THE SCOTTISH OFFICE

Department of Health

NHS
MEL(1998)62

NHS Management Executive
St. Andrew's House
Edinburgh EH1 3DG

17th September 1998

Dear Colleague

SCREENING FOR COLORECTAL CANCER

Summary

1. This letter provides information about the pilot studies Ministers have decided to establish to screen for colorectal cancer and about the procedures for expressing an interest in being a pilot site.

Background

2. On 10 September, Ministers announced that they had accepted the advice of the UK National Screening Committee to commission 2 pilot studies, one in England, the other in Scotland, of colorectal cancer screening.

3. Further information is set out in the Annex to this letter.

Action

4. Board General Managers and Trust Chief Executives are asked to ensure that this information is circulated widely within the Service, and in particular that it reaches those who might be interested in expressing an interest in being a pilot site.

5. Such expressions of interest are to be submitted to Dr Muir Gray CBE, Regional Director of Research and Development, Anglia and Oxford Regional Office, Institute of Health Sciences, Old Road, Headington, Oxford, OX3 7LF, copied to Sir David Carter, Chief Medical Officer, The Scottish Office, by **Wednesday 14 October 1998.**

Yours sincerely

DR KEVIN J WOODS
Director of Strategy and
Performance Management

Addressees

For action:
Board General Managers
Trust Chief Executives

For information:
General Manager, CSA
General Manager, State Hospitals Board for Scotland
Chief Executive, Health Education Board for Scotland
Executive Director, SCPMDE
Scottish Secretary, Marie Curie Cancer Care
Regional Director, Macmillan Cancer Relief
Project Manager, BACUP Scotland Cancer Counselling Service

Enquiries to:

Dr Rosalind Skinner
Room 322
St Andrew's House
EDINBURGH EH1 3DG

Tel: 0131-244 2296
Fax: 0131-244 2030

PME03209.089

National Screening Committee

A Proposal for Colorectal Cancer Screening Pilots

Introduction

The Colorectal Cancer Workshops hosted by The Scottish and Welsh Offices and held in Edinburgh on 21 May 1997 and in Cardiff on 16 March 1998 opened up the opportunity for debate on the need for and feasibility of a population screening programme for cancer of the colon and rectum. The first workshop debated the evidence, whilst the second concentrated on the practicalities of putting policy into practice. A summary of the Workshops and background papers are available from the National Screening Committee secretariat and are on the NSC website: **http://www.open.gov.uk/doh/nsc/nsch.htm**

Research evidence supports the potential of screening to reduce mortality from cancer of the colon and the rectum in males and females. However reservations expressed about both the practicality and the general acceptability of the screening test and the follow-up confirmatory tests resulted in the main recommendation of the second workshop, that pilot (or demonstration) sites should be set up to test these concerns.

These pilots will provide further opportunity to educate everyone about the risks, benefits and disbenefits of population screening, and above all the need for informed consent, to ensure that individuals, invited to take part, fully understand the screening programme prior to consenting to the process.

The differences between seeking out the presence or absence of a disorder in a healthy person and diagnosing the cause of illness in an already sick person, are not yet widely appreciated. The chances of any one of the many healthy persons being screened being found to have the disorder are very small. On the other hand, every sick person should be effectively, rapidly and accurately diagnosed in the shortest possible time. In screening, just one test is utilised to indicate the presence or absence of a condition whilst in diagnosing a condition in a sick patient, a whole range of questions and tests may be required before a conclusion is reached.

Neither the colon nor the rectum are glamorous parts of our body and many of us try to ignore their existence especially when they seem to be working well. We rarely if ever think to go for regular check-ups on them as we do for our eyes, teeth, blood, heart and blood pressure etc., and yet they are every bit as important as any other part of our body that we try to keep in good working order with diet, exercise or check-ups. Indeed, if we paid more attention to eating a high fruit and fibre diet the digestive system would be kept working at closer to optimal efficiency, but many of us are still attracted to high fat content snack foods, such as chips and crisps.

The more population screening programmes we have, the better the chance to reinforce the messages about them. Inevitably some healthy people may be wrongly identified as having the disorder, whilst others who actually have the disorder may have results indicating that they are free from disease. On balance, however, in an effective programme, whilst a few individuals may be disadvantaged by the programme the vast majority will benefit.

The proposed pilots will offer the opportunity to test both the practicalities and acceptability of a screening programme for colorectal cancer and it is hoped they will provide evidence to demonstrate whether or not a UK screening programme should be introduced.

Contents

The National Screening Committee is interested in your comments on this document ; please send them to Dr Muir Gray, address, fax & email address details can be found in paragraph 6.3.1.

SCREENING FOR COLORECTAL CANCER

Executive Summary

Colorectal cancer is a major public health problem. It is the second most common cause of cancer deaths in the United Kingdom. The National Screening Committee has appraised the evidence about primary and secondary prevention of colorectal cancer and has decided that the quality of the evidence is sufficiently high for policy recommendations to be made.

Having appraised the evidence, the National Screening Committee used this evidence to test colorectal cancer screening against the criteria it has developed to assess proposed new programmes.

There is scope for reducing the incidence of colorectal cancer by dietary change and this paper contains a recommendation to plan population-based educational programmes to accelerate dietary change. This proposal is in line with the policy proposals in the Green Papers: *Our Healthier Nation* in England; *Working Together for a Healthier Scotland*; *Better Health, Better Wales*, and *Well Into 2000*, in Northern Ireland Two high quality randomised controlled trials of colorectal cancer screening were published in *The Lancet* in 1996 and these demonstrated that, in the research setting with screening provided by very highly specialised trained and committed teams, it was possible to reduce mortality through screening which was both acceptable and safe.

For good to outweigh harm it will be necessary to have a national screening programme that reaches defined quality standards which, although not necessarily as high as the exceptional standards reached in the research programmes, is sufficiently high to produce benefit while minimising adverse effects.

The National Screening Committee, therefore, recommends two pilots of screening be organised.

