

Results of the first round of a demonstration pilot of screening for colorectal cancer in the United Kingdom

UK Colorectal Cancer Screening Pilot Group

Abstract

Objective To assess the feasibility of introducing into the UK's NHS a national screening programme for colorectal cancer based on faecal occult blood testing.

Design Demonstration pilot.

Setting Two English health authorities and three Scottish health boards.

Participants People aged 50-69 years.

Results 478 250 residents of the pilot areas were invited to take part in the screening programme. Uptake (the proportion in whom a final faecal occult blood test result was available) was 56.8% (n = 271 646). The overall rate of a positive test result was 1.9% and the rate for detecting cancer was 1.62 per 1000 people screened. Both these values were higher in Scotland than in England, higher in men than in women, and increased with age. The positive predictive value was 10.9% for cancer and 35.0% for adenoma. 552 cancers were detected by screening; 92 (16.6%) were polyp cancers. 48% of all screen detected cancers were Dukes's stage A, and 1% had metastasised at the time of diagnosis.

Conclusions Screening for colorectal cancer by testing for faecal occult blood is feasible within the context of the United Kingdom's NHS. Screening should lead to a reduction in deaths from colorectal cancer in the population offered screening.

Introduction

Population based randomised trials are necessary to demonstrate the efficacy of a screening strategy.¹ In colorectal cancer, guaiac based testing of faecal occult blood is the only screening modality that has been shown to reduce disease specific mortality by means of such trials. Studies of most relevance for the United Kingdom were those carried out in Nottingham, England, and in Funen, Denmark, which showed reductions in deaths from colorectal cancer of 15% and 18%, respectively, after screening.^{2 3}

Although it is accepted that screening for faecal occult blood is efficacious, randomised trials are carried out by highly motivated research teams.⁴ On the advice of the National Screening Committee, the UK Department of Health carried out a demonstration pilot to test the feasibility of a national screening programme for colorectal cancer. We report on the uptake, outcomes, and consequences of the project.

Methods

The methods used to set up and run the pilot are described elsewhere.⁵ Briefly, the pilot was carried out in two areas: Coventry

and Warwickshire (two English health authorities, population around 800 000), and Grampian, Tayside, and Fife (three Scottish health boards, population around 1.2m). Guaiac based faecal occult blood tests were carried out over a two year period. The pilot was designed to assess the short term outcomes that would indicate whether a national programme would reduce mortality from colorectal cancer.

Participants and screening process

The faecal occult blood test used in the pilot (Hema-screen; Immunostics, NJ, USA) had identical biochemical characteristics to that of the test in the Nottingham and Funen trials. Faecal material was assessed from two samples taken from each of three stools from each participant, with repeat testing for weak positive results (one to four samples positive) after appropriate dietary restriction. People who had a positive test result and therefore needed further investigation were defined as test positive.

All residents of the pilot areas aged 50-69 were invited to participate. They were sent a test kit by post from a central office. The kit included information on the nature and purpose of screening and instructions on how to complete the test and return it to a central laboratory. This information, developed to explain the concept of false positive and false negative test results and possible adverse effects of screening, had been tested by an independent market research organisation. The two laboratories used for the pilot were accredited by Clinical Pathology Accreditation (UK), Sheffield.

Colonoscopy was carried out by endoscopists who attended evaluation sessions at the endoscopy unit at St Mark's Hospital, Northwick Park, and who agreed to submit their results to a central database and quality assurance programme. Patients who had an incomplete colonoscopy were offered a double contrast barium enema. Histopathological examination of specimens (biopsy, polypectomy, and resection) was carried out by specialist gastrointestinal pathologists, with quality assured by circulation of a pertinent slide.

The pilot was evaluated independently by a multidisciplinary group from the universities of Edinburgh, Warwick, and Essex. The group examined performance against central benchmarks derived from the Nottingham trial. We set out the key findings of the pilot in this context. The group also examined psychosocial and ethnicity issues related to acceptability and uptake of screening, the impact of screening on routine services, stakeholders' attitudes to screening, and the health economics of screening. Details can be found in the final report of the evaluation group (www.cancerscreening.nhs.uk/colorectal/finalreport.pdf).



