Original article

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Faecal occult blood testing in areas of high incidence and mortality; the effect of screening the population aged 50 to 59

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Abstract

Aim In central Liverpool, the incidence of colorectal cancer (CRC) is 119% of the national average. Currently, screening is offered to those aged 60–70 through the National Bowel Cancer screening programme. A theoretical model showing the effect of the introduction of biennial screening in individuals aged 50–59 has been applied to the population of central Liverpool.

Method The impact of screening using faecal occult blood testing (FOBT) in individuals aged 50–59 in central Liverpool (n = 47 440; males 23 312) was assessed by a model based on three levels of compliance.

Results After modelling, the positive FOBT result for increased incidence of CRC, the positive predictive value for adenoma and cancer detection was calculated using age-specific positivity rates. The results indicate that between 120 and 162 new diagnoses of CRC per 100 000 population aged 50–59 could be detected by biennial screening, dependant on compliance rates.

Conclusion Screening individuals aged 50–59 can identify early cancers and significant adenomas, which may contribute to a reduction in the expected high mortality rate found in this geographical area.

Keywords Colorectal cancer, population screening, faecal occult blood testing, individuals aged 50–59

Introduction

Cancer incidence and prevalence are high in industrial areas. In central Liverpool, the incidence of colorectal cancer (CRC) is 119% of the United Kingdom (UK) national average [1]. CRC is the second leading cause of death from malignant disease in the UK [2]. Screening by faecal occult blood testing (FOBT) detects cancers at an earlier stage, often before symptomatic presentation. Previous randomized controlled trials (RCT) [3–5] and a meta-analysis [6] have shown a reduction in cancer-specific mortality of between 15% and 33%.

Following these trials, a national pilot scheme [7] was developed to screen individuals over 60 years in England. The National Bowel Cancer screening programme, introduced in 2006, is offered to all people between 60 and 70 years [8] with the aim of reducing mortality as reported by others [9]. If calculations are adjusted for attendance rates, the overall mortality reduction has been estimated by Hewitson *et al.* [9] to be 25% (RR 0.75, 95% CI 0.66–0.84).

In Scotland, a similar screening programme is already available from the age of 50. The age threshold in that study took into account the higher geographical incidence of disease, the age standardized incidence of 50 cases per 100 000 (age 50–59) [10] and a mortality rate of 23.1 per 100 000 population [5]. In Liverpool, the same age standardized incidence is 45.5 per 100 000 and, between 2000 and 2004, 174 cases of CRC were diagnosed in the population aged 50–59 [1]. The associated mortality rate is 25.7 per 100 000 [1]. It is clear that the impact of CRC on the population of Liverpool is comparable with that in Scotland.

Owing to the high incidence of the disease in Liverpool, we aimed to determine the effect of implementing screening at 50 rather than 60 years of age. A theoretical model was created showing the effect of biennial screening of the population aged 50–59 in central Liverpool.

Development of the model

The study aimed to determine the following: the size of the population included in the study, the level of

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expected participation rate, the test positivity rates for the population, the yield of diagnoses of CRC, the yield of significant adenomata detected, and the stage of detected disease.

The size of the population included in the study

Using the latest available (2001) national census information, the population size was calculated to be 47 440 (23 312 men, 24 128 women; 26 987 aged 50–54, 20 453 aged 55–59) [11].

The expected participation rate

Expected levels of test participation were calculated based on previously obtained levels in the British bowel cancer screening programme (BBCSP) pilot studies [12,13] and previous RCTs [3–6]. It was decided to model the results using three levels of compliance as follows:

High (60%): This value, obtained from the national pilot uptake target, [12] was the highest level of compliance recorded in our literature review (57% was obtained through the main study by Hardcastle *et al.* [2]).

Medium (54.8%): This was the level of compliance achieved in the first round of the pilot study [13].

Low (44.5%): This was the level of compliance in the second round of the BBCSP pilot study [13].

The number of patients attending one screening round in the three main RCTs [2–4] was between 66.8% [4] and 53.4% [2]. The uptake on a second round of screening was less, 44.5%; so this was used to estimate the lowest participation rate in our model. Similar assumptions based on the highest level of participation have been made. Although the Funen trial [4] reported an initial uptake of 66.8%, the Nottingham trial [2] reported a maximum compliance of 57%. Since our model was to apply to the UK, we felt that an uptake of 60% would be a reasonable figure. It was shown in the British pilot studies that uptake was much lower in the 50–54- year-old groups [12,13]. This was a factor in the decision for the implementation of screening at an older age. In the first round of the pilot, the uptake in men aged 50–54 was 47.2%, which was the lowest age-specific uptake rate.

