# National Screening Committee

## *A Summary of the Colorectal Cancer Screening Workshops and Background Papers*

# Contents

## INTRODUCTION

Colorectal cancer is a serious health problem with an overall 5-year survival rate of 35% (England). This low survival is mainly attributable to the fact that the disease usually presents with non-specific symptoms which are either ignored by the patient or lead to delayed diagnosis. Screening methods might therefore result in earlier diagnosis and reduce both mortality and morbidity. Three randomised controlled trials have demonstrated that population screening of people over 50 years of age for non-visible (occult) blood in faeces can reduce the colorectal cancer death-rate. The first workshop in Edinburgh was therefore organised to consider the evidence and the second workshop in Cardiff to consider the practicalities of introducing a population screening programme.

## THE DISEASE AND DIAGNOSIS[1]

### 1. Incidence, staging and mortality

The incidence rate for colorectal cancer is 53.5 for men and 36.7 for women per 100,000 (all ages). Incidence rises sharply with age and age-standardised rates in 1992 were 4 per 100,000 among people aged under 50, 100 per 100,000 among those aged 50-69, and over 300 per 100,000 among people over the age of 70 years.

The effectiveness of treatment and prospects for survival depend on the stage of cancer at diagnosis, usually described in terms of a modified Dukes' classification, see below:-

| Dukes' Stage (modified) | Definition | Approximate frequency at diagnosis | Approximate 5-year survival |
|---|---|---|---|
| A | cancer localised within the bowel wall | 11% | 83% |
| B | cancer which penetrates the bowel | 35% | 64% |
| C | cancer spread to lymph nodes | 26% | 38% |
| D | cancer with distant metastases (most often in the liver) | 29% | 3% |

### 2. High risk groups

There are however two genetic syndromes that lead to cancer at a relatively early age: hereditary non-polyposis colorectal cancer (HNPCC) and familial adenomatous polyposis (FAP). The HNPCC mutation, which affects 2-5% of colorectal cancer patients, is associated with an 80% lifetime risk. Without treatment, people with FAP(1% of patients) would usually die of bowel cancer before the age of 40 years. In addition to these rare genetic disorders , close relatives of people diagnosed with colorectal cancer are at increased risk. The risk is greater the larger the number of relatives affected, the closer the family relationship, and the younger they are at the time of diagnosis. However, the disease is so common that 10% of people over the age of 50 will have an affected relative. Those with a single relative over the age of 60 have the same risk as the general population. About 25% of patients with colorectal cancer have a positive family history.

## 3. Symptoms and diagnosis

The most common presenting symptoms of colorectal cancer include change of bowel habit, rectal bleeding, abdominal pain and anaemia. These are non-specific , occur frequently in the population and have a wide variety of causes. Any or all of these symptoms may lead to problems with diagnosis and to referral to a wide range of hospital specialties. Dutch, Australian and US studies have shown that visible rectal bleeding in older people is an important indicator of possible colorectal cancer. Around 20% of patients aged over 60, and 10% of those aged over 40 reporting visible rectal bleeding had colorectal cancer. In the USA study none of the cancers occurred in people aged under 50. UK studies report delays of around 10 months between the onset of symptoms and treatment. The median patient delay is approximately 3 months, usually because patients do not think the symptoms signify serious illness. Professional delay may be the result of mis-diagnosis, often due to the assumption that symptoms are caused by haemorrhoids. However, there is little evidence that such delays affect health outcomes.

## 4. Investigations

In cases of suspected colorectal cancer, the large bowel can be completely examined by one of two methods: colonoscopy or sigmoidoscopy plus double-contrast barium enema. In colonoscopy, a flexible tubular device (endoscope) is inserted into the anus and threaded along the whole of the large bowel. In sigmoidoscopy, a shorter instrument (rigid or flexible) is used to examine the lower part of the bowel. The flexible sigmoidoscope being able to reach farther into the colon than the rigid one. In double contrast barium enema the lining of the bowel is first of all coated with barium and then distended by air to allow the whole of the bowel to be visualised using X-rays.

A US randomised controlled trial and UK and Swedish studies found that these diagnostic methods have similar yields and costs. This equivalence depends, however, on operator competence. Colonoscopy is a technically difficult procedure which can yield reliable results if the tip of the colonoscope reaches the caecum (or proximal end) of the colon and is commonly known as “completion”. Although published series, mainly from the US, report completion rates of 85% or more, audit data from the Trent Region and Wales suggest that completion rates in many British hospitals may be below 50%. The colonoscopy technique improves with practice. A study of training in colonoscopy found that physicians are normally able to achieve completion 80% of the time after 50 colonoscopies, rising to 95% after 200. Competence in flexible sigmoidoscopy can be achieved after 24 to 30 examinations. A US study found that trained nurses were as likely to discover cancers by sigmoidoscopy as gastroenterologists (and patients were more willing to return for a repeat procedure after examination by a nurse). Further research on nurse endoscopy is being commissioned by the NHS Health Technology Assessment programme.

## 5. Treatment

Once diagnosed colorectal cancer is usually treated by surgery with or without the use of radiotherapy or chemotherapy. About 80% of patients undergo surgery, usually with the hope of being cured. Fewer than half survive more than 5 years. Therefore it is hoped that the research findings, which have demonstrated that population screening of people over 50 years of age using Faecal Occult Blood (FOB) tests can reduce the mortality from colorectal cancer, can be rolled out to benefit the whole population.

## THE FIRST WORKSHOP

## COLORECTAL CANCER SCREENING WORKSHOP
## EDINBURGH - 21 MAY 1997

The National Screening Committee's first workshop on colorectal cancer screening, was held on Wednesday 21 May 1997 in Edinburgh. The event was hosted by The Scottish Office and chaired by Sir David Carter, the Chief Medical Officer of Scotland.

The purpose of the workshop was to:

(i) analyse the extent to which colorectal cancer screening meets the recognised criteria for population screening programmes
(ii) identify the quality standards for a colorectal cancer screening programme
(iii) identify the critical success factors for a colorectal cancer screening programme

The main objective of the workshop was to highlight key issues for further consideration at a second workshop on colorectal cancer screening to be held in Cardiff.

The workshop participants were mainly healthcare professionals with an interest in colorectal cancer and included specialists from the UK, Europe and the USA. The overseas experts attending the workshop were specifically asked to apply their perspective to the UK situation.

### 6. Session 1

The Workshop considered six papers in the morning session:

What makes screening different? -
and why we need a National Screening Committee. *(Dr J A Muir Gray),*
A Colorectal Cancer Control Programme:
primary, secondary and tertiary prevention. *(Professor Robert Haward),*
The Nottingham Colorectal Cancer Screening Study. *(Professor Jack Hardcastle)*[2],
Scandinavian reaction to the Funen study. *(Professor Ole Kronborg)*[3],
Screening and case-finding of people at high risk. *(Mr Malcolm Dunlop),*
Critical success factors:
what could go wrong in a colorectal cancer screening programme?
*(Professor Colin McArdle).*

**Expert Overseas Advisers:**

Professor Robert Fletcher[6], Professor of Ambulatory Care & Prevention, Harvard Medical School, Boston, USA.
Professor Theodore Ganiats, Associate Professor of Family Medicine, University of California, San Diego, USA.
Professor Ole Kronborg, Professor of Surgery, Odense University Hospital, Denmark

See references[2,3,4,5,6,7] for the full papers which were used as background information to this workshop session.

## 7. Session 2

In the second session in the afternoon the participants were split into discussion groups to consider the topics set out below and to report back their findings in a plenary session.

- to decide on the degree to which the evidence available for colorectal cancer screening meets the criteria agreed by the National Screening Committee for appraising population screening.

- to agree a set of objectives for a colorectal screening programme using breast screening objectives as a template and basis for discussion.

- to identify critical success factors that would need to be in place to ensure that a screening programme of adequate quality could be set up and maintained over a ten year period.

## 8. Summary of Outcomes

The main points to emerge from both of the sessions were:-

8.1. The FOB test was broadly sensitive and specific enough to take forward a screening programme. This had been demonstrated with good quality data from three Randomised Controlled Trials. However there was a need to ensure that specificity was high in order to minimize the disbenefits associated with false positive results and to control the workload resulting from the screening programme.

8.2. In view of the recognised morbidity and mortality associated with colonoscopy, there were concerns about the adverse effects of colonoscopy if the quality of care was not of the highest. The problems of providing the manpower to staff a national screening programme needed to be analysed. Genetic issues related to colorectal cancer need to be addressed in much greater detail.

8.3. The critical success factors for a colorectal cancer screening programme could be grouped into:

8.3.1. Resource limitations e.g. the availability of radiologists

8.3.2. Quality limitations e.g. ability to reproduce the standards achieved in research settings

8.4. A draft set of objectives and quality standards was developed by one workshop group. The criteria for population screening in relation to colorectal cancer screening were considered by another workgroup (Chapter 6.2: The First Report of the National Screening Committee).

8.5. There is no evidence of effectiveness for screening sub groups of the population, identified on the basis of family history, with FOB or sigmoidoscopy. However well organised case-finding for relatives of cases of Familial Adenomatous Polyposis or Hereditary Non-polyposis Colorectal Cancer is of benefit but is not considered by the National Screening Committee to be population screening.

## 9. Conclusions

### KEY ISSUES IDENTIFIED FOR CONSIDERATION IN CARDIFF

9.1. **Integration of colorectal cancer screening with the Calman/Hine recommendations**

Any programme for colorectal cancer screening should be integrated with the national implementation of the Calman/Hine recommendations or their equivalent in Scotland. A key consideration for colorectal cancer screening will be the opportunity cost of implementing a national programme. A possible way forward in terms of resources would be to consider the opportunity cost of colorectal cancer screening within a national programme budget for the management of colorectal cancer

9.2. **Pilots**

The possibility of introducing colorectal cancer screening in pilot sites needs to be addressed. It is unclear what form these pilots might take and whether such a policy would be feasible. Such a policy will need to address specific issues:

9.2.1. public perception of risk and the consumer reaction to "piloting" an intervention

9.2.2. reproducibility of results achieved from the pilot sites

9.2.3. the adverse effects of screening - for example - what is the risk from colonoscopy and how this should be expressed to people invited for screening?

9.2.4. the resources required for screening

9.3. **Colorectal cancer screening policy options**

The precise screening policy option in order to proceed with colorectal cancer screening has not yet been agreed. Examples of major decisions which still need to be agreed are:

9.3.1. Should FOB testing be performed annually or biennially?

9.3.2. What combination of positive FOB card squares will constitute a "positive result"?

9.3.3. What is the precise policy for managing individuals with a "positive result"?

9.3.4. What is the most appropriate balance between complete and incomplete colonoscopy ?

9.3.5. What is the best balance between colonoscopy and double contrast barium enema?

9.4. **Decision analysis**

A decision analysis of a colorectal cancer screening programme will need to be undertaken. This will allow decision trees for the various policy options and resource implications to be mapped out and a sensitivity analysis to be applied to the options. This could take into account the impact of variations in quality or outcome. Other considerations may also need to be included in such an analysis e.g. the risk of screening. The end result will be a spectrum of analyses policy options which will be used to aid further decision making.

## THE SECOND WORKSHOP

## COLORECTAL CANCER SCREENING WORKSHOP
## CARDIFF - 16 MARCH 1998

The National Screening Committee's second workshop on colorectal cancer screening, was held on Monday 16 March 1998 in Cardiff. The event was hosted by The Welsh Office and chaired by Dr Ruth Hall, the Chief Medical Officer of Wales.

The first workshop on colorectal cancer examined the evidence for the efficacy of colorectal cancer screening and came to the conclusion that there was good evidence of beneficial effect at the standards of screening achieved in the screening trials.

Potential barriers to achieving this standard of service in ordinary service settings were identified at the workshop and in the period since the first workshop the following work has been undertaken.

- A decision analysis of different screening options and the consequences of screening to a standard lower than that achieved in the populations covered by research screening programmes.

- A service plan simulation was carried out, based on certain assumptions about the screening policy and its performance standards. The main objective of this exercise was to identify the resources required for screening both nationally and for a population such as that which might be covered by a single screening programme.

- An analysis of the screening programme, and the options to be offered the public, was undertaken from the perception of the individual invited to be screened. The National Screening Committee, reflecting changes in public attitudes towards informed consent and bearing in mind the possible medico-legal consequences, has proposed that one intermediate outcome of screening was the degree to which the decision to participate was based on well-informed choice. This marks a new emphasis for hitherto intermediate outcomes have focused on criteria such as the proportion of the population covered by screening. This analysis has focused particularly on communicating the magnitude and probability of the adverse effects of participating in screening and on those choices which participants in screening have to make, choices based on incomplete or unsatisfactory evidence.

### 10. Objectives of the workshop

The aim of the Worksop is to guide the Secretariat of the National Screening Committee in the preparation of their final report to the National Screening Committee about colorectal cancer screening. In addition, it will be expected to make recommendations to the National Screening Committee and three different recommendations will be considered in the discussion groups.

### *10.1 Recommendation A*

The first recommendation is whether to proceed further with colorectal cancer screening or whether to ask the National Screening Committee to recommend to Ministers that colorectal cancer screening, although having evidence of efficacy in ideal circumstances, cannot be recommended for further investigation or implementation at present. Alternatively, the National Screening Committee could be advised that one or two pilot schemes should be implemented to test not the efficacy of screening in best hands but the feasibility of organising screening in a new environment sufficiently well to achieve adequate levels of quality to reproduce the results found in research settings.

### *10.2 Recommendation B*

If it is decided to go ahead with the recommendation for a pilot, or pilots, then the policy to be recommended will need to be clear and simply expressed. One issue that has emerged in preparing the decision analysis and simulated service plan is the best balance of endoscopic and radiological follow-up of people with positive FOB tests. Two different options are discussed in the simulated plan and it is essential to recommend either one option or the other to the National Screening Committee, or to propose that research needs to be done which could, of course, be done in the context of the pilot, or pilots.