Details of the pilot group are on bmj.com

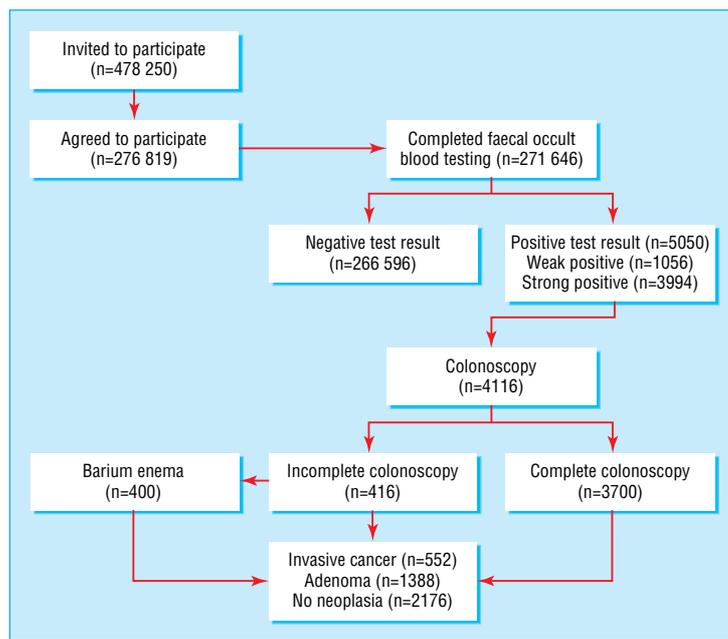


Fig 1 Flow diagram of pilot

Results

Screening started on 29 March 2000 with the despatch of the first test kits. The prevalence (first) round was completed on 19 May 2003 with the last colonoscopy. The results presented here pertain to uptake, the rate of positive test results (positivity), colonoscopy, positive predictive value, and distribution of stage of cancer. Figure 1 details the flow of participants through the pilot.

Uptake and positivity

Overall, 478 250 residents (England 185 267, Scotland 292 983) were invited to participate; testing was completed for 271 646 (56.8%). This uptake was higher for England than for Scotland (table 1), higher in women than in men, and increased with age (fig 2). Of 276 819 responders, 98.1% (n = 271 646) completed

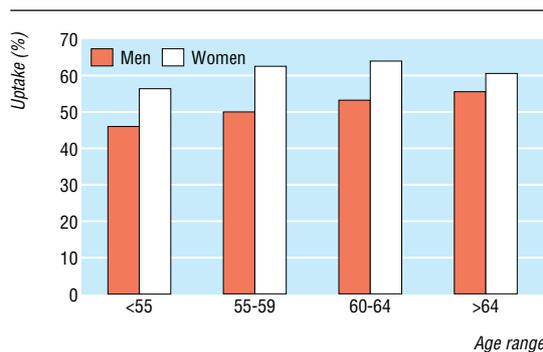


Fig 2 Variations in uptake of faecal occult blood test by age and sex

the test. The overall uptake (56.8%) was comparable to the Nottingham study (57% in the prevalence round).²

The overall positivity rate was 1.9% (England 1.6%, Scotland 2.1%; P < 0.001). Although the positivity rate in the Nottingham study was 2.1%, this trial embraced a wider age range (50-74) than the pilot; the rate was 1.8% for the 50-69 age range (J H Scholefield, personal communication, 2003).² Thus, although the results for England were similar to those for Nottingham, the positivity rate for Scotland was higher (see table 1). Men had a higher rate than women, and positivity increased with age (fig 3).

Colonoscopy

Overall, 3700 of 4116 people had a complete colonoscopy (completion rate 89.9%). The uptake of colonoscopy among people with a positive test result was 81.5% (4116 of 5050), and only 76 (1.5%) were deemed medically unfit to undergo the examination. In total, 858 (16.9%) did not attend, but 172 (20%) of these were under follow up, 69 (8%) had undergone recent colonoscopy, 51 (6%) had opted for colonoscopy in a private clinic, and 17 (2%) had no colon.

Colonoscopy was accompanied by some morbidity. Ten patients (0.24%) were admitted for overnight observation because of bleeding or abdominal pain; 13 (0.32%) were readmitted for the same reasons. None required intervention. Two people had perforations (0.05%), one owing to the size of a polyp after polypectomy.