The test positivity rates

The age-specific positivity rates were taken from the BBCSP pilot study [12]. A Liverpool-specific value was calculated based on an incidence rate of 119% [1] of the national average and multiplied with the expected test positivity. This process was completed for both men and women in the two age categories, 50–54 and 55–59 years.

It has been assumed that cancer detection through screening would be higher in this population by a factor of 1.19. This postulated increase in detection rates is credible, since the FOBT positivity rate in the population of Liverpool is currently approximately 3%, higher than the national average. The calculated increase in detection proportional to the increased incidence in the population may be a conservative underestimate of the true potential benefit of FOBT in this population group.

The incidence of CRC and significant adenomas identified by FOBT

Using the calculated age-specific positive predicted values, as calculated from the first round of the BBCSP pilot study and presented in the calculations in its second round [13] multiplied by 119% to reflect the increased incidence in Liverpool, the expected numbers of cancers and adenomas detected by screening were calculated using the three levels of predicted compliance for all four sub-population groups (males aged 50–54 and 55–59, and females aged 50–54 and 55–59) (Tables 1–4).

Assuming similar positive detection rates, the overall number of CRC cases that could be detected through screening would be between 20 and 27, dependant on participation rates. Based on the same assumptions of

Table 1 Predicted numbers of significant neoplasms in central Liverpool for men aged between 50 and 54, based on an incidence of 119% of the national average. Age-specific FOBT positivity rates and PPV from British bowel cancer screening programme data [12,13].

Participation rate	Population screened – total population 13 259	Positive FOBT – 1.38 × 1.19 = 1.64	PPV for +ve FOBT and neoplasia – 34.72 × 1.19 = 41.32	PPV for +ve FOBT and cancer – 6.94 × 1.19 = 8.26
Males 50–54				
High: 60	7955	130	54	11
Medium: 54.8	7266	119	49	10
Low: 44.5	5900	97	40	8

FOBT, faecal occult blood testing; PPV, positive predictive value.

Table 2 Predicted numbers of significant neoplasms in central Liverpool for men aged between 55 and 59, based on an incidence of 119% of the national average. Age-specific FOBT positivity rates and PPV from British bowel cancer screening programme data [12,13].

Participation rate	Population screened – total population 10 053	Positive FOBT – 1.53 × 1.19 = 1.82	PPV for +ve FOBT and neoplasia – 37.36 × 1.19 = 44.46	PPV for +ve FOBT and cancer – 6.32 × 1.19 = 7.52
Males 55–59				
High: 60	6032	110	49	8
Medium: 54.8	5509	100	45	8
Low: 44.5	4474	81	36	6

FOBT, faecal occult blood testing; PPV, positive predictive value.

Table 3 Predicted numbers of significant neoplasms in central Liverpool for women aged between 50 and 54, based on an incidence of the 119% of the national average. Age-specific FOBT positivity rates and PPV from British bowel cancer screening programme data [12,13].

Participation rate	Population screened – total population 13 728	Positive FOBT – 0.83 × 1.19 = 0.99	PPV for +ve FOBT and neoplasia – 28.13 × 1.19 = 33.47	PPV for +ve FOBT and cancer – 4.17 × 1.19 = 4.96
Females 50–54				
High: 60	8237	82	27	4
Medium: 54.8	7523	74	25	4
Low: 44.5	6109	60	20	3

FOBT, faecal occult blood testing; PPV, positive predictive value.

Table 4 Predicted numbers of significant neoplasms in central Liverpool for women aged between 55 and 59, based on an incidence of 119% of the national average. Age-specific FOBT positivity rates and PPV from British bowel cancer screening programme data [12,13].

Participation rate	Population screened – total population 10 400	Positive FOBT – 0.92 × 1.19 = 1.09	PPV for +ve FOBT and neoplasia – 30.25 × 1.19 = 36	PPV for +ve FOBT and cancer – 5.04 × 1.19 = 6
Females 55–59				
High: 60	6240	68	24	4
Medium: 54.8	5699	62	22	4
Low: 44.5	4628	50	18	3

FOBT, faecal occult blood testing; PPV, positive predictive value.

positivity, relative risk and participation, the predicted range in the number of neoplasms detected ranged from 114 to 154. It is likely that the number of adenomas detected would be approximately the number of neoplasms minus the number of cancers between 87 and 134.