> The target population for the purposes of the pilot programmes would be for people aged 50 to 69. The primary test will be the faecal occult blood (FOB) test without dietary restriction and without rehydration of the test sample.
>
> Follow-up for people with positive tests will be by colonoscopy, with double contrast barium enema for those people in whom a complete colonoscopy is not possible. The alternative of using double contrast barium enema and flexible sigmoidoscopy will 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 pilot project is not to assess the effectiveness of colorectal cancer screening; randomised controlled trials have already demonstrated the effectiveness of screening when delivered in research conditions. Nevertheless it should be noted that colorectal cancer

screening offers a smaller relative mortality reduction than breast or cervical screening, and carries a higher risk of complications in those investigated, thus informed participation will be an important consideration for the pilots.

The pilots will start in 1999 and run for two years. Paragraphs 6.3 et al give more details about how potential pilot sites can express an interest and the key criteria that should be met.

During the pilot phase preparatory planning work will take place to allow rapid implementation of a national screening programme should the results in the pilot studies show that more good than harm can be done at reasonable cost.

A central feature of the pilots will be the provision of clear and explicit information to people invited for screening not only about the benefits of colorectal cancer screening but also about its adverse effects and limitations.

A Summary of the Colorectal Cancer Screening Workshops and Background Papers are available from the NSC Secretariat. This report includes a summary of the two workshops and papers on informed choice, decision analysis, planning and costing studies. Please ring the Secretariat on 0113 254 7366 or fax on 0113 254 5831 if you would like a copy of the report.

The report is also available on the NSC website: http://www.open.gov.uk/doh/nsc/nsch.htm

COLORECTAL CANCER SCREENING

Colorectal cancer is a major public health problem. It is the second most common cause of cancer deaths in the United Kingdom and for this reason a manual to improve outcomes in colorectal cancer was published by the NHS Executive as part of its programme on commissioning cancer services (1). A report was also issued on cancer services in Wales by the Cancer Services Expert Group in November 1996 and in Scotland by a sub-committee of the Scottish Cancer Coordinating and Advisory Committee. The need to improve the effectiveness and quality of cancer care is an issue that all four Health Departments in the United Kingdom have addressed, based on the Calman/Hine Report on the policy framework for commissioning cancer services (2). The manual did not make a definite recommendation about colorectal cancer screening, as two major trials on colorectal cancer screening were about to report.

This document complements the effective Healthcare Bulletin on the management of colorectal cancer produced by the NHS Centre for Reviews and Dissemination (3), Colorectal Cancer, a national Clinical Guideline produced by the Scottish Intercollegiate Guidelines Network (SIGN) and other documents produced by the four Health Departments on colorectal cancer care (Appendix 1), and makes a proposal for the pilot programmes of colorectal cancer screening. The workshop summaries and key papers will be published separately and made available on the NSC Website (http://www.open.gov.uk/doh/nsc/nsch.htm); hard copies will be available on request.

1. The challenge of colorectal cancer

There are almost 20,000 deaths each year from colorectal cancer, 93 per cent of them in people over the age of 55. The incidence of cancer increases with age and the lifetime risk of colorectal cancer is 1 in 25.

Colorectal cancer is classified as a cancer of four stages. Stage A is the early stage of cancer with the cancer limited to the lining of the colon. Five year survival with colorectal cancer can be 80 per cent in Stage A. 50 per cent of cancers have spread and are of Stage C or D at diagnosis at the present time, and the survival for cancers of Stage C or D is less than half of that when diagnosis is made at Stage A.

Early diagnosis would therefore appear to be beneficial but when considering whether or not to screen for cancer, or indeed any other disease, it is important to be aware of what is called lead time bias, for early diagnosis does not necessarily improve outcome or survival.

2. Lead time bias

Proponents of the introduction of any screening programme sometimes base their argument on cohort studies, which are designed to follow a series of people who have had a screening test and compare their survival with that of the general population. However, this is a poor method of evaluating screening, principally because of what is called lead-time bias.

Imagine a disease that has a natural history of ten years from its beginning to its fatal end, and that causes symptoms after five years, which usually prompt the sufferer to visit a doctor; the survival time from the point of symptomatic diagnosis is five years (Figure 1A). A test that enables a diagnosis of the disease to be made at an earlier, pre-symptomatic, stage, for example, at three years, will apparently increase survival time (Figure 1B).

This apparent increase in survival time does not necessarily mean that screening is effective; it may simply mean that the person with the pre-symptomatic disease found by screening is aware of the condition for seven years as opposed to five. This is referred to as lead-time bias. It is essential that any screening programme is evaluated within an RCT which has been designed with death as the outcome in order to control for lead-time bias.

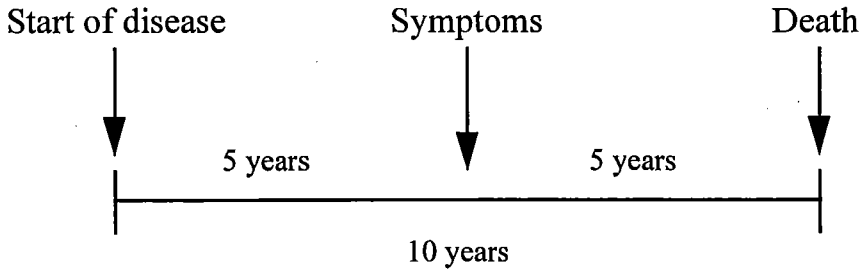


Figure 1A

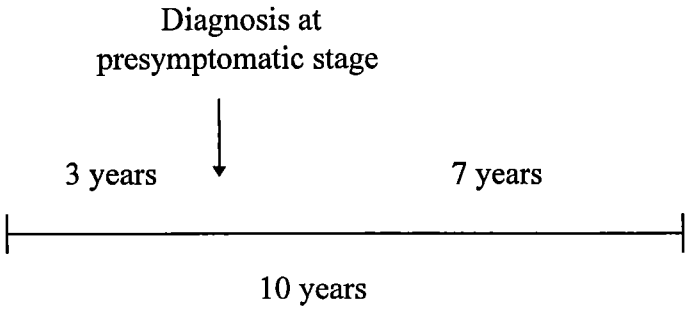


Figure 1B

For this reason is it essential that new screening programmes are assessed not only by measuring the impact that the screening programme may have on the stage of presentation and survival time in a defined population but also the impact that screening has when tested in a randomised controlled trial.

