

**Next Steps Towards a Feasibility Study for
Colorectal Cancer Screening in New Zealand:
Report for the Ministry of Health**

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Executive Summary

New Zealand has high rates of colorectal cancer (CRC) in comparison to many other countries, and has now twice considered whether population based colorectal cancer screening would be appropriate as an intervention to reduce mortality. A feasibility study of CRC screening has been recommended by an expert advisory group to inform a future decision about whether New Zealand should have a national programme.

This report reviews the current international status in relation to CRC screening, examines feasibility/pilot studies that have been conducted, looks at the information a feasibility study would provide New Zealand, provides an outline study design, and outlines the work that needs to be done prior to a feasibility study including an indicative timeline.

Internationally opportunistic testing remains the most common modality of 'screening' for CRC. However there is increasing interest in population based organised screening programmes, reflected in recommendations that programmes be implemented in some countries and more concrete action in others. Feasibility/pilot studies of screening have been or are being conducted in the UK, Australia, France, Italy, Spain, the Netherlands, Switzerland, Denmark and Finland. Programmes are being implemented at a national or state level in the UK, Australia, France, Italy, Canada, and Finland. All feasibility studies/pilots that have been completed have been described as successful, despite varying results in terms of participation and test positivity. There is a slight favouring of the use of guaiac faecal occult blood tests (FOBTg) in both feasibility/pilot studies and programmes, which is in part because of the lower positivity rate and thus reduced implications for diagnostic colonoscopy services.

A New Zealand prevalence and incidence round of screening would give valuable information on participation, test positivity, preliminary information on economics and cost, potential equity effects and health service implications. This information is not able to be reliably extrapolated from other jurisdictions. This screening could occur as part of a feasibility study, a pilot study or staged implementation of a programme.

In order to provide adequate information a feasibility study needs to detect a reasonable number of cancers, 40 would seem a sensible minimum. In order to ensure precise estimation of participation rates and test positivity rates for Maori as well as comparisons between Maori and non-Maori, at least 6000 Maori need to be invited to participate in screening. Assuming that Maori comprise about 10% of the population in this age range then 60 000 people would need to be invited to participate in screening. Should the Ministry of Health want to look at other population groups, such as Pacific peoples and Asian, a similar number of these groups would need to be invited to participate in screening. This may require further increases in the overall study size. Sample size calculations should be revisited once the final screening pathway and objectives are decided on.

In order to conduct a prevalence and incidence round of screening a number of steps need to occur. These include:

- Agreement on leadership and decision making process including incorporation of reducing inequalities in both of these aspects
- Agreement on key policy parameters (e.g. age range, screening interval)
- Development of information systems
- Finalising the details of the screening pathway, including the development of comprehensive quality indicators for the pathway and a monitoring framework.

These are substantive projects.

Full evaluation of the project is required and success criteria for a feasibility study are discussed. There are two possible types of success criteria, firstly minimum acceptable targets and secondly more aspirational goals. There are no precedents that we have been able to find for the use of minimum acceptable targets in a feasibility study and there are a number of difficulties around setting them. Options are provided for the latter.

Planning, delivering and evaluating a feasibility study is a long process. Realistic timeframes need to be set, including two years planning time before the commencement of screening, followed by four years of screening, with ongoing evaluation.

Finally in the writing of this report we have substantially quoted from and referenced the reports of the Gisborne Inquiry, the Cervical Cancer audit, the evaluations and critiques

of the breast cancer screening pilots and programme planning and the Chamberlain review of BreastScreen Aotearoa. Almost all the issues that need to be grappled with for CRC screening have already been faced in cervical and breast cancer screening.

Recommendations

The following recommendations are made in this report:

- Direct contact is made with countries that are currently conducting pilot/feasibility studies or are in the early stages of programme implementation to get further information and assistance.
- A prevalence and incidence round of CRC screening should be carried out in New Zealand within geographically defined populations to answer key questions relating to implementing CRC screening in the New Zealand context.
- The study is set up with the goal of addressing the question:
 - Can CRC screening be introduced in New Zealand in a way that is effective, safe and acceptable for participants, equitable and economically efficient?
- Specific aims and objectives for the study should be agreed upon by the implementation group and members of the pilot sites.
- A feasibility study needs to detect a minimum of 40 cancers, which requires a minimum of 40,000 people be invited for screening. To ensure adequate explanatory power for participation and test positivity rates for Maori, at least 6000 Maori participants need to be invited. This requires an increase of the total study numbers to 60 000 invited to participate in screening.
- The calculations around numbers invited to participate in screening should be reviewed once the screening pathway is finalised, as in the absence of decisions around key parameters and questions of the study it is not entirely straight forward to calculate sample size.
- The study should include a full prevalence, and incidence round of screening, and therefore be a minimum of four years duration.
- A multicentre study should be carried out with a minimum of two sites meeting the following criteria:
 - A diverse ethnic population
 - Urban and rural mix
 - Personnel with capacity and experience to deliver a screening programme
 - Service capacity and quality to manage the requirements of a screening programme

- Willingness of local DHB management, hospital clinicians, pathologists and primary care to participate in a screening feasibility study
- Demonstrated experience in reducing or eliminating inequalities in services.
- The feasibility study should have a monitoring system in place to allow detection of any issues or problems as they arise, so they can be resolved speedily.
- The work is managed by the National Screening Unit due to their considerable experience in, and understanding of, screening and cancer screening programmes.
- Eliminating inequalities is a main focus for leadership, process and planning of this feasibility study.
- A leadership structure and decision making and stakeholder engagement processes are agreed to early in the process.
- The pilot sites are selected early in the process so they can contribute to decisions.
- Screening policy parameters, such as age range, are reviewed for their implications on inequalities before being confirmed.
- Information systems are developed that incorporate functions that span the screening pathway as detailed in section 5.3.
- The feasibility study pilots the use of a population register to identify and invite eligible participants. This register could be based on Primary Health Organisation enrolment or National Health Index databases.
- Decisions about how people are invited are based on evidence, and on the approaches that are most effective for groups that screening programmes do not usually serve well.
- The decision about the type of FOBT is considered against the following parameters: evidence of mortality benefit, acceptability and participation, cost, inequalities, resource implications, sensitivity and specificity, quality control, acceptability to service providers.
- The role of primary care and GPs in the screening pathway needs to be elucidated. These groups need to be involved in developing the screening pathway and planning the feasibility study.
- High risk people identified through the feasibility study have their ongoing surveillance needs co-ordinated through the screening programme.

- The approach to individuals who are at high risk of CRC and thus not eligible for FOBT screening needs to be considered at the outset of the screening pathway design and feasibility study design.
- There is independent, on-going, multi-disciplinary evaluation, conducted by a group with relevant expertise (including in Maori health), planned as part of the study, and that it covers the four areas of effectiveness, safety and acceptability, equity and economics.
- Ideal/aspirational targets for the study be developed with the input of the implementation group and pilot sites, once the screening pathway has been finalised
- A minimum of two years is allowed for planning, and preparation before screening is initiated at study sites.

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Authors' conflict of interest statement

- Dr Shaw has previously worked for the Ministry of Health, at the National Screening Unit on colorectal cancer screening policy and in the Healthy Eating-Healthy Action Team.
- Dr Sarfati currently has contracts via the University of Otago with the Ministry of Health to produce reports relating to colon cancer management in New Zealand, and the quality of NZ Cancer Registry data in relation to colon cancer.
- Dr Cunningham is involved in the writing of reports for the Ministry of Health relating to colon cancer management in New Zealand, and the quality of NZ Cancer Registry data in relation to colon cancer.

All researchers state that they would consider applying for future work on colorectal cancer screening if the opportunity arises.

Peer Reviewers' conflict of interest statement

Tony Blakely, Liz Dennett, John McMenemy, Nick Chamberlain and Nina Scott all declare no conflict of interest.

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Glossary

Adenoma – a non-cancerous growth in the lining of the bowel that can progress to cancer.

BreastScreen Aotearoa – New Zealand's population based national breast cancer screening programme, managed by the National Screening Unit.

Colonoscopy – a procedure which uses a flexible fibre-optic endoscope to directly examine the bowel for polyps or cancer. It requires bowel preparation in the form of diet restriction and laxatives in the preceding days.

Cancer detection rate – the proportion of people screened in which cancers are detected.

Double Contrast Barium Enema – an X-ray examination using barium sulphate and air to outline the contour of the large bowel.

Ethnicity – the current official (Statistics New Zealand) definition of an ethnic group is a social group whose members share a common origin; claim a common and distinctive history and destiny; possess one or more dimensions of collective and cultural individuality such as unique language, religion, customs, mythology or folklore; feel a sense of unique collective solidarity. In New Zealand, ethnicity is based on self-identification.

Faecal occult blood tests – a type of test that involves taking a sample or samples of faecal matter and testing it for occult (unseen) blood or blood products which may indicate the presence of pathology in the bowel. This can be used as a screening test for colorectal cancer. The two main types of faecal occult blood tests are guaiac and immunochemical.

False negative – a normal (negative) test result in a person who has the target condition. This is important in quantifying the number of cancers that will be missed by the screening test.

False positive – an abnormal (positive) result in a person who does not have the target condition. This is important in quantifying the number of people without cancer who will need further investigation.

Flexible Sigmoidoscopy – a flexible fibre-optic endoscope used to directly examine the lower bowel for polyps or cancer.

Incidence – the number of new cases of a disease in a given population during a given period of time. Incidence is usually expressed per 100,000 people per year.

Inequalities in health – differences in health status between groups that are unnecessary, avoidable and unjust.

Interval cancer – a cancer that is diagnosed after a normal screening test result was given and before the next scheduled screening examination (or during some defined period after the screening test). Interval cancers include a spectrum of cancers, from those which did not exist or were undetectable at the previous round of screening to those that were detectable but missed.

National Cervical Screening Programme – New Zealand's population based cervical screening programme.

National Cancer Register – a population-based register of all primary malignant diseases diagnosed in New Zealand, excluding squamous cell and basal skin cancers.

Negative Predictive Value – the proportion of individuals with a negative (normal) test result who do not have the target condition.

Opportunistic screening – screening initiated through practitioner offer or patient request, with no coordinated system of follow up.

Organised screening – all of those eligible for screening are systematically identified and offered screening. Centralised systems are used for follow up and quality monitoring.

Perforation – a complication of colonoscopy where a small hole is accidentally made in the bowel wall.

Population register – a database holding selected information about each member of the resident population in a defined geographical area.

Positive Predictive Value – the proportion of individuals with an abnormal test result who have the target condition.

Prevalence – the number of cases of a specified disease in a given population at a designated point in time.

Randomised controlled trial – an epidemiological experiment in which subjects are randomly assigned into groups to receive or not receive an experimental preventive or therapeutic treatment, intervention, procedure or manoeuvre. Randomised controlled trial evidence of benefit of screening is one of the criteria used to assess potential screening programmes.

Screening pathway – the sequence of steps involved in a screening programme, which includes the promotion of the programme, the identification and invitation of eligible participants, the screening test itself, and appropriate diagnostic investigations and treatment for those testing positive. It is important to note that the offer of a screening test in isolation is not a screening programme.

Sensitivity – the proportion of individuals who have a target condition who receive a positive (abnormal) test result. A screening test that is more sensitive will pick up a greater proportion of those with the target condition. However, it is possible that a more sensitive test may worsen the trade-off between benefits and harms if the test picks up more cases of inconsequential disease.

Socio-economic position – the social and economic factors that influence what position(s) individuals and groups hold within the structure of society (e.g. someone's social class, income or relative deprivation).

Specificity – the proportion of individuals who are free of the target condition who are correctly identified by the screening test as being free of the condition. If a new screening test is more specific (results in fewer false positives) then the potential harm of screening may be reduced.

Surveillance – monitoring individuals known to have a disease or to be at increased risk of a disease.

Test positivity rate – the proportion of people being tested who return a positive result.

Abbreviations

BSA	BreastScreen Aotearoa
CRC	Colorectal cancer
CRCSAG	Colorectal Cancer Screening Advisory Group
DCBE	Double contrast barium enema
DHB	District Health Board
FOBT	Faecal occult blood test
FOBTi	Faecal occult blood test- immunochemical
FOBTg	Faecal occult blood test- guaiac
FS	Flexible sigmoidoscopy
GP	General Practitioner
IBD	Inflammatory bowel disease
NCSP	National Cervical Screening Programme
NHI	National Health Index
NHS	National Health System
NMDS	National minimum dataset
NSU	National Screening Unit
NPV	Negative predictive value
NZCR	New Zealand Cancer Register
NZHTA	New Zealand Health Technology Assessment
OECD	Organisation for Economic Cooperation and Development
PHO	Primary health organisation
PPV	Positive predictive value
RCT	Randomised controlled trial

Chapter 1 CRC screening in NZ

1.1 Background

Reaching agreement on what constitutes screening is difficult. One definition proposed by Wald (2006) is contained in Box 1.