### *10.3 Recommendation C*

The traditional approach for evaluating the effect of screening programmes is to assess their effect on mortality and to use intermediate measures such as the population coverage and sensitivity. As attitudes towards screening change, it is proposed that it may be necessary to introduce a third type of outcome, namely the proportion of people achieving adequately informed choice about whether or not they wish to participate in screening. The practical implications of this are that if adequately informed choice is taken as an outcome of importance to the programme, steps need to be taken not only to define criteria that could be used to measure "adequately informed choice" but also to ensure that participants or potential participants have been "adequately informed". The provision of adequate information may reduce compliance when people appreciate the NNS, the namely the number needed to be screened to detect one case that will benefit.

## 11. Session 1

The Workshop considered four papers in the morning session:

Planning for Colorectal Cancer Screening *(Dr Linda Garvican),*
Decision Analysis of Colorectal Cancer Screening Options *(Dr Alastair Gray),*
Competing Priorities for Commissioners *(Dr Gordon Patterson and Dr John Pritchard),*
Informed Choice - the Patient's Dilemma *(Dr Angela Raffle).*

Papers were circulated by Dr Linda Garvican, Dr Alastair Gray and Dr Angela Raffle and updated versions of these can be found in Appendices 1, 2, 3. In addition the Workshop considered EFFECTIVE HEALTH CARE, *The management of colorectal cancer, Vol.3 No. 6 December*

*1997* and a paper from *Gastroenterology* on the proportion of adenomas missed by colonoscopic examination (1).

The Workshop also received the report of the First Workshop which had identified possible constraints which might impair the effectiveness and quality of the programme.

## 12. Session 2

In the second session in the afternoon the participants were split into discussion groups to consider the topics set out below and to report back their findings in a plenary session.

- to agree on the balance between endoscopic and radiological investigation of people with positive tests.

- to identify the objectives , criteria used to measure the impact, as well as the strengths and weaknesses of using pilots to assess the practical problems of implementing research findings.

- to decide on the role and impact that "informed choice" might have on a population screening programme.

## 13. Summary of Outcomes

13.1 High quality research evidence from more than one randomised controlled trial supports the hypothesis that, with care of the quality provided by the research teams, screening for colorectal cancer does more good than harm at reasonable cost.

13.2 Although it would be unrealistic to expect to reproduce these standards across the whole country, it was concluded that an adequate level of quality to achieve a significant reduction in mortality could be achieved.

13.3 The barriers to good quality were identified and all are potentially able to be overcome or minimised, but a shortage of skilled staff may prove the most difficult to overcome.

13.4 There is scope for the primary intervention of colorectal cancer through dietary change.

13.5 There is no place at present for trying to identify a high risk subgroup of the whole population by enquiring about family history, but the identification of people with Familial Adenomatous Polyposis (FAP) and Hereditary Non Polyposis Colonic Cancer (HNPCC) could be significantly improved by systematic follow-up of the relatives of young people diagnosed to have colonic cancer.

13.6 Any programme must be based on complete disclosure of benefits, limitations and adverse effects of screening to people invited for screening so that they can make an informed choice.

## 14. Conclusions

14.1 The National Screening Committee was asked to note these conclusions and to consider testing the feasibility of colorectal screening through pilot programmes.

14.2 Systems, based on registers, for the identification and follow-up of people who are at very high risk of FAP and HNPCC should be instituted.

## RECOMMENDATIONS

It was agreed that the following recommendations would go forward to the National Screening Committee:-

- that two pilots be organised.
- the target population would be for people between the ages of 50 to 69.
- the primary test would be the faecal occult blood (FOB) test without dietary restriction and rehydration of the test sample.
- follow-up of people with positive tests would be by colonoscopy, with double contrast barium enema for those people in whom complete colonoscopy was not possible. The alternative of using double contrast barium enema and flexible sigmiodoscopy would be explored as an alternative to colonoscopy, should problems of staffing and facilities for colonoscopy appear to be a significant constraint.

The aim of the pilots is not to assess the effectiveness of colorectal screening; randomised controlled trials have already demonstrated the effectiveness of screening in research conditions.

**References**


1. Extracted from EFFECTIVE HEALTH CARE, *The management of colorectal cancer*, Vol.3 No.6 December 1997, ISSN: 0965-0288

2. Hardcastle J D, Chamberlain J O, Robinson M E H et al
   Randomised controlled trial of faecal-occult-blood screening for colorectal cancer.
   *Lancet 1996, 348: 1472-7*

3. Kronborg O, Fenger C, Olsen J et al
   Randomised study of screening for colorectal cancer with faecal-occult-blood test.
   *Lancet 1996, 348: 1467-71*

4. Mandel J S, Bond JH, Church T R et al
   Reducing mortality from colorectal cancer by screening with fecal occult blood.
   *New Eng J Med 1993, 328: 1365-71*

5. Mulcahy H E, Farthing M J G, O'Donoghue D P
   Screening for asymptomatic colorectal cancer
   *BMJ 1997, 314: 285-91*

6. Winawer S J, Fletcher R H, Miller L et al
   Colorectal cancer screening: clinical guidelines and rationale
   Expert Advisory Group for the Federal Agency for Health Care Policy & Research in the United States
   *Gastroenterology 1997, 112: 594-642*

7. Burke W, Petersen G, Lynch P et al
   Recommendations for follow-up care of individuals with an inherited predisposition to cancer
   JAMA 1997, 277: 915-9

8. Rex DK et al
   Colonoscopic miss rates of adenomas determined by back-to-back colonoscopies.
   *Gastroenterology 1997; 112: 24-28.*

**APPENDIX 1**

# Planning for a possible National Colorectal Cancer Screening Programme

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## Abstract

This report presents the planning, projected costs and manpower requirements for a possible National Colorectal Cancer Screening Programme. Screening would be offered to all those aged 50-69, comprising 20% of the UK population. The initial screening test would be faecal occult blood testing (FOBT), every two years. A local programme, administered by a Screening Centre serving a population of 1 million, would be responsible for inviting 100,000 individuals per annum.

The response rate in Nottingham, the UK trial centre, was below 60%. Good informed compliance would require the active support of primary care. The invitation and test kit would be sent by post, and completed tests returned to the Screening Centre, for reading and reporting.

Those with a positive initial screen (about 2%) would be recalled for assessment. This would result in 60,000 investigations each year across England and Wales, given a screening uptake rate of 60%. Clearly any deviation from this predicted rate would have major resource implications. Assessment and any subsequent treatment would involve a multi-disciplinary team, working at the Cancer Unit, as recommended in recent NHS Executive guidance.

The gold standard for investigation is colonoscopy. When completed successfully this allows visualisation of the whole bowel. However performance varies widely across the UK, and there is insufficient skilled manpower to undertake this additional workload. Most significantly the technique has a mortality rate quoted at 0.02%, so the programme could expect 12 deaths per annum, which would not be acceptable. Alternatively, assessment of screen-positive cases could be by a combination of double contrast barium enema and flexible sigmoidoscopy, with a comparable sensitivity. Both procedures have much lower morbidity and mortality rates. Colonoscopy would then only be required for a smaller number of patients, with cancer or suspicious lesions, or following unsatisfactory investigations.

Quality Assurance should be an integral part of the programme, as in the other NHS cancer screening programmes, involving all professional groups and coordinated by a regional quality assurance reference centre.

Cost estimates are over £40 million a year, plus any allowance for general practitioners, with additional capital and training costs at the start of the programme. Given a 60% overall uptake rate, a test sensitivity of 60%, and a recall rate of 2%, approximately 35% of the cases of colorectal cancer in the eligible population, i.e. about 5400 cases, could be detected per year. As this would also depend on maintaining good compliance, an ongoing 4000 cases is a more realistic figure. Significant savings on treatment costs are unlikely, as aggressive curative therapies would be expensive.

## Introduction

Colorectal cancer is the second most common cause of cancer deaths in the United Kingdom, with over 30,000 new cases and almost 20,000 deaths each year (1). 93% of these deaths occur in people over 55, and incidence increases with age, with a lifetime risk of 1 in 25. The estimated annual treatment cost in the UK is over £250 million (2). Overall 5 year survival is less than 40%, but can be 80% in tumours detected at Duke's stage A, whilst still confined to the bowel wall (3). 50% of cases are stage C or D at diagnosis, when prognosis is poor.

Three randomised controlled trials (4-6) have shown reduced mortality from colorectal cancer in study populations offered annual or biennial faecal occult blood testing (FOBT). No country has a national screening programme at present, but the United States Preventive Task Force endorses annual FOBT or sigmoidoscopy every 5 years in those over 50 (7).

This paper was commissioned by the Secretariat of the National Screening Committee and was presented at the Second National Workshop on Colorectal Cancer Screening, held in Cardiff in March 1998. The brief was to plan a biennial programme based on FOBT, for a resident population of 1 million, and for England and Wales. Eligible age range and details of screening protocol were not specified.

## Definition of proposed programme

The proposal under consideration is a biennial screening programme for those aged 50-69 using faecal occult blood (FOB) tests. Participants would receive an invitation by mail from their General Practitioner, together with the test kit, and would perform the test as directed at home, collecting specimens from 3 consecutive bowel motions onto the special cards provided. Completed tests would be returned to the Screening Centre in a special metallised envelope suitable for posting.

The planning proposals are based on programmes for resident populations of 1 million, comprising one or more Health Authorities, and 2/3 Cancer Units. All the administration and reading of the test slides would be carried out in the Screening Centre. Patients requiring investigation would attend Assessment Clinics run by designated teams, at the nearest Cancer Units. The usual investigative technique is colonoscopy, followed by double contrast barium enema (DCBE) when complete colonoscopy has not been achieved. Those diagnosed with colorectal cancer would be treated at these Cancer Units as appropriate, in conjunction with the local Cancer Centre.

Quality assurance mechanisms would be integral to the programme, involving all professional groups and coordinated through regional Quality Assurance Reference Centres. These would each be responsible for 5-7 programmes and would provide a performance monitoring role to the NHS Executive.

## Planning assumptions and evidence

### 1. Age Range:

Participants in the Minnesota study (4) were aged 50-80 whilst those in the Danish (5) and Nottingham (6) studies were 45-74. However, colorectal cancer is rare in those under 50, with only 5% of cases diagnosed, and these may have genetic implications. About 50% of cases occur in the age range 50-69 (7). In the Nottingham trial uptake at initial invitation was significantly lower both in those aged 45-49 (37%) and in those aged over 70 (48%) than in the 50-69 age group (55%) (6). The colorectal cancer mortality benefit was divided into two age groups. It was 19% better for those under 65 at the start of the study but only a nonsignificant 10% better for those 65 or over, giving the quoted 15% overall figure. The NHS Breast Screening Programme (NHSBSP) routinely invites only those aged 50-64, but a pilot study has shown attendance is also high in women aged 65-69, when invited to attend (8). Thus 50-69 seems sensible to optimise both uptake and benefit.

### 2. Biennial Screening:

The Danish and Nottingham trials both showed benefit in terms of mortality reduction from biennial screening (5,6). The Minnesota study (4) showed a greater benefit from annual screening, but at greater cost. A very large number of investigations were performed, due to the higher sensitivity of the test, and it is possible the greater mortality benefit derived at least partly from the removal of more precancerous lesions rather than more frequent screening.

### 3. Screening Protocol

#### a) Use of Haemoccult-II or similar FOBT

Several other types of FOBT are now available, including versions where the kit is thrown in the toilet and read by the patient. However these have not been evaluated in randomised controlled trials. Some are reported to have higher sensitivities, but this may lead to large numbers of false positives (9).

#### b) No dietary restriction at initial screen.

Danish participants were asked to consume no red meat, fresh fruit, iron preparations, vitamin C, aspirin or other non-steroidal antirheumatics during the 3 days before the samples were taken. In Nottingham no dietary restrictions were suggested at the initial screen, but those with up to 4 of the 6 possible test squares positive were asked to repeat the procedure with the restricted diet, in order to reduce the false positive rate. The result of this revised protocol was a similar proportion deemed ‘screen positive’, and thus requiring investigation, to that observed in Denmark. Uptake in Nottingham was only 57%. Diet restriction may significantly reduce the acceptability of the test, and is impossible to control effectively.

**c) Reminder letter after 4-6 weeks.**

It is standard practice in the NHS Breast and Cervical Screening programmes to give non-attenders a second opportunity. For equity, an NHS programme would need to re-invite all those eligible every two years, unless they signed a disclaimer.

**d) Rehydration of samples.**

The Minnesota study involved rehydration of samples, giving a sensitivity of 92.2 and specificity of 90.4 (4), but with a very high false positive rate. This meant that 50 people had to be investigated for each cancer detected. Ceasing rehydration reduced the positive rate from 9.8% to 2.4%, with decreased sensitivity (80.8%), but increased specificity (97.7%). Slides were not rehydrated in either the Nottingham or Danish studies.

**e) Criteria for investigation**

Participants initially testing positive on 1-4 squares would be invited to retake the test with dietary restriction. Those with 5-6 positive squares on the initial screen or any positive squares on the retest would be referred for investigation. Those rescreening negative would be offered retesting 3 months later, as in the Nottingham protocol. At this stage any positive squares would result in further investigation. In this study less than 2% of those screened required further investigation and about 11% of these had cancer (6). In the view of the author this seems an acceptable false positive level.

## 4. Further investigations

Three diagnostic procedures can be used to investigate those with positive screens.

**a) Colonoscopy**

This is the 'gold standard' technique because the whole bowel can be visualised and biopsies taken. It is technically difficult and requires thorough preparation and sedation of the patient. The procedure can usually be performed as a day-case. Only medically-qualified staff have carried out colonoscopy, and there is good evidence that competence increases with training and experience of over 200 procedures (10,11). Thorough audit of these diagnostic investigations is recommended (11). Most publications report completion rates of 85-95%, but UK audit data indicates rates as low as 50% in some areas (11). When the endoscope does not reach the caecum and the examination is incomplete it may be necessary to refer patients for follow-up DCBE. In the Danish trial about 8% of those who screened positive also had DCBE following incomplete colonoscopy (5). The rate would probably be higher in less experienced centres - about 25% is quoted in an Italian study (12).