Positive predictive value

The positive predictive values of a positive test result were 10.9% for invasive cancer and 35.0% for adenoma. The values for cancer were higher for Scotland and in men. All values compared

Table 1 Uptake and positivity rate in pilot screening for colorectal cancer compared with prevalence round of Nottingham trial. Values are numbers (percentages)

Variable	England (n=185 267)	Scotland (n=292 983)	Both (n=478 250)	Nottingham (n=53 810)
Uptake*	109 609 (59.2)	162 037 (55.3)	271 646 (56.8)	30 672 (57.0)
Positive test result†	1714 (1.6)	3331 (2.1)	5050 (1.9)	552 (1.8)

Values are standardised to population of men and women aged 50-69 years.

*Participants with final test result.

†Result indicating further investigation.

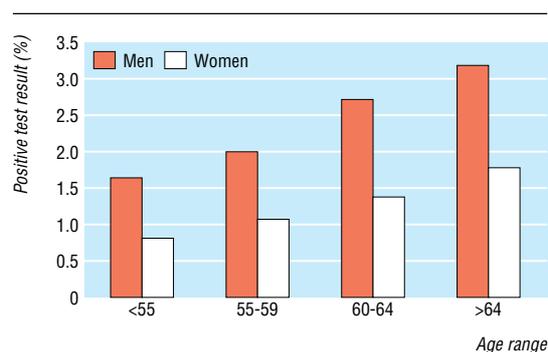


Fig 3 Variations in positivity of faecal occult blood test by age and sex

favourably to those of the Nottingham study in the 50-69 age range (table 2).

Stage distribution of screen detected cancer

Overall, 552 cancers detected by screening were diagnosed, of which 92 (16.6%) were invasive polyp cancers, removed at colonoscopy. In the pilot, if polyp cancers with no information on staging (colectomy to remove residual disease after polypectomy not carried out) were classified as Dukes's stage A, then 265 (48%) of the screen detected cancers would be at stage A and five (1%) at stage D (with metastases; fig 4).

The proportions of screen detected cancers presenting at Dukes's stages A or B were similar for England and Scotland. Both were comparable to the Nottingham values at the first invitation to participate (table 3).

Neoplasia detection rates

The cancer detection rate for the pilot was 1.62 per 1000 people screened, and 6.91 for all neoplasia (cancers and adenomas). The cancer detection rate in England was comparable to the 50-69 age range in the prevalence round of the Nottingham trial whereas it was higher in Scotland (table 4). The overall detection rate for neoplasia was higher in Scotland than in England, particularly for men.

Discussion

Screening for colorectal cancer by testing for faecal occult blood is feasible within the context of the United Kingdom's NHS, as shown by this demonstration pilot conducted in two health authorities in England and three health boards in Scotland. Randomised trials of screening by faecal occult blood testing have shown reduced disease specific mortality, but screening for cancer remains controversial.^{2 3 6 7} The most important question was whether the short term outcomes of the randomised trials could be achieved by a comprehensive screening programme covering large, representative areas of Britain; if this was possible, then a national programme could reasonably be expected to bring about a comparable reduction in mortality from colorectal cancer. The results of the trial from Nottingham were used as benchmarks as this was the largest population based trial of

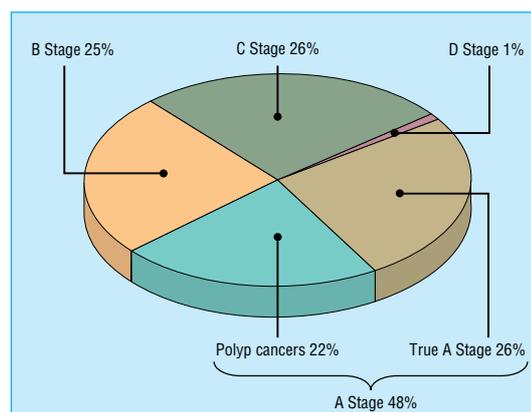


Fig 4 Dukes's stage of cancers detected by screening in pilot. "Polyp cancers" are defined as invasive cancers removed at colonoscopy when colectomy was not carried out

screening for colorectal cancer and was carried out in the United Kingdom.