3. Randomised controlled trials of colorectal cancer screening

In a randomised controlled trial, the people who are thought might benefit from colorectal cancer screening, for example people aged 50 to 69, are randomly allocated to receive screening or not receive screening. The group allocated to the screening programme then

receives the screening and the other half, who were not randomly selected for screening, are not offered an opportunity for screening and receive the usual type of health care. Both groups are followed up over a long period of time and a number of variables are measured, notably:

the incidence of colorectal cancer, namely the number of new cases arising in each group;

the mortality within each group from colorectal cancer;

the mortality within each group from all types of cancer.

3.1 Minimising chance and bias

The main reason why randomised controlled trials are used to assess the effectiveness of a new procedure or programme is to minimise bias; for example if screening is assessed by its effect on the whole population it may be that within that population the people who come for screening are quite different from the rest of the population, for example by being more health conscious and being the sort of people who would have presented with cancer early whether or not there was a screening programme. Only a randomised controlled trial which allocates people to either receive an invitation for screening or not is able to assess the effects of screening without bias.

Bias is a form of systematic error. Researchers can also be misled by chance, for although research studies may be carefully designed they can still give the wrong answer by chance, particularly if the beneficial or adverse effects of the intervention are small. The best way to minimise the possibility of chance giving the wrong answer is to make the trial large enough, for the larger the trial the higher the probability that any result found will really be due to the procedure or programme.

There have now been three randomised controlled trials of colorectal cancer screening, of high quality and with sufficient power to assess the magnitude of the benefits and harms that would result were a colorectal cancer screening programme to be introduced (4, 5 & 6).

These trials show that screening for colorectal cancer is effective in reducing mortality, by around 15%, from the disease when the screening is done at the quality of service offered by the research teams.

The effects of such a screening programme on a population of a million people are set out in the flow chart shown as Figure 2.

4. Randomised controlled trials are necessary but not sufficient

The demonstration of a beneficial effect in a randomised controlled trial or, preferably, a systematic review of randomised controlled trials is an essential prerequisite for the introduction of a cancer screening programme but this type of technology assessment does

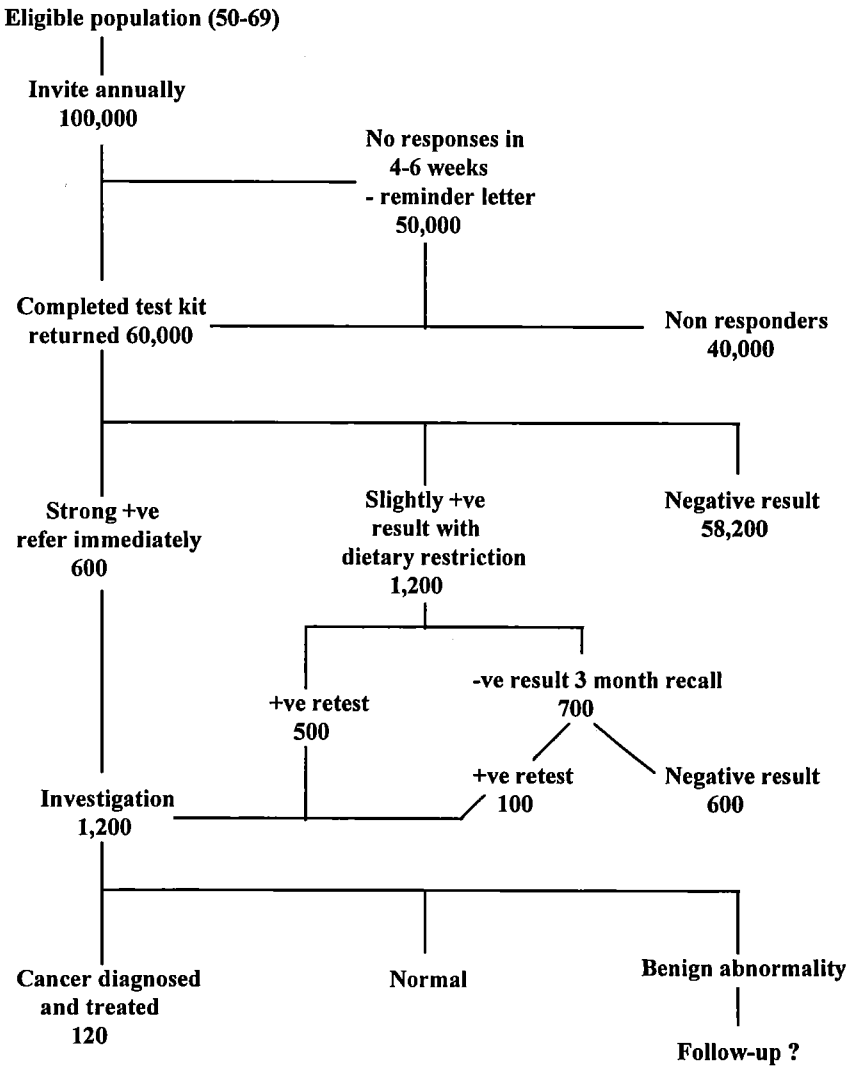
not by itself provide all the information that is needed to make a policy decision about cancer screening.

In the 1960s the World Health Organisation produced a report setting out criteria that could be used to appraise potential new screening programmes (7). These criteria are commonly known as the Wilson and Jungner criteria after the authors of the report but the National Screening Committee came to the opinion that these criteria did not give sufficient weighting to:

the adverse effects of screening,
the strength of the evidence about the effectiveness of the screening programme,
the opportunity costs of screening.

They have therefore drawn up a new set of criteria, based on the Wilson and Jungner criteria, and the appraisal of colorectal cancer screening using these criteria is set out below.

Figure 2 Colorectal Cancer Screening programme for a Population of 1 Million. Projected numbers involved at each stage



The condition

1. The condition should be an important health problem.

2. The epidemiology and natural history of the condition, including development from latent to declared disease, should be understood adequately and there should be a detectable risk factor, disease marker, latent period or early symptomatic stage.

3. All the cost-effective primary prevention interventions should have been implemented as far as practicable.

The test

4. There should be a simple, safe, precise and validated screening test.

5. The distribution of test values in the target population should be known and a suitable cut-off level defined and agreed.

6. The test should be acceptable to the population.

7. There should be an agreed policy on the further diagnostic investigation of individuals with a positive test result and on the choices available to those individuals.

The treatment

8. There should be an effective treatment or intervention for patients identified through early detection, with evidence of early treatment leading to better outcomes than late treatment.