Box 1 Definition of medical screening

There is no universally accepted definition of medical screening, but there is general agreement that the activity contains three elements:

(1) It is a process of selection with the purpose of identifying those individuals who are at a sufficiently high risk of a specific disorder to warrant further investigation, or sometimes direct preventive action. It is usually a preliminary process to offering a diagnostic test and, if required, preventive action.

(2) It is systematically offered to a population who have not sought medical attention on account of symptoms of the disease for which screening is being conducted. It is normally initiated by medical authorities and not by a patient's request for help on account of a specific complaint.

(3) Its purpose is to benefit the individuals being screened. On this basis, mass testing activities such as surveillance for HIV infection or pre-employment examinations to test fitness for work would not be classified as medical screening.

In an attempt to encapsulate these elements the following definition is proposed:

Screening is the systematic application of a test or inquiry to identify those individuals at sufficient risk of a specific disorder to benefit from further investigation or direct preventive action, among persons who have not sought medical attention on account of symptoms of that disorder. [1]

Meta-analysis of randomised controlled trials conducted in recent decades has shown that screening using the FOBTg Haemoccult can reduce population mortality from CRC by 16% (95% confidence range 10%-22%). [2] In view of this evidence and high rates of

CRC, New Zealand has twice considered whether a national population based CRC screening programme for people at average risk of the disease would be suitable.

In 1998 the National Health Committee published a discussion document containing the recommendations of a working party that had considered the appropriateness of colorectal cancer screening in New Zealand. The following recommendations were made:

- Given the modest potential benefit, the considerable commitment of health sector resources and the small but real potential for harm, population-based screening for colorectal cancer with faecal occult blood tests is not recommended for New Zealand.
- Population-based screening for colorectal cancer with other modalities, such as flexible sigmoidoscopy, colonoscopy or double contrast barium enema, is also not recommended as there is not yet evidence from randomised controlled trials that screening with any of these modalities produces a reduction in colorectal cancer mortality.
- Decisions should be reviewed as evidence of benefit from new faecal occult blood tests and other screening modalities becomes available.
- Colorectal cancer is recognised as an important cause of morbidity and mortality and it is recommended that New Zealand participate in international research in this area.
- Wider consultation and further consideration should be undertaken to develop appropriate advice on surveillance recommendations for groups identified to be at increased risk of colorectal cancer. [3]

In 2004, in response to international developments, the National Screening Unit (NSU) commenced a review of this policy. To inform this policy review the NSU commissioned primary research, a systematic evidence review, discussion documents and convened an advisory group. The advisory group wrote a comprehensive report and made a number of recommendations. The recommendations specifically relevant to this report include:

- A feasibility study of CRC screening with immunochemical faecal occult blood test (FOBTi) as the screening test be undertaken in New Zealand. The study would address several key research questions specific to New Zealand and assess

feasibility by monitoring the acceptability and impact of screening on participants and service providers across the screening pathway.

- The feasibility study design should incorporate an initial phase that determines optimum positivity rates of the chosen FOBTi(s). This phase may involve comparing the performance with that of the FOBTg used in the published randomised controlled trials and the United Kingdom pilots.
- A feasibility study is a pre-requisite to a decision regarding a pilot study. [4]

The authors' understanding of the current status of CRC screening policy in New Zealand is as follows:

- No decision on whether to proceed with a national programme of CRC screening has currently been made.
- In order to provide the information required to make a decision on whether to proceed with a national programme a feasibility study is being considered.

This report is written based on this understanding.

1.2 Scope of this report

This report has been commissioned by the Ministry of Health to inform planning of a feasibility or pilot study of CRC screening in New Zealand. The report was to cover the following:

- Review the colorectal screening feasibility and/or pilot studies and screening programme implementation internationally. This was to include the experience of other countries in establishing criteria, the criteria they used in the design of their feasibility and/or pilot studies, the outcomes of the feasibility and/or pilot studies and the reasons why some countries did not continue with colorectal screening after the completion of the feasibility and/or pilot studies. This work was to build on (but not be a replication of) existing literature reviews already produced to date (such as the reports produced by the National Screening Unit, Colorectal Screening Advisory Group and the NZHTA Literature Review).
- Recommend whether a study could be used to establish the feasibility of screening in the New Zealand setting using evidence based reasoning and based on the review of international studies and suitable criteria.

- Recommend suitable success criteria for a feasibility or pilot study in New Zealand including consideration of (but not limited to) the following:
 - type of tests;
 - acceptability of tests;
 - required participation rates to achieve a valid study and the minimum size of the trial population that New Zealand could base a study on;
 - the demographic composition of the population to be trialled;
 - the cost effectiveness;
 - effect on reducing inequalities;
 - other suitable success criteria included in international feasibility and/or pilot studies.
- Provide outline options for a feasibility and/or pilot study design for a population based colorectal cancer screening programme in New Zealand. This outline design was to include (but was not limited to):
 - The advantages and disadvantages of the proposed option(s) of the feasibility and/or pilot study design;
 - A broad timeline and tasks for implementing the feasibility study;
 - Suggested infrastructure for implementing the feasibility study;
 - Identification of the equity considerations

The contract timeframe was five weeks so the report covers many of these issues at a high level, and identifies areas for further work. A large amount of work has already been done on this issue in New Zealand and internationally, so it is inevitable that this report distils and summarises some of this information.

1.3 Improving population health and reducing inequalities

The New Zealand Health Strategy and Cancer Control Strategy have the dual aims of improving population health and reducing inequalities. [5, 6] The New Zealand Health Strategy notes that: “to improve the overall health of New Zealanders, particular attention must be paid to those with the poorest health.” [5] Inequalities in health are differences in health status which are unnecessary, avoidable, and unjust. [7]

Inequalities currently exist in New Zealand between ethnic groups, between genders, between age groups, and between geographic and socio-economic groups.

This report has a focus on eliminating inequalities, particularly between Maori and non-Maori. Inequalities between Maori and non-Maori are the largest and most consistent inequalities in health in New Zealand, [8, 9] and so must be a focus of initiatives to improve the health status of New Zealanders. Moreover, Maori are tangata whenua and have a special relationship with the Crown under the Treaty of Waitangi. National screening programmes currently operating for breast and cervical cancer have not achieved equitable coverage for Maori women. [10, 11] If colorectal cancer screening is introduced it represents an opportunity to learn from the experiences of other screening programmes and focus on getting screening right for those generally least well served by screening programmes.

Colorectal cancer screening has the potential to increase inequalities between Maori and non-Maori. If a screening programme is established which is much more acceptable to non-Maori New Zealanders it may improve survival in non-Maori but not Maori, worsening the existing differences in survival. It is therefore essential that CRC screening is established in a way which is acceptable to Maori in the first instance, in order to prevent the disparities in uptake seen in other screening programmes. Box 2 summarises inequalities in CRC in New Zealand between Maori and non-Maori.

Box 2 Inequalities in CRC in New Zealand between Maori and non-Maori

Inequalities currently exist in colorectal cancer. While Maori are less likely to be diagnosed with CRC than non-Maori, they are just as likely to die from it (i.e. Maori are less likely to survive CRC). [9] Hence Maori/non-Maori disparities in CRC mortality are due to factors around diagnosis, treatment and support. Compared to non-Maori, Maori are less likely to have stage at diagnosis recorded on the Cancer Register, are less likely to have localised disease and more likely to have disseminated disease. [12] Survival differences may also be explained by differences in treatment received or differences in co-morbidities. Approximately half of the 60% higher risk of death from dying from colorectal cancer for Maori (relative to non-Maori) is accounted for by differences in stage at diagnosis, the other half may be influenced by differences in treatment received and differences in co-morbidities. [12]

Chapter 2 CRC screening activity internationally

This section summarises the current practice of CRC screening internationally, then reviews pilot/feasibility studies and/or experience in programme implementation in more detail.

Chapter 2 Summary and Recommendations

- Organised population based CRC screening activity has been increasing internationally in the last decade.
- Opportunistic screening is common.
- New Zealand has high rates of CRC compared to many other Organisation for Economic Cooperation and Development (OECD) countries.
- Italy, France, Spain, the UK, and Australia have conducted feasibility/pilot studies of faecal occult blood test (FOBT) screening.
- Denmark, Switzerland and the Netherlands are in the process of conducting feasibility studies.
- Italy, France, the UK, Australia, Canada, Finland are implementing organised population based screening programmes. A number of other countries have recommendations but do not yet appear to have programmes.
- Slightly more feasibility studies and programmes use guaiac FOBT than immunochemical.
- All pilot/feasibility studies have used a population register to invite participants to attend.
- Participation in pilot/feasibility studies varied from 17% to 70%, despite this all pilot/feasibility studies concluded that population based screening was feasible.

We recommend that :

- Direct contact is made with countries that are currently conducting pilot/feasibility studies or are in the early stages of programme implementation to get further information and assistance.

2.1 *International stocktake*

Table 1 summarises colorectal cancer mortality rates and screening programme status for OECD countries. It specifically distinguishes organised population-based programmes (which include the three key elements of screening as described in section 1.1) from opportunistic screening. Opportunistic screening/testing is dependent on practitioner offer or patient request, and so will not be offered to all eligible subjects, and tends not to have the elements that ensure quality and safety of the process. [13]

As can be seen from Table 1, many countries have opportunistic screening for colorectal cancer, using a variety of screening tests including FOBT, flexible sigmoidoscopy and colonoscopy. Population-based screening has been recommended in a number of countries, and several have undertaken or are undertaking feasibility or pilot studies of screening. The UK, Australia and Finland are the only OECD countries currently with national population-based CRC screening programmes, and all of these are in their early stages of implementation. Canada, France and Italy are either planning to, or are currently implementing state-based programmes. No information could be found on Mexico and the Slovak Republic, and information in English was not always readily available.

Table 1 CRC mortality rates and screening status for all OECD countries

OECD country	Female CRC mortality/100 000*	Male CRC mortality/100 000*	CRC screening programme status
Australia	13.3	18.7	Pilot study 2002-4 Implementing a national population-based CRC screening programme [14, 15]
Austria	13.9	20.1	Annual FOBT for individuals over 40 as part of preventive examination (opportunistic screening) No national population-based screening programme [16]
Belgium	14.1	18.7	Feasibility study of screening using FS undertaken in 1990s [17] No national population-based screening programme
Canada	11.7	16.1	Population-based screening has been recommended and is currently being implemented at a state level [16, 18-22] No population based feasibility/pilot study appears to have been conducted.
Czech republic	18.0	34.0	Biennial guaiac FOBT for individuals over 50 offered by GPs (opportunistic). No national population-based screening programme [16]
Denmark	19.2	23.3	Feasibility studies being undertaken looking at participation and stage distribution [23] No national population-based screening programme at present [16, 21]
Finland	9.8	11.5	Implementing a national population-based CRC screening programme, with phased implementation over 10 years from 2004 [23, 24]
France	11.8	18.2	A pilot trial in 23 districts to assess feasibility is being conducted Decision made to implement a national population based CRC screening programme [21, 25]
Germany	15.7	19.9	Guidelines recommend opportunistic screening with biennial FOBT or two colonoscopies (10 years apart) from age 55 No national population based screening programme, although data on screening is centrally managed [16, 21, 26]
Greece	18.7	9.7	Opportunistic FOBT screening available for individuals aged 45-75. No national programme [16]
Hungary	21.2	35.6	Feasibility study in Budapest in 1983 using FOBT, found to be very high cost[27]. Several regional programmes National programme using FOBT is planned [28].
Iceland	13.2	12.8	Population based screening has been recommended [16, 21] Unable to determine if this is being implemented
Ireland	13.7	23.6	No national screening programme, although it has been recommended. [29]

OECD country	Female CRC mortality/100 000*	Male CRC mortality/100 000*	CRC screening programme status
Italy	10.9	16.5	National screening using FOBT recommended [26] Screening programmes operating in 11 of 21 regions [30-32]
Japan	11.1	17.3	National screening programme since 1992, annual FOBTi for individuals aged over 40, low participation rate (17%) [21, 33]
Korea	6.7	10.9	National screening programme since 2004 (probably opportunistic), annual FOBTi for individuals aged 50+ (as part of screening programme for breast, cervical, colon, stomach and liver cancers) [21]
Luxembourg	13.4	18.6	No national population-based screening programme [21]
Mexico	4.1	4.5	No information found
Netherlands	14.4	18.9	National programme has been recommended and several pilot and feasibility studies are in progress. [21, 34]
New Zealand	18.6	23.2	Considering a feasibility study
Norway	16.8	20.1	No national population-based screening programme, although there is an RCT occurring comparing FS with FS plus FOBT (once only screening exam) [23, 35]
Poland	11.4	18.2	Opportunistic screening by colonoscopy [36] No national population-based screening programme.
Portugal	11.9	20.0	Identified as a goal but no national programme [21, 37].
Slovak Republic	16.0	33.2	No information found
Spain	11.3	18.5	Feasibility study in Catalonia in 2000 [38] No national population-based screening programme at present [21]
Sweden	11.1	14.9	No national population-based screening programme [21]
Switzerland	9.7	15.3	Feasibility study/trial assessing different tests in 50-80 year olds, national programme planned [16, 21].
Turkey	5.4	5.8	No national population-based screening programme [39]
United Kingdom	12.4	17.5	Pilot study in 2000-2003 [40] Now implementing a national population-based CRC screening programme.[41]
United States	11.6	15.2	No national population-based screening programme [26] Opportunistic screening recommended [42]

* Source: GLOBOCAN 2002 Age standardised to world population, ICD-10 C18-21

2.2 Feasibility/pilot study summary

This section looks at feasibility and pilot studies of population-based colorectal cancer screening that have been conducted internationally over the past decade.