Using data from Cancer Research UK [5], the age-specific incidence of bowel cancer per 100 000 was obtained. This expressed as cases per 100 000 and was then calculated from the predicted number of cases diagnosed from screening in the Liverpool population. In the female population, the overall detection rate in the population aged 50–59 was estimated to be between 51 and 68 cases per 100 000, and the male population of the same age range had between 120 and 162 cases per 100 000 (Fig. 1).

The stage of detected cancers

It is assumed that, by screening for CRC, detection will occur earlier in the disease process. Using the staging results from the British pilot study [7] and the

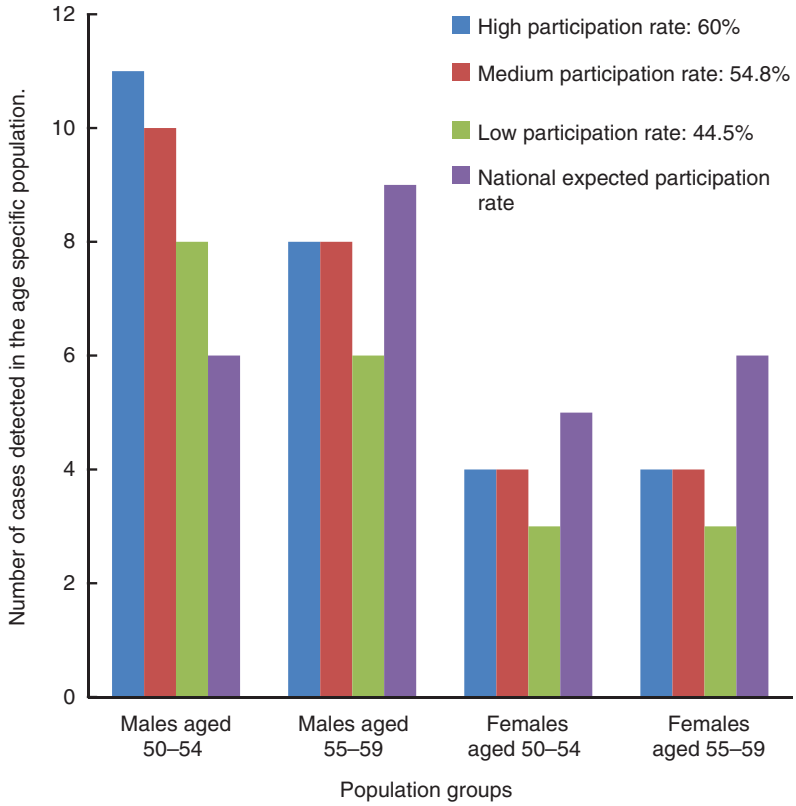

Figure 1 Graph showing the expected number of detected cancers following faecal occult blood testing with variable participation rates in the population of Liverpool compared with the expected national rate.

Nottingham RCT [2], the expected distribution of detected cancers in relation to Dukes stage was calculated, based on an average of these two trials. Although not age-specific, these data were used to show the expected overall distribution of staging through screening. It is possible that because of the younger age range in our model's population that the staging of screen-detected cancers could shift even more dramatically towards an earlier stage.

The results were compared with the expected distribution of stage without screening in the Liverpool area. These showed an obvious stage migration towards earlier disease (Fig. 2).

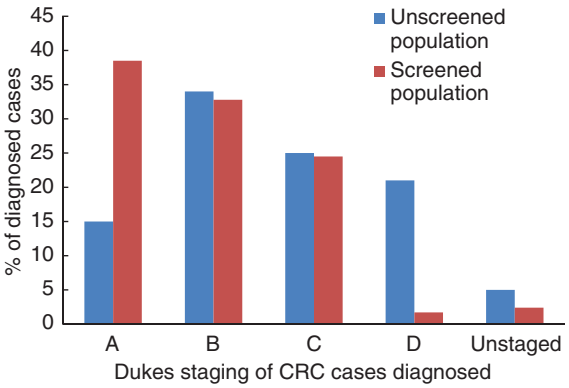

Figure 2 Graph comparing the staging of cancers detected through screening with presentation without screening in the population in Liverpool.

Discussion

This study was conducted to establish if there was a valid reason to extend the existing screening programme to patients aged 50–59 in central Liverpool, an area with an above-average CRC incidence rate. It is evident that the incidence and mortality of CRC in Liverpool is above the national average, but this study did not take into account the deprivation factors associated with the area and the effect on CRC incidence, although this undoubtedly would have an influence [12,13].

