Colorectal cancer

The Department of Health has recently announced the rollout of the NHS National Bowel Cancer Screening Programme (NBCSP). The following article outlines the principles of bowel cancer screening and examines the evidence supporting such a programme, including economic factors. In addition, the implications of colorectal cancer screening for individuals outside of the target age range of the NBCSP are considered.

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Colorectal cancer is the second most common cause of malignant death within the UK.[1] It is a significant health problem, with an annual mortality of approximately 16,000 deaths.[1] The aetiology is well documented and understood; pre-cancerous adenomatous polyps undergo malignant change giving rise to adenocarcinoma.[2] Furthermore, a strong correlation between stage at diagnosis and outcome exists confirmed by cancer registry data. Several safe and validated screening modalities have been investigated[3] and the treatment protocol for both pre-cancerous and malignant lesions are well defined. Finally high quality evidence from randomised controlled trials demonstrates that faecal occult blood testing (FOBT) reduces mortality and morbidity from colorectal cancer within the screened populations.[4-6] The criteria defining a successful screening programme have been well documented,[7] but are less frequently adhered to. However the pathophysiology of colorectal cancer does lend itself to screening.

In May 1997 the National Screening Committee held their first workshop on colorectal screening in Edinburgh, which set out to examine evidence to support colorectal cancer screening. A subsequent meeting in Cardiff on 1998 advised the Secretariat of the National Screening Committee on the potential future of colorectal cancer screening in the UK and proposed the implementation of two pilot screening studies. The aim was to assess the feasibility and acceptability of biennial FOBT as a means of national bowel cancer screening. Three pilot screening rounds have successfully taken place in Coventry and north Warwickshire in England; and in Tayside, Grampian and Fife in Scotland. The results of the first two rounds of screening[8,9] led the Department of Health to issue a statement in April 2006 officially outlining the rollout of the NHS Bowel Cancer Screening Programme (NHS BCSP), which is expected to be fully operational by 2009.

How will the programme work?

The NHS BCSP will be co-ordinated by five programme hubs and 90–100 screening centres. The programme hubs will be responsible for inviting subjects on (or around) their 60th birthday to complete a postal FOBT. Routine recall for testing will subsequently occur every two years until the individual's 70th birthday. Importantly, individuals are permitted to self-refer (at intervals of not less than 2 years) to the screening programme above the age of 70 years.

Screening will be carried out using postal guaiac FOBT kits. Testing kits comprise a triple-slide set, with each slide consisting of two testing windows. Screening candidates will be expected to apply faecal matter to the two testing windows of a slide, for three consecutive bowel motions. Kits are then sealed and returned to the local screening centre for interpretation.

FOBT will yield one of four results:

- Subjects with spoiled, inadequate or technically-failed kits will be invited to repeat the test
- Individuals with a negative result test will be informed in writing and given an information sheet specifying the symptoms of bowel cancer, to increase awareness between rounds of screening
- A weak positive test, defined as one-to-four positive

testing windows, will require retesting following dietary advice. A subsequent weak positive result will trigger a nurse-led clinic appointment and assessment of suitability for colonoscopy. After one weak-positive FOBT result, two negative tests must be recorded before the subject can be discharged from the current round of screening.

- Subjects with a positive test, defined as five or six positive testing windows, will be invited to meet with a screening nurse to discuss the individuals' suitability for colonoscopy. This appointment should occur within one week of the positive result and the GP will be informed.

A suitable subject with a positive test will undergo colonoscopy at the screening centre, remaining under their care until discharge. Discharge may be back into the screening programme, to the GP for follow-up, or into the care of a hospital consultant.

Colonoscopic diagnoses will be managed according to normal protocols, most commonly resulting in either discharge, polyp surveillance according to the British Society of Gastroenterology guidelines,[10] or cancer treatment consistent with the recent Association of Coloproctology of Great Britain and Ireland guidelines.[11]

Is FOBT the most effective method of detecting colorectal cancer in a population?

There are several methods for detecting asymptomatic bowel cancers including FOBT, flexible (fibre-optic) sigmoidoscopy (FOS), colonoscopy and double contrast barium enema.