The overall uptake and number of positive test results were almost identical to those of the Nottingham trial. The higher positivity rate in Scotland was probably related to the higher rate of cancer detection. The positive predictive value of the faecal occult blood test and the distribution of stage of screen detected cancers were comparable to the Nottingham trial. Thus the pilot has shown that the outcomes believed necessary to bring about a reduction in mortality from colorectal cancer can be achieved by the UK's NHS outside the context of a randomised trial. There are, however, some other important considerations.

Age range and uptake

Firstly, only those aged 50-69 years were offered screening on the basis of the fall off in uptake in people over 70 in the Nottingham study.² It is likely that the elderly population would be more willing to accept screening than was the case when the Nottingham trial was in progress. Furthermore, data from the Funen trial indicate that if the age at entry to the study had been raised from 50 to 55 then this would have missed 3% of the screen detected cancers whereas lowering the age at completing the study from 74 to 69 would have missed 25%.⁸ Before implementing national screening, therefore, consideration should be given to the appropriate age range to be invited to participate.

Secondly, around 40% of the population declined to take part in the pilot. Uptake tended to increase with age, further highlighting the need to reconsider the age range to be invited. Women were more likely to comply than men, which may be related to women's greater exposure to screening. This indicates the need to improve awareness of screening in men. Over 10% of participants with a positive result for faecal occult blood testing did not take up the offer of colonoscopy despite the implications of the result being explained by the pilot nurses. This may reflect a lack of understanding of the screening process at the time of initial acceptance, and calls into question the adequacy of the information provided to participants.

Table 2 Positive predictive values of colonoscopies conducted in screening pilot and Nottingham trial

Variable	Men			Women			Both		
	England	Scotland	Nottingham	England	Scotland	Nottingham	England	Scotland	Nottingham
Cancer*	11.6	12.7	10.1	9.9	10.3	8.5	10.2	11.8	9.5
Neoplasia†	53.7	53.6	—	36.1	37.3	—	46.9	47.3	—

Nottingham values are for prevalence round and age corrected for 50-69 years but do not include all polyp cancers (age corrected values for total neoplasia not available).

*Includes polyp cancers.

†Includes all invasive cancers and adenomas.

Table 3 Dukes's stage of colorectal cancer in pilot and in Nottingham trial at first invitation to participate. Values are numbers (percentages)

Dukes's stage	England	Scotland	Nottingham
Not available	7 (5.3)	28 (9.4)	0
Available:	124 (95.3)	270 (90.6)	83 (100.0)
A or B	89 (71.8)	197 (73.0)	59 (71.1)
C or D	35 (28.2)	73 (27.0)	24 (28.9)

Polyp cancers included in category A when nodal status is unknown.

Colonoscopy

The completion rate for colonoscopy of around 90% was better than the UK average,⁹ but the pilot areas were chosen on the basis of being able to provide colonoscopy to the required standard. National programmes will require a high quality colonoscopy service. This service will need to accommodate screening colonoscopies as well as the increased demand created by the surveillance of patients with screen detected adenomas, and it will also need to reduce waiting lists for patients with symptoms. It is therefore timely that endoscopy training centres have been established in England, and that guidelines for surveillance by colonoscopy of patients with adenomas have recently been issued.¹⁰⁻¹² It will, however, require a concerted effort from the training centres and the organisations governing gastroenterology and colorectal surgery to effect a programme of accelerated training to meet the demand. The role of nurse endoscopists within the screening process will also have to be clarified.¹³

Primary care involvement

One of the concerns at the beginning of the pilot was the involvement of general practitioners at the invitation stage. Previous research by the Nottingham group had shown that screening invitations signed by a general practitioner were more likely to be accepted than those issued by an unfamiliar individual or organisation.¹⁴ To minimise the impact on primary care it was decided that the invitation letters should be signed by the lead clinicians. The uptake was similar to the first round of the Nottingham study.

Sensitivity and specificity

Another source of concern is the diagnostic sensitivity and specificity of the guaiac based faecal occult blood test. Interval data on cancer from the Nottingham study have indicated that the test may only be about 50% sensitive in a screening context, and that about half of all colonoscopies carried out on the basis of a positive test result show no evidence of neoplasia.² Endoscopy of the lower gastrointestinal tract is widely used for screening, and both colonoscopy and flexible sigmoidoscopy have their proponents.¹⁵⁻¹⁶ Colonoscopy has the advantage of high sensitivity and specificity, but it is expensive and associated with morbidity, and in the absence of randomised trials, the cost and benefit ratio for population screening is difficult to determine.

