Screening for colorectal cancer

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Screening for colorectal cancer is feasible and there is increasingly compelling evidence to show that such programmes can save lives at a cost similar to that of the existing breast cancer screening programme.

Colorectal cancer is the third commonest malignancy in the UK, killing around 20,000 people per annum. Colorectal cancer is equally prevalent in men and women, and usually occurs in later life (aged 60–70 years). The incidence and mortality of colorectal cancer have remained approximately static for the past 40 years, although there are recent trends showing slight declines in both in the UK and in the US. The decrease in mortality may reflect a tendency towards earlier diagnosis, possibly as a result of increased public awareness of the disease. Surgery remains the mainstay of treatment for colorectal cancer, but early diagnosis makes it more likely that the tumour can be completely resected and thereby improves the chance of a cure.

Early diagnosis in colorectal cancer is challenging because the symptoms of bowel cancer are very similar to the symptoms of a number of benign bowel conditions such as haemorrhoids, irritable bowel syndrome and diverticular disease. Population screening may provide a good opportunity to improve survival and reduce the incidence of this important condition, but which test and can we afford it?

Why screen for colorectal cancer?

It is widely accepted that the vast majority of colorectal cancers result from malignant change in polyps (adenomas) occurring in the lining of the bowel 10–15 years before malignant change occurs. The best available evidence suggests that only 10% of 1 cm adenomas undergo malignant change after 10 years. The incidence of adenomatous polyps in the colon increases with age, and although adenomatous polyps can be identified in up to 20% of the population, most of these are small and unlikely to undergo malignant change. The vast majority (90%) of adenomas can be removed at colonoscopy, obviating the need for surgery. Other types of polyps occurring in the colon such as metaplastic...
(alternatively known as hyperplastic) polyps are usually small and have much lower malignant potential than adenomas.

Colorectal cancer is a common condition with a known pre-malignant lesion (adenoma). There is a relatively long time course for malignant transformation from adenoma to carcinoma and outcomes are markedly improved by early detection of adenomas and early cancers. Thus there is great potential to reduce the mortality from this disease by detecting adenomas and early cancers through screening asymptomatic individuals.

Which screening test(s) for population screening?

Since bowels are something of a taboo subject, education about bowel cancer is poor. A recent survey revealed that only 30% of the British population were aware that cancer of the bowel occurred. Such ignorance only adds to the difficulties of early detection for this form of cancer.

In order for a screening test to be applicable to large populations, it has to be inexpensive, reliable and acceptable. Many different screening tests have been tried in order to detect early colorectal cancer (Table 1). Perhaps the simplest and least expensive is symptom questionnaire, but this has proved predictably insensitive and only becomes reliable when the tumour is relatively advanced. Digital rectal examination and rigid sigmoidoscopy both suffer from the limitation that they only detect rectal or rectosigmoid cancers, are unpleasant and invasive.

Flexible sigmoidoscopy has the capacity to detect 80% of colorectal cancers as it can examine the whole of the left colon and rectum. A strategy to provide a single flexible sigmoidoscopy for adults aged 55–65 years aimed at detecting adenomas may be cost effective. A multicentre trial of this strategy for population screening is currently under evaluation. Although flexible sigmoidoscopy is more expensive than rigid sigmoidoscopy, it is generally more acceptable to patients (less uncom-
fortable) and has much higher yield than the rigid instrument. Many nurses are now trained to undertake flexible sigmoidoscopy making potential screening programmes using this modality more cost effective. In a population screening programme, uptake of the offer of the screening test is crucial; it seems that compliance with flexible sigmoidoscopy is likely to be around 45% and, of these, 6% will subsequently require full colonoscopy. The effect this will have on the incidence of and mortality from colorectal cancer is uncertain. A large multicentre trial is underway and will provide much needed information in 2003.

Colonoscopy is the gold standard technique for examination of the colon and rectum, but it is expensive. The need for full bowel preparation, sedation and the small risk of colonic perforation make it unacceptable for population screening. Colonoscopy is, however, the investigation of choice for screening high risk patients (hereditary non-polyposis colorectal cancer and patients with long-standing ulcerative colitis).

Barium enema like colonoscopy examines the whole colon and rectum; however, although it is cheaper and has a lower complication rate than colonoscopy, it is invasive and requires full bowel preparation. Whereas colonoscopy may be therapeutic (polypectomy), barium enema does not allow removal or biopsy of lesions seen. There are no population screening studies using barium enema.

CT colography (virtual colonoscopy) is a new radiological technique which may have a role in population screening for colorectal cancer. Although it requires full bowel preparation, very expensive CT scanners and computing facilities, it is minimally invasive and views of the whole colon can be obtained within 5 min. Preliminary data suggest that this technique has a similar sensitivity for large polyps and cancers to colonoscopy or barium enema. As yet, there are no published trials of CT colography in population screening, but this is surely only a matter of time. CT colography has the potential to be cost effective and to reduce the need for colonoscopy in population screening.

Faecal occult blood tests are the most extensively studied screening tests for colorectal cancer. These tests detect haematin from partially digested blood in the stool. The overall sensitivity of faecal occult blood tests for colorectal neoplasia is, therefore, only 50–60%, though their specificity is high. In screening studies using faecal occult blood tests, individuals are invited to take two samples from each of three consecutive stools. Compliance tends to be around 50–60%, but with population education this could be improved significantly. Individuals with more than 4/6 positive tests (around 2% of ‘acceptors’) need colonoscopy.

