial programme, which began in 2002, to test the feasibility and acceptability of colorectal cancer screening using faecal occult blood testing (FOBT). The project involves the recruitment of up to 50,000 people between 50 and 75 years of age.¹ Firm recommendations are not expected to emerge before 2007.

Given that such an undertaking will consume measurable health resources, it is worthwhile examining the issues surrounding colorectal cancer detection, particularly in view of the diametrically opposed views of countries with similar disease incidences, such as the US and New Zealand, concerning the role of mass population screening. Both the US Preventive Services Task Force and the American Cancer Society^{2, 3} recommend screening be performed for all asymptomatic people at average risk for colorectal cancer, by annual FOBTs from age 50 years, plus periodic flexible sigmoidoscopy (ACS recommendation five-yearly if results remain negative). These guidelines are in close accord with those of Canada.⁴ In contrast, however, neither population nor pilot colorectal cancer screening programmes have recently been recommended by New Zealand health authorities.⁵ In the UK, a middle road is being pursued, in which a pilot study to determine the feasibility of a population-based screening programme has been implemented, as in Australia. No results are yet available from the UK trial, which is however now in the completion phase.⁶

To more fully understand the reasons for such opposing views, one needs to look at early cancer detection not just from a clinical viewpoint, but also socially, economically, philosophically and psychologically.

It is well-recognised that, in developed countries:

- colorectal cancer is the commonest internal malignancy, and the second leading cause of death from cancer, with a lifetime risk of disease of about 1 in 40 and risk of death 1 in 20;^{7, 8}
- prognosis is closely related to disease stage at diagnosis, with five-year survivals of 90% for

localised disease, 60% for regional disease and 6% for those with distant disease. About one-quarter of patients currently present with metastatic disease;⁷

- 75% of the population are at average risk for colorectal cancer, 20% at moderate risk and 5% at high risk, with family history a major factor in determining individual susceptibility;⁹
- almost all colorectal cancers originate from adenomatous polyps, with about a ten-year interval between the development of a small polyp (1 cm) and presence of established cancer, providing an opportunity for early detection of pre-existing lesions and prevention of malignancy by polypectomy;
- mass screening by FOBT (and probably also flexible sigmoidoscopy, colonoscopy and double-contrast barium enema) can reduce colorectal cancer mortality;¹⁰⁻¹⁹ and
- environmental factors play a significant role in colorectal cancer development, as shown by migrant studies and 20-fold international variations in colorectal cancer disease incidence.^{20, 21}

The above points appear to present a strong case for cancer prevention through early detection of this disease, but there are a number of major difficulties to consider.

One of the most important such issues is compliance. In the three major randomised controlled trials of FOBT population screening, the Minnesota USA trial by Mandel *et al.* achieved over 90% compliance for at least one FOBT, but only 45–60% compliance for all tests over a 13-year period. Kronborg's group in Funen, Denmark achieved 67% compliance for initial screening but only 46% for all five biennial tests, and the Nottingham UK trial led by Hardcastle reported 60% compliance for at least one test but only 24% of the screened cohort completed all biennial tests over a ten-year period.

Given that these trials were organised and managed by committed researchers, it is unlikely these figures would be bettered at national levels. In Japan, the national CRC programme introduced in 1998 has achieved a population uptake of less than 20%,²² and after more than 25 years, national FOBT compliance in Germany is 20% for men and 30% for women.²³ These figures from actual national programmes are in line with calculations of workers such as Delco and Sonnenborg, who predicted a 6% average decline in FOBT compliance,

with an initial compliance of 40–75%.²⁴ It is worth noting that similar low levels of compliance have been observed using other screening methods to detect bowel cancer – with, for example, only 30% of even high-risk patients attending for regular sigmoidoscopy over a seven-year period.²⁵

Obtaining high levels of population recruitment for colorectal cancer screening is clearly a major determinant of consequent health outcomes. There is evidence that people do not simply fail to attend for screening in a passive fashion, but often make an active decision not to be tested, the commonest reasons including feeling well (most common reason), fear of cancer or further tests, and lack of time.²⁶ Although patient education may improve screening acceptance,^{27,28} the general population's disinclination to be as concerned about certain health matters as their doctors appears worthy of acknowledgment and understanding, even if it is not ultimately respected.