Flexible sigmoidoscopy

Flexible sigmoidoscopy is the subject of an ongoing randomised trial, and preliminary results are encouraging.¹⁶ Higher detection

What is already known on this topic

Population based randomised controlled trials have shown that screening by faecal occult blood testing for colorectal cancer can reduce mortality

What this study adds

A screening programme for colorectal cancer using faecal occult blood testing is feasible in the United Kingdom

Such a programme should lead to a reduction in mortality from colorectal cancer

rates were achieved for cancer and adenoma using a single examination at age 55-64 than by using a single round of screening by faecal occult blood testing. The proportion of cancers detected at Dukes's stage A (62%) was also more favourable. However, non-randomised evidence from Denmark comparing a single flexible sigmoidoscopy and faecal occult blood test with biennial testing over 16 years indicates that a screening programme using faecal occult blood testing has a similar diagnostic yield to once only flexible sigmoidoscopy.¹⁷ Mortality data from the flexible sigmoidoscopy trial are not yet available, but only people expressing an interest in screening were recruited and randomised so that compliance is impossible to estimate for the population.

Conclusion

Health ministers in England and Scotland have indicated that national colorectal cancer screening programmes will be introduced, but the screening modalities and time scales have yet to be decided.¹⁸⁻¹⁹ Screening by faecal occult blood testing is not perfect, but it seems viable within the UK NHS, and there is now abundant evidence that it can have a major impact on mortality from colorectal cancer. On the basis of available data from the literature, it has been calculated that screening by faecal occult blood testing costs about £5900 (\$10 800; €9000) per life year saved, which is well below the threshold most European countries are willing to pay, and therefore represents a cost effective intervention.²⁰⁻²¹ In the United Kingdom, however, there is little doubt that a screening programme would put further pressure on an already overstretched endoscopy service, and the introduction of screening must go hand in hand with improvements in provision of services.¹⁸

This study forms part of the independent evaluation of the UK colorectal cancer screening pilot commissioned by the policy research programme at the Department of Health, England. The views expressed are those of the authors and not necessarily those of the Department of Health. We thank JH Scholefield, Queen's Medical Centre, Nottingham, for providing unpublished data from the Nottingham trial.

Contributors: RJCS was director of the Scottish arm and lead clinician for Tayside; he will act as guarantor for the paper. R Parker was director of the English arm and lead clinician for the English site. FE Alexander and D Weller evaluated the results. FA Carey was the lead pathologist of the Scottish arm. C Fraser led the selection process of the faecal occult blood test and ensured the quality of the testing process. C Morton was project man-

Table 4 Detection rates for cancer and neoplasia per 1000 people screened (faecal occult blood testing complete) for pilot and prevalence screen of Nottingham trial

Variable	Men			Women			Both		
	England	Scotland	Nottingham	England	Scotland	Nottingham	England	Scotland	Nottingham
Cancer	1.8	2.9	1.7	0.8	1.2	1.1	1.3	2.0	1.6
Neoplasia	8.3	12.4	—	3.7	4.4	—	5.8	8.0	—

Values are standardised for age or age and sex to age range in pilot (50-69 years).

ager for the Scottish arm. NAG Mowat was the lead clinician for the pilot in Grampian. M Newbold was the lead pathologist of the English arm. JG Paterson was chairman of the steering group for the pilot. J Patnick was national coordinator of NHS screening programmes. K Robertshaw was project manager for the English arm. SCH Smith oversaw the testing process in England. J Wilson was the lead clinician for the pilot in Fife.

Funding: Departments of Health in England and Scotland.

Competing interests: None declared.

Ethical approval: Ethical approval was not sought for the pilot. This was a decision made by the National Screening Committee, and endorsed by the Departments of Health, on the grounds that faecal occult blood screening for colorectal cancer is a technology of proved efficacy, and that the study was not research based but rather evaluated the feasibility of introducing a screening programme into the NHS.

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