The predominant location of bowel cancer and adenomas has been well documented with 70% being detectable by flexible sigmoidoscopy. Several trials, including the Medical Research Council UK Flexible Sigmoidoscopy trial,[12] investigated the use of FOS as a screening tool. The baseline findings from this study have demonstrated cancer detection rates of 0·3% and an adenoma rate of 12%; comparable with FOBT. The uptake and acceptability rates for FOS were high; only 2% of participants wished that they had not partaken. A randomised controlled trial from Italy has also highlighted detection rates of advanced neoplasia to be almost three-times higher using FOS based screening protocol when compared to FOBT.[13] Similar cancer detection rates were shown in the MRC trial. However, mortality reduction from FOS-based screening has not been demonstrated in another trial and fears regarding perforation rates and incomplete examination of the colon have limited its appeal .

Colonoscopy offers the most sensitive means of detecting bowel pathology, however analysis from the USA has unequivocally demonstrated FOBT to be capable of screening a greater proportion of the population for a fraction of the cost.[14] Again the risk of colonic perforation, raised concerns about this modality of screening.

What is the evidence that FOBT screening reduces mortality?

Three large randomised controlled trials from Nottingham (UK), Funen (Denmark) and Minnesota (USA), support the use of guaiac FOBT for bowel cancer screening.[5-7]

The Nottingham trial recruited 150,251 subjects aged between 45 and 74 years over 10 years. Subjects were randomised into a control group and a cohort undertaking biennial FOBT screening. The uptake rate was 53·4% and a statistically significant reduction in disease-specific colorectal cancer mortality (of 15%) was observed. Positive FOBT results were seen in 2·1% of whom 11% were diagnosed with malignancy.[7] The Danish study was similar in design, although recruiting a smaller cohort of 31,000 subjects into each arm.[5] The trial showed a reduction in colorectal cancer mortality of 18% at 10 years follow up, although interestingly, the rates of colorectal cancer and overall mortality were similar in both arms. The Minnesota trial was perhaps the least convincing, despite showing the largest reductions in colorectal cancer mortality. A total of 46,551 subjects were assigned to three groups; annual screening, biennial screening and control. The group receiving biennial FOBT tests showed a colorectal cancer mortality reduction of 33%.[6] This trial has attracted criticism due to the participation of volunteer subjects and the use of rehydrated Haemoccult®, potentially yielding an artificially high proportion of positive results and thus an elevated colonoscopy rate.

A systematic review and meta-analysis including the results of six randomised controlled trials using haemoccult demonstrated a 16% reduction in colorectal cancer mortality for the screened cohorts.[15]

However, it is important to remember that FOBT does not detect all colorectal cancer within the screened groups and little data on interval cancers exists. The best evidence, published by the Nottingham group in 1992[16] suggests that haemoccult has a sensitivity of 67·6%, missing 36 out of 111 cancers, with significantly greater sensitivity for carcinoma of the sigmoid and descending colon than for

right-sided or rectal cancers. Data from the second round of pilot screening gives a similar sensitivity of 64·4%.

Is a national screening programme viable?

There seems to be little doubt from the above evidence that FOBT reduces colorectal cancer mortality within a screened population. The three pilot rounds of FOBT screening were therefore designed to assess the feasibility of introducing a nationwide screening programme. Data from the pilot was therefore not designed to conclusively demonstrate reductions in mortality.

The first round of screening took place from March 2000 to May 2003 and invited 478,250 individuals aged between 50–69 years to take part. A total of 271,646 people accepted, yielding an uptake rate of 56·8%. The rate of positive FOBT was 1·9%, of which 35% had adenomas and 10.9% were diagnosed with malignancy. A high proportion of cancers were either polyp cancers (16·6%) or Dukes A disease (48%), with only 1% of subjects diagnosed with neoplasia exhibiting metastases at the time of diagnosis.[8] The overall cancer detection-rate of FOBT screening was 1·62 per 1000. These data are consistent with results of the previously described randomised controlled trials and therefore it is plausible that a similar reduction in mortality will ultimately be seen in the screened population.