In addition to poor compliance, inadequate follow-up of positive FOBT tests, and investigative limitations have been shown to have further adverse impact on screening attempts. In one recent study, 37–63% of FOBT-positive patients were reported as having not received appropriate further evaluation.²⁹ Of those patients who are properly investigated, usually by endoscopy or radiology, about 5–20% will be falsely negative for significant neoplasia.^{30,31}

Although general consensus exists that the cost-effectiveness of colorectal cancer screening lies midway between that for breast and cervical cancer,³² major differences of opinion persist regarding the appropriate screening test to employ and the optimal time interval between tests. Recommendations range from FOBT (annually or biannually from age 50 in normal-risk asymptomatic patients),^{9–11} through flexible sigmoidoscopy 5–10-yearly,^{33, 34} or double-contrast barium enema three-yearly as a first-line approach,³⁵ to the view that colonoscopy once every 5–10 years is the best method.^{36,37} Among those who agree that FOBT is the most suitable test for screening, there is uncertainty as to the optimal type of FOBT to use and the number of samples to be taken.³⁸

At the root of these arguments lies a complex web of factors, which include costs, personnel and equipment availability, test performance characteristics, complication rates, infrastructure needs, individual attitudes and perceived health priorities.^{34,39,40–2}

A different perspective on the topic may be obtained by an examination of the relationship between screening by an individual clinician and mortality reduction. It has been estimated that 1,250 patients would need to be screened to prevent one death from colorectal cancer.⁴³

In Australia, the average GP has 210–20 patients between 50 and 70 years of age on his or her list.^{44,45} For such a doctor, it would take about ten years to prevent one death from colorectal cancer within the practice, even if every single eligible patient was screened at each of the five biennial FOBT test intervals. Given the probable patient-compliance rate, the real time period required is closer to 40 years, i.e. beyond the working life of many GPs today.

This basic equation does not include important negative factors for those screened, such as:

- psychological distress from false-positive results, which comprise 65–80%+ of positive FOBTs;^{24,43}
- incorrect reassurance from false-negative results (<1–30% for cancers, and 10–85% for adenomas, depending on size);^{24,43}
- economic and time costs related to further investigations;⁴⁵
- risks and complications of follow-up procedures, including many unnecessary colonoscopies (2% serious sequelae, 0.02% mortality), and bowel surgery (mortality rate variously reported between 1–30% at different centres);^{43,46,47} and
- no reduction in overall mortality (there appeared to be a slight increase in cardiovascular mortality among screened cohorts, which offset reduced deaths from colorectal cancer).^{10–12}

Many GPs focus early detection efforts on patients perceived as 'at increased risk', with colonoscopy the favoured screening modality but, since the majority of colorectal cancers occur in patients at average risk, this approach has no potential in it to significantly reduce mortality.⁴⁹

Clinicians cannot therefore expect to obtain identifiable reductions in colorectal cancer mortality through individual efforts – in this sense, population screening may be much like taking hypotensive medication – the benefits may never be actually felt, but the side-effects are. A long-term community-based view is needed to properly assess the role of early bowel cancer detection and, as in any mass screening programme, 'most people receive a little harm so that a few may benefit greatly'.