9. There should be agreed evidence-based policies covering which individuals should be offered treatment and the appropriate treatment to be offered.

10. Clinical management of the condition and patient outcomes should be optimised by all health care providers prior to participation in a screening programme.

The screening programme

11. There should be evidence from high quality randomised controlled trials that the screening programme is effective in reducing mortality or morbidity.

12. There should be evidence that the complete screening programme (test, diagnostic procedures, treatment/intervention) is clinically, socially and ethically acceptable to the public and health professionals .

13. The benefit from the screening programme should outweigh the physical and psychological harm (caused by the test, diagnostic procedures and treatment).

14. The opportunity cost of the screening programme (including testing, diagnosis and treatment) should be economically balanced in relation to expenditure on medical care as a whole.

15. There should be a plan for managing and monitoring the screening programme and an agreed set of quality assurance standards.

16. Adequate staffing and facilities for testing, diagnosis, treatment and programme management should be available prior to the commencement of the screening programme.

17. All other options for managing the condition should have been considered (e.g. improving treatment, providing other services).

The application of these criteria to colorectal cancer screening is set out in Section 5.

5. Testing colorectal cancer screening against the criteria

5.1. The condition should be an important health problem.

Colorectal cancer is a major public health problem, being the second most common cause of death from cancer in the UK.

5.2. The epidemiology and natural history of the condition, including development from latent to declared disease, should be understood adequately

The epidemiology of colorectal cancer has been well studied but the natural history is not fully understood yet. The contribution that genetic factors play in the general population is not understood fully although the contribution of genetic factors in certain conditions in which there is a very high risk of colorectal cancer in affected families is now understood sufficiently well to provide a basis for effective action.

There is not, however, sufficient evidence to use any form of genetic screening, including enquiry about family history for colorectal cancer in the general population except as part of a research programme that has been approved by an ethics committee (see Section 5.2.1).

Although it is "generally accepted that most cancers of the colon and rectum develop from adenomatous polyps, direct evidence for this assertion is sparse; for obvious reasons it is not ethical to study the natural history of polyps by leaving them in place and observing the consequences" (8). It is, however, possible to make assumptions about the rate of progress from an adenoma, which is non-invasive, to a carcinoma and the general consensus is that the period of time required for a benign non-invasive adenoma to proceed to cancer is at least five years and it may be much longer. The adenoma may form a prominence or bump on the lining of the colon and this is called a polyp.

The passage of small amounts of blood in the faeces allows the disease to be detected at an early stage if appropriate tests are used to detect what is called occult blood in the faeces for these small amounts of blood are altered chemically in the colon but are not obvious to the naked eye.

5.2.1 Genetic risk

Colorectal cancer is a common disease and, by chance, several members of one family will develop colorectal cancer while in other families no-one will be affected. It is clear now, however, that sometimes the distribution of colorectal cancer in families is not simply a matter of chance alone but reflects the inheritance of genetic factors which increase the risk of colorectal cancer.

The National Screening Committee commissioned work from the leading research workers and clinicians in the field and this work was co-ordinated by Professor John Burn of the University of Newcastle. A separate report is being prepared on this topic for consideration by both the National Screening Committee and the Advisory Committee on Genetic Testing. In Scotland, a report on Cancer Genetic Services in Scotland was produced by a sub-

committee of the Priority Areas Cancer Team in 1997, building on earlier work carried out by a sub-committee of the Scottish Cancer Coordinating and Advisory Committee.

It is clear that there are two conditions in which people are at very high risk of colorectal cancer - familial adenomatous polyposis (FAP) and hereditary non-polyposis colon cancer (HNPCC). General population screening for these conditions is not feasible currently but a systematic approach to the identification and testing of relatives of people presenting with cancer at an early age, and certain other characteristics, would allow a high proportion of people who carry the genetic risk to be identified, counselled and treated appropriately. This is not screening in the sense of the term used by the National Screening Committee but as part of its investigation into colorectal cancer screening the need for such a system of care has been identified and is recommended.

In the general population it can now be concluded that people are at different degrees of risk because of their genetic composition and the population is sometimes arbitrarily divided into those at low and medium risk. Some people have advocated the identification of people at medium risk by taking a family history systematically, for example during a health check or the registration of new patients in primary care.

There is, however, no strong evidence that this technique does more good than harm. Questions about the family history of colorectal cancer should not be asked as part of general health screening, except in the context of high quality research designed to address the benefits and harms of such techniques. This issue requires further consideration.

5.3. All the cost-effective primary prevention interventions should have been implemented as far as practicable

There is some evidence suggesting that aspirin reduces the risk for colorectal cancer (Section 5.3.2) and there is increasing evidence about the scope for primary prevention by dietary change; there are now interventions which have been demonstrated, in randomised controlled trials, as being effective in facilitating and accelerating a change in diet. These have not been implemented as far as possible.

5.3.1 Primary prevention of colorectal cancer through diet

The Committee on Medical Aspects of Food and Nutritional Policy (COMA) have recently published an extensive report on the Nutritional Aspects of the Development of Cancer (9). The overall conclusions were that "there is moderate evidence to conclude that higher intakes of vegetables, lower red meat and processed meat consumption and diets rich in NSP (dietary fibre) would reduce the risk of colorectal cancer"

Other reports have reached similar conclusions (10).

5.3.1.1 Potential for improvement

The Report on the Scottish Diet in 1993 noted that existing data provide support for a protective role for vegetables and fruit in relation to cancer, with fibre-containing starchy foods also having a possibly protective function in bowel cancer. Targets for dietary

improvement in Scotland, based on this Report, and aimed in particular at increasing consumption of fruit and vegetables and complex carbohydrates, were set in Scotland in 1994 for the year 2005. 'Eating for Health, A Diet Action Plan for Scotland' issued in 1996, set out a framework in which all the interests with an influence on diet - from food producers and processors to consumers themselves - could work together to bring about dietary improvement in Scotland and make progress towards the targets.

Work to support the target setting for Our Healthier Nation (11) suggests that an increase in fruit and vegetable consumption and dietary fibre could result in a 20% reduction in mortality rate for people under 65 years by the year 2010, and recommends an interim target in England of a reduction of 50% in the proportion of the population who consume less than 5 portions of fruit and vegetables per day by the year 2005. This work is being validated at present.