The second round of pilot screening has been less publicised. A total of 127,746 subjects were invited for screening, 15·9% of these were new invitees (mostly aged 49-51 years). The results were less encouraging than the first round. The uptake rate was lower (51·7%), and shown to decrease in areas of socioeconomic deprivation and with high densities of immigrant population.[9] The rate of positive FOBT was 1·77% with a colorectal cancer detection rate of 0·94 per 1000; lower than the first round of screening and than shown in the Nottingham and Funen trials. Decreased detection rates were reflected by a lower positive predictive value for FOBT. The reduction in uptake was attributed to decreased public awareness and a smaller advertising campaign. This is supported by evidence highlighting that increased awareness of the benefits of screening results in increased compliance.[17]

It should be noted that South Warwickshire General Hospitals NHS Trust did not participate in the second and third round of the screening pilot, due to resource availability, contributing to the decreased cohort of subjects.

It is important to consider the differences between the randomised controlled trials, the pilot screening studies and the NHS BCSP; the most important of which is the age of the population to be screened. The Nottingham trial; often used as the benchmark to which the pilot screening programme has been compared, incorporated the largest age range (45–74 years) whereas the NHS BCSP will have the smallest (60–69 years). As the incidence of bowel cancer increases with age, a smaller, but more elderly age-group is more likely to generate a higher cancer detection rate for the population screened. This will not necessarily translate into an overall reduction in colorectal cancer mortality and increased efficacy of the programme as there are a number of confounding variables such as differential uptake rates, fitness for surgery and overall survival between age groups.

The Nottingham study showed a reduction in screening uptake for individuals over the age of 70 years. However, data from the Funen trial highlighted that the 70–75 year age group accounted for 25% of cancers, whereas the 50–55 year old group yielded only 3%; in keeping with the population distribution of colorectal cancer. In an ageing population, it is reasonable to assume that the trend of reduced uptake may regress and an increasing proportion of elderly subjects with colorectal cancer may be suitable for surgery. This has been reflected in the expansion of the NHS BCSP to include the 70–75 year old age group by 2010.

Is bowel cancer screening economically viable?

The economic impact of any screening programme cannot be underestimated. As society moves closer to defining acceptable levels of funding for quality-adjusted life-years (QUALYs), it becomes imperative to ensure cost-effective screening in order to promote longevity of the programme. Unfortunately, the models used to predict cost-effectiveness are complex and incorporate numerous variables, which are often prone to error or bias.[18] In conjunction with the constant economic flux, it is likely that any estimate of cost-effectiveness is likely to be open to criticisms. A report to the English Bowel Cancer Screening Working Group by the School of Health and Related Research has used a prediction model based on the best available evidence.[18] It demonstrated that in terms of cost-effectiveness, FOBT screening within the 60–69 year cohort is likely to give QUALY savings at levels acceptable to society and below the cost of alternate health interventions available from the NHS. However, the report also concluded that FOS-based screening programmes were likely to be more cost-effective than FOBT, potentially even generating a cost saving for the NHS. The report suggested that a larger age range (50-69

years) would be viable, although imposing a concurrent increase in initial set-up costs and larger ongoing resource implications. It is therefore likely that the limitations in service provision will dictate the level of screening permissible, rather than overall cost-effectiveness.

What is the effect of screening outside of the screened population?

It has been shown that colonoscopic activity outside of the screening programme, including two-week wait referrals, have also increased since the inception of the bowel cancer screening pilot.[9] A recent study from our unit has also demonstrated a decrease in emergency colorectal cancer admissions for individuals beyond the age-range of the pilot study (ie, over 69 years) between 1999 and 2005. It is thought that publicity-related increase in awareness of the symptoms and signs of colorectal cancer has led to greater GP-referral of symptomatic, anxious and high-risk individuals of all ages.[19] One may also assume that members of the screened population may request further screening after surpassing the upper age boundary for the NHS BCSP.

Conclusion

The Department of Health has introduced the NHS BCSP following three rounds of pilot screening, based upon robust clinical evidence.[4,5,7-9,13,15,18-21] It is likely that there will be cost-effective reduction in colorectal cancer mortality for the screened groups in addition to beneficial effects for the unscreened population. The future of the NHS BCSP may, however, be decided by the factor that was not considered in this manuscript; the political ramifications of continuing or abandoning the screening process.

Conflict of interest: none declared

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