Medline and internet searches were performed to identify studies meeting the following criteria:

- FOBT as screening test only (guaiac or immunochemical)
- Pilots or feasibility studies for population based screening programmes (not opportunistic screening)
- Articles published in English

Available grey literature for the UK and Australian pilots was also obtained. The staged implementation of the Finnish screening programme has also been included in this review as it aimed in its first three years to produce information about the feasibility of screening in the Finnish context, a similar aim to the pilot and feasibility studies reviewed. The terms feasibility and pilot studies are used synonymously in most literature.

Sections 2.2.1 and 2.2.2 present the design and results of feasibility and pilot studies reviewed respectively. With the exception of the Spanish study, only results of prevalence (first) screening rounds are included.ⁱ Other feasibility studies are in progress internationally, for example in Denmark, Switzerland and the Netherlands, but design and results have not yet been reported. [16, 23, 34] Variable amounts of information were available on the studies presented here, with the most information being available on the UK and Australian pilots, where the full evaluation reports are publically available (and in English). In all the other studies considered, information was obtained from journal articles, which provide more limited information.

ⁱ The only other study that has reported an incidence (second) round of screening is the English pilot. However the evaluation of the prevalence round was of both the English and Scottish sites so it is not directly comparable.

2.2.1 Design of feasibility/pilot studies

Key design features of each feasibility/pilot study are detailed in Table 2. Some of the key points include:

- All of these studies utilised a population register to identify people eligible for screening, either using General Practice enrolment data or municipal registers.
- Most excluded those at high risk of colorectal cancer, including individuals with a personal history, or who had recently been screened for colorectal cancer, although in some studies these people were only excluded from follow up and not from the initial round of FOB testing.
- Various age ranges between 50 and 74 were chosen for the studies.
- Invitation was by post in all these studies, with letters coming either from general practitioners, the screening programme itself, or from local mayors in the Italian studies. Half of the studies included here sent the test kit out with the invitation, while the others required the person to visit their GP or another venue to receive a test kit, and tests kits were returned either by post or in person.
- Guaiac FOBT has been used in the UK, France, Spain and Finland, while Australia and Italy have opted for immunochemical FOBT.
- For countries using a guaiac test no dietary restrictions were required for the initial test, except in Finland. However dietary restrictions were required for repeat indeterminate tests in the UK and Spain.
- Criteria for test positivity varied between the studies. In Spain and the UK a weakly positive or indeterminate category was used for guaiac testing, while France and Finland regarded any positive result on guaiac testing as requiring follow up.
- Colonoscopy was used as the diagnostic test of choice in all countries, with DCBE being an acceptable alternative in most when colonoscopy could not be completed.
- GP referral for colonoscopy was required in the Australian, French and Finnish programmes, but occurred via the screening programme in other countries.

Table 2 Design of feasibility and pilot studies

Country name	Australia [14, 43]	UK [40, 44]	Italy - Valle d'Aosta [30]	Italy – Florence [45]	France [25]	Spain [38]	Finland ⁱⁱ [24, 46]
Type of Study	Pilot study to assess feasibility, acceptability and cost-effectiveness of screening using FOBT	Pilot programme to assess acceptability and feasibility of population based screening	Feasibility study of CRC screening using FOBTi (NB screening programmes already established in other parts of Italy)	“Experimental screening protocol” Trial of different methods of invitation	Pilot screening programme to assess feasibility and effectiveness (23 pilot areas, one reported on here: Haut-Rhin)	Pilot screening programme in Catalonia (2 rounds)	Implementation of screening programme with staged roll out. Individual level randomisation to screening or control, with screening offered to controls after 6 years.
Years conducted	2002 – 2004	2000 – 2003	2001	1996 – 1998	2003 – 2006	2000 - ?	2004 –
Method for identifying eligible population	Medicare enrolment files used to develop Bowel Cancer Screening Pilot Register	Primary care (GP) registers	Municipal rosters, matched to GP files	Resident lists from municipal archives matched with GP patient registers	Sickness Fund database files	Primary Health Care database	Central Population Register
Screening register established	yes	yes	Not stated	yes	yes	yes	yes

ⁱⁱ Implementation of screening programme rather than pilot/feasibility study, although also designed to test feasibility as the programme is gradually expanded.

Country name	Australia [14, 43]	UK [40, 44]	Italy - Valle d'Aosta [30]	Italy – Florence [45]	France [25]	Spain [38]	Finland ⁱⁱ [24, 46]
Age Range	55-74	50-70	50-74	50-70	50-74	50-69	60-69
Exclusion criteria	Recent colonoscopy, personal history of CRC,	Those with a personal history of CRC do not seem to have been excluded.	No exclusion of those at high risk of CRC.	Recent CRC screening (FOBT, DCBE, colonoscopy), Personal history of CRC or adenomas.	Recent CRC screening, high CRC risk, serious illness.	High CRC risk (personal history of CRC, adenoma, or IBD, or meeting criteria for hereditary CRC syndromes)	Nil stated
Method of invitation	Postal invitation from screening programme. Including test kit.	Postal, signed by clinical directors of screening pilot programme. Including test kit.	Postal, signed by the mayor of the municipality. Not including test kit, but including addresses for sites to collect test kits.	A: letter from GP instructing to pick up kit from volunteer centre B: letter from GP instructing to pick up kit from GP clinic C: letter from mayor instructing to pick up kit from volunteer centre	Postal, inviting to visit GP for screening. Not including test kit.	Postal: personal invitation letter signed by person in charge of screening programme. Not including test kit. Test kit sent to those who indicated willingness (and automatically if had participated in 1 st round).	Postal, personal invitation letter from national screening centre. Including test kit.
Reminder	Letter after six weeks if test not returned.	Letter after 4-6 weeks if test not returned.	Letter after 2 months if no response or didn't return test.	Letter, time interval not indicated.	Recall letter after 6 months if had not visited GP, another 4 months later FOBTg sent	Letter after six weeks if test not returned.	Not stated

Country name	Australia [14, 43]	UK [40, 44]	Italy - Valle d'Aosta [30]	Italy – Florence [45]	France [25]	Spain [38]	Finland ⁱⁱ [24, 46]
					directly in mail to non-responders, another letter after 6 weeks if necessary.		
Type of screening test	Immunochemical FOBT (2 different brands of test used – Bayer Detect and Inform, randomly allocated)	Guaiac FOBT (Hema-screen)	Immunochemical FOBT (latex agglutination, OC Hemodia)	Immunochemical FOBT	Guaiac FOBT (Hemoccult II)	Guaiac FOBT (Hema-screen)	Guaiac FOBT (Hemoccult)
Samples	1 sample each from 2 separate bowel motions	2 samples from 3 consecutive stools	Single sample	One day (single sample?)	2 samples from 3 consecutive stools	2 samples from 3 consecutive stools	1 sample from 3 consecutive stools
Delivery of samples to laboratory for analysis	Postal	Postal	In person	In person	Postal	Postal	Postal
Dietary restrictions required?	No	No. Dietary restrictions for repeat test if first test weakly positive.	No.	No.	No. Asked not to use >1g of acetylsalicylic acid or vitamin C.	No. Dietary restrictions for repeat test if first test weakly positive.	Yes. Avoid raw meat, liver, blood dishes and >250mg/day of vitamin C for 3 days.
Positivity criteria	According to manufacturers specifications, (quantitative	Indeterminate: 1-4 spots (repeat test) Positive: 5 or 6	Cut off: haemoglobin 100ng/ml of sample solution	Not Stated	One slide positive	Indeterminate: 1-4 spots (repeat test) Positive: 5 or 6	Any blood observed

Country name	Australia [14, 43]	UK [40, 44]	Italy - Valle d'Aosta [30]	Italy – Florence [45]	France [25]	Spain [38]	Finland ⁱⁱ [24, 46]
	results also recorded for future analyses of adjusting positivity cut off)	spots				spots	
Method to deliver results	Postal, to participant, GP and Register. Advised to see GP if positive for referral for colonoscopy	Postal Invited to attend nurse appt to discuss results and further investigations.	Postal if negative. Telephone if positive.	Postal if negative. Telephone if positive.	Postal, to participants and GPs, advised to see GP if positive for referral for colonoscopy.	Postal if negative. Telephone if positive, with offer of colonoscopy.	Postal. If positive result also sent to local health centre to organise colonoscopy.
Diagnostic test	Colonoscopy	Colonoscopy DCBE if incomplete colonoscopy, but no DCBE if unfit for colonoscopy	Colonoscopy, DCBE if not possible to complete colonoscopy	Colonoscopy, DCBE if not possible to complete colonoscopy	Colonoscopy	Colonoscopy, DCBE if incomplete or contraindicated	Colonoscopy
Role of GP	GPs asked to explain pilot to their patients. Test results sent to GPs. Asked to see GP after positive test for referral for colonoscopy, or if symptoms or family history	Letter indicates don't need to contact GP, contact screening office of phone hotline instead.	Dispensed testing kits (as did pharmacies and health district staff)	Invitation letters were from GP (Groups A and B), GP dispensed testing kits (Group B)	Referral for colonoscopy	Asked to see GP after positive test to confirm suitability for colonoscopy	Responsible for organising colonoscopy and further management.

Country name	Australia [14, 43]	UK [40, 44]	Italy - Valle d'Aosta [30]	Italy – Florence [45]	France [25]	Spain [38]	Finland ⁱⁱ [24, 46]
	(impact on GPs included in evaluation)						
Screening interval	Biennial (re-invited after 5 years if negative colonoscopy)	Biennial	Biennial	Biennial	Not stated (assume biennial)	Not stated (assume biennial)	Biennial
Method of recall	Postal – by Screening Register	Not Stated	Not Stated	Not Stated	Not Stated	Postal - Central screening unit established	Postal - National screening unit responsible for invitations
Methods to encourage uptake	Educational material included with invitation (available in common languages), local press, radio and TV campaigns	Local publicity in pilot areas, radio campaigns, posters	Involvement of GPs in planning, letters of invitation signed by the mayor. Health education campaign prior to mailing invitations.	Local mass media and leaflets in doctors offices and pharmacies prior to invitations.	Not Stated	Not Stated	Not Stated
Methods of providing information to participants	Pilot phone helpline established. Website established. GP and specialist information kits.	Phone hotline established	Not Stated	Not Stated	Not Stated	Not Stated	Not Stated

2.2.2 Results of feasibility/pilot studies

The results of the feasibility and pilot studies are detailed in Table 3. This text contains some of the key points:

- Studies varied in size from 3,000 to nearly 480,000 people invited.
- Participation rates varied from 17% in Spain to 70% in Finland, with the remaining studies between 42 and 57%. (The randomised controlled trials (RCTs) which provide evidence for a mortality benefit had approximately 60% participation. [2])
- There was higher participation by women in all studies, and by less disadvantaged and older people. Differences in participation between ethnic groups were noted in the UK and Australian studies.
- Over 95% of all tests returned were able to be analysed in all studies.
- Test positivity varied between 1.9% and 3.4% for guaiac tests and between 4.2% and 9.0% for immunochemical tests.
- Waiting time for colonoscopy was not uniformly recorded across the studies. Colonoscopy rates following a positive test were over 80% in all but the Australian study, although data issues meant that the Australian rate is likely to be an underestimate. Over 85% of all colonoscopies were completed satisfactorily (although different definitions of satisfactory colonoscopy were used in the different studies).
- Colonoscopy complication rates were only stated for 3 studies, and very few serious complications were reported. Perforation rates were between 0.05% and 0.2%.
- Cancers were detected in 0.2-0.5% of those screened (with most studies finding cancer in 0.2%), and the positive predictive value (PPV) for cancer varied between 4.5% and 14.3%.
- The proportion of those having screening who went on to require surveillance colonoscopy was not stated in any of the study reports available.
- All the studies were reported as demonstrating the feasibility of wider screening programmes, including those with very low participation rates (Spain) and those with significant problems with the screening pathway and with the evaluation (Australia).
- The UK, Australia and Finland are currently implementing screening programmes nationally, Italy has regional programmes and France is reported to be intending to implement a national programme, following on from the 22 pilots occurring.