In Australia, Agrez and colleagues carried out a review of the evidence on population screening for colorectal cancer (12). They concluded that 'data suggest that educational strategies directed at primary prevention could effect a reduction in mortality from colorectal carcinoma that equals the magnitude in mortality achieved by screening.'

However, to come to that conclusion, the authors drew on the examples of other primary prevention programmes for cancer (lung and melanoma), rather than direct evidence of achievement of dietary change.

5.3.1.2 Dietary change

Dietary patterns can and do change, as witnessed by the change in the range of food consumed in the UK over the past 20 years. The Food Tables prepared by the Ministry of Agriculture, Fisheries and Food shows substantial changes over time in the pattern of food consumption and in overall nutritional balance, including a modest increase in the consumption of fresh fruit and fruit juice offset by a slight decline in the consumption of vegetables in recent years.

Nevertheless, to achieve the order of change necessary, specific targeted interventions would be needed. Most of the research into dietary change in the UK has been related to cardiovascular disease, and in particular the reduction in the percentage of energy of the diet from fats.

The Health Education Authority have commissioned a series of Health Promotion Effectiveness reviews, including a number relating to healthy eating, both in the general population and amongst specific groups (13). Much of the research was based in the United States but showed that interventions for changing dietary behaviour can be successful in a number of settings, and set out their characteristics.

In the USA there has been a major research programme aimed at changing dietary behaviour in terms of fruit and vegetables (14). The results are starting to be published and look encouraging.

There has also been a major research programme funded by the UK Economic and Social Research Council, The Nation's Diet: The Social Science of Food Choice (1992-1998). A report setting out the findings is due to be published in September, although interim results have been published (15) These should contribute to the theoretical basis for interventions.

5.3.1.3 Programme for action

From this initial work, it would appear to be possible to achieve a reduction in mortality by primary prevention equal to that from screening using dietary measures. However the research demonstrates that interventions need to be well planned, comprehensive, and sustained to be effective. This would require investment alongside that for screening. On the other hand, an increase in the intake in fruit and vegetables would also have a beneficial effect on other health problems, in particular heart disease, which would increase its potential for being cost effective.

The following work needs to be carried out.

- A further analysis to assess the potential reduction in mortality in a wider age group
- A detailed review of the evidence of dietary interventions to determine an estimate of the potential for change.
- The development of a costed proposal for a pilot project to be carried out in parallel with the pilots for screening.

Further consideration will need to be given to a feasibility study and the cost implications of parallel pilot studies.

5.3.2 Aspirin and colorectal cancer risk

It is clear from studies of populations using aspirin that the use of aspirin and non-steroidal anti-inflammatory drugs for pain relief reduce the risk of colorectal cancer (16) but this reported effect has not been found consistently (17), and on the basis of present evidence there is no place for recommending the use of aspirin for the prevention of colorectal adenoma and carcinoma.

5.4. There should be a simple, safe, precise and validated screening test

The faecal occult blood test is now a well evaluated test and it is proposed that:

biennial screening using the faecal occult blood test, with

a reminder letter after four weeks to those who have not responded to the initial invitation to be screened, and

no rehydration of samples to minimise the false positive rate.

no dietary restrictions

The FOB test consists of a piece of specially treated paper cut into six squares. Those with five or six positive squares will be referred for further investigation. Those who are positive on one to four squares will be invited to retake the test after restricting meat intake in their diet.

The age range 50 to 69 has been chosen as the age range at which to start screening in the pilots for two reasons. The first is that some defined age range is essential so that there is a clearly defined population for which those responsible for screening have to be accountable. Resources will be limited for a national colorectal cancer screening programme were one to be introduced, principally the human resources required to carry out the skilled investigations of those who have positive tests for faecal occult blood screening. It is therefore essential that these resources be used to best effect for the whole population. Secondly, the acceptance of the offer of screening was lower in people aged over 70 in the one randomised controlled trial carried out in the UK. The best use of resources for the population as a whole is to concentrate on the age range 50 to 69 in the first instance, with a review of this policy after the whole national programme has had two completed rounds of screening. Screening under the age of 50 is not justified because of the low incidence of cancer in this age group.

The contribution of primary care to colorectal cancer screening is of great importance and the involvement of general practitioners would be central to the development of an effective and acceptable programme.

5.5. The distribution of test values in the target population should be known and a suitable cut-off level defined and agreed

New types of test for faecal occult blood are being developed and will be evaluated during the pilot phase of the programme.

5.6. The test should be acceptable to the population

The test was acceptable to members of the public in the research studies although in the pilot studies, proposed it would be important to emphasise both the limitations of the test and the possible adverse effects of screening.

5.7. There should be an agreed policy on the further diagnostic investigation of individuals with a positive test result and on the choices available to those individuals

The standard follow-up for people with positive tests is colonoscopy, with double contrast barium enema for those for whom a complete colonoscopy cannot be carried out.

Another option is to offer a combination of double contrast barium enema and sigmoidoscopy and this may be evaluated in one of the pilots. A randomised controlled trial of screening by sigmoidoscopy alone for cancer of the lower half of the colon and rectum is being carried out by the Medical Research Council and its findings, which are not due for at least three years, will be taken into account when available.

It is important for the public and the individuals who are invited for screening to appreciate that at each stage of the screening programme there will be both false positives and false negatives, and that these are an essential part of a high quality screening programme. The magnitude of false positives and false negatives should be assessed as part of quality assurance but they must occur in even the best programme because:

a screening programme that had no false negatives would have too many false positives, and

a screening programme that had no false positives would have too many false negatives.

A balance always has to be struck and it is important also that those invited for screening are given information that helps them appreciate the inherent limitations of any screening programme.

It is important to point out that colonoscopy and double contrast barium enema carry risks, particularly the former, and that it is possible to perforate the colon while carrying out colonoscopy, particularly in difficult examinations. Too much pressure on colonoscopists to ensure that their colonoscopy is complete, with the colonoscope going to the furthest point of the colon, can result in an increased incidence of perforation. If the colon is perforated an operation is required and death could result.