The results derived from this model indicate that implementing screening in the male population aged 50–59 would result in a greater detection rate of CRC than in the female population of the same age range (14–17 cancers in men compared with 6–8 cancers in women). This cannot be explained by population distribution, since the two gender populations were comparable in numbers. It could be attributed to

demographic variables, environmental factors or the natural history of the condition.

The detection rate results appeared to be below the average national detection rate in all sub-populations except for men aged 50–54 (Fig. 1). To interpret the postulated effect of screening, the national average value must be taken into account and used as a comparator for all cases diagnosed in all age groups. Our screening model is based on a maximum uptake of 60%, with a population-specific sensitivity rate for FOBT. For example, in men aged 50–54 , the FOBT sensitivity is calculated to be 44.8%, resulting in a maximum detection rate of 27% of all adenomas and cancers in this group. The lowest detection rates would be found in women aged 50–54 , if compliance was 44.5% with a FOBT sensitivity of 33.7%, resulting in detection of 15% of cases. It is therefore sensible to assume even with FOBT that a number of cancers would present symptomatically. This is often seen in older age groups involved in screening programmes and explains the apparent reduced detection rate compared with national averages.

Population screening programmes result in earlier diagnosis. This is clearly demonstrated in the redistribution of expected Dukes staging of detected cancers, showing a shift to earlier stages at diagnosis. A reduction in the number of cases diagnosed as Dukes D and an increase in Dukes A tumours would be expected to result in a reduction in mortality, and this has been shown in the Cochrane review of CRC screening techniques [14]. The distribution of cancer stages shown in Fig. 2 is based on all age groups within the Liverpool area because age-specific data could not be obtained.

In conjunction with a shift to earlier stage, the overall neoplasm detection rate is calculated to be between 114 and 154 cases. Of these, a large proportion will be adenomas. Removal of premalignant adenomas when they are detected should result in a reduction in the future incidence of cancer that normally follows adenoma formation after an interval of around 18 years [15].

Previous work assessed the cost-effectiveness of introducing alternative screening strategies for CRC within the UK [16]. It was concluded that by extending biennial FOBT to the population aged 50–59, that the total cost in the first year would increase by over £50 million from £75 501 096 to £128 486 326. There would also be an associated increase in the manpower required to serve this increase, including diagnosis and treatment. The quality-adjusted life days saved per person would, however, increase significantly from 3.8 to 8.29 [16]. Detecting cancers earlier by screening means that patients will not present later with more invasive disease, require more costly treatment and increased mortality. Although screening incurs increased costs to the health care system, when compared with no screening, it is likely to result in health gains at acceptable costs [16].

The detection of early cancers and adenomas has an effect on mortality. There is some evidence that the stage of CRC has no correlation with the symptoms or timing of presentation [17], although it has been known for a long time that patients presenting as an emergency have a much higher postoperative mortality and a lower cancer-specific survival [18]. It is highly likely, therefore, that early detection can reduce the incidence of emergency presentation with a decrease in mortality and an increase in survival, which would have a great impact on public health [18]. This conclusion is further supported by Goodyear *et al.* [19] who showed that FOBT led to an increase in the diagnosis of asymptomatic disease. It has also been noted that the substantial fall in emergency admissions cannot be attributed to screening unless the decline is in the screened population [20]; by screening a larger population, therefore, it should be possible to reduce emergency admissions in a larger population. FOBT has a proven efficacy in reducing mortality [3,17] and, if applied to a young population, could reduce the incidence and mortality of individuals at the time of screening and of the whole population in the future [15].

FOBT was recommended in the European Community to members of the general population aged between 50 and 74 [21] and also by the British bowel cancer screening pilot [13,14]. The restriction of screening to people aged 60–69 in England may have resulted in cancers developing and advancing unnecessarily in younger age groups. Parkin *et al.* [22] postulated that the degree of protection offered by screening was much the same throughout life, and therefore, screening at a younger age would protect the population aged 50–59 from the development and reduce the future incidence of CRC.

Screening programmes are costly, both in terms of actual screening and follow-up of patients with a positive result. By extending screening to a greater proportion of the population, there could be an initial increase in workload, but the patients identified would be likely to require less expensive treatment. It is possible, therefore, that the system could result in similar costs.

Conflict of interest

No competing interests.

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