**TABLE 1: Sensitivity, specificity and complication rate for investigative techniques (from Winawer et al).**

| | Colonoscopy | DCBE | FSIG | DCBE/FSIG |
|---|---|---|---|---|
| Sensitivity for cancers (%) | 97 | 84 | 97 (for 50% colon) | 98 |
| Specificity for cancers (%) | 98 | 97 | 94 (for 50% colon) | 98 |
| Morbidity (%) perforation haemorrhage | 0.1 0.3 | 0.03 | 0.015 | 0.045 |
| Mortality (%) | 0.02 | 0.003 | | 0.003 |

Complication rates are much higher than for alternative techniques (Table 1), with a significant mortality rate, usually quoted as 0.02% (13,14). A mortality risk justifiable in symptomatic patients presents major difficulties for a screening programme. No deaths attributable to colonoscopy have been reported in the published trials (4-6). However a national programme would involve a projected 60,000 investigations and could therefore experience 12 deaths per annum, which would clearly be unacceptable. Sensitivity and specificity are 97% and 98% respectively for cancers, but even this technique can miss important lesions (13,15).

**b) Double contrast barium enema (DCBE)**

This technique images the whole bowel in most completed examinations, but 10% may be unsatisfactory, due to differences in clinical skill or patient's anatomy. Most studies have been conducted on symptomatic rather than screened patients, but sensitivities in the range 55-85% are quoted for Duke's stage A and B cancers (13,16-19). False positives are less than 1% for cancers and 5-10% for large polyps. It is thus possible to detect the majority of clinically important lesions (13), but some examinations do have to be repeated due to technical difficulties. Complications and mortality rates are low (Table 1).

Until recently radiologists administered the barium enema, but senior radiographers can now undertake this following training. This can be more cost-effective as the throughput of the fluoroscopy room is increased. The radiologist is then only required to report the films, taking about 5 min. per patient.

There is a small risk of radiation-induced cancer, with an average radiation dose quoted as 7mSv (International Commission on Radiation protection, 1990). Minimisation of number of films and adherence to radiological quality assurance should keep this to acceptable levels.

### c) Flexible sigmoidoscopy

This allows clinicians to visualise the lower bowel directly and biopsy lesions as part of the procedure. Patients do not require sedation, and can therefore be examined as outpatients. The procedure is quick, taking about 5-10 min, depending on experience (13). Competence can be achieved after 24-30 examinations. There is good evidence that non-medical health professionals can be trained to do this as competently as gastroenterologists, with similar cancer detection and complication rates (20,21) although they do not usually perform polypectomy. Patients were more willing to return for a repeat procedure after examination by a nurse (21).

The limitation of this process is the proportion of colon visualised, about 50% of the total (13), with a sensitivity of 96%. It should therefore be possible to detect about half the colon cancers and all the rectal cancers i.e. 66% of all colorectal cancers (13). Guidelines would need to be produced on follow-up of individuals with small (<1 cm) adenomas. There is a 1 in 3 chance that they will also have additional proximal adenomas.

### d) Combined DCBE and sigmoidoscopy

This combination is the diagnostic evaluation technique in the ongoing Swedish trial. There is good evidence from an American randomised controlled trial that this combination is as effective as colonoscopy for detection of clinically significant lesions (22), and costs are similar (23). The Swedish group reported a combined sensitivity of 98% (24), although with no mortality benefit to date. It is standard practice to confirm the diagnosis by an alternative technique before proceeding to an expensive and hazardous operation. It has therefore been assumed that following DCBE/FSIG, 12.5% would require either confirmatory or follow-up colonoscopy.

## 5. Options for discussion

The main screening trials have used colonoscopy as the major investigative technique, and a programme has been planned accordingly. This is Option 1. However in view of the technical difficulty of this procedure, the shortage of skilled personnel and above all the unacceptable risk of mortality, it seems reasonable to consider an alternative option, with similar sensitivity and specificity , but a lower rate of complications. The programme has therefore also been planned with a combination of double contrast barium enema and flexible sigmoidoscopy (DCBE/FSIG) as assessment techniques. This is Option 2, recommended for consideration by the National Screening Committee.

## 6. Natural history of colorectal cancer

Mucosal masses in the bowel- 'polyps'- represent different kinds of histology, with varying clinical importance. About 25% of the population have premalignant adenomatous polyps by the age of 50, and prevalence increases with age (25). The probability of progression to invasive cancer can theoretically be estimated on histological examination. Those individuals with polyps which are large, of tubulovillous or villous histology, and multiple occurrence are at greater risk of developing both further adenomatous polyps and cancer.

The general consensus is that most cancers of the colon and rectum arise from adenomatous polyps, however few actually progress to cancer (about 2.5 polyps per 1000 per year). The recent American review estimated an average of 10 years for a polyp of less than 1cm diameter to transform into invasive cancer (12).

The major difficulty envisaged with those recalled for assessment relates to follow-up and/or treatment of those found to have benign lesions, polyps and adenomas. The numbers of these cases will rise rapidly over the years, causing both considerable anxiety for patients, and diagnostic workload for the cancer centres. Once in the system there will be a tendency to recall these individuals for regular investigations, without good evidence of clinical benefit. It may be appropriate to return all patients to normal recall, following excision of benign polyps.

## Programme Organisation

Approximately 20% of a population of 1 million would be in the eligible age range of 50-69. On a biennial frequency it would therefore be necessary to invite 100,000 individuals each year. In addition to the staff at a Screening Centre, a large number of individuals from different specialties and professional groups would be involved in the programme:

- Health Authority: Screening section, health promotion and public health
- Primary care: GPs, practice nurses and administrative staff
- Screening centre: Office staff. Nurses/MLSOs/other technical staff.
- Cancer Units: Multidisciplinary team i.e. Radiologists and radiographers, gastro-intestinal surgeons, gastroenterologists, endoscopy nurses & other endoscopy unit staff. Specialist colorectal cancer nurses. Pathologists & MLSOs. Clerical staff.

As the test kit would be sent by mail and the screening test performed by the individual at home, personal contact with participants would be limited. The main elements of personal contact would be in primary care, and at the Cancer Units during investigation and treatment.

### Detailed Planning

### 1. Health Promotion

Uptake in the Nottingham study was 51-54% for men aged 50-69 and 54-59% for women, at the first invitation. Overall 59.6% completed at least one test. Acceptance varied from 29-74% according to general practice (6). Randomisation was by household, limiting the scope for health promotion activities at either practice level or across the city.

A variety of health promotion activities would be required to ensure that everyone eligible for a test was fully informed about the screening programme, and able to take up the offer of a test if they so wished. The Forrest report paid little regard to health promotion and no specific resources were allocated. In this case it would be important to include an allowance in the overall cost projections.

### 2. Primary Care role

### a) Patient information lists

General practitioners would be required to check their lists for 20% of their patients every two years, for correct addresses and recent deaths. It would seem sensible to invite whole practices and indeed whole towns over a limited time period for ease of administration and health promotion, even though there is no geographical constraint, as with the mobile units involved in breast screening. At present general practitioners check about 7% of their lists every three years for the NHSBSP, without payment. Patients should be invited unless currently being treated for colorectal cancer, terminally ill, or they had signed a disclaimer.

## b) Support for programme

Given that the screening invitation would purport to come from the general practitioner and there would be no personal contact with the Screening Centre, primary care would be the natural point of referral for those with questions, and active support by the practice crucial to good informed compliance rates. There would inevitably be questions about the test, and particularly about abnormal results, and the nature of the investigations advised. Patient anxieties would need to be managed properly, and this would increase the workload of the practice nurse. In this case it may therefore be appropriate to provide a fee, although this would significantly increase the costs of the programme.

## 3. Screening Centre

The screening centre would serve a population of about one million and be responsible for all the administration and FOBT testing for 100,000 individuals invited each year. The Screening Centre could be located on any convenient NHS site in the area served. The centre would require 4 or 5 large rooms, one of which was used as the laboratory for processing and reading the completed test slides, plus facilities for slide disposal. At present there is no system of automation for slide reading. The Nottingham experience is that only about 40-50 sets can be read per hour and the results logged on the test envelope by one experienced reader. Assuming an uptake of 60%, the centre would have to read 60,000 sets per annum. A blue colour indicates the presence of occult blood, but readers would need to become experienced on the intensity of colour associated with such a positive result. Although the slide reading is straightforward, and requires no extended training, a suitable state-registered health professional (MLSO or nurse) would need to take clinical responsibility for reporting the results. It might be appropriate for this individual to be the Screening Centre Manager.

Test instructions require slides to be read two minutes after adding the developer solution, and to ignore any later colour changes. A separate section of the slide can be used for internal quality assurance testing (both positive and negative). However there is no mechanism for storing the test slide, or even re-reading it some time later. This has both benefits and disadvantages for a screening programme- any evidence of missed positives will be destroyed. External quality assurance poses problems, and would need to involve inclusion of standard ‘test’ slides into the routine screening batches.

It is estimated that about 10-12 staff of various grades would be required to read the slides, handle the administration of the programme, and send out all the necessary letters. This is based on the current workload in NHSBSP screening offices. Reminder and normal result letters could use Economailer systems. An envelope-filling machine could be customised to handle the invitation test packs. The only other item of capital expenditure would be for the computer system.

Over 200,000 letters per annum would be required, because each patient would need to be contacted at least twice. If they responded quickly to the invitation they would receive the test results, and if not they would be sent a reminder. The volume of correspondence is therefore not very sensitive to the uptake rate, unless a decision is taken not to issue reminders.

## 4. Investigation/assessment

The Screening Centre would arrange appointments sessions. Patients would go to their local Cancer Unit for assessment, and, for a programme serving a total population of 1 million, 2 or 3 Cancer Units would share the workload of about 27 cases per week. It may be possible to accommodate the necessary sessions in existing Out Patient and Radiology Departments, although some specialist centres across the UK have waiting lists of 3-4 months due to shortage of manpower, and/or facilities.

### a) Investigation by colonoscopy

About 6 patients could be accommodated in one session, involving a specialist gastrointestinal surgeon and two endoscopy nurses. The workload and manpower projections are shown in Tables 2 and 4, based on an uptake rate of 60% and a recall rate of 2%, so that nationally 60,000 patients would require assessment.

Clearly any variation from this projected rate of 1200 screening investigations per million per year would have major resource implications for the programme. A 3% recall rate would involve a 50% increase in assessment clinics - and associated costs. Similarly uptake of 70% would result in a further 200 investigations per annum per screening programme.

### b) Investigation by DCBE/FSIG

These techniques can both be performed as outpatient procedures, and have the advantage of a lower level of medical intervention. DCBE administered by radiographers is becoming widely accepted, and a growing number of colorectal cancer clinical nurse specialists or nurse endoscopists are trained to carry out FSIG.

**TABLE 2: Option 1: Investigation by colonoscopy, as first line technique (assuming 60% uptake and 2% recall rate)**

| | **Single programme** | | **National requirement** |
|---|---|---|---|
| | **per week** | **per annum** | **per annum** |
| Numbers of patients recalled | 27 | 1,200 | 60,000 |
| Number endoscopy sessions | 4-5 | 200 | 10,000 |
| Number DCBE examinations if 7-10% of colonoscopies are incomplete | 2-3 | 84 -120 | 4200 - 6000 |
| Number DCBE sessions | 0.25 - 0.3 | 11-15 | 550 - 750 |
| Associated pathology sessions | 2 | 90-100 | 4500-5000 |

**TABLE 3: Option 2: Investigation by DCBE/FSIG (assuming 60% uptake and 2% recall rate)**

| | Single programme | | National requirement |
|---|---|---|---|
| | **per week** | **per annum** | **per annum** |
| No. of patients recalled for both investigations | 27 | 1,200 | 60,000 |
| Number of DCBE sessions | 3-4 | 135-150 | 6500 - 7500 |
| No. of endoscopy sessions | 3 | 130 | 6500 |
| No. of follow-up colonoscopies | 3-4 | 150 | 7500 |
| No. of colonoscopy sessions | 0.5-0.7 | 25 | 1250 |
| No. of associated pathology sessions | 2 | 90 | 4500 |

Although biopsy and polypectomy are possible during the course of FSIG, standard practice is to book patients with identified lesions/polyps for full colonoscopy. In the costings projected for a national programme it has been assumed that 12.5% of those recalled for assessment would go on to have colonoscopy, either for suspected cancer or due to unsatisfactory investigations. However overt lesions could be biopsied during the FSIG.

## 5. Manpower

Manpower requirements are indicated in Table 4. Most of these involve small sessional commitments, which are unlikely to be accommodated by existing staff, but would pose serious recruitment problems. At the present time there are not enough colorectal surgeons across the UK to cope with this additional workload, and recent guidance (11) highlights the need for more specialists in this field. Certainly there are not enough gastroenterologists (physicians or surgeons) to undertake an additional 60,000 investigations per annum.

The requirement for additional radiology and pathology manpower could possibly by accommodated. Radiology is a shortage specialty and the NHSBSP has experienced difficulties in attracting enough consultant staff, but for colorectal cancer screening the time commitment of only 1 or 2 sessions per week would fit in more easily with other interests.

**TABLE 4: Manpower requirements for colorectal cancer screening programme (in whole time equivalents)**

| | **Single programme (serving 1 million)** | **National programme (50 million)** |
|---|---|---|
| **Screening Centre** | | |
| Screening centre manager | 1 | 50 |
| Admin & clerical) | | |
| Test readers ) | 10-11 | 500-550 |
| **Cancer Units** | | |
| **Either (Option 1)** | | |
| Consultant GI surgeon | 0.5 | 25 |
| Endoscopy nurses | 1 | 50 |
| Radiologist | 0.1 | 5 |
| Radiographer (Snr II) | 0.1 | 5 |
| **or (Option 2)** | | |
| Radiologist | 0.15 | 8 |
| Radiographer (Snr II) | 0.5 | 25 |
| Endoscopy specialist (gastroenterologist, GI surgeon or nurse endoscopist) | 0.4 | 20 |
| Endoscopy nurses | 0.7 | 35 |
| GI surgeon | 0.1 | 5 |
| **Plus (both Options)** | | |
| Pathologist | 0.2 | 10 |
| MLSO | 0.25 | 13 |
| Clerical support (for all investigations) | 0.6 - 1 per CU | 100 |
| Colorectal cancer specialist nurse | 0.5 | 25 |

## 6. Training & educational issues

A national programme could only be rolled out progressively as staff were trained to their roles.