Several large randomised studies have shown that faecal occult blood screening is feasible and two studies have shown that such screening reduces mortality from colorectal cancer. In the Nottingham study, for
every 100 Haemoccult-positive individuals, 12 had cancer and 23 had adenomatous polyps. The screen-detected cancers tended to be at an earlier stage than those presenting symptomatically (26% Dukes’ stage A screen detected versus 11% Dukes’ stage A in controls). The downside of faecal occult blood screening at present is its relatively low sensitivity which means that some cancers will be missed on each round of screening. The Nottingham data suggest that screening every 2 years only detects 72% of cancers. This could be improved by testing annually and by using more sensitive immunologically based faecal occult blood tests.

**Who should be screened?**

There is a spectrum of risk for colorectal cancer. Although 19% of the population will develop adenomatous polyps, only 5% will develop colorectal cancer. This equates to a 1 in 20 life-time risk for colorectal cancer. Most of these cancers will occur in people between the ages of 65–75 years, but the peak incidence for adenomas is slightly earlier at 55–65 years of age. Thus population screening for colorectal cancer should target these age groups starting at age 55 years and ending at 75 years. In addition, there are some individuals in the population who will have inherited a much higher susceptibility to colorectal cancer (Table 2). Some individuals will have inherited a well-recognised single gene disorder such as familial adenomatous polyposis or HNPCC, whereas others (the vast majority) will have inherited an undetermined, and often unknown, genetic abnormality. These individuals tend to develop colorectal cancer before the age of 50 years and, therefore, screening for these high-risk individuals needs to be tailored to their individual risk pattern. Such individuals may also be at risk for cancers at other sites and screening for ovarian, breast and endometrial cancers may be appropriate in some of these cases. The advice of clinical geneticists in these cases can be invaluable.

**Table 2 Inherited risk of colorectal cancer**

<table>
<thead>
<tr>
<th>High risk</th>
<th>Medium risk</th>
<th>Low risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Familial adenomatous polyposis (FAP)</td>
<td>One first degree relative with colorectal cancer presenting &lt; 45 years of age</td>
<td>One first degree relative only with colorectal cancer presenting &gt; 55 years of age</td>
</tr>
<tr>
<td>Hereditary non-polyposis coli (HNPCC)</td>
<td>Two or more first degree relatives with colorectal cancer</td>
<td>No family history of colorectal cancer</td>
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**Advances in colorectal cancer**

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Cost effectiveness of screening

An economic evaluation conducted in parallel with the Nottingham trial demonstrated that, even within the then-existing follow-up period, the cost per life-year gained as a result of faecal occult blood screening was superior to that of many other interventions currently being introduced into the UK health care system. Extrapolations beyond the trial period suggested that cost-effectiveness would improve with follow-up, as longer-term survival advantages became more prominent. This conclusion appeared robust against plausible variations in compliance rates and target age ranges, because of approximately equivalent cost-outcome compensations (for example, lower compliance reduces the overall effectiveness of screening, but it also reduces the costs). The Danish Faecal Occult Blood Screening Trial employed a similar clinical protocol to that of Nottingham, and also encompassed a parallel economic evaluation. Although they employed somewhat different economic evaluation methodologies, both groups of researchers came essentially to the same conclusion, namely, that in each of their countries, faecal occult blood screening for colorectal cancer would represent better value-for-money than did existing programmes of screening for breast cancer.

Beyond faecal occult blood screening, mathematical modellers working independently of trials have evaluated a wide range of other theoretical screening protocols, involving endoscopy, radiology and faecal occult blood tests, in various combinations, at various ages and at various screening intervals. The confidence intervals surrounding estimates derived from theoretical models are invariably wider than those derived from trial data, because so much more has to be assumed (e.g., compliance rates and likely procedure costs). Whilst modelling exercises have to be interpreted cautiously, the message is emerging that some combined modality screening strategies are capable of offering acceptable value-for-money. Many are likely to be more effective, given the relatively poor sensitivity of faecal occult blood tests, and some might even prove to be more cost effective.

Potential harm from screening for colorectal cancer

Although it has been suggested that considerable anxiety and psychological morbidity may be caused by inviting populations to participate in screening for colorectal cancer, there is little evidence to substantiate this. Indeed, in the Nottingham trial, there was no evidence of any long-standing psychological morbidity from the screening programme. Similarly, there is no evidence that screening for colorectal
cancer leads to false re-assurance from negative tests. However, there are complications from colonoscopy (perforation and haemorrhage). The incidence of these complications is around 1 in 2000 procedures, and usually occurs in therapeutic colonoscopy (endoscopic polypectomy) rather than in diagnostic procedures. Mortality from such events is fortunately very rare.

**Key points for clinical practice**

- Screening for colorectal cancer using faecal occult blood tests is feasible and there is increasingly compelling evidence to show that such programmes can save lives at a cost similar to that of the existing breast cancer screening programme.
- Only flexible sigmoidoscopy presents a promising alternative to faecal occult blood screening, but conclusive data will not be available for another 5–7 years.
- To undertake such a programme in the UK, there would need to be a considerable investment in colonoscopy facilities and expertise.
- Several countries, including the US, have instituted screening programmes utilising one or both of these modalities. Whether the UK follows will be determined by political decisions.

**Bibliography**