Although colonoscopy has been the standard method of follow-up in the UK trial, another trial currently taking place uses a combination of double contrast barium enema and sigmoidoscopy, direct visualisation of the lower part of the colon. This approach appears to give results that are similar to those obtained by using colonoscopy as the initial follow-up investigation. There is concern that there may be insufficient experienced colonoscopists to allow a programme of this sort to be delivered nationally. Further work therefore needs to be done to investigate the feasibility of either using specially trained nurses to carry out colonoscopy or using double contrast barium enema with sigmoidoscopy as an alternative. If the latter approach were adopted the constraint on implementation of the programme nationally would switch from a shortage of clinicians able to do colonoscopy to a shortage of radiologists able to carry out double contrast barium enema and if the latter course were to be explored, for example in a pilot study, the possibility of training radiographers to carry out some of the tasks currently carried out by radiologists should be explored and evaluated.

5.8. There should be an effective treatment or intervention for patients identified through early detection, with evidence of early treatment leading to better outcomes than late treatment.

The randomised controlled trials demonstrate the benefits of early treatment. The risk to benefit ratio for treatment of benign and suspicious lesions is less certain.

5.9. There should be agreed evidence-based policies covering which individuals should be offered treatment and the appropriate treatment to be offered.

Two documents have been produced in England which give clear guidance on the management of colorectal cancer at different stages (1, 3) as well as the SIGN guideline on Colorectal Cancer in Scotland. These will be used to inform treatment guidelines for cancer detected in the screening programme.

5.10. Clinical management of the condition and patient outcomes should be optimised by all health care providers prior to participation in a screening programme

The screening programme, including all the investigations and the treatment of people with cancers or adenomas identified as part of the screening programme, will be governed by the principles and practices set out in the Calman/Hine recommendations for the organisation of cancer services.

5.11. There should be evidence from high quality randomised controlled trials that the screening programme is effective in reducing mortality and morbidity

The three trials of screening on which the recommendations are based are trials of high quality, well designed to minimise bias, and large enough to give sufficient power for the conclusions of the trials to be acceptable as reflecting what would happen if screening were offered to the whole population. The evidence supports the potential of screening to reduce mortality from cancer of the colon and rectum in males and females by between 10% and 20%. The Nottingham trial found a 15% (confidence interval 2% to 26%) cumulative mortality reduction with a median follow-up of 7.8 years. The Denmark trial found a 18% (confidence interval 1% to 32%) relative mortality reduction over 10 years. However, this means that screening would be unable to avert colorectal cancer deaths in the remaining 80% to 90% of those offered screening, nevertheless the number of lives saved nationally would be substantial.

5.12. There should be evidence that the complete screening programme (test, diagnostic procedures, treatment/intervention) is clinically, socially and ethically acceptable to health professionals and the public

The high rates of acceptance of both the test and subsequent follow-up indicates acceptability to the public with a proviso that people must be given information not only about the test but also about the limitations and potential harms of the whole screening programme.

5.13. The benefit from the screening programme should outweigh the physical and psychological harm (caused by the test, diagnostic procedures and treatment)

Decision analysis has shown that more people benefit than are harmed from screening but the balance of benefit to harm in a screening programme is an ethical and not only an arithmetical issue. The National Screening Committee has drawn up a set of ethical principles on which screening policies and programmes should be based and these have been published in its Annual Report (18).

One of the ethical issues in screening is that healthy people are exposed to adverse effects of screening without a guarantee of benefit and some healthy people will be harmed by any screening programme. There are two ways of looking at this. One is to say that the individual is clearly accepting the probability of harm without benefit when agreeing to participate in screening and that this is acceptable, provided they are given all the information in a way that allows them to be fully informed when they make the choice. Another way of looking at this is to say that some people who do not have the disease will be harmed, and that the decision to introduce and manage a programme that will benefit many but seriously harm a few poses serious ethical dilemmas.

This is of particular concern in colorectal cancer screening for it is possible that some people who do not have colorectal cancer will die as a result of the screening programme for colonoscopy is not a procedure free from risk. No fatalities were recorded in the trial in Denmark or the UK but these were services of the highest quality, large specialist centres with staff whose principal interest was screening and colonoscopy. This level of quality cannot necessarily be reproduced throughout the whole country and although sufficient quality can be achieved to ensure that an adequate number of cancers are detected, complication rates may be higher than were observed in the trials.

One feature illustrated well by the cervical screening programme is that individuals who are not technically harmed in anyway, nevertheless feel considerable aggrievement if they suffer misleading test results, or if they develop cancer despite participation in the screening programme. However, this harm should be much ameliorated if clear information about the benefits and limitations of screening are given to participants from the outset, in order to avoid falsely high expectations about the preventability of colorectal cancer through screening.

5.14. The opportunity cost of the screening programme (including testing, diagnosis and treatment) should be economically balanced in relation to expenditure on medical care as a whole.

The cost effectiveness of colorectal cancer screening has been examined in two studies, one of them based on the trial of colorectal cancer screening in the UK (19, 20), the other on a decision analysis commissioned by the National Screening Committee. The decision analysis allowed a number of different options to be examined and the cost for every extra year of life gained using different screening policies could be calculated. The decision analysis model allowed different scenarios to be explored but even taking an approach which assumed the worst case, with relatively high cost and low levels of detection, the cost effectiveness of colorectal cancer screening appeared similar to that of breast cancer screening and to many other procedures currently provided as standard by the National Health Service.

The opportunity cost of screening would need to be examined were the decision to implement a whole programme, which would cost between £45 and £50 million a year for the UK, to be made.

Opportunity costs can be calculated either by comparing the cost of colorectal cancer screening with some other intervention designed to control colorectal cancer, for example the effect of investing the same amount of money in either primary prevention or treatment services. Alternatively, opportunity costs can be assessed by comparing the effect of investing in colorectal cancer screening with the effect of investing the same amount of money on treating other bowel disorders or other cancers. This work is beyond the remit of the National Screening Committee.

5.15. There should be a plan for managing and monitoring the screening programme and an agreed set of quality assurance standards

A plan has been prepared for the provision of an integrated programme of colorectal cancer screening.

Colorectal cancer screening would only take place in the context of a national quality assurance programme. The precise arrangements for managing the quality assurance programme cannot be defined until the National Screening Committee has considered the report of the Quality Assurance Workshop held in July 1998 and made recommendations about the framework to which all quality assurance management should conform. A draft set of standards was produced for the Cardiff Workshop and these will form the basis of the standards to be used by the national programme and the basis of a specification for an information system to allow each programme to be informed about its own level of performance so that it can compare its performance with the standards.