### a) Medical staff

Additional specialists need to be trained in colonoscopy, both to improve symptomatic diagnoses (8) and for any national screening programme. The annex to the Executive Letter accompanying the guidance (26) recognises additional costs of the order of £30,000 per million population for such training. There is evidence that satisfactory performance requires experience of 50 procedures for trainees to reach the caecum 80% of the time, but those who had done over 200 succeeded with 95% of investigations (10,11).

Reading of double contrast barium enema films is a standard part of a radiologist's workload, so additional training should not be required.

### b) Radiographers

There is an existing course to train Senior II radiographers to administer DCBE, but numbers would have to be expanded considerably to cope with the increased demand resulting from colorectal cancer screening. Only a small number have completed the course to date.

### c) Nurses

Nurse endoscopists

Only a few nurses across the UK are fully trained to carry out FSIG. Others have completed the formal course, but this needs to be followed by performance of some 50 investigations under supervision and recorded on video. This training capacity would need to be expanded considerably if nurses were to be generally responsible this assessment. It is likely to be a more practical approach than training additional consultants or other doctors, but they are not taught to perform polypectomy.

Clinical nurse specialists

Whilst the role of specialist breast care nurses is becoming established, that of nurses specialising in colorectal cancer diagnosis and care is not well developed. It is broader than the existing stoma nurses' remit, and may be combined with endoscopy.

### d) Screening centre

The greatest training requirement would be for the screening centre staff in principles and operation of the programme, the computer system and FOBT slide reading. Recruitment and retention of staff would probably be enhanced by job descriptions covering a variety of functions in the screening centre, but this would increase the level of training required.

### e) Primary care

This training requirement should include both practice nurses and reception staff, who would bear the brunt of patients enquiries and concerns, and would need a very clear understanding of the principles and operation of the programme, its limitations and grey areas.

## 7. Quality Assurance

This must be integral to the programme and involve all professional groups. A culture of excellence needs to permeate the whole programme. Screening should not be done at all if it is not of high quality. The following would be required:

- Regional quality assurance reference centre covering about 6 screening centres.
- Regular local multidisciplinary meetings to discuss cases
  - allowance has been made for attendance at these meetings in the projected manpower levels
  - attendance should be mandatory, but the meetings could be combined with those envisaged for symptomatic work (11).
- FOB slide quality assurance scheme
- Audit of colonoscopy, FSIG and DCBE, including completeness, complication and mortality rates and detection of cancers and adenomas.
- Audit of office procedures and failsafe.
- Audit of interval cancers and those non-compliers, in conjunction with local Cancer Registry.
- National system of professional quality assurance monitoring groups.
- Performance management by NHS Executive, with accountability to Regional Director of Public Health.

## 8. Setting-up Costs and Capital Equipment

Equipment requirements are listed in Table 6. Provision of imaging equipment or endoscopy facilities are likely to vary widely across the country. In some Cancer Units investment may be needed to implement the guidance for symptomatic colorectal cancer management (11,26).

Costs of building additional rooms have not been included, so this would be an additional setting-up cost, if suitable vacant accommodation were unavailable.

It would be necessary to design and implement computer systems, i.e. software for health authorities to produce call-and-recall data and a dedicated system for the screening centres**.** Both would need constant maintenance and updating

**TABLE 5: Capital Equipment Requirements**

| Location | Equipment | Cost |
|---|---|---|
| Screening Centre | Computer system<br>Envelope filling machine | £25,000<br>£30,000 |
| Cancer Unit | X-ray fluoroscopy equipment (1)<br>Daylight processor<br>Colonoscopy and associated equipment<br>Flexible sigmoidoscope<br>Complete endoscopy suite | £250,000<br>£25,000<br>£45,000+ per set<br>£10,000+ per set<br>£500,000 minimum |

Note 1. This cost estimate is for equipment for a basic x-ray room only. A multipurpose/digital room would be more expensive, but possibly more flexible for the imaging department, and would obviate the need for film storage. Additional installation charges would depend on room configuration, etc.

## 9. Costings for a Colorectal cancer Programme

The main quantifiable costs are shown in Tables 6 and 7, for staff and non-staff costs respectively. Staff costs are based on midpoints of scales for 1997/8 and include 20% on-costs. The annual cost for a programme serving a population of 1 million is therefore estimated at **over £800,000** including NHS Trust overheads and/or screening centre rental. The main burden of these costs is due to the expensive investigations necessary on about 2% of those screened, even though over 90% of them will turn out not to have cancer (9). Until a more specific test is developed (and recent attempts with other technologies have been no better) COLORECTAL CANCER screening will be an expensive programme, even though the initial FOBT is cheap.

These projections are based on an assumed uptake rate of 60%, with 2% of those screened requiring investigation. Sensitivity analysis showed this to be very dependent on the recall rate, but not to variations in uptake, as the screening centre costs are largely fixed (Table 9).

Other potential costs, which have not been included, are:

* Setting up and training costs
* Allowance for primary care
* Treatment costs for cancers detected
* Costs of follow-up for benign lesions.
* Legal costs resulting from missed cancers or complications during diagnosis.

Colorectal cancer treatment is estimated at over £4 million per annum per million population, at 1991 prices (3). Implementation of the recent guidance to improve outcomes of symptomatic cases is estimated at £406,000 per million population per annum, plus about £150,000 in one-off change costs (26). Over 50% relates to adjuvant chemotherapy provision and improved palliative care.

**TABLE 6: Staff costs for national colorectal cancer screening programme (based on first line investigation by DCBE/FSIG)**

| Staff | Annual Salary + 20% oncosts (£) | Local Screening Programme (£) | National Programme (£ million) |
|---|---|---|---|
| Screening centre manager | 30,000 | 30,000 | 1.5 |
| Screening Centre Staff | 15-20,000 | 170,000 | 8.5 |
| Consultants (various specialties) | 65,000 | 55,000 | 2.75 |
| Endoscopy nurses | 20,000 | 14,000 | 0.7 |
| Radiographers (Senior II grade) | 22,000 | 11,000 | 0.55 |
| MLSO | 20,000 | 5000 | 0.25 |
| Colorectal cancer specialist nurse | 30,000 | 15,000 | 0.75 |
| Clerical | 15,000 | 30,000 | 1.5 |
| **Total** | | **330,000** | **16.5** |

Notes:

1. Costs based on consultant grade endoscopists. A saving of £14,000 per annum per local programme is possible if FSIG is carried out by a nurse endoscopist.

2. Clerical support shared between endoscopy unit, radiology and pathology in all cancer units involved in programme.

**TABLE 7: Annual Non-staff costs for a national colorectal cancer screening programme**

| | Single programme for 1 million population (£) | National programme (£ million) |
|---|---|---|
| **Screening centre** | | |
| Test kits | 150,000 | 7.5 |
| Stationary ) | | |
| Postage ) | 120,000 | 6.0 |
| Computer maintenance | 5,000 | 0.25 |
| Rental/ | | |
| Utilities/overheads | 20,000 (variable) | 1.0 |
| **Cancer Units:** | | |
| Films, chemicals barium, etc @ £25 per exam. | 30,000 | 1.5 |
| Radiology equipment maintenance | 20,000 | 1.0 |
| Endoscopy unit consumables drugs, etc. @ £10 per exam. | 12,000 | 0.6 |
| Equipment maintenance | 5,000 | 0.25 |
| Pathology nonstaff costs @ £5 per patient | 6,000 | 0.3 |
| Trust overheads | 20,000 (variable) | 1.0 |
| **Other costs:** | | |
| Health promotion | 50,000 | 2.5 |
| PNL generation (Health Authority) | 50,000 | 2.5 |
| QA Reference Centre contribution | 15,000 | 0.75 |
| (Primary care allowance) | ? | ? |
| **Total** | **503,000** | **25.15** |
| **Staff costs brought forward from TABLE 6** | **330,000** | **16.5** |
| **Total costs** | **833,000** | **41.65** |

A district with a population of 1 million would expect 600 cases of colorectal cancer to be diagnosed per annum. Of these a maximum of 50% would be likely to be detectable in the screening age range. If the screening programme succeeded in detecting 120 cases, which would be a similar proportion to the yield of the NHSBSP (19), this would work out at £6,5000 per cancer detected. This may be an optimistic outcome because the FOBT sensitivity is only about 60%. A decision analysis was conducted alongside this conventional planning exercise (28). The model was built up from first principles, using published data and indicated the yield of cancers could be less than 80 per annum, or £10,000 per cancer detected.

It is also possible that compliance will decrease in subsequent screening rounds, especially in those who have had investigations. In the Nottingham trial only 38% completed all the tests offered. However the NHSBSP has demonstrated that in an established programme, up to 90% of previous attenders return (8), so this fear may not be justified.

**TABLE 8: Sensitivity analysis on cost projections, assuming investigation by initial colonoscopy and follow-up DCBE.**

| Uptake (% of those invited) | Recall for assessment (% of those screened) | Number of investigations (per million population) | Number of colonoscopy sessions per annum | Estimated cost of programme (per million population) |
|---|---|---|---|---|
| 60 | 2 | 1200 | 200 | £833,000 |
| 60 | 3 | 1800 | 300 | £1,055,000 |
| 60 | 4 | 2400 | 400 | £1,275,000 |
| 50 | 2 | 1000 | 170 | £770,000 |
| 50 | 3 | 1500 | 250 | £945,000 |
| 70 | 2 | 1400 | 235 | £915,000 |
| 70 | 3 | 2100 | 350 | £1,165,000 |

## References


1. Austoker J. Screening for colorectal cancer *BMJ* 1994;**309:**382-6

2. Dunlop MG. Colorectal cancer: Clinical review: Science Medicine & the future. *BMJ* 1997;**314:**1882-5

3. Mountrey L, Sanderson H, Harns J. Colorectal Cancer in *Health Care Needs Assessment vol.1* edited by A Stevens & J Rafferty, Radcliffe, Oxford, 1994.

4. Mandel JS, Bard JH, Church TR, Snover DC, Bradley GM, Schuman LM & Ederer F for the Minnesota Colon Cancer Control Study. Reducing Mortality from Colorectal Cancer by Screening for Faecal Occult Blood. *N.Eng.J.Med.* 1993;**328:**1365-71.

5. Kronborg O, Fenger C, Olsen J, Jorgensen OD, Sandergaard O. Randomised study of screening for colorectal cancer with faecal occult blood test. *Lancet* 1996;**348:**1467-71.

6. Hardcastle JD, Chamberlain JO, Robinson MHE, Moss SM, Amar SA, Balfour TW, James PD, Mangham CM. Randomised controlled trial of faecal occult blood screening for colorectal cancer. *Lancet* 1996;**348:**1472-7.

7. Lieberman D, Sleisenger MH. Is it time to recommend screening for edorectal cancer? (Commentary) *Lancet* 1996;**348:**1463-4.

8. Rubin G, Garvican L, Moss S. "Routine Invitation of Women aged 65-69 for Breast Cancer Screening: Results of the first year at the East Sussex, Brighton and Hove Breast Screening Service pilot site. *BMJ*, 1998, in press.

9. Simon JB. Fecal Occult blood testing: Clinical value and limitations. *The Gastroenterologist* 1998;**6:**66-78.

10. Cass O, Freeman M, Peine C, Zera R, Onstad G. Objective analysis of endoscopy skills during training. *Annals. Int. Med.* 1993;**118:**40-44.

11. NHS Executive Guidance on Commissioning Cancer Services. *Improving Outcomes in Colorectal Cancer. The Manual & Research Evidence.* Department of Health, London, 1997.

12. Castiglione G, Zappa M, Grazzinig, Sani C, Mazzotta A, Mantellini P, Ciatto S. Cost analysis in a population based screening programme for colorectal cancer: comparison of immunochemical and guirac faecal occult blood resting. *J.Med.Screening* 1997;**4:**142-6.

13. Winawer SJ, Fletcher RH, Miller L et al. Colorectal Cancer Screening: Clinical Guidelines and Rationale. *Gastroenterology* 1997;**112:**594-642.

14. Waye JD, Kahn O, Auerbach ME. Complications of colonoscopy and flexible sigmoidoscopy. Gastrointest Endosc Clin N Am.1996; **6:**343-377.

15. Rex DK, Cutler CS, Lemmel GT et al. Colonoscopic miss rates of adenomas determined by back to back colonoscopies. *Gastroenterology* 1997;**112:**24-28.

16. Hixson LJ, Fennerty MB, Sampliner RE, McGee D Garewal H. Prospective study of the frequency and size distribution of polyps missed by colonoscopy. *J. Natl Cancer Inst.*1990: **82:**1769-72

17. Fork FT. Double contrast barium enema and colonoscopy in polyp detection. *Gut* 1981;**22:**971-7.

18. Steine S, Stordahl A, Lunde OC, Loken K, Laerum E. Double contrast barium enema versus colonoscopy in the diagnosis of neoplastic disorders: aspects of decision making in general practice. *Fam. Pract* 1993;**10:**288-91.

19. Hixson LJ, Fennerty MB, Sampliner RE, Garewal HS. Prospective blinded trial of the colonoscopic miss-rate of large colorectal polyps. *Gastrointest Endosc* 1991;**37:**125-7.

20. NHS Centre for Reviews & Dissemination. The Management of Colorectal Cancer. *Effective Health Care Bulletin* 1997;**3(6):**1-12.

21. Maule WF. Screening for colorectal cancer by nurse endoscopists. *N.Eng.J.Med* 1994;**330:**183-7.

22. Rex D, Waddle R, Ga L, Pound D, O'Connor K, Hawes R, Dittus R, Lappas J, Lumeng L. Flexible sigmoidoscopy plus air contrast barium enema versus colonoscopy for suspected lower gastrointestinal bleeding. *Gastroenterology* 1990;**98:**855-861.