- We were unable to find evidence of any country that has conducted a feasibility or pilot study that has definitively decided **not** to proceed with a CRC screening programme. However for Spain we are unable to determine what has happened subsequent to the feasibility study conducted in Catalonia.

Table 3 Results of feasibility and pilot studies

Country name	Australia [14, 43]	UK [40, 44, 47]	Italy - Valle d'Aosta [30]	Italy - Florence [45]	France [25]	Spain [38]	Finland [24, 46]
Eligible population	Men and women aged 55-74 in three geographical areas (2 urban, 1 rural)	Men and women aged 50-70 in two geographical areas in England and Scotland	Men and Women aged 50-74 in small geographical area	Men and women aged 50-70 in a small town	Men and women aged 50-74 in geographical area (Haut Rhin) Also 22 other area-based pilots in France.	Men and women aged 50-69 in town of 239,000 inhabitants.	Men and women aged 60-69 (eventually all in Finland, with gradual inclusion of more municipalities over time)
Population theoretically eligible to be screened	Not stated	Not stated	Not stated	Not stated	186 592.	Round 1: 64,886 Round 2: 67,239	52,994 (half of the 105,992 eligible to be randomised to screening or control groups)
Population invited to be screened	60,792	478,250	2,961	15,235	182,981 (97.9%)	Round 1: 63,880 Round 2: 66,534	52,994
Population actually eligible to be screened	56,907 ⁱⁱⁱ	Not stated	Not stated	Not stated	163,707	Not stated	52,994
Population participated in screening	25,840 (45.4% of eligible)	276,819 (57.9% of invited)	1,693 (57.2% of invited)	6,418 (42.1% of invited)	Not Stated	Round 1: 10987 (17.2% of eligible) Round 2: 14837 (22.3% of eligible)	37,514 (70.8%)

ⁱⁱⁱ Some of those invited were not actually eligible, for example because they no longer lived in the pilot areas or were deceased.

Country name	Australia [14, 43]	UK [40, 44, 47]	Italy - Valle d'Aosta [30]	Italy Florence [45]	France [25]	Spain [38]	Finland [24, 46]
Screening test completion	25,688 (45.1%) (95% of tests returned)	271,646 (56.8%) (98% of those who agreed to participate)	1,631 (55.1%) (96% of tests returned)	6,393 (41.9%) (99% of tests returned)	90,706 (55.4% of eligible)	Round 1: 96.4 % Round 2: 95.5%	36,556 (97.4% of tests, others recollected)
Participation by groups	Higher in women and the least disadvantaged groups, and English speaking and non-indigenous groups.	Higher in women and older and the least disadvantaged groups, lower amongst some ethnic groups.	Higher in women.	Higher in women, married people, and people living in the centre of town. Higher participation among those invited by their GP and among those who received test kits from their GP. (B>A>C)	Higher in women than men and in those aged 55-69 than in older or younger groups.	Higher in women.	Higher in women, married people, and the oldest age group.
Overall test positivity rate (number of positive tests)	9.0% (2308) Inform: 9.9 Bayer: 8.2 Higher in men and older age groups (Inform: 14.2% in men 65-69 and 13.9% in men 70-74).	1.9% (5050)	4.4% (72)	4.2% (268)	3.4% (3100)	Round 1: 3.4% Round 2: 0.8%	2.1% (803) (higher in men)
Time to follow up	Time from FOBT result to GP consultation:	Time from positive FOBT to colonoscopy: 2-6	Not Stated	Not Stated	Not Stated	Median time from positive FOBT to	82% had colonoscopy within 3

Country name	Australia [14, 43]	UK [40, 44, 47]	Italy - Valle d'Aosta [30]	Italy Florence [45]	France [25]	Spain [38]	Finland [24, 46]
	Mean 9 days Time from GP consultation to colonoscopy: Mean: 38.5 days Median: 30 days	weeks average in 2001 (longer for symptomatic patients) (NB invitations for screening had to be suspended in several areas because waiting times for colonoscopy were becoming >2-4 weeks average)				colonoscopy: Round 1: 41 days Round 2: 47 days	months of test, 91% within 4 months.
Attended colonoscopy after positive FOBT (% of those with positive FOBT)	1,265/2,317 (55%) ^{iv}	4,116/5,050 (81.5%)	67/72 (93.1%)	231/268 (86.2%)	2,724/3,100 (87.9%)	Round 1: 334 (89.8%) Round 2: 108 (87.8%)	723 (90.0%)
Completed colonoscopy	Whole colon visualised: Men: 97.3% Women: 94.2% Adequate colonoscopy (all polyps removed): Men: 86.9% Women: 88.8% ^v	89.9%	94%	Not Stated	50-69: 88.6% 70-74: 84.9%	92.3%	Not Stated

^{iv} Likely to be an underestimation due to data collection issues, however many of those with +ve FOBT did not attend their GPs, which was required for colonoscopy referral.

Country name	Australia [14, 43]	UK [40, 44, 47]	Italy - Valle d'Aosta [30]	Italy - Florence [45]	France [25]	Spain [38]	Finland [24, 46]
Colonoscopy complications	Not Stated	2 perforations (0.05%) 23 required admission for pain or bleeding	Not Stated	Not Stated	6 serious complications (0.2%) (2 perforations, 4 bleeding), 9 required admission for pain or minor bleeding	6/623 (1.0%) 1 perforation (0.2%)	Not Stated
Number of cancers detected (% of people participated in screening)	67 ^{vi} (0.26%)	552 (0.19%)	3 (0.2%)	33 (0.51%)	206 (0.23%)	Round 1: 23 (0.2%) Round 2: 13 (0.1%)	62 (0.16%)
Adenoma detection	176 high risk	1388 (0.5%)	27 (21 high risk)	75	958 (1.1%)	Round 1: 109 (0.9%) Round 2: 49 (0.3%) (high risk 79;42)	312 (0.8%)
PPV (denominator number of colonoscopies)	Cancer: 5.2% High risk adenoma: 13.9%	Cancer: 10.9%	Cancer: 4.5% High risk adenoma: 31.3%	Cancer: 14.3%	Cancer: 7.6% High risk adenoma: 23.6% Neoplasia (cancer and all adenomas): 42.7%	Cancer: 6.2% (Round 1) High risk adenoma: 22.5%	Cancer: 8.6% Adenoma: 43.2%

^v Actual numbers not given

^{vi} These are suspected rather than confirmed cancers because of data collection issues. At the time of the evaluation only 20 of these had been confirmed as carcinoma.

Country name	Australia [14, 43]	UK [40, 44, 47]	Italy - Valle d'Aosta [30]	Italy - Florence [45]	France [25]	Spain [38]	Finland [24, 46]
Stage of cancers	Not known at time evaluation report published	Dukes stage A: 48% ^{vii} B: 25% C: 26% D: 1%	Not stated	Astler and Coller A: 39.3% B1: 33.3% B2: 12.1%	TNM stage I: 47.6% II: 23.8% III: 20.5% IV: 8.1%	TNM stage I: 41.7% II: 19.4% III: 27.8% IV: 11.1%	Not stated
Surveillance colonoscopy recommended	Not Stated	Not Stated	Not Stated	Not Stated	Not Stated	Not Stated	Not Stated
Treated by endoscopic polypectomy only	Not Stated	16.7% of cancers	Not Stated	48.4% of cancers	38.8% of cancers	Not Stated	Not Stated
Costs/cost effectiveness (Note these are not directly comparable)	\$A 24,000 per life saved	2,650 pounds per QALY	Not Stated	Not Stated	Euro 13,466 (2006 Euros) per cancer detected	Not Stated	Not Stated
Conclusions reached	Proceed with national screening programme (decision made prior to evaluation of pilot)	Screening using FOBT is feasible in the UK. Proceed with national screening programme. Decision to restrict age range in England (not Scotland) to 60-69 for national	Extension to regionally based screening programme suggested Criteria: participation, organisational capacity	GP involvement in screening increases participation. Screening is feasible.	Population based screening is feasible in France. FOBTg is the only tool compatible with existing colonoscopy capacity. Criteria:	Screening is feasible in Catalonia.	Screening is feasible and implementation has been successful. Continue implementation of national screening programme. Criteria: participation

^{vii} Including polyp cancers

Country name	Australia [14, 43]	UK [40, 44, 47]	Italy - Valle d'Aosta [30]	Italy - Florence [45]	France [25]	Spain [38]	Finland [24, 46]
		programme because of colonoscopy capacity concerns.			cost participation diagnostic yield		and test performance.
National programme implemented?	yes	yes	Regional programme	Regional programme	planned	Regional programme	Continued roll-out

2.2.3 Ethnic inequalities in pilot and feasibility studies

The UK pilot team commissioned a separate evaluation of the pilot looking at the performance of the programme for different ethnic groups. Uptake by South-Asian groups was compared with uptake by non-Asian groups, and was found to be significantly lower even after adjusting for age, gender, date of invitation and deprivation. The Muslim community had the lowest uptake at 31.9%, compared to 63.7% for non-Asians. The difficulties of using the test were the most important factors influencing uptake. The rates of proceeding to colonoscopy after a positive FOBT were also lower amongst Asian communities (54.9% versus 74.4% for non-Asians) and the difference remained significant after adjustment for age, gender and deprivation. The large inequalities in uptake by ethnic group found in this evaluation were felt to be a considerable concern for the roll-out of a national programme, and strategies to address these inequalities were suggested. [48]

The Australian evaluation also considered differences by ethnicity. The overall participation was significantly lower for Aboriginal and Torres Strait Islander people (25.7%) than the general population (45.5%) after adjusting for age and sex. However there were some concerns about the accuracy of this estimate because of difficulties identifying the target (denominator) population. There were also very low numbers of Aboriginal and Torres Strait Islanders participating (62 in total), despite assessing participation by indigenous people being a “focus of the Pilot”, and it was not possible to analyse participation at later points in the pathway such as colonoscopy. Language and literacy issues were considered to be a major impediment to participation. Difficulties in making postal contact with Aboriginal and Torres Strait Islander were also a problem for delivering the invitation to screening.[14, 43]

The other feasibility studies examined reported differences in participation by age and gender only, with the exception of the Florence pilot, which also looked at differences by marital status, place of birth, and neighbourhood. [31] None of these studies reported differences by ethnicity and it not clear from the reports whether ethnic differences were examined.

2.2.4 Success criteria used for feasibility/pilot studies

The Ministry of Health is specifically interested in criteria used to judge the ‘success’ of feasibility or pilot studies conducted internationally.

We were unable to find any specific ‘success’ criteria for any of the pilot or feasibility studies that have been conducted. The UK had pre-stated ‘benchmarks’ and Australia had a number of objectives; these are discussed in sections 2.2.4.1 and 2.2.4.2 respectively.[14, 49] Most published reports of pilot/feasibility studies had a generic aim to determine the ‘feasibility of population screening’ with no specific details of how feasibility would be determined. These reports concluded with a subjective statement that screening was feasible and a discussion of issues that would need to be addressed prior to implementation of a full programme.[25, 30, 38, 46]

2.2.4.1 *United Kingdom*

The UK explicitly stated that the demonstration pilots would be assessed on key short term outcomes which would indicate “whether or not a full scale programme would be likely to reduce mortality at reasonable cost without undue effects”. [49] These “benchmarks” were described as “short term outcomes derived from the Nottingham and Funen trials which the pilot aims to emulate”.^{viii} [49] The expected benchmarks and actual outcomes are in Table 4. There was no statement about what would happen if these benchmarks were not achieved.

^{viii} See Hewitson et al 2006 for a summary of the design and outcomes of the Nottingham and Funen trials.

Table 4 Benchmarks of UK CRC screening pilots and results of the pilots.