5.16. Adequate staffing and facilities for testing, diagnosis, treatment and programme management should be available prior to the commencement of the screening programme

Adequate staffing and facilities will be available for the two pilot sites for this will be a necessary precondition. The possibility of inadequate staffing will be explored during the piloting of the programme and a plan to overcome any shortages identified will be developed during the pilot phase and implemented should a decision be made to have a national screening programme.

5.17. All other options for managing the condition should have been considered (e.g. improving treatment, providing other services)

Steps have already been taken to improve the management of colorectal cancer treatment as part of the UK Health Departments' initiative to improve the quality and effectiveness of cancer services.

6. Pilot screening programmes

Having reviewed the evidence and appraised its relevance to the UK population, the National Screening Committee proposes that two pilots be set up to offer two defined populations screening for colorectal cancer.

6.1 The protocol for the pilot projects

The target population for the pilot projects would cover all people aged 50 to 69 over a two year period. The primary test will be the faecal occult blood (FOB) test without dietary restriction and without rehydration of the test sample.

Follow-up for people with positive tests will be by colonoscopy, with double contrast barium enema for those people in whom a complete colonoscopy is not possible. The alternative of using double contrast barium enema and flexible sigmoidoscopy will 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 pilot project is not to assess the effectiveness of colorectal cancer screening; randomised controlled trials have already demonstrated the effectiveness of screening when delivered in research conditions.

6.2 Objectives of the pilot projects

The objectives of the pilots are to:

a) develop and evaluate a system for commissioning colorectal cancer screening;

b) evaluate the acceptability of the programme to the population when they receive full information about the limitations of screening and possible adverse effects;

c) clarify the part that primary care should play in screening and the implications of that for a national screening programme, taking into account all the changes that are currently taking place in primary care;

d) develop the most efficient means of distributing testing kits and reminders, and processing very large numbers of FOB tests; and design a system for carrying out FOB tests for the number of people that would be covered by a national screening programme;

e) set up and evaluate a structure for managing colorectal cancer screening for a total population of up to one million, taking into account the development of cancer units;

f) clarify and reach agreement on minimal acceptable and achievable quality standards and set up a quality assurance system for the two pilots that could be expanded into a national quality assurance system;

g) ensure that the quality of care provided in the research setting can be sufficiently reproduced in the service setting;

h) develop an information system that would allow the programme to be run efficiently and quality to be measured continuously;

i) identify possible staffing problems and take such steps as may be necessary to preclude or overcome such problems;

j) test planning assumptions, including the cost assumptions, in practice and refine the plan;

k) consider ways in which the public can be best involved in the colorectal cancer screening programme both locally and nationally;

l) develop a national training strategy for the national screening programme should the decision be made to introduce it.

m) Evaluate the cost-effectiveness of the promotion of dietary change as an alternative to screening.

6.3 Invitation to Express an Interest:

6.3.1 Partnerships of Health Boards, Trusts and Primary Care teams that meet the key criteria outlined below and wish to express an interest in being a colorectal cancer screening pilot site should write by the 14 October 1998 to:

Dr Muir Gray CBE, Regional Director of Research & Development, Anglia & Oxford Regional Office, Institute of Health Sciences, Old Road, Headington, OXFORD OX3 7LF. Tel: 01865 226833; Fax: 01865 226775;
E-mail address:- graym@rdd-phru.cam.ac.uk

Applications from Scotland should be copied to:

Sir David Carter
Chief Medical Officer
The Scottish Office Department of Health
St Andrew's House
EDINBURGH EH1 3DG

6.3.2 Expressions of interest should give details of: how the criteria are met; any relevant pre-existing expertise; the prospective project leader and key personnel.

6.3.3 Key design features of pilot location:

<u>Demographic</u>

a) There will be one pilot site in England, one in Scotland. Each pilot site might typically cover a population between 0.75-1m. Typically this might involve 4 DGHs/cancer units linked to one health board/cancer centre. Alternatively it might be two HBs/cancer centres if the DGHs/cancer units are geographically adjacent, provided one HB clearly has the lead responsibility.

b) Applications involving city, urban and rural populations would be the preferred option.

c) Confirmatory tests might typically require around one session per week for colonoscopies (based on six evaluation per session) and one examination per week for barium enema following incomplete colonoscopy. On the other hand, flexible sigmoidoscopy and barium enema examinations whilst not expected, are not excluded. Centres with little or no waiting lists for examination will be preferred.

Screening centre - laboratory capacity

d) The main focus for the pilot will be in the screening centre where the FOB tests would be read and administered. In theory, this could be sited anywhere but might in practice be best situated within the NHS family.

e) An appropriate number of rooms, perhaps five or six, will be needed for the centre to process and read the slides (which might be 60,000 pa). At least 2.0 wte trained readers will be needed and one MLSO to take clinical responsibility. Sufficient clerical staff will be required to handle approximately 200,000 letters pa (two letters for 100,000, including reminders and results); this might be between 8 and 10; those in supervisory roles will need some experience of handling a screening programme.

f) Pilot sites will need to demonstrate access and availability to screening centre facilities and staff working within the Scottish equivalent of the Calman/Hine guidelines, with minimum capital cost.

Cancer Unit Capacity

g) Prospective pilot sites will need to demonstrate capacity within the cancer centres, particularly the Departments of Radiology and Pathology, to offer prompt and efficient follow-up services to those patients with positive FOB tests. The follow-up service would be that outlined in the main proposal document. This might typically be 1,200 new investigations per year for 1m population. Appropriately trained clinicians, suitably skilled in the proposed techniques should be in post and responsive to the plans to offer these services or there should be good prospects of attracting high calibre staff at short notice.

h) It is essential that sites have effective multi-disciplinary teams working within the Calman-Hine principles, with good opportunities for Continuing Professional Development to keep abreast of the latest research and techniques. Sites should be able to demonstrate that they meet the six key recommendations set out in *Improving Outcomes in Colorectal Cancer*, published in November 1997, which have been adopted for this UK study. Sites should also be able to offer appointments for follow-up assessments within 2 weeks without detriment to waiting times for symptomatic patients.