23. Walker AR, Whynes DK, Chamberlain JO, Hardcastle JD. The hospital costs of diagnostic procedures for colorectal cancer. *J.Clin.Epidemiol*. 1991;**44:**907-14.

24. Kewenter J, Brevinge H, Engaras B, Haglind E. The yield of flexible sigmoidoscopy and double contrast barium enema and the diagnosis of neoplasia in the large bowel in patients with a positive haemoccult test. *Endoscopy* 1995;**27:**159-63.

25. Williams AR, Balasooriya BAW, Day DW. Polyps and cancer of the large bowel: an autopsy survey. Gut 1982;123:835-42.

26. NHS Executive. Guidance on commissioning cancer services. EL (97)66 Annex A.

27. Garvican L, Littlejohns P. An evaluation of the prevalent round of the NHS Breast Screening Programme in South East Thames, 1988-1993: Achievement of Quality Standards and Population Impact. J.Med. Screening 1996;3:123-128.

28. Gray A, Briggs A. The benefits and adverse effects of screening for colorectal cancer: a decision analysis. Report for the National Screening Committee. March 1998.

# APPENDIX 2

# The benefits and adverse effects of screening for colorectal cancer: a decision analysis[1]

**Prepared for the National Screening Committee**

**by**

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**March 1998**

[1] This paper is currently being redrafted prior to submission for publication.

## Introduction

This draft report sets out the methods, data and results of a decision analysis performed by the Health Economics Research Centre, University of Oxford, on behalf of the National Screening Committee. The report is intended as the starting point for a debate about the benefits and adverse effects of such a programme, rather than as a definitive statement. It can usefully be read in conjunction with the report by Linda Garvican for the Committee,(1) from which the screening options have been taken.

## Methods

*Population*

The baseline model assumes that everyone aged 50-69 would be invited to participate in the programme.

*Screening options considered*

Two options are considered: these are called Option A and Option B. Both options involve a biennial screen, both include all adults aged 50-69, and have the same initial test procedure (set out below). The main difference concerns the method of investigation, Option A relying on colonoscopy as the first line method of investigation, while in Option B the initial method of investigation is flexible sigmoidoscopy and double contrast barium enema.

*Test procedure*

Figure 1 sets out the tree for the test procedure. The initial test procedure is identical in the two options considered (Option A and Option B). Persons complete one FOB test, and those who test strongly positive on this test (5 or 6 squares positive) proceed straight to investigation. Persons who test positive (1 to 4 squares positive) proceed to another FOB. If the second test is also positive persons proceed to investigation; if it is negative persons proceed to a third test; if this is positive they proceed to investigation; if it is negative they return to the overall programme.

*Investigative procedure*

Figure 2 sets out the method of investigation in Option A. Persons proceeding to investigation following test results have a colonoscopy as the first line method of investigation. This is followed by double contrast barium enema if the investigation is not successfully completed.

Figure 3 sets out the method of investigation in Option B. Persons who screen positive proceed to flexible sigmoidoscopy as the first line method of investigation; the tree differentiates cancers in the upper and in the lower colon, as the flexible sigmoidoscope will not allow the upper colon to be visualised. Flexible sigmoidoscopy is followed by double contrast barium enema. If either of these two investigations is positive, colonoscopy is then performed.

*Overall model*

For Option A and Option B, the results of the test and investigation trees then feed into overall model tree, shown in Figure 4. The structure of this model is the same for each Option. The at risk population divides into those who comply with the initial FOB test and those who do not. Those who comply may either screen positive or negative, and those who screen positive proceed to investigation which may result in detection of a cancer, detection of a polyp, no abnormality detected, or investigative mortality. Full compliance is assumed if the person is referred for investigation following FOB test result.

Pathway probabilities are then attached to these trees, and the numbers of persons finishing up in each terminal node of the model are computed. We report for each Option the numbers tested and investigated, the number of cancers detected and missed, the number of polyps detected and excised, and the numbers of deaths induced.

*Cost-effectiveness*

In addition, we attach resource valuations to each event in order to calculate a total cost for each Option. We define the health outcome in terms of life-years gained. The distributions by Dukes Stage of colorectal cancer cases detected in a screening programme and in routine clinical practice are taken from published studies, alongside data on survival from date of detection for each stage. The benefit of the screening programme is then defined in terms of the improvement in survival measured in life years gained arising from earlier detection of cancer cases. Finally, cost-effectiveness is defined as the incremental costs per life year gained of a screening programme compared with no programme. Note that for the purposes of this analysis we have not discounted future costs and benefits to present values.

## Data

Evidence on colorectal cancer screening has recently been collected in an Effective Health Care Bulletin,(2) and as supporting material for the clinical guideline recommendations of an American panel on colorectal cancer screening. (3) These were the principle sources for the decision analysis.

*Sensitivity and specificity of FOBT*

Table 1 sets out the parameter values used in the test sub-model. The same values are entered for both Options. We assume a nonhydrated test, and no dietary restrictions in the first test. Reported sensitivities of the FOBT for cancer range from 38% to 92%, with figures of 53.6% from Nottingham and 51% from Denmark.(4,5) We follow the American panel in using a value of 60% in the base case. Specificity of the FOBT ranges from 90% to 98% for a nonhydrated test.(3) Our base case specificity is set at 0.94.

For the purposes of the model we have to make some assumption concerning the proportion of First FOBTs that are weakly or strongly positive. We assume that, amongst persons with cancer, 80% of positive tests will be strongly positive and 20% weakly positive. Among persons without cancer, we assume that 80% of positives will be weakly positive and 20% strongly positive.

Persons progressing to a 2$^{nd}$ or 3$^{rd}$ FOBT are assumed to adhere to dietary restrictions prior to the test; for these tests we use a sensitivity of 80.8% and a specificity of 97.7%, as found in the Minnesota trial.(6)

*Investigation*

Table 2 sets out the parameter values and sources for the investigations in Option A. The sensitivity of the colonoscope in the detection of cancer is set at 96.7%. The specificity of the colonoscope in the detection of cancer is set at 98%. The sensitivity of double contrast barium enema in the detection of cancer is set at 84%, and its specificity at 97.5%.(3). Previous studies have found that between 8%(5) and 25% of persons undergoing colonoscopy had DCBE as a result of incomplete colonoscopy. We assume in our base case that 15% of patients will have an incomplete colonoscopy. Our costs for colonoscopy (£143) and xray (£55) are based on the costing assumptions in the programme analysis.(1)

Table 3 sets out the parameter values and sources for the investigations in Option B. We assume that 0ne-third of cancers are located in the upper colon and therefore cannot be visualised by the flexible sigmoidoscope. The sensitivity of the flexible sigmoidoscope is set at 96.7%, and its specificity at 94%. The sensitivity and specificity of double contrast barium enema in the detection of cancer is set as in Option A, at 84% and 97.5% respectively.(3). Our cost of £75 per flexible sigmoidoscope procedure is based on a 1991 cost analysis, updated to 1997 prices.(7)

*Overall model*

Tables 4 and 5 shows the parameter values and sources for the overall model using Option A and B respectively. Both Options have the same values for all parameters, except that the sensitivity and specificity of their investigation procedures differ (i.e. the output of the investigation sub-model; individual procedures have the same sensitivity and specificity in each Option). The investigative approach of Option has a sensitivity of 0.948 and a specificity of 0.979. The investigative approach of Option B has a sensitivity of 0.912 and a specificity of 0.998.

Our base case assumes a health authority with a total population of 1 million, of whom 20% are in the age range 50-69. In line with the Nottingham figures, we assume that 57% of those invited for an initial screening test will agree.(8) The annual incidence of colorectal cancer is set at 100 per 100,000 amongst those aged 50-59, as stated in the Effective Health Care Bulletin, based on ONS Monitor statistics.(2) The incidence rate within the screening period (biennial) is therefore 200 per 100,000.

All the investigative procedures have complication rates; the best documented evidence of serious complication relates to colonoscopy, where 6 prospective studies have reported mortality rates of between 1 and 3 per 10,000 procedures: we use a base case figure of 2.36 per 10,000.(3)
The proportion of persons who are found to have benign polyps is set at 10%, in line with the Effective Health Care Bulletin finding from the literature. In the model, we document the number of polyps detected, but make no other assumptions concerning the benefits or adverse effects of removing them.

*Survival*

Table 6 summarises the model calculations on the gain in life expectancy from earlier detection of colorectal cancer. In the base case, 5-year survival rates by Dukes' Stage at diagnosis are taken from data from St Vincent's Hospital, Dublin, as quoted in the Effective Health Care Bulletin.(2) The distribution by Dukes' Stage of cases of colorectal cancer in unscreened and screened populations are taken from the Dublin data and from Nottingham respectively.(8) It is assumed that persons who survive for 5 years will thereafter approximate to the population life expectancy, which is taken from interim English Life Tables for 1994-96. From these data it is estimated that life expectancy on diagnosis of colorectal cancer is 10.3 years in an unscreened group and 12.3 years in a screened group, a gain in life expectancy of 2.00 years per case detected.

## Results

*Cases*

Table 7 summarises the screening results for Option A, and Table 8 shows the same information for Option B. Taking Option A first (Table 7), in a typical health authority of 1 million people, each year 100,000 persons will be screened (i.e., half the total number aged 50-69). 57,000 will be tested, of whom 875 (0.87%) will be investigated. 64 cancers will be detected but 136 cancers will be missed. Hence the number of incident cancers detected by Option A will be 32%. Each year there will be 17 persons whose test and investigation results are false positive and who therefore proceed to surgery. From all investigations, 79 polyps will be detected and excised. Finally, there will be 0.21 induced deaths each year, or one per 5 years.

Turning to Option B (Table 8), in a typical health authority of 1 million people, each year 100,000 persons will be screened (i.e., half the total number aged 50-69). 57,000 will be tested, of whom 875 (0.87%) will be investigated. 62 cancers will be detected but 138 cancers will be missed. Hence the number of incident cancers detected by Option B will be 31%. Each year there will be 1 person whose test and investigation results are false positive and who therefore proceeds to surgery. From all investigations 81 polyps will be detected and excised. Finally, there will be 0.02 induced deaths each year, or one per 50 years.

*Costs*

Tables 9 and 10 show the costs of option A and B respectively. In both options the fixed costs of the programme amount to £360,000 per year. Details of these are set out in the accompanying report. (1) Variable costs associated with letters, testes and investigations overhead costs are £427,507 in Option A and £419,979 in Option B. Consequently total costs per annum are £787,507 in Option A and £779,979 in Option B.

*Cost-effectiveness*

Tables 11 and 12 show the cost-effectiveness of Option A and Option B respectively. In the course of the year Option A detects 64 colorectal cancer cases which yield 128.94 life years gained. Set against this are 4.23 years of life lost from investigative mortality, giving a net gain in life years of 124.71. The total programme cost is £787,507 and in addition £50,211 will be spent on operating on false positives (we assume a unit cost of £3000 per operation). Hence the incremental cost per life year gained of Option A over no screening programme is £6,717 per life year gained. Note that these figures are not discounted.

Table 12 shows the cost-effectiveness of Option B. In the course of the year Option B detects 62 colorectal cancer cases which yield 124.08 life years gained. Set against this are 0.36 years of life lost from investigative mortality, giving a net gain in life years of 123.72. £4,042 is incurred in operations of false positives. Hence the incremental cost per life year gained of Option B over no screening programme is £6,337 per life year gained.

*Sensitivity analysis*

Many of the parameters used in Option A and B are subject to uncertainty. In order to examine the degree to which the results obtained might be affected by this uncertainty, a number of key parameters were varied within plausible ranges to assess the resulting changes in the results. In this analysis we have performed one-way sensitivity analyses, varying each parameter separately. This shows clearly the individual effect of each change, but is likely to understate the degree of uncertainty, as it does not capture the effect of simultaneous changes in a number of values.

Table 13 shows that the cost-effectiveness ratio in Option A is sensitive to changes in compliance and in the assumed sensitivity and specificity of the FOB test. However, changes in most of the other values have little effect on the results.

Table 14 shows a similar pattern for Option B.

Changing other aspects of the model will also have an effect on the results. For example, if the 5-year survival rates by Dukes' Stage and unscreened distribution by Dukes' Stage are taken from the Needs Assessment document rather than the Effective Health Care Bulletin, the gain in life expectancy per case detected falls from 2 years to 1.35 years, and consequently the cost per life year gained rises from £6,717 to £10,134 in Option A, and from £6,337 to £9,417 in Option B.

## Discussion

The decision analysis presented above gives some initial estimates of the benefits and adverse effects associated with two options for a national screening programme for colorectal cancer. There are a number of ways in which the analysis can be improved and extended:

- Variations in the basic structure of the model could be examined
- Some features of the model, such as the benefits and adverse effects of detecting polyps, could be developed
- The costings for investigations and for the programme could be refined
- To make comparisons with other health care interventions for which cost-effectiveness data are known, the results need to be discounted to present values.
- More comprehensive sensitivity analyses - including scenario analyses - could be performed.

However, by setting out a transparent structure and explicit parameter values, the model and its results should serve as a basis for discussion.

## Reference List


1. Garvican, L. Planning for a colorectal cancer screening programme in England and Wales: a report for the National Screening Committee. Tunbridge Wells, Kent. South east Institute of Public Health. 1998; p.1
2. NHSCRD. The management of colorectal cancer. Effective Health Care 1998;(3;6).
3. Winawer SJ, Fletcher RH, Miller L, Godlee F, Stolar MH, Mulrow CD, Woolf SH, Glick SN, Ganiats TG, Bond JH, et al. Colorectal cancer screening: clinical guidelines and rationale. Gastroenterology 1997;112(2):594-642.
4. Robinson MH, Moss SM, Hardcastle JD, Whynes DK, Chamberlain JO, Mangham CM. Effect of retesting with dietary restriction in Haemoccult screening for colorectal cancer. J Med.Screen. 1995;2(1):41-4.
5. Kronborg O, Fenger C, Olsen J, Bech K, Sondergaard O. Repeated screening for colorectal cancer with fecal occult blood test. A prospective randomized study at Funen, Denmark. SCAND.J GASTROENTEROL. 1989;24(5):599-606.
6. Mandel JS, Bond JH, Church TR, Snover DC, Bradley GM, Schuman LM, Ederer F. Reducing mortality from colorectal cancer by screening for fecal occult blood. Minnesota Colon Cancer Control Study [published erratum appears in N Engl J Med 1993 Aug 26;329(9):672] [see comments]. N.Engl.J Med. 1993;328(19):1365-71.
7. Walker AR, Whynes DK, Chamberlain JO, Hardcastle JD. The hospital costs of diagnostic procedures for colorectal cancer. J Clin.Epidemiol. 1991;44(9):907-14.
8. Hardcastle JD, Chamberlain JO, Robinson MH, Moss SM, Amar SS, Balfour TW, James PD, Mangham CM. Randomised controlled trial of faecal-occult-blood screening for colorectal cancer. Lancet 1996;348(9040):1472-7.