Benchmark	Expected outcome (%) [49]	Achieved outcome in first round of pilot [40]
Compliance	60 (in first round)	56.8
Final positivity rate of FOB test	2 (in first round)	1.9%
Positive predictive value cancer*	10	10.2% England 11.8% Scotland*
Positive predictive value adenoma	40	46.9% England 47.3% Scotland [#]
Stage of cancer	50 at Dukes stage A	48% (Dukes A and polyp cancers)

[#] These are PPVs for neoplasia rather than PPVs of adenoma. * Includes polyp cancers

In addition the independent evaluation of the UK pilots was expected to provide information on the following:

- Economic evaluation
- Impact of screening on primary care
- Impact of screening on secondary care
- Screening compliance and reasons for non-compliance
- Physical and psychological morbidity created by screening.[49]

The results of all aspects of the evaluation are publically available. [40, 44, 48, 50]

2.2.4.2 Australia

The Australian CRC screening pilot evaluation, which was published after the pilots were largely concluded, stated it was designed to assess the “feasibility, acceptability and cost-effectiveness of bowel cancer screening, aiming to inform consideration of whether, and how, to introduce a national, organised population based bowel cancer screening program using faecal occult blood testing in Australia”. [14] A comprehensive monitoring and evaluation framework with ten objectives was set (see Box 3). To our knowledge there were no specific criteria set to judge whether these aims were met. A commitment to implementing a national programme was made prior to the publication of the final evaluation report (see Table 12).

Box 3 Evaluation objectives of Australian CRC screening pilot sites

- To pilot processes for providing screening information and support to the target population and service providers to facilitate informed participation in screening
- To compare costs and performance of at least two immunochemical FOBTs in detecting bowel cancers and significant adenomas in the Australian target population in order to determine which test(s) to use in a subsequent national program.
- To monitor the impact of bowel cancer screening on the primary health care sector (GP screening role; education and training; GP knowledge, attitudes and satisfaction with screening; GP financing; workforce issues) and the implications of this for a national programme.
- To monitor the impact of bowel cancer screening on tertiary services (specialist consultations, referral patterns, waiting times, costs, colonoscopy provision, workforce issues, satisfaction with screening service) and the implications of this for a national programme.
- To develop and trial the Pilot a national bowel cancer screening register within the Health Insurance Commission. Functions of the register will include invitation of the target population, register recall, reminder and clinical data functions, capacity for monitoring of screening clinical and cost indicators.
- To evaluate the acceptability of FOBT screening to a representative cross-section of the Australian target population, and equitable access within that sample.
- To evaluate screening knowledge, attitudes and satisfaction with service delivery amongst those invited to participate, especially factors associated with not participating.
- To agree minimal acceptable and achievable quality standards along the screening pathway and set up quality assurance systems for the Pilot which can be expanded into a national quality assurance system.
- To determine the costs of all services provided along the screening pathway in order to provide estimates of screening cost-effectiveness and funding required for a national programme.
- To compare the impact (and anticipated impact) of bowel cancer screening in the Australian health care environment with results achieved in international screening trials.[14]

Chapter 3 The role of a feasibility study in New Zealand

The National Health Committee screening criteria provide a way to identify conditions for which organised population based screening programmes may benefit the population.[13] However for condition that have a 'successful' assessment against the screening criteria, such as CRC, this represents only one phase in a process of successfully implementing population based screening. Next steps can include project planning, a 'test' round of screening in a community, and scaling up services to be able to deliver a national programme.

One of the recommendations of the CRCSAG was that a feasibility study would be an appropriate next step in order to clarify specific issues (see Appendix 6 of the CRCSAG report for details). [4] This section looks at what the key unanswered questions are in New Zealand, considers whether a feasibility study can answer these questions and, briefly, whether there are any other options available to obtain this information.

Chapter 3 Summary and Recommendations

- There are a number of issues relating to the feasibility of CRC screening in New Zealand that can only be addressed by carrying out a study of such screening in the New Zealand context. Key questions include:
 - What would the coverage and participation rates be in New Zealand?
 - What would the FOBT positivity rate be in New Zealand?
 - What would the impacts of screening be on primary, and secondary/tertiary services?
 - Would such a screening programme be cost-effective in New Zealand?
 - What would the impact of CRC screening be on inequalities in health in the New Zealand context?
- These questions could be addressed as part of a feasibility or pilot study, or a staged implementation process.
- A prevalence and incidence round of screening will provide essential information on

how to implement CRC screening in New Zealand, however whether it will answer the question of **should** there be CRC screening in New Zealand is less clear. Unlike a randomised controlled trial, a feasibility study does not result in a yes/no answer, but rather identifies issues which may need to be addressed prior to a national roll-out of a screening programme. This is reflected in the fact that every other country that has conducted a similar study has concluded that screening is feasible.

We recommend that:

- A prevalence and incidence round of CRC screening should be carried out in New Zealand within geographically defined populations to answer key questions relating to how to implement CRC screening in the New Zealand context.

3.1 Key issues to be resolved by a feasibility study

First a couple of definitions:

- Feasible means practicable, possible, easily or conveniently done. [51]
- A feasibility study is defined as “a preliminary study undertaken to determine and document a project's viability.”[52]

The CRCSAG specifically noted that a feasibility study should occur prior to the decision about a national screening programme. The group made a number of comments about what a feasibility study could achieve (see Box 4).

Box 4 CRCSAG statement on what a feasibility study would achieve in New Zealand

“A feasibility study of CRC screening using FOBTg or FOBTi should be considered. Such a study would inform a decision on whether the New Zealand health system could support a national CRC screening programme by determining:

- consumer participation and the preferred method of invitation/ follow-up for positive tests
- the acceptability of FOBTs in general, and specifically with regard to the preferred means of collecting samples and performing such tests
- test positivity of FOBTg

- which FOBT to use
- appropriate positivity rate if FOBTi is chosen
- the impact of screening on service providers
- whether routine care for symptomatic individuals is compromised by screening particularly in respect of colonoscopy
- how to monitor the quality of overall components of the CRC screening pathway
- economic efficiency.”[4]

In addition to these considerations, a feasibility study needs to be designed to provide information on likely impacts of CRC screening programme on inequalities in CRC in New Zealand.

A feasibility study would involve commitment of considerable time, money and other resources. Logically it would only be worth this commitment if it is able to provide information which is essential to inform a decision about implementing a screening programme, and which cannot be extrapolated from the experiences of other countries.

This information cannot be gleaned from experience in other jurisdictions for the following reasons:

- Review of feasibility studies shows a wide range of experience in terms of participation (from 17 - 70%) and FOBT positivity rate (from 1.9 - 9% for the prevalence round). These are essential determinants of the ability of a population screening programme to achieve the mortality benefit seen in RCTs.
- The impact of a screening programme on primary care, secondary care and on existing services for symptomatic individuals cannot be properly assessed without having some idea of **both** positivity rate and participation.
- The New Zealand health system is unique and so how it will respond to the increased demands of screening cannot be extrapolated from other countries.
- The translation of costs between health care systems is problematic due to different structures, costs and funding, and so economic evaluation needs to be undertaken in the New Zealand context.
- While inequalities in screening programmes are reported in a number of countries including New Zealand, [14, 48, 53] there are a number of special equity considerations for a CRC feasibility study in NZ. These include:

- The nature of the test requiring the handling and possibly storage of faeces
- This is the first screening programme to include men in New Zealand.
- CRC is of different importance as a cause of cancer related morbidity and mortality for different ethnic groups in New Zealand. [12, 54]
- Inequalities are not universal in current screening programmes in New Zealand (e.g. BreastScreen South has equal participation for women of all ethnic groups). This shows that system design is a vital factor in determining participation of target ethnic groups.

3.2 *Would a feasibility study answer these questions?*

The CRCSAG have recommended a feasibility study, which would involve a prevalence (first) round and then (at least) a partial incidence (second) round of screening in a community, [4] on the assumption that information obtained from this study could be extrapolated to the New Zealand population. This next section examines this assumption in more detail in order to clarify what a prevalence round of screening can and cannot deliver.

3.2.1 Consumer participation

While a feasibility study will give us a signal of participation levels in any future screening CRC programme, it is difficult to know how accurately participation levels in a pilot or feasibility study will predict participation in a national programme.

As noted previously, participation in recently conducted international pilot/feasibility studies varied from 17-70% in the prevalence round (see Table 2 3). For Catalonia (Spain) and England, who have reported on incidence screening rounds in their studies, participation increased (from 17.2 – 22.3%) and declined (from 58.5 – 51.9%) respectively. [38, 50] For Australia, France and the UK it is too early to determine how participation in feasibility studies relates to participation in national programmes.

In terms of New Zealand experience, the Otago/Southland breast screening pilot site had 75% participation between 1991 and 1996, and the Waikato site had 63%. [55, 56] Coverage, in the BSA programme, between 2004-2006, in the Otago/Southland region was 66.2% in 50-69 year olds and the Midland region (which includes the Waikato pilot site) was 58.7%. [10] However the pilot programmes had access to a population register based on the electoral roll, whereas BSA does not. Thus, in the absence of a population register, we can probably expect coverage in a feasibility study to be at the upper end of any eventual programme.

3.2.2 Test positivity

Assuming an appropriate sample size, and that the population that participates in a screening feasibility study is similar to the population that would participate in a full programme, test positivity rates should be an accurate representation of what would be seen in a full programme.

Interestingly the UK evaluation found that individuals and groups that did not participate in screening were likely to be at higher risk for CRC than those that did participate. [44] If the same occurred in New Zealand 'true' positivity rates in the entire population may be higher than observed.

3.2.3 Health service implications

Health service implications include those for:

- Laboratories
- Primary care and general practitioners
- Secondary/tertiary care (both diagnostic investigations and treatment). Both the direct effect of screening pathway activities and indirect effects on routine care need to be considered.

A feasibility study will produce good information on the direct effects of screening activities through various evaluation methods (e.g. surveys of practitioners). This

information will be essential in planning for a programme, for example informing workforce planning.

Assessing the effect on routine care, for example for individuals who are not eligible for population based screening because they already have symptoms suggestive of CRC, will be more challenging. Monitoring the effect of screening on routine care is vital as a screening programme must not simply shift existing colonoscopy resources from current requirements to the screening programme.

The authors are uncertain of the extent of routine monitoring of current colonoscopy services (numbers performed and waiting lists) by District Health Boards and the Ministry of Health. However the best publically available information is from an ad-hoc survey, funded by the NSU, conducted in 2005.^{ix} [57] In order to examine the effect of a screening programme on routine colonoscopies, systems would need to be developed and tested prior to the commencement of a feasibility study, so that baseline findings can be recorded before screening commences.

3.2.4 Equity

A feasibility study will give valuable information on equity which will be useful for planning for any future programme. This information includes:

- System factors, i.e. those factors related to the screening site that impact on differences in participation or waiting times between groups. It would also be important to evaluate factors that result in successful elimination of inequalities.
- A baseline indication of the extent of current differences between groups in acceptability and participation, and other factors such as colonoscopy rates, waiting times and other effectiveness and quality measures along the continuum of care.
- An indication on whether there are likely to be any rural/urban equity issues.^x

^{ix} The fact that this survey was conducted suggests that there may be limitations in the information available.

^x note that there are few in breast cancer which may be a consequence of screening (see Bennett et al, 2007)

It is, however, unlikely that a feasibility study would be able to detect differences between groups for 'rare' events such as cancer detection (see section 4.3).

3.2.5 Economics of screening

As identified in the CRCSAG report, a feasibility study will give information on some economic measures related to screening. [4] These include unit costs and total costs of services along the screening pathway, and can be reported as cost per eligible individual, cost per person invited, cost per person screened, and cost per cancer detected.

This information will allow calculation of cost effectiveness of screening and costs of funding of a national programme, possibly with more certainty than previous modelling work done in New Zealand. ^{xi}[58]

3.3 *Alternative options*

This section considers whether there are other possible mechanisms for gathering the information required to make decisions about the feasibility of CRC screening in the New Zealand context

3.3.1 A specific research project

Research projects could be undertaken, for example looking at the factors influencing uptake of an offer of screening or the positivity of a particular test. Such projects would also require mechanisms for those involved to go on to be offered the appropriate follow

^{xi} However it is possible that, once the screening pathway is finalised, many of these costs, and thus the cost effectiveness, would be able to be calculated from current information already available to the Ministry of Health.

up. As the systems for the entire screening pathway would need to be established for a research project looking at any aspect of the pathway, it makes sense to conduct a prevalence round of screening which allows information to be gathered about every step on the pathway. Moreover, specific research projects will not answer questions about the impact of a screening programme on the New Zealand health sector, or be as generalisable as an actual round of screening.

3.3.2 A pilot study

The CRCSAG specifically advised that a feasibility study rather than a pilot study be conducted, in order that it is explicit that a decision to proceed with a national programme had not been made. [4] However as can be seen from the review in Chapter 2, the terms pilot study and feasibility study are generally used synonymously in the literature. Most countries opt to conduct a pilot study to assess the feasibility of CRC screening in the local context. There are no differences in design of feasibility and pilot studies, and so the decision between the two will be based on other considerations such as Government commitment to screening and public perception of the implications of the two terms.