Primary Care

i) Good relationships with primary care teams are essential. Sites should have established robust and credible links with practice teams and primary care administration, who will need to be supportive of the application for pilot site status. These teams will have an active role as the first source of advice and counselling in the screening programme, dealing with anxieties and misunderstandings; as well as helping to lead proactive public awareness and promotion activities. Accurate maintenance of the prior notification lists will fall to primary care services and accuracy will be essential.

j) Sites should be in localities which can demonstrate achievement of national targets for uptake in breast and cervical screening.

Public Awareness

k) Each site will need to conduct a public awareness campaign to promote the screening service for the duration of the pilot. This will need to include active participation from all the key health partners. Good links will need to be demonstrated with local media, and access and cooperation with pharmacy outlets, or perhaps retail centres.

l) The key messages about CRC screening are not straightforward, often awkward and need to be consistent with broader messages promoted about the benefits and limitations of other cancer screening programmes. Innovative but sensitive health promotion skills will be required.

Informed Consent

m) Further national debate will be ongoing about the best routes for balancing a maximised uptake against a clear public understanding of the possible consequences of entering the screening programme. Patients and special interest groups have an important role to play in establishing the most appropriate environment for screening to be successful.

n) A workshop is to be organised, through the National Screening Committee, with representatives of the public and the media to consider the image and reality of screening, the implications in the offer of the screening test, the relationship between those implications and the probabilities of benefit or harm, and the concept of informed choice.

o) Pilot sites will need to engage actively with this process, demonstrate a clear appreciation of the different ethical contract that screening brings up and be open to challenging new partnerships.

Quality Management

p) Quality assurance and clinical excellence will be an integral part of any pilot service offered. Sites will need to demonstrate that suitably robust audit and accountability lines exist at all levels and will need to be willing to participate in the development of external quality management arrangements.

Research

q) Potential pilot sites cannot be part of any current research trial in colorectal cancer screening, diagnosis or treatment e.g. the 14 sites presently involved in the MRC Flexible Sigmoidoscopy Trial.

6.3.4 Additional research questions:

It is recognised that additional complementary research will be needed to help fill the gaps in knowledge. The National Screening Committee Directors will work closely with the Health Technology Assessment programme to ensure these issues are addressed in a planned and systematic way.

APPENDIX 1

This paper is a report of the National Screening Committee which is a UK Committee, but each of the four Health Departments have different policy documents that relate to different aspects of this paper. The key policy documents from each of the four Health Departments, many of them based on the Calman/Hine report (2), are listed below:-

England

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

Scotland

Colorectal Cancer. A National Clinical Guideline recommended for use in Scotland by the Scottish Intercollegiate Guidelines Network. June 1997.

Eating for Health. A diet action plan for Scotland. July 1996.

The Scottish Diet. Report of a Working Party to the Chief Medical Officer for Scotland. December 1993.

Cancer Genetic Services in Scotland. Report by the Genetics Sub-Committee of the Priority Areas Cancer Team. September 1997.

Commissioning Cancer Services in Scotland. Report to the Chief Medical Officer. Scottish Office Department of Health. April 1996.

Wales

Cancer Services in Wales: A Report by the Cancer Services Expert Group (Cameron Report). November 1996.

Northern Ireland

Cancer Services: Investing in the Future. The Campbell Report.

Cancer Services: Investing in the Future. A report of the Cancer Working Group. May 1996.

Cancer Services: A framework for the multi-professional contribution to cancer care in Northern Ireland. A report by the Central Nursing Advisory Committee. July 1996.

References

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

2. A Policy Framework for commissioning cancer services:
A report by the Expert Advisory Group on cancer to the Chief Medical Officers of England and Wales. April 1995

3. NHS Centre for Reviews and Dissemination, University of York 1997. Effective Health Care Bulletin: The management of colorectal cancer. FT Healthcare

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

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

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

7. Wilson JMG, Jungner G. 1968 Principles and Practice of Screening for Disease. World Health Organisation, Geneva

8. Winawer SJ, Fletcher RH, Miller L, Godlee F, et al. 1997
Colorectal cancer screening: clinical guidelines and rationale.
Gastroenterology 112: 594-642.

9. Working Group on diet and cancer of the Committee of Medical Aspects of food and nutritional policy (COMA), Nutritional aspects of the development of cancer: 1998 Department of Health

10 American Institute for Cancer Research. 1997
Food nutrition and the prevention of cancer.
World Cancer Research Fund

11. Day N. 1998.
Monitoring the progress to the 2010 target for cancer mortality.
Personal communication

12. Agrez MV, Coory M. and Cockburn J. 1998
Population screening for colorectal carcinoma with fecal-occult blood testing, Are we sufficiently informed?.
Cancer Vol 82 No 10

13. Roe L, et al. 1997
Health promotion interventions to promote health eating in the general population: a review.
Health Education Authority

14. Havas S. et al. 1994
5 a day for better health: a new research initiative.
J. Amer. Dietetic Assoc. 94: 32-36.

15. Murcott A. 1997
The nation's diet: an overview of early results.
British Food Journal 99(3): 89-96

16. Sandler RS, Calanko JC, Murray SC, Helm JF and Woosley JT. 1998
Aspirin and nonsteroidal anti-inflammatory agents and risk for colorectal adenomas.
Gastroenterology 114: 441-7.

17. Stürmer T, Glynn RJ, Lee I-M, Manson JE, Buring JE, et al. 1998;
Aspirin use and colorectal cancer: post-trial follow-up data from the Physicians' Health Study.
Ann. Intern. Med. 128: 713-720.

18. National Screening Committee 1998.
First Report of the National Screening Committee
Health Departments of the United Kingdom,
Web site: http://www.open.gov.uk/doh/nsc/nsch/htm

19. Harcastle J, Chamberlain JO, Robinson MHE, Moss SM, Amar SS, Balfour TW, James PD, Mangham CM. 1996 Randomised controlled trial for faecal-occult-blood screening for colorectal cancer. Lancet; 348: 1472-77.

20. Gray A, Briggs A. March, 1998.
The benefits and adverse effects of screening for colorectal cancer: a decision analysis. Draft report prepared for the National Screening Committee.
Health Economics Research Centre, Institute of Health Sciences, University of Oxford.

 ISBN 0 7480 7801 0