**Figure 1: Structure of model for test procedure, Options A and B.**

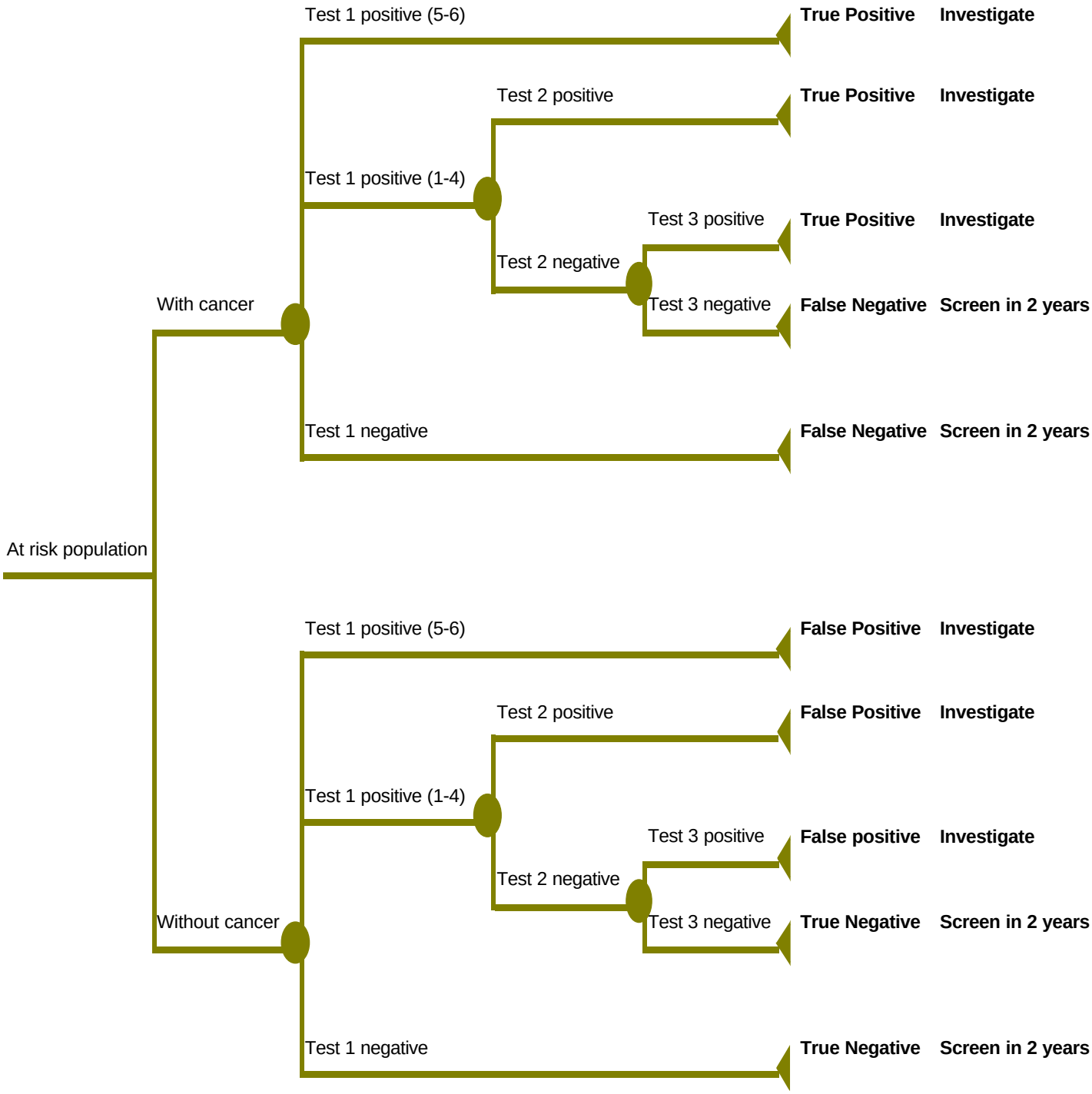

**Figure 2: Structure of model for investigation procedure, Option A**

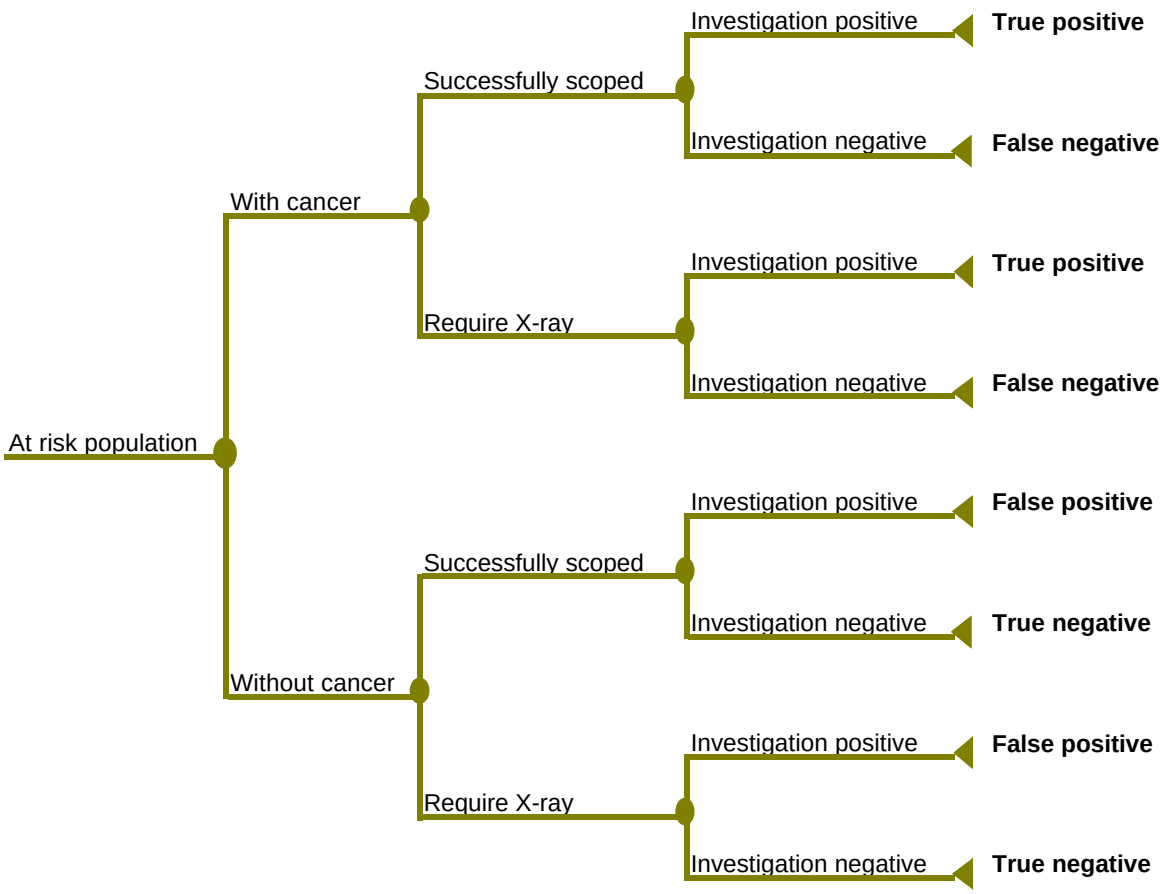

**Figure 3: Structure of model for investigation procedure, Option B**

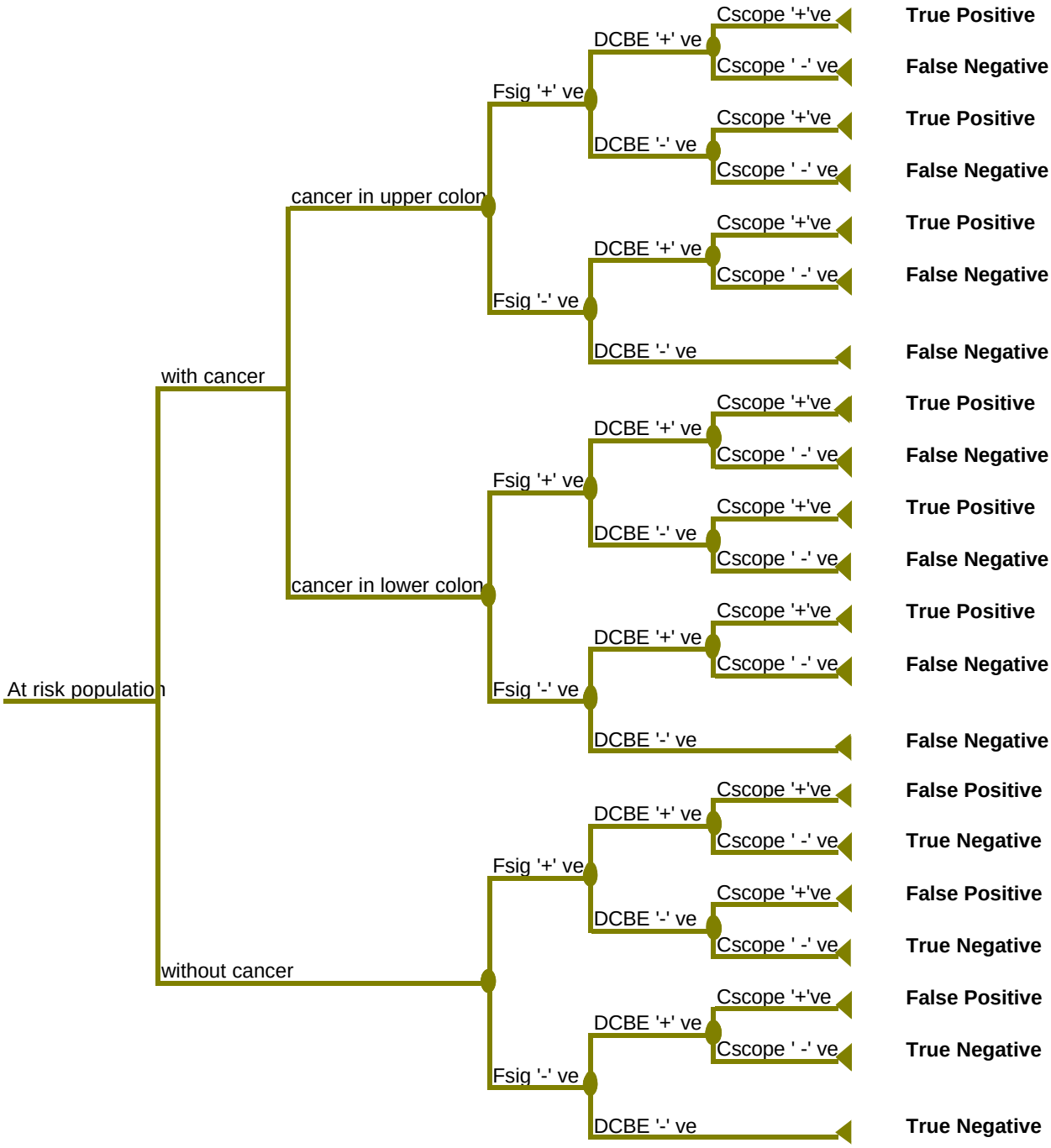

**Figure 4: Structure of overall model for Options A and B.**

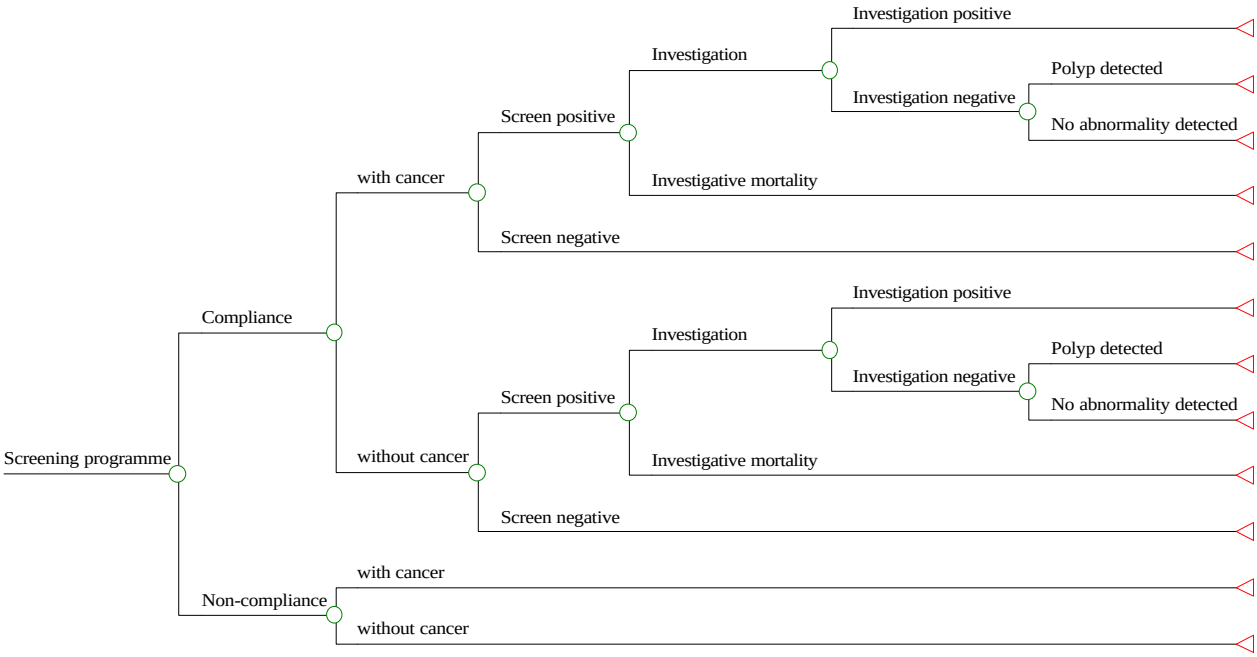

**Table 1: Parameter values and sources for test sub-model, Option A and B**

| Value | Name | Description | Source |
|---|---|---|---|
| 0.6 | SensTest1 | Sensitivity of the FOB test (no dietary restrictions) | Winawer, 1997 |
| 0.94 | SpecTest1 | Specificity of the FOB test (no dietary restrictions) | Winawer, 1997 |
| 0.2 | pwpc | Proportion of Test 1 positives 'weakly positive' (with cancer) | Assumed |
| 0.8 | pwpnc | Proportion of Test 1 positives 'weakly positive' (no cancer) | Garvican, 1998 |
| 0.808 | SensTest23 | Sensitivity of the FOB test (dietary restrictions) | Mandel, 1993 |
| 0.977 | SpecTest23 | Specificity of the FOB test (dietary restrictions) | Mandel, 1993 |