3.3.3 Staged implementation

In Finland a decision was taken to stage implementation. This was in order to monitor the effects of the roll out of screening as it was implemented, and to establish feasibility in a Finnish context before screening was rolled out on a large scale. As with pilot or feasibility studies, staged implementation involves conducting a prevalence round of screening on a subset of the eligible population, so that lessons can be learnt and applied in the wider implementation of screening. The advantage of this approach is that implementation is already underway, meaning that workforce expansion (e.g. training) can be commenced, there is a shorter time lag until screening is available to all those eligible and it provides more certainty to the sector. However it requires a decision to

proceed with population based CRC screening which has not yet been made in New Zealand.

3.4 Conclusion

The Ministry of Health has asked that we “recommend whether a study could be used to establish the feasibility of screening in the New Zealand setting”.

A well designed, adequately resourced, well run and evaluated study of a prevalence and incidence round of screening in a community setting,^{xii} with a clear set of goals and objectives, has the potential to provide rich information on many aspects of CRC screening in the NZ context. This information will include the key issues of participation, test positivity, equity implications, health service implications of screening and information on economics of screening. Inevitably, there will be some limitations to the information available and some questions will not be answered fully unless a programme is implemented.

This information will be vital to inform **how** a national CRC screening programme would be delivered in New Zealand and what would need to be done in order to ensure this is a successful programme. However whether this information will allow the Ministry and the Minister to decide whether New Zealand **should** proceed to a full screening programme is less clear. This is for a number of reasons:

- Results from a feasibility study of screening are not pass/fail. Minimum success criteria for a study would be difficult to set (see discussion in chapter 6) and areas of weakness are likely to respond to further work and/or resourcing.
- This report shows that no other country has determined that CRC screening is not feasible after a prevalence round of screening. This would make it difficult for New Zealand to argue that we have such a unique experience that we are unable to proceed with screening.

^{xii} At least one geographic community is required for a feasibility study to ensure that systems are fully saturated and tested by a round of screening, thus mimicking conditions of a national programme.

Ultimately whether to proceed with a screening programme is a decision for Government, which is able to consider competing health priorities. Information from a feasibility study will contribute to this decision but is unlikely to give a clear cut answer.

Prevalence and incidence rounds of screening, offered to a geographic subset of those eligible for screening, are a good next step to examine practicalities of CRC screening in the New Zealand context. The following sections outline the recommended design and key features of this study, which could equally be called a feasibility or a pilot study, or be part of a staged roll out. (For consistency it is referred to as a feasibility study in the next sections).

Chapter 4 Key parameters of a study

This section outlines key principles to guide next steps in CRC screening, identifies suggested aims and objectives for a study, and considers the population required for a study, study duration, criteria to select pilot sites and stopping rules.

Chapter 4 Summary and Recommendations

We recommend that:

- The study is set up with the goal of addressing the question:
 - Can CRC screening be introduced in New Zealand in a way that is effective, safe and acceptable for participants, equitable and economically efficient?
- Specific aims and objectives for the study should be agreed upon by the implementation group and members of the pilot sites.
- A feasibility study needs to detect a minimum of 40 cancers, which requires a minimum of 40,000 people be invited for screening. To ensure adequate explanatory power for participation and test positivity rates for Maori, at least 6000 Maori participants need to be invited. This requires an increase of the total study numbers to 60 000 invited to participate in screening.
- The calculations around numbers invited to participate in screening should be reviewed once the screening pathway is finalised, as in the absence of decisions around key parameters and questions of the study it is not entirely straight forward to calculate sample size.
- The study should include a full prevalence, and incidence round of screening, and therefore be a minimum of four years duration.
- A multicentre study should be carried out with a minimum of two sites meeting the following criteria:
 - Diverse demographic characteristics within the populations(s) with special emphasis on ethnic diversity
 - Urban and rural mix
 - Personnel with capacity and experience to deliver a screening programme
 - Service capacity and quality to manage the requirements of a screening

- programme
- Willingness of local DHB management, hospital clinicians, pathologists and primary care to participate in a screening feasibility study
 - Demonstrated experience in reducing or eliminating inequalities in services.
 - The feasibility study has a monitoring system that will allow detection of any issues or problems as they arise so they can be resolved speedily.

4.1 Key principles

Table 5 outlines key areas/principles for consideration in the planning, design, implementation and evaluation of future work around CRC screening. These principles are broadly the same as the dimensions of quality as outlined in the Improving Quality: A framework for screening programmes in New Zealand, and are similar to principles proposed for breast screening pilot evaluations. [59, 60] The answers to these questions will only be fully answered by implementing a national CRC screening programme, but information from a feasibility study will provide a preliminary information. The remaining sections of this report refer to these concepts frequently.

Table 5 Principles to guide planning, implementation and evaluation of CRC screening

Principle	Translating the principle
Effectiveness	Can NZ achieve the mortality reduction from CRC seen in RCTs for Maori and non-Maori in a national CRC screening programme?
Safety and acceptability	Will a CRC screening programme be safe and acceptable for participants?
Equity	Will a CRC screening programme be equitable for Maori and other population groups?
Economic efficiency	Will a CRC screening programme represent value for money for taxpayers?

4.2 Goals, aims and objectives of a feasibility study

The following section has suggestions for the proposed goals, aims and objectives for a feasibility study. However these need to be further discussed, amended and agreed by the group tasked with implementing this work and representatives of the pilot sites.

4.2.1 Goal

The overarching question that the feasibility study must answer is:

Can colorectal cancer screening be introduced in New Zealand in a way that is effective, safe and acceptable for participants, equitable and economically efficient?

The specific research questions have been grouped under the headings of effectiveness, safety and acceptability, equity and economic efficiency.

4.2.2 Aims and objectives

4.2.2.1 Effectiveness

Aim

To assess whether a national CRC screening programme in New Zealand is likely to achieve the mortality reduction from CRC for Maori and non-Maori seen in international randomised controlled trials.

Objectives

- To pilot the use of a population register (for example based on PHO enrolment data) to identify those eligible for screening.
- To pilot processes for invitation and provision of information to the target population.
- To measure coverage and participation rates in the eligible and invited populations including measuring Maori and non-Maori rates.
- To pilot the use of a screening database/register for CRC, and to assess its ability to facilitate the coordination of the screening process including sending invitations to screen, providing recall and reminder letters, managing clinical data, and providing information for monitoring and evaluation.
- To assess the performance of one or more FOBT in the New Zealand context including assessing (and comparing) cost of test/s, positivity rates overall, technical

repeat rates, positive predictive values for adenomas and CRC, and false positive rates, including comparing between Maori and non-Maori.

- To evaluate the impact of screening on primary care services, including time and resource implications of screening activities, knowledge, attitudes and acceptability of CRC screening to all primary care workers including general practitioners.
- To evaluate the direct and indirect impact of screening activities on secondary and tertiary services including colonoscopy referral rates, rates of specialist consultations, waiting times from referral to colonoscopy, waiting times from diagnosis to treatment, time taken to provide results of screening test, colonoscopy and pathology tests, and knowledge, attitudes and acceptability of CRC screening to specialists (including gastroenterology, surgical, pathology and radiology specialists) and other health professionals working in secondary/ tertiary services.
- To assess the early indicators of effectiveness of CRC screening including
 - Colonoscopy completion rate
 - Adenoma detection rate and size distribution of adenomas
 - CRC detection rate and stage distribution of cancers detected

4.2.2.2 Safety and acceptability

Aim

To assess whether a New Zealand CRC screening programme can be delivered in a manner that is safe and acceptable.

Objectives

- To pilot quality and monitoring standards for CRC screening, including the acceptability of the standards.
- To evaluate knowledge, attitudes and satisfaction of participants in the screening pathway and programme, and to identify factors associated with non-participation including non-uptake of colonoscopy after referral.
- To measure and report number and type of adverse events following colonoscopy.

- To measure and report safety and acceptability of CRC screening for Maori and non-Maori.

4.2.2.3 Equity

Aim

To assess whether a CRC screening programme can be delivered in a manner that eliminates (or does not increase) current inequalities between Maori and non-Maori.

Objectives

- To evaluate the process of adopting an eliminating inequalities focus in the leadership, decision making processes and implementation of the feasibility study.
- To evaluate the services of different pilot sites to identify the factors that act to eliminate or reduce inequalities, as well as any factors that exacerbate or maintain current inequalities.
- To evaluate how participation rates vary by sex, ethnicity, socioeconomic status and rurality.
- To evaluate knowledge, attitudes and satisfaction of groups of participants (defined by sex, ethnicity, socioeconomic status and rurality) in the screening programme, and to identify factors associated with non-participation, particularly among groups the screening programme does not serve well.

4.2.2.4 Economic efficiency

Aim

To assess whether a CRC screening programme can be delivered in an economically efficient manner.

Objectives

- To determine the costs of tests and screening-related services.
- To provide more detailed local information in order to estimate the cost-effectiveness of screening, for example, in terms of cost per cancer detected, and cost per life year saved.
- To compare the cost-effectiveness of CRC screening in New Zealand with other preventive programmes, including screening, in New Zealand.

4.3 Study population

Internationally feasibility/ pilot studies have varied enormously in terms of size of the population invited to participate; ranging from 3,000 (Italy – Valle d’Aosta) to nearly 480,000 (UK) (see Table 3). None of the studies we reviewed provided a clear rationale for the population size chosen. The breast cancer screening pilots carried out in Otago/Southland, and Waikato faced many of the same issues as the CRC screening feasibility study. In the breast screening pilots approximately 20,000 women were invited for screening at each site. [55, 61]

In this section we provide a number of sample size calculations to provide background information to inform any decision on optimal size of study population. The final decision is likely to be based on a combination of scientific and practical considerations. Ideally, though, the number of people participating in the trial would be sufficiently large to provide adequate statistical power to answer the key questions identified above. The following provides some of the important considerations in deciding on a sample size.

4.3.1.1 Numbers of cancers detected

It would be essential to identify enough cancers to calculate key measures such as the positive predictive value of tests. We would expect approximately 40 cancers to be identified in an eligible population of 40,000, assuming 50% participation rate, and a 0.2% cancer detection rate (see Table 3). Assuming an underlying PPV of 10% (UK

study was 10.9% for cancer), this number of cancers would give an estimated PPV of approximately 10%, with a 95% confidence interval of 7% to 13%.

4.3.1.2 Estimating point estimates for population groups

One of the aims of the study is to calculate point estimates for a range of parameters such as participation and positivity rates.

- For participation rates, to estimate participation of 50% with confidence intervals of 45%-55%, we would require just over 380 participants. For increased precision to 48-52%, the sample size would need to be between 2300 and 2400. These numbers would be similar for any sub-population we would be likely to want to measure with this level of precision e.g. ethnic group, sex, age group, deprivation group.
- Positivity rates will vary depending on the test chosen. Assuming a positivity rate of 2-3%, and 95% confidence intervals of +/- 0.5%, the sample size needed would be approximately 3000 screened (around 6000 invited) for any major population group for which this level of precision was required. With an immunochemical test, the positivity rate will be higher, perhaps 8-9%. With 95% confidence intervals of +/- 1.0%, this would require a sample size in the range of 2700-3200 screened per population group studied.
- To estimate a cancer detection rate of 0.2%, with 95% confidence intervals of 0.15%-0.25%, we would need an overall sample size of 28,000-30,000 people undergoing screening, which is likely to equate to around 60,000 people invited to screen. For an estimate of 0.2% with the wider confidence intervals of 0.1-0.3, the number invited would have to be around 15,000.
- Note the above calculations provide estimates only. They assume that the populations invited to attend in the study are a randomly selected group from the New Zealand population. This is clearly not the case, although the sites selected will hopefully be representative of the whole population.

4.3.1.3 *Estimating differences between population groups*

- It will be important to accurately estimate participation rates between population groups. Assuming 10% of the population in the age group invited for screening is Maori, a sample size of just over 8000 non-Maori and 900 Maori will give 80% power (alpha 5%) to detect a 5% difference in participation rates between Maori and non-Maori.
- Assuming approximately 5% of the invited population is Pacific, the respective numbers would be approximately 16,000 non-Pacific, and 845 Pacific people, to detect a 5% difference in participation rates. This sample size will be adequately powered to detect differences for any characteristic that is more evenly spread in the population (e.g. sex).
- To detect differences in cancer detection rates between ethnic groups, a much larger sample would be required. For example, if we assume that the non-Maori cancer detection rate is 0.2%, and that for Maori it is only 0.1% we would need 140,000 non-Maori and 15,000 Maori screened to have 80% power to detect this difference.

4.3.1.4 *Conclusion*

The decision on the size of a study population in this context is largely a pragmatic one. Clearly there is a balance between obtaining sufficiently rich and powerful data to fully answer all the research questions, and the resources required to run such a study. If it is decided that additional aspects are to be examined in a feasibility study (e.g. more than one type of screening test –see section 5.4.4.1) this may impact on numbers required for a study.