Population screening for colorectal cancer also requires the infrastructure and resources to effectively evaluate positive results (one of ten World Health Organization criteria for effective population screening).⁵⁰ Where FOBT or double-contrast barium enema is used as a screening modality, patients showing possible evidence of neoplasia will usually require colonoscopy.¹⁰ This will also apply to a significant number of patients with distal polyps identified by flexible sigmoidoscopy, in order to exclude concurrent proximal lesions.⁵¹

In 1999, the European Group for Colorectal Cancer

Screening issued a strong recommendation for the widespread use of repeated FOBT tests in the early detection of colorectal cancer.⁵² This recommendation was based on Level I evidence indicating a reduction in colorectal cancer mortality was achievable by such means.¹⁰⁻¹² In contrast, however, the UK joint position statement in 2000, released by the British Society of Gastroenterology, the Royal Colleges of Physicians, and the Association of Coloproctology of Great Britain and Ireland, did not recommend mass screening at that time. The joint report concluded that, in view of the inadequacy of current resources for bowel cancer investigation, the extra demands from mass screening could not be met, and had the potential to further compromise the diagnosis and management of symptomatic patients.⁵³ Future decisions were regarded as dependent on the results of ongoing UK trials.

These views were echoed in New Zealand, where, in 1999, the National Health Committee Working Party on Population Screening for Colorectal Cancer strongly advised against the introduction of mass screening.⁵⁴ The recommendations were based on a careful and comprehensive assessment of the major factors involved in establishing a mass colorectal cancer screening programme in a developed country, which are summarised in Table 1.

TABLE 1
Expected outcomes of a national screening programme.

• Unit of eligible population (50–74)	1,000,000
• Expected participation rate 60%	600,000
• Number of FOBTs (dependent on type)	1.2–3.6 million
• Cost of FOBTs (annual screening)	£10–15 million*
• Number of annual colonoscopies generated	5,000 (30–5% increase)
• People diagnosed with cancer	10,000
• Deaths from all causes	150,000
• Deaths from colonoscopy	5
• Deaths from colorectal cancer	5,000
• Screening deaths averted by screening	750

*£ sterling

These disparate views may be understood from the

standpoint of the relationship between research and reality. The potential lack of concordance can be illustrated by recent studies of mammography in Sweden, in which significant mortality reductions obtained in pilot programmes, were not matched by those obtained 'in the field'.⁵⁵ Differing opinions concerning the role of mass colorectal cancer screening may therefore depend, at least in part, on the extent to which research trial findings are extrapolated to the wider community. This type of evaluation will be an important aspect of future screening decisions based on the outcomes of trials such as those now underway in both Australia and the UK.

For the UK, a mass screening programme based on FOBTs would translate into total costs in the order of £100 million. This financial outlay would need to be accompanied by support and infrastructure including public education,^{56,57} the establishment of quality control systems⁵⁸ and personnel training. The latter is of particular importance in regard to endoscopic follow-up services, where complication rates are significantly higher amongst inexperienced operators.⁵⁹ There are now attempts by some authorities to address some of these concerns by minimising or bypassing FOBTs in favour of ten-yearly colonoscopy as the procedure of choice for reducing colorectal cancer mortality.^{60,61} This approach has not yet been formally adopted by any country, however.

Given the widely differing opinions pertaining to major aspects of early colorectal cancer detection, it appears difficult to draw any firm conclusions concerning the role of mass screening. To add to the problem, it is known that external factors play a significant role in the pathogenesis of bowel cancer. Migrant studies indicate that environmental changes rapidly alter the incidence of bowel cancer, and have been estimated to be the main cause of disease in up to 35% of patients.⁶² Very low physical activity, alcohol consumption, cigarette smoking and high fat intake all increase disease risk, whereas a combination of regular exercise plus a diet rich in fruits and vegetables appears to be protective.⁶³

In view of the lack of consensus concerning secondary prevention, and the significant influence of lifestyle on the incidence of bowel cancer, should the focus be instead on primary prevention? If the suggestions that this entails a concerted effort to encourage people to lose weight, stop smoking, avoid excessive alcohol, eat healthy foods, and exercise regularly sound familiar, that is probably because they are!

Perhaps the question should not relate to the pros and cons of screening for colorectal cancer, but instead to the level of commitment of both patients and doctors to ensure that prevention rather than detection is the real starting point for good health.

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