**Table 2: Parameter values and sources for investigation sub-model, Option A**

| Value | Name | Description | Source |
|---|---|---|---|
| 0.967 | SensScope | Sensitivity of the scope | Winawer, 1997 |
| 0.98 | SpecScope | Specificity of the scope | Winawer, 1997 |
| 0.84 | SensXray | Sensitivity of the Xray | Winawer, 1997 |
| 0.975 | SpecXray | Specificity of the Xray | Winawer, 1997 |
| 15% | prXray | Proportion of patients requiring Xray | Kronborg, 1996; Castiglione, 1997 |
| 143 | ucCol | Unit cost of a colonoscopy procedure | Garvican, 1998 |
| 55 | ucXray | Unit cost of an Xray and barium enema | Garvican, 1998 |

**Table 3: Parameter values and sources for investigation sub-model, Option B**

| Value | Name | Description | Source |
|---|---|---|---|
| 0.333 | prCUC | proportion of cancers in the upper colon | ONS monitor |
| 0.967 | SensScope | Sensitivity of the colonoscope | Winawer, 1997 |
| 0.98 | SpecScope | Specificity of the colonoscope | Winawer, 1997 |
| 0.84 | SensXray | Sensitivity of the Xray | Winawer, 1997 |
| 0.975 | SpecXray | Specificity of the Xray | Winawer, 1997 |
| 0.967 | SensFsig | Sensitivity of flexible sigmoidoscope | Winawer, 1997 |
| 0.94 | SpecFsig | Specificity of flexible sigmoidoscope | Winawer, 1997 |
| 75 | ucFsig | Unit cost of the sigmoidoscope procedure | Walker et al 1991(£50) updated |
| 143 | ucCol | Unit cost of a colonoscopy procedure | Garvican 1998 |
| 55 | ucXray | Unit cost of an Xray and barium enema | Garvican 1998 |

**Table 4: Parameter values and sources for overall model. Option A**

| Value | Name | Description | Source |
|---|---|---|---|
| 1,000,000 | pop | Total population in typical health authority | ONS |
| 20% | pr50_69 | Proportion of population in 50-69 age band | ONS |
| 0.57 | comp | Compliance rate | Hardcastle 1996 |
| | | | |
| 0.002 | incid | Incidence rate of cancer (within screening period) | Endogenous to model |
| 0.001 | incidA | Annual incidence of cancer | ONS monitor 1997 |
| 2 | freq | frequency of screen (years) | Endogenous to model |
| 0.000236 | mort | Mortality rate from colonoscopy | Winawer, 1997 |
| 0.1 | polyp | Proportion of subjects with benign polyps | Clinical Outcomes Group |
| | | | |
| 0.94795 | SensIn | Sensitivity of investigation for detecting cancer: Option A | Endogenous to model |
| 0.595576 | SensSc | Sensitivity of screening for detecting cancer: Option A | Endogenous to model |
| 0.97925 | SpecIn | Specificity of investigation: Option A | Endogenous to model |
| 0.985817 | SpecSc | Specificity of screening: Option A | Endogenous to model |
| 1.094992 | RuTest | Average number of tests used in the screen: Option A | Endogenous to model |

**Table 5: Parameter values and sources for overall model. Option B**

| Value | Name | Description | Source |
|---|---|---|---|
| 1000000 | pop | Total population in typical health authority | |
| 20% | pr50_69 | Proportion of population in 50-69 age band | ONS |
| 0.57 | comp | Compliance rate | Hardcastle 1996 |
| | | | |
| 0.002 | incid | Incidence rate of cancer (within screening period) | Endogenous to model |
| 0.001 | incidA | Annual incidence of cancer | ONS monitor 1997 |
| 2 | freq | frequency of screen (years) | |
| 0.0002363 | mort | Mortality rate from colonoscopy | Winawer, 1997 |
| 0.1 | polyp | Proportion of subjects with benign polyps | Clinical Outcomes Group |
| | | | |
| 0.912022827 | SensIn | Sensitivity of investigation for detecting cancer: Option B | Endogenous to model |
| 0.59557632 | SensSc | Sensitivity of screening for detecting cancer: Option B | Endogenous to model |
| 0.99833 | SpecIn | Specificity of investigation: Option B | Endogenous to model |
| 0.985817392 | SpecSc | Specificity of screening: Option B | Endogenous to model |
| 1.094992288 | RuTest | Average number of tests used in the screen: Option B | Endogenous to model |

**Table 6: Calculated gain in life expectancy from earlier detection of colorectal cancer**

| | Dukes' Stage: | | | | |
|---|---|---|---|---|---|
| | **A** | **B** | **C** | **D** | **All** |
| Five-year survival, Dublin (NHSCRD) | 0.83 | 0.64 | 0.38 | 0.03 | |
| Stage distribution: Dublin unscreened (NHSCRD) | 0.11 | 0.35 | 0.26 | 0.29 | |
| Stage distribution: Needs assessment unscreened | 0.12 | 0.38 | 0.3 | 0.2 | |
| Stage distribution: Nottingham post screen | 0.31 | 0.3 | 0.19 | 0.19 | |
| Life expectancy in population, age 65 | | | | | 16.58 |
| Life expectancy on diagnosis of cancer, aged 60, unscreened: | | | | | 10.30 |
| Life expectancy on diagnosis of cancer, aged 60, screened: | | | | | 12.30 |
| Gain in life expectancy from screening: | | | | | 2.00 |

**Table 7: Screening results, Option A**

| | **Invited** | **Tested** | **Investigated** | **Cancer detected** | **Cancer missed** | **False positives proceeding to surgery** | **Polyps excised** | **Induced death** |
|---|---|---|---|---|---|---|---|---|
| Numbers of cohort | 100000 | 57000 | 875 | 64 | 136 | 17 | 79 | 0.21 |
| Percentage of cohort | 100% | 57% | 0.8747% | 0.0643% | 0.1357% | 0.0167% | 0.0793% | 0.0002% |

**Table 8: Screening results, Option B**

| | **Invited** | **Tested** | **Investigated** | **Cancer detected** | **Cancer missed** | **False positives proceeding to surgery** | **Polyps excised** | **Induced death** |
|---|---|---|---|---|---|---|---|---|
| Numbers of cohort | 100000 | 57000 | 875 | 62 | 138 | 1 | 81 | 0.02 |
| Percentage of cohort | 100% | 57% | 0.8747% | 0.0619% | 0.1381% | 0.0013% | 0.0811% | 0.0000 % |

**Table 9: Costs of Option A**

| Item | Volume | Unit cost | Total cost | Description |
|---|---|---|---|---|
| Fixed costs | 1 | 150,000 | £150,000 | (inc. health promotion etc.) |
| Staff overhead | 10 | £20,000 | £200,000 | (number of staff to deal with invitations and processing test results) |
| Annual equivalent capital costs | 1 | 10,000 | £10,000 | (annual equivalent capital cost for computers, envelope filling and rooms) |
| Letters | 109499 | £1.20 | £131,399 | (the cost of sending the kit, leaflet and reminders) |
| Test kits | 109499 | £1.50 | £164,249 | (the cost of the kit included in the invitation) |
| Investigations | 875 | £151 | £131,859 | |
| | | | | |
| Fixed programme costs | | | £360,000 | |
| Variable costs | | | £427,507 | |
| Total costs | | | £787,507 | |

**Table 10: Costs of Option B**

| Item | Volume | Unit cost | Total cost | Description |
|---|---|---|---|---|
| Fixed costs | 1 | 150,000 | £150,000 | (inc. health promotion etc.) |
| Staff overhead | 10 | £20,000 | £200,000 | (number of staff to deal with invitations and processing test results) |
| Annual equivalent capital costs | 1 | 10,000 | £10,000 | (annual equivalent capital cost for computers, envelope filling and rooms) |
| Letters | 109499 | £1.20 | £131,399 | (the cost of sending the kit, leaflet and reminders) |
| Test kits | 109499 | £1.50 | £164,249 | (the cost of the kit included in the invitation) |
| Investigations | 875 | £142 | £124,331 | |
| | | | | |
| Fixed programme costs | | | £360,000 | |
| Variable costs | | | £419,979 | |
| Total costs | | | £779,979 | |

**Table 11: Cost-effectiveness of Option A**

| | |
|---|---|
| Cancers detected | 64 |
| Average life-years gained | 2.00 |
| Total life years gained | 128.94 |
| Life years lost (investigative mortality) | 4.23 |
| Net life years gained | 124.71 |
| Total programme cost | 787,507 |
| Cost of surgery on false positives | 50,211 |
| Total cost | 837,718 |
| Incremental cost per life year gained | £6,717 |

**Table 12: Cost-effectiveness of Option B**

| | |
|---|---|
| Cancers detected: | 62 |
| Average life-years gained: | 2.00 |
| Total life years gained | 124.08 |
| Life years lost (investigative mortality) | 0.36 |
| Net life years gained | 123.72 |
| Total programme cost | 779,979 |
| Cost of surgery on false positives | 4,042 |
| Total cost | 784,021 |
| Incremental cost per life year gained | £6,337 |

**Table 13: Sensitivity of cost-effectiveness results to changes in parameter values, Option A**

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Compliance | 0.45 | 0.5 | 0.55 | 0.6 | 0.65 | 0.7 | 0.75 | 0.8 | |
| Cost per life year gained: | 8119 | 7453 | 6908 | 6454 | 6070 | 5741 | 5455 | 5206 | |
| FOB sensitivity | 0.4 | 0.45 | 0.5 | 0.55 | 0.6 | 0.65 | 0.7 | 0.75 | 0.8 |
| Cost per life year gained: | 10194 | 9023 | 8095 | 7341 | 6717 | 6192 | 5744 | 5357 | 5019 |
| FOB specificity | 0.9 | 0.91 | 0.92 | 0.93 | 0.94 | 0.95 | 0.96 | 0.97 | 0.98 |
| Cost per life year gained: | 7938 | 7628 | 7321 | 7018 | 6717 | 6420 | 6126 | 5834 | 5546 |
| Colonoscopy sensitivity | 0.95 | 0.955 | 0.96 | 0.965 | 0.97 | 0.975 | 0.98 | | |
| Cost per life year gained: | 6825 | 6793 | 6761 | 6730 | 6698 | 6668 | 6637 | | |
| Colonoscopy specificity | 0.95 | 0.955 | 0.96 | 0.965 | 0.97 | 0.975 | 0.98 | 0.985 | 0.99 |
| Cost per life year gained: | 7212 | 7129 | 7047 | 6965 | 6882 | 6800 | 6717 | 6635 | 6552 |
| DCBE sensitivity | 0.74 | 0.76 | 0.78 | 0.80 | 0.82 | 0.84 | 0.86 | 0.88 | 0.90 |
| Cost per life year gained: | 6829 | 6806 | 6784 | 6761 | 6739 | 6717 | 6695 | 6673 | 6652 |
| DCBE specificity | 0.95 | 0.955 | 0.96 | 0.965 | 0.97 | 0.975 | 0.98 | 0.985 | 0.99 |
| Cost per life year gained: | 6790 | 6775 | 6761 | 6746 | 6732 | 6717 | 6703 | 6688 | 6673 |
| Unit cost of colonoscopy | 120 | 130 | 140 | 150 | 160 | 170 | 180 | 190 | 200 |
| Cost per life year gained: | 6559 | 6629 | 6700 | 6770 | 6840 | 6910 | 6980 | 7050 | 7120 |