We have estimated that a sample of 40,000 invited to participate in screening will result in approximately 40 cancers being detected. This number of cancers seems a reasonable minimum to ensure adequate precision around the calculation of the positive predictive value of the screening test, as well as giving a good estimate of the cancer detection rate in the study.

In order to ensure precise estimation of participation rates and test positivity rates for Maori as well as comparisons between Maori and non-Maori, at least 6000 Maori need to be invited to participate in screening. Assuming that Maori comprise about 10% of the population in this age range then this increases the total study size to 60 000. Should the Ministry of Health want to look at other population groups such as Pacific and Asian a similar number of these groups would need to be invited to participate in screening. This may require further increases in the study size.

A New Zealand feasibility study will not be able to provide detailed data on some issues. For example, colonoscopy complication rates have been found to be very low in other pilot/ feasibility studies. In the UK pilot study (with 478 250 people invited to participate in screening) there were 2 perforations at colonoscopy among more than 3600 individuals who underwent colonoscopy (see Table 3). A NZ study of 40 000 people would result in between 380 and 1800 colonoscopies being required depending on the type of FOBT selected. Assuming UK rates of complications we might reasonably expect 0-2 perforations. (We have been unable to find published New Zealand complication rates for colonoscopy). Additionally it is unlikely that we would be able to compare rare events between population groups, such as cancer detection rates.

Finally we recommend that these calculations are reviewed once a final screening pathway is agreed on. If a feasibility study were to include more than one type of FOBT or other methods of diagnosis, [62] the implications of these decisions on the numbers invited to participate in screening would need to be reviewed.

4.4 Duration of study

The CRC Screening Advisory Group recommended that the feasibility study would be a minimum of three years, involving one complete (prevalence) round (two years) and one partial incidence round (one year). A complete incidence round would provide richer data in terms of changes in participation and test positivity, which will be important in the planning for a national programme (test positivity will decrease after the prevalence round). A full incidence round may also be easier to communicate to participants.

4.5 Criteria for consideration in selection of study sites

There are a number of factors which would have to be considered in the selection of screening sites. The study would need to be multicentre, with a minimum of two centres in order to reduce the possibility that findings are not largely driven by specific local factors. Sites selected to carry out the feasibility studies would meet the following criteria:

- A diverse ethnic population
- Urban and rural mix.
- Personnel with capacity and experience to initiate a screening programme including individuals with experience in screening, relevant clinical and laboratory expertise, and project management.
- Service capacity and quality, particularly in regards to colonoscopy services, to manage the requirements of the screening programme.
- Willingness of local DHB management, hospital clinicians, pathologists and primary care to participate in a screening feasibility study
- At least one site must have demonstrated experience in reducing or eliminating inequalities between Maori and non-Maori in services.

While it is important to select sites that are capable of and keen to undertake the a feasibility study, due to having these specific requirements it is likely that the sites selected will be atypical from other sites in New Zealand and thus may present the best picture of CRC screening.

4.6 Stopping rules

The CRCSAG stated that criteria for termination of the feasibility study would need to be determined in advance. [4] We were not able to identify any pilot or feasibility study that clearly articulated rules for terminating the study under specified circumstances. Predetermined rules relating to lack of efficacy or an unacceptable level of harm would be in place for randomised controlled trial which is testing a hypothesis. However a feasibility study is an investigation of the processes and outcomes of screening within

communities in New Zealand. It is possible the feasibility study will identify unacceptable impacts on services, or major quality/ safety concerns, although as discussed in section 4.3 the study is unlikely to detect a large number of adverse events. In most instances, where such issues were identified, the appropriate response would be to alter the screening process, or to actively address the issue that had arisen before continuing with the screening programme. For example:

- A study of cervical screening in Otago during the late 1980's was stopped after three years because of low participation in voluntary registration for the programme. [63] Since then, procedures have changed considerably allowing the functioning of a successful national cervical screening programme.
- In the United Kingdom, colonoscopy waiting times for symptomatic patients were noted to increase in most centres after the commencement of the pilot study, and in all but one site invitations for screening were suspended for periods during the pilot to ease the burden on diagnostic services.[47]

Hence instead of a priori 'stopping rules' we suggest that the feasibility study is accompanied by a monitoring system that will allow detection and notification of issues to facilitate investigation and rectification as necessary.

Chapter 5 Key tasks required to implement a study

This section looks at key practical issues around delivery of a feasibility study. Firstly leadership and process, then key screening policy parameters, information system requirements and, lastly, finalising the screening pathway.

Chapter 5 Summary and Recommendations

- Implementing a feasibility study for colorectal cancer screening is a large and complex task requiring substantial staff and resources.

We recommend:

- The work is managed by the National Screening Unit due to their considerable experience in, and understanding of, screening and cancer screening programmes.
- Eliminating inequalities is a main focus for, and of, leadership, process and planning of this feasibility study.
- A leadership structure and decision making and stakeholder engagement processes are agreed to early in the process.
- The pilot sites are selected early in the process so they can contribute to decisions.
- Screening policy parameters, such as age range, are reviewed for their implications on inequalities before being confirmed.
- Information systems are developed that incorporate functions that span the screening pathway as detailed in section 5.3.
- The feasibility study pilots the use of a population register to identify and invite eligible participants. This register could be based on Primary Health Organisation enrolment or National Health Index databases.
- Decisions about how people are invited are based on evidence, and on the approaches that are most effective for groups that screening programmes do not usually serve well.
- The decision about the type of test FOBT is considered against the following parameters: evidence of mortality benefit, acceptability and participation, cost, inequalities, resource implications, sensitivity and specificity, quality control,

acceptability to service providers.

- The role of primary care and GPs in the screening pathway needs to be elucidated. These groups need to be involved in developing the screening pathway and planning the feasibility study.
- High risk people identified through the feasibility study have their ongoing surveillance needs co-ordinated through the screening programme.
- The approach to individuals who are at high risk of CRC and thus not eligible for FOBT screening needs to be considered at the outset of the screening pathway design and feasibility study design.

5.1 Leadership and process

A critical first step, along with securing funding, is to determine appropriate leadership, agree on the process to make necessary decisions and engage relevant stakeholders.^{xiii} The Ministry of Health has considerable experience in successfully delivering large and controversial public health projects (such as the meningococcal vaccine project), however we would like to make four points specific to CRC screening:

- Firstly this is a unique opportunity to make eliminating inequalities the focus of screening programme planning, design and implementation. This needs to be done at the outset. A number of ideas about how this could be done have been detailed in previous discussions of these issues. [4, 54] In order to truly focus on eliminating inequalities it is essential to have leadership that are skilled and knowledgeable in Maori health, Maori development and screening. An implementation group that has strong representation, including technical experts, from Maori would be a good starting point.
- Secondly it may be useful to be aware of the leadership structures and processes put in place to implement pilot studies in Australia and the UK, which look to be

^{xiii} Stakeholders in this area include Consumers, Maori, Pacific people, Surgeons, Gastroenterologists, Pathologists, Laboratories, Academics, radiation specialists, oncologists, Potential providers of any services such as laboratories, private specialists, FOBT manufacturers General practitioners, National Screening Unit Cancer NGOs, DHBs, Ministry of Health, Treasury, Minister of Health

easily applicable to New Zealand, although would need to be adapted slightly to ensure a focus on eliminating inequalities. [14, 49]

- Thirdly the screening expertise and experience in the Ministry of Health resides in the National Screening Unit, which currently manages the two national cancer screening programmes. Given New Zealand's experience (mistakes) in the initiation and delivery of cancer screening programmes, [64-66] and that the benefits and harms of CRC screening are even more finely balanced than other cancer screening programmes any CRC screening work should be managed by the National Screening Unit, with close links to other relevant parts of the Ministry of Health.
- Finally selection of the feasibility study sites needs to occur early in the process so they can input into the decision making and planning of the study. The pilot sites' input will be essential in determining the aims and objectives, approaches to eliminating inequalities, targets, screening pathway details and evaluation criteria of the screening activities they will deliver.

5.2 Key screening policy parameters

The basic parameters of the population to be invited to participate in a feasibility study need to be finalised. Table 6 details the parameters, the CRCSAG recommendations and any additional comments.

These decisions will have impacts on equity that need to be considered. For example Maori have a younger age structure; hence proportionately more CRC is in ages that would not be eligible to be screened.[67] This is also likely to apply to Pacific people. The impact of the different age structures on expected changes in CRC mortality in ethnic groups due to screening needs to be considered further. As the RCTs covered a wide age range from 45-80, [2] it would be useful to model potential mortality effects/benefits of a range screening age parameters for each of the population groups. It is possible that screening age ranges could be slightly different for different groups. There is a precedent for this approach, with Maori having cardio-vascular risk assessment ten years earlier than non-Maori. [68]

Table 6 Basic policy parameters of screening

Parameter	CRCSAG Recommendation	Comment
Sex	Men and women	Based on RCT evidence.
Age range	55-74	RCTs covered a range of ages from 45-80 [2] Feasibility studies' age ranges vary considerably (see Table 2) and actual implementation age ranges are different again (see Table 3)
Exclusion criteria	Previously diagnosed CRC Already in a colonoscopy surveillance programme Undergoing treatment for CRC	Those at high risk of CRC should be managed as set out in the guidelines for Surveillance and Management of Groups at Increased Risk of Colorectal Cancer [69] Those with symptoms of CRC require diagnostic services and so should not be offered screening. Some feasibility studies also excluded those who had recently been screened for CRC by FOBT or colonoscopy [14, 25, 45]
Screening interval	Biennial	Based on RCT evidence.

5.3 Information systems

Good information systems are crucial the success of population-based screening programmes. In New Zealand and internationally, many of the problems identified in screening programme pilots and implementation have been related to inadequate information systems. For example:

- The Gisborne inquiry highlighted problems with correlation of histology and cytology information and the lack of centralised information in the New Zealand cervical cancer screening programme.[65]
- Breast cancer screening pilots in New Zealand ran into problems because of changing data systems and the lack of centralised access to data.[61, 70]
- In the Australian colorectal cancer screening pilot the resources required to set up a central screening register were significantly underestimated, and there were significant problems with capturing colonoscopy and diagnosis data making evaluation of the pilot difficult. [43]

Setting up good information systems for the feasibility study will allow useful evaluation and will provide a foundation for a functional screening programme in the future.

Key features of information systems for screening:

- A centralised database, with all those invited for testing identified, and all test results and follow up diagnostic and treatment information (all information required for clinical management and for evaluation included).
- Links with other databases, including the information source used to identify the eligible population (for example PHO enrolment data), and those holding diagnosis and treatment information (NMDS, NZCR)
- Efficient and timely provision of information to those being screened and health care providers
- Confidentiality and privacy
- Quality assurance and improvement systems

It is recommended that a central database or register is established to manage the information needs of the screening programme. Functions of a screening register include:

- Invitation
- Notification of results, plus or minus coordination of referral for diagnostic investigations
- Holding data on those participating in screening, including test results and subsequent diagnosis and treatment information
- Monitoring how closely the screening pathway is being followed, including waiting times
- Safety-net alerts when the screening pathway is not being followed^{xiv}
- Coordination of information
- Recall for repeat tests
- Providing information on those not attending following invitation (assuming a population-based invitation system) to enable targeted health promotion interventions

A screening database would not necessarily perform all these functions, although there are good reasons why these functions would be desirable. Functions should also be built

^{xiv} This could include alerts for total population data as well as when there are inequalities between groups occurring in the screening pathway, to allow further investigation and correction and provide information on those not attending following invitation (assuming a population-based invitation system) to enable targeted health promotion interventions.

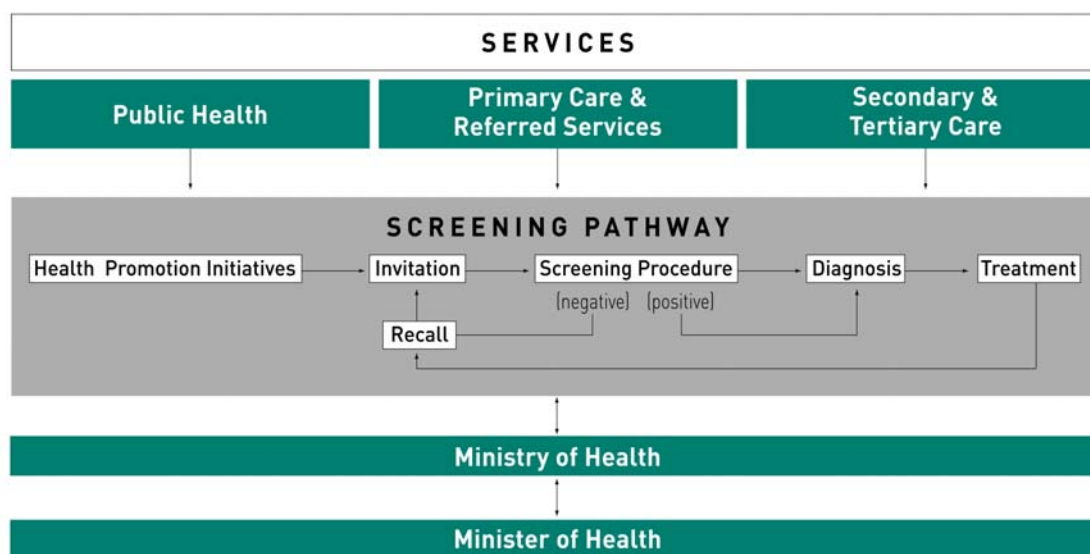
into the register to provide alerts when there are inequalities between different groups occurring in the screening pathway, to allow further investigation and correction.