**Table 14: Sensitivity of cost-effectiveness results to changes in parameter values, Option B**

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Compliance | 0.45 | 0.5 | 0.55 | 0.6 | 0.65 | 0.7 | 0.75 | 0.8 | |
| Cost per life year gained: | 7750 | 7079 | 6530 | 6072 | 5685 | 5353 | 5065 | 4813 | |
| FOB sensitivity | 0.4 | 0.45 | 0.5 | 0.55 | 0.6 | 0.65 | 0.7 | 0.75 | 0.8 |
| Cost per life year gained: | 9479 | 8431 | 7593 | 6908 | 6337 | 5854 | 5441 | 5083 | 4769 |
| FOB specificity | 0.9 | 0.91 | 0.92 | 0.93 | 0.94 | 0.95 | 0.96 | 0.97 | 0.98 |
| Cost per life year gained: | 7127 | 6929 | 6732 | 6534 | 6337 | 6140 | 5943 | 5746 | 5550 |
| Colonoscopy sensitivity | 0.95 | 0.955 | 0.96 | 0.965 | 0.97 | 0.975 | 0.98 | | |
| Cost per life year gained: | 6451 | 6417 | 6383 | 6350 | 6317 | 6285 | 6253 | | |
| Colonoscopy specificity | 0.95 | 0.955 | 0.96 | 0.965 | 0.97 | 0.975 | 0.98 | 0.985 | 0.99 |
| Cost per life year gained: | 6386 | 6378 | 6370 | 6362 | 6353 | 6345 | 6337 | 6329 | 6321 |
| Flexible sigmoidoscopy sensitivity | 0.950 | 0.955 | 0.960 | 0.965 | 0.970 | 0.975 | 0.980 | | |
| Cost per life year gained: | 6349 | 6346 | 6342 | 6338 | 6335 | 6331 | 6328 | | |
| Flexible sigmoidoscopy specificity | 0.9 | 0.91 | 0.92 | 0.93 | 0.94 | 0.95 | 0.96 | 0.97 | 0.98 |
| Cost per life year gained: | 6400 | 6384 | 6369 | 6353 | 6337 | 6321 | 6306 | 6290 | 6274 |
| DCBE sensitivity | 0.74 | 0.76 | 0.78 | 0.80 | 0.82 | 0.84 | 0.86 | 0.88 | 0.90 |
| Cost per life year gained: | 6586 | 6534 | 6484 | 6434 | 6385 | 6337 | 6290 | 6243 | 6197 |
| DCBE specificity | 0.95 | 0.955 | 0.96 | 0.965 | 0.97 | 0.975 | 0.98 | 0.985 | 0.99 |
| Cost per life year gained: | 6375 | 6367 | 6360 | 6352 | 6345 | 6337 | 6329 | 6322 | 6314 |
| Unit cost of colonoscopy | 120 | 130 | 140 | 150 | 160 | 170 | 180 | 190 | 200 |
| Cost per life year gained: | 6323 | 6329 | 6336 | 6342 | 6348 | 6354 | 6360 | 6366 | 6372 |

# APPENDIX 3

# SCREENING FOR CANCER OF THE BOWEL
# INFORMATION FOR THE PUBLIC

**March 1998 (revised July 1998)**
**For the**
**National Screening Committee**

Angela E Raffle

# Screening for cancer of the bowel
# Information for the public

***NOTES***

1. *This document gives information that needs to be available for potential participants in colorectal cancer screening. It is drafted as though a national programme were in place offering two yearly faecal occult blood testing to people aged 50 to 69. Some of the information on the diagnostic procedures is not yet complete since this will vary from hospital to hospital.*

2. *An important step in developing information of this kind will be its testing for comprehensibility and completeness with groups of intended recipients.*

3. *At this stage, no reference is made to groups for whom screening would be difficult i.e. frail, bedbound, sensory impaired, mental health problems, learning difficulties, minority ethnic groups. Special arrangements will need to be planned, and explained in the information for participants.*

4. *All the figures about probabilities are at this stage provisional. It is not easy to give precise and accurate estimates as figures from RCTs vary, and may not even be the same as will result once routine screening is up and running.*

**Who is this information for?**

This information is for anyone who is interested in knowing more about bowel cancer screening. It is designed for those who are being offered testing, and for anyone else who wants to know more about the screening programme. The first section of this leaflet explains the screening programme. The second section gives more general information about bowel cancer. At the end there is a glossary, and information about key evidence sources for the information in this leaflet.

**What is bowel cancer screening?**

The NHS bowel cancer screening programme organises early detection tests offered from the age of 50 through to 69. The purpose is to find small malignant cancers of the colon and the rectum. Small malignant cancers can be treated more easily than larger cancers, and the long term results of treatment for small malignant cancers are better than for large malignant cancers.

National screening is offered because it is certain that bowel cancer screening can save lives. But screening is not completely straightforward:

- The screening programme will only pick up some, not all, of the cancers that exist in people coming forward for screening.
- Some cancers, even if they are found by screening, will not be curable.
- As well as finding malignant cancers, many people will be found to have benign tumours of the bowel. For these people with benign tumours treatment and follow up will be recommended, even though most people in this group would never experience any problem from these conditions if left alone.
- A very small number of people will suffer complications from the investigations.

It is therefore important that you think carefully before deciding to have a bowel screening test. The screening programme is not a guarantee against bowel cancer and it inevitably involves investigations and treatments for some who do not actually stand to benefit.

**What is the screening test?**

The test is called the “faecal occult blood test”, or FOBT for short. It is a test that you do yourself in your own home and it involves putting a very small amount of faeces onto a piece of special blotting paper. The testing pack is sent by post, once every two years, to everyone aged 50 to 69 and registered with a general practitioner. Detailed instructions explaining exactly how to do the test are enclosed inside the testing pack. When you have completed the test you send it back by post to the screening centre.

The completed tests are processed at the screening centre to measure if blood is present in the blotting paper samples. It is important to realise that like many other medical tests, the FOBT only gives an indication or *probability* for you having bowel cancer. At this stage there are three different results possible:

1. **Negative -** 951[2] percent of people tested (or 95 out of every 100) have no blood present in the first test sample, and the test is called "negative". If you have a negative test result you will be sent a letter telling you, and you will receive a testing kit for another routine screening test two years later. If you have reached 69 years of age you will not be sent any more routine tests.

   **what does a negative result mean?** a negative result means that you are very unlikely to have bowel cancer. Out of 1,000 people with a negative FOBT, less than 1 will be diagnosed with bowel cancer before the next routine test two years later.

2. **Weakly positive** - 3.3 percent of people tested (between 3 and 4 in every 100) have a weakly positive result. If this happens then you will be asked to carry out the test again, but this time you will be advised to avoid certain foods and medications for six days before doing the test. This makes the test more reliable. If the second test shows no sign of blood being present in the faeces then you are counted as having a negative test result. This means that you are very unlikely to have bowel cancer. You will be sent a letter telling you, and you will receive a testing kit for another routine screening test two years later (if you have reached 69 years of age you will not be sent any more routine tests). The number of people with negative tests after retesting brings the total with negative results up to 98%.

   If the second test is positive, or if it is again weakly positive, you are counted as having a positive test. You will receive an invitation to attend for further investigations of the bowel. The number of people with positive tests after retesting brings the total with positive tests up to 2% or 2 out of every 100.

3. **Positive -** 1.8 percent[3] of people tested (or nearly 2 out of every 100) have a first result that indicates the likelihood of blood in the faeces. Altogether (including those who have a weakly positive result followed by a positive retest) the percentage of people with a positive test is 2%. If you have a positive result you will receive an invitation to attend for further investigations of the bowel.

   **what does a positive result mean?** a positive FOBT means that you have a roughly 6% chance of being diagnosed with bowel cancer once further investigations are carried out. The majority of people (94%) with a positive FOBT are not found to have bowel cancer when the investigations are carried out. As well as the 6% found to have bowel cancer, there will be a further x%[4] who will be found to have benign tumours in the bowel. Your chance of being found to have a benign tumour rises considerably with age.

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[2] These percentages are derived from the accompanying decision analysis

[3] The Danish study is now in its 6th round of screening and the percent of people with positive tests is 3%

[2,3,4] Figures relating to the detection rates for adenomatous polyps with varying degrees of dysplasia, and for flat adenomas, vary according to the classification, the investigation used, and the composition of the study population. A systematic review will be conducted to ensure that accurate information can be given to the public.

**What happens next after the screening test result?**

**After a negative result** - you will receive a letter within a few weeks telling you of the result. Two years later when it is time for your next routine test you will receive another testing kit through the post. Once you reach 69 and if you have never had any abnormality found during screening, then you will not receive any more tests.

**After a positive result** - you will receive a letter within a few weeks telling you of the result and giving you information about a hospital appointment to attend for further investigation of the bowel. The three main investigations that are used are *colonoscopy*, *double contrast barium enema*, and *flexible sigmoidoscopy*. Exactly which investigation or which combination of investigations you will be offered depends on the latest national advice, and the circumstances of your individual case. You will receive information about the investigations, and any preparations you need to make, with the appointment details that are sent to you. There is likely to be a wait of several weeks before your appointment for the investigations. This is a worrying time for most people because of the uncertainty about whether cancer is present or not. Unfortunately it is seldom possible to guarantee an immediate appointment for everyone. The delay of a few weeks makes no difference to the success of treatment

**What do the bowel investigations involve?**

**1. Colonoscopy**

**what is the procedure?**
*(to be completed by local centre)*

**what are the possible complications[5] ?**
Serious complications from colonoscopy are very rare when the procedure is carried out by an experienced and skilled operator, but even so they do occur. In approximately 4 patients out of every 1,000 the examination will cause either perforation of the bowel wall, or a serious haemorrhage. Abdominal surgery with a general anaesthetic may then be needed to repair the gut or stop the bleeding. Very occasionally death can result from a complication of colonoscopy. This occurs in approximately 2 out of every 10,000 examinations.

**how accurate is the investigation?**
In between 5% and 50% of patients it is not possible to "complete" colonoscopy because the scope instrument cannot be safely made to reach all the bowel. When colonoscopy is successfully carried out it will miss around 3 out of every 100 cancers. It will give a misleading result (suggesting cancer when in fact no cancer is present) in 2 out of every 100 people without cancer.

[5] The figures about accuracy and complications are all taken from the accompanying Planning document.

## 2. Double contrast barium enema (DCBE)

**what is the procedure?**
*(to be completed by local centre)*

**what are the possible complications?**
Complications from barium enema examinations are extremely rare. Perforation of the bowel has been known to occur. The likelihood of this is 1 case in 2,500 examinations. Surgery with a general anaesthetic might then be needed to repair the perforation, leading to a risk of death of 1 in 33,000 examinations.

**how accurate is the investigation?**
In approximately 10% of patients the barium enema does not give a technically satisfactory result, and a good view of the whole bowel cannot be obtained. When barium enema is successfully carried out it will miss between 15 and 45 out of every 100 cancers. It will give a misleading result (suggesting cancer when in fact no cancer is present) in 3 out of every 100 people without cancer, and suggesting benign tumours when in fact none are present in around 5 to 10 out of every 100 patients..

## 3. Flexible sigmoidoscopy (FSIG)

**what is the procedure?**
*(to be completed by local centre)*

**what are the possible complications?**
Complications from flexible sigmoidoscopy are extremely rare indeed. Perforation of the bowel has been known to occur. The likelihood of this is 1 case in 7,000 examinations. No deaths have been reported as a complication of sigmoidoscopy.

**how accurate is the investigation?**
Flexible sigmoidoscopy only examines the lower half of the colon. It therefore cannot detect any cancers that are above the reach of the sigmoidoscope. For cancers in the lower half of the colon it will miss approximately 3 out of every 100. It will give a misleading result (suggesting cancer in the lower bowel when in fact no cancer is present) in 6 out of every 100 people without cancer.

**What will happen if I am diagnosed with bowel cancer?**

Depending on the type of cancer it is, you will be offered surgery, together with chemotherapy or radiotherapy as appropriate. Your care will be undertaken by a specialist cancer team working to agreed standards of good quality practice.

Although the purpose of screening is to find cancers when they are very small and when cure is possible, not all cancers detected by screening are in this category. The major studies of screening (in Nottingham and in Denmark) found that deaths were cut by around 15%. This still means that 85% of fatal cases of bowel cancer cannot be helped by screening. This is because some occur in people who do not attend, but also because some are not detected even by good quality screening, and some are not curable even if they are found. For every 10 people who are diagnosed with bowel cancer on screening, approximately 3 live longer as a direct result of the early detection of their cancer.

**What will happen if I am found to have a benign tumour?**

If you are found to have one or more benign tumours (*adenomas*) of the bowel then these will be removed during colonoscopy. It is not necessary to have abdominal surgery or a general anaesthetic in order for these tumours to be treated. The tumours will be sent to a laboratory and carefully examined under a microscope to check that they are benign. You will then continue to be offered two yearly FOBT as usual (unless you are already 69).

A small percentage of adenomas when examined in the laboratory show "*high grade dysplasia*". This is thought to suggest a possibility that the tumours might become malignant in the future. If you have an adenoma showing high grade dysplasia then you may be offered follow up and repeat investigations to treat any further tumours if they develop.

**Weighing up the benefits of screening**

There is quite a lot of information in this leaflet. This is because screening is a fairly complex undertaking. The following table summarises what happens when 100,000 people accept the offer of screening during a two year period. Before you participate in screening it is impossible to know whether you are one of the few who will have your life saved by screening, whether you will be amongst the many who are correctly reassured by a negative result, whether you will be amongst those who undergo investigations even though you do not have cancer, or whether you will be in the small minority who suffer misleading test results or complications.

## Table: the consequences for 100,000 people screened over two years

| | | | |
|---|---|---|---|
| 3,269 | need repeat FOBT before they can be given a definite result | | |
| 98,064 | have negative FOBT | | |
| | of these | 98,010 | do not have cancer |
| | | 55 | false reassurance - bowel cancer diagnosed within 2 years |
| 1,936 | have positive FOBT | | |
| | of these | 35 | diagnosed with bowel cancer and have benefit |
| | | 82 | diagnosed with bowel cancer but do not benefit |
| | | 1,619 | diagnosed not cancer and have no cancer |
| | | 6 | diagnosed not cancer but do have cancer within 2 years |
| | | 550[6] | diagnosed and treated for benign tumour |
| | | 25[7] | diagnosed with suspicious benign tumour and followed up |
| | between 1 and 8 if DCBE + FSIG<br>8 if colonoscopy | | suffer complications from the investigation |

*The following are not yet included in this document*:

**General information about bowel cancer**
**Glossary**
**Key References**

[6] Based on average prevalence in 50-69 age group of 30% (Winawar et al. 1997)
[7] Assuming that 5% of polyps are found to show high-grade dysplasia

**There are further questions that will arise once the screening programme is underway which will therefore need to be addressed prior to the programme or pilots starting, and these are:-**

1. Why can't people under 50 have screening?
2. Why can't people over 69 have screening?
3. Why is it not every year?
4. Small cancers aren't likely to bleed, so why do FOB test?
5. I'm disabled, how will you cater for my needs?
6. If polyps need removing, surely everyone should have barium or scope investigations?
7. Why can't you add more tests to predict which polyps will progress to cancer?
8. I've read about flat adenomas, what do you do for those?
9. If I feel that the screening service has let me down, how will I be compensated?