5.4 *Screening pathway finalisation*

The details of the screening pathway (see Figure 1) need to be finalised. The pathway needs to mimic a programme as much as possible, in order to provide an accurate 'dress rehearsal' of a screening programme. Hence this section highlights some quite fine detail. For some of the aspects of the screening pathway the decision will be clear, others are more complex, and there is inevitably a certain amount of interdependency. Decisions around the final shape of the screening pathway need to be part of the responsibility of the group formed to implement a feasibility study. However as a feasibility study is a 'dress rehearsal' stakeholders need to be engaged in decision making as decisions made about the feasibility study will shape any national programme.

The remainder of this section details aspects of the screening pathway, highlighting specific issues that need to be clarified. This should be thought of as an introduction only as inevitably other issues will arise. The NHS bowel cancer screening programme website contains a wealth of information about the UK screening pathway and programme and should be consulted.

Figure 1 Screening pathway in New Zealand



Source: National Screening Unit

5.4.1 Identifying eligible participants

Identifying individuals who would benefit from screening and being able to invite them to participate is absolutely key to programme success. New Zealand does not currently have a population register used to invite eligible people to participate in screening, although it has been recommended on a number of occasions. [53, 64-66] There are a number of ways that are currently or have previously been used to identify persons eligible for screening in the New Zealand context (see Table 7).

Table 7 Methods used to identify eligible participants in screening pilots or programmes in New Zealand

Screening activity	Method of invitation	of	Comment
Breast screening pilots	Predominately the electoral roll [70]		An amendment to the Electoral Act 1988 was required to allow this. The amendment allows the electoral roll to be used for health research purposes, hence while it could be used for a CRC screening feasibility study it cannot then be used a basis to identify eligible participants for a national programme, unless there is a change to legislation. Coverage not 100% of the population and accuracy probably varies according to the electoral

		cycle. No recording of ethnicity or sex on the electoral roll.
BSA programme	Social marketing GP referral	Social marketing might be difficult in a feasibility study setting as it would need to be confined to a specific area. Unclear if social marketing would be successful in the setting of a feasibility/pilot study (no NZ pilots have used it and all international CRC pilot studies used population registers) GP referral for screening might be possible but would impose a significant burden on GPs and their practices.
NCSP (note there was no formal pilot programme of cervical screening undertaken in New Zealand)	Opportunistic via GP	Unlikely that this would be successful in a feasibility study setting as participation would be dependent on GP attendance or GPs going through their records to identify people, which again would pose a significant burden on GPs and their practices
Antenatal HIV screening pilot	Attached to an existing programme of antenatal blood testing	Not relevant to CRC screening
Newborn metabolic screening	Initiated after birth.	
Newborn hearing screening programme	Initiated while in hospital after birth.	

None of the methods identified in Table 7 is ideal for a CRC feasibility study and then as a basis for subsequent programme implementation. Of concern is that all the pilot studies reviewed used a population register to directly invite people to participate (see Table 2), and participation was, despite this, not as good as hoped.

5.4.1.1 A population register

A population register is a database holding selected information about each member of the resident population in a defined geographical area. In order to be used to identify and invite people for screening, the register needs to include unique identifiers, demographic information, and up to date contact details.

There are inequalities in participation in the screening programmes currently operating in New Zealand, with Maori and Pacific women being less likely to participate in breast and

cervical screening programmes, although this varies by region. Differences in participation may be related to lower invitation rates in these groups. The use of a population register has been identified by the National Health Committee as a specific mechanism to ensure equity of access by providing a fair opportunity to participate to all. [13] A population register has also been recommended by the NSU Maori Advisory Group as a way to improve Maori women's coverage. (personal communication Dr N Scott)

There are two health databases in New Zealand that could be considered as potentially forming the basis of a population register. They are the National Health Index (NHI) and Primary Health Organisation (PHO) enrolment databases.

A register based on the NHI has been proposed for use by the breast screening and cervical screening programmes. [64, 65] However there are a number of issues with the NHI database including a large number of duplicate entries, non-entry on the database, inaccurate ethnicity data, people are not removed when they leave New Zealand and address information is problematic, as the NHI is only updated on contact with secondary and tertiary health services.

The better source of population data would most likely be the Primary Health Organisation enrolment data, which currently covers approximately 94% of the population (although there are likely to be differences by ethnicity in the level of enrolment). [71] General practice enrolment data has been used in the United Kingdom and Australia to identify those eligible for colorectal cancer screening.

There would be many issues to be worked through before PHO enrolment data (or NHI if that was ultimately thought to be more suitable) could be used for screening invitations. This includes practicalities as well as issues such as privacy concerns. However a colorectal cancer screening feasibility study would provide a good opportunity to explore this approach. If such a register were in place for colorectal cancer screening it could also be utilised by other national screening programmes. The use of a population register is essential for ensuring that all those eligible for screening have the opportunity to participate, and should be explored in the proposed feasibility study.

5.4.2 Inviting people to participate

Ascertaining optimal methods of inviting people to screen is critical for maintaining high participation rates. Even if it is assumed that written invitations will be sent to named individuals through the postal system, a number of issues need to be considered including:

- Who should a letter of invitation come from?
 - Screening programme?
 - Individuals' general practitioner? (there is evidence that letters from individuals' primary care practitioners improve participation [72])
 - Other?
- How will the invitation be framed?
- How will information on benefits and harms of screening be presented?
- How much detail will be provided on colorectal cancer, the screening process etc?
- How will those who are not eligible for population-based FOBT screening be identified, and directed into appropriate pathways?
- Will the test be delivered with the letter of invitation?
- Who will people contact if they require more information?
- How will people with language or reading difficulties be identified?
- Will different methods of invitation be required for different groups within the population?
- What are the follow-up protocols, for non-response, wrong addresses and inadequate tests?

There is evidence from other NZ screening programmes and from CRC feasibility studies of effective approaches for some of these considerations. This evidence needs to be gathered and reviewed. Decisions on these aspects of the invitation process need to be based on best practice, as well as practicalities. Importantly these decisions need to reflect what is most effective for groups that screening programmes do not usually serve well.

5.4.3 Role of primary care and GPs

The New Zealand primary care system has a number of players including Primary Health Organisations, general practices, and Maori and Pacific health providers. All providers need to be meaningfully engaged in decisions around CRC screening.

The CRCSAG discussed the roles of primary care and GPs in the Australian and UK pilot studies in their report. [4] In a sense the roles were almost polar opposites, with little involvement of GPs in the UK pilot and a much bigger role in Australia, with GPs being responsible for managing all steps after a positive FOBTi test result. The UK pilots deliberately aimed to minimise primary care workload while the Australian pilot notes that the programme will have better buy in from primary care if GPs are involved. [14, 44] These roles have continued in the newly established national programmes. If the Australian approach was used in NZ there would need to be significant change to address the high proportion of people (37.9%) who appear not to have visited their GP after a positive test.[43]

Primary care involvement in current NZ screening programmes spans both ends of the spectrum already, with extensive involvement in the NCSP, and more minimal involvement in the BSA programme. The issue of GP's not being supportive of CRC screening in New Zealand because of screening test sensitivity has also been flagged.[4]

Consultation with stakeholders needs to be undertaken to gain support for the study and to decide what the best role for primary care and GPs in the screening pathway and in a feasibility study of CRC screening in NZ would be. The role of primary care that is most likely to eliminate inequalities needs to be determined. The role that is eventually selected will need to be reviewed as part of an evaluation.

5.4.4 Screening test

There are two types of faecal occult blood tests; guaiac and immunochemical. They use different methods to detect blood in faeces and thus have different implications in terms

of screening test features such as sensitivity and specificity, as well as other issues such as cost and quality issues.

5.4.4.1 Type of test

Neither FOBT screening test is ideal, both have advantages and disadvantages. Of the feasibility studies reviewed only two countries (Italy and Australia) used FOBTi, while the UK, France, Spain and Finland used FOBTg (see Table 2 and Table 3). In terms of population-based CRC screening programmes; Finland, England, and France are using guaiac tests, Scotland is using FOBTg followed by FOBTi in the case of ‘weak positive’ results, and Australia and Italy are using FOBTi. [15, 25, 45, 46, 73, 74] At least some of the Canadian states implementing CRC screening programmes appear to be using guaiac tests as well, although details are sparse. [18, 75]

In the NZ context the choice is between FOBTg, FOBTi or a combination (two step process involving guaiac and then immunochemical). The advantages and disadvantages of the options have been canvassed thoroughly in many forums including the CRCSAG report and the NZHTA review. [4, 76] Some of the issues to consider when choosing which screening test to opt for are summarised in Table 8.

Table 8 Considerations when deciding between types of FOBT

Parameter	Considerations
Evidence of mortality benefit	Is there evidence that application of the screening test will reduce CRC mortality?
Acceptability and participation	How easy is the test to perform? Will people feel comfortable with the test? Is dietary restriction required?
Inequalities	Is there evidence of different uptake of the test by different population groups?
Costs	What are the direct costs of the test (per unit)?
Resource implications	What are implications of test chosen on diagnostic services? How many colonoscopies are likely to be required (this will vary with the test positivity rate)?
Sensitivity and specificity	How sensitive is the test (what is the rate of false negatives likely to be)? How specific is the test (what is the rate of false positives likely to be)?
Quality control mechanisms	Can adequate quality control systems be instituted to ensure that the test is being

	reported appropriately?
Acceptability to service providers	Is the test acceptable to service providers, including those who will be recommending testing in primary and secondary services and those who will be analysing samples?

The CRCAG recommended that FOBTi be trialled in a feasibility study in New Zealand. This recommendation is based on the higher sensitivity of FOBTi, some evidence of the greater acceptability of FOBTi to the public, and of the greater acceptability of FOBTi to general practitioners and pathologists because of sensitivity and quality control concerns.[4]

The most profound impact of choosing FOBTi is the higher positivity rate and hence the higher colonoscopy requirement. The implications of this choice on the screening programme are far reaching: if 100 000 people aged 50-70^{xv} were invited for screening, and 60% participated, the potential number of colonoscopies required over a two year period could vary from 1140 (1.9% positivity –UK guaiac test) to 5400 (9% positivity-Australia immunochemical tests). This would likely decline after the prevalence round when positivity would decrease, but there would also be a concomitant increase in people requiring surveillance colonoscopies. France made the decision to use guaiac tests partly because it will have less impact on colonoscopy services. [25] The UK, with the lowest test positivity rate, had to cease inviting individuals for periods during their pilot because colonoscopy services were unable to cope.[47]

A NZ feasibility study could be an opportunity to test different approaches of FOBT (see Table 9).

Table 9 Options for FOBT in a feasibility study

Options	Advantages	Disadvantages
Guaiac alone	Consistent with RCT based evidence Would allow comparison with international positivity rates Known to have lower positivity rates than immunochemical tests so health service more	Sensitivity of the test problematic. Dietary restrictions need to be clarified (note inconsistent approach to this in different pilot studies) Need more samples than

^{xv} As a reference point there were approximately 70 000 men and women aged 50-70 in Waikato DHB in the 2006 census.

	likely to have capacity Cost less than immunochemical	immunochemical Quality assurance concerns (although presumably countries with guaiac as a screening test must have quality procedures)
Immunochemical alone-either one brand or more than one brand	Some research evidence of increase in participation with immunochemical tests, although this is not reflected in pilot study results. Higher sensitivity than guaiac	Would probably be a advantageous to test more than one type of FOBTi, and this may increase the numbers required in the study.(although this would need to be calculated) No RCT evidence related to FOBTi and CRC screening. Lower specificity than FOBTg
Two step- guaiac followed by immunochemical if 'weak positive' result	Less health service implications for pilot sites as decreases the number of false positives.[77] Cost less than immunochemical alone as only some people will have FOBTi tests.	No RCT evidence Would require infrastructure to support both types of tests
Both immunochemical and guaiac- randomise study population to receive either FOBTi or FOBTg	Could determine if there were participation differences in different types of test in NZ population Would have NZ specific information on positivity for both types of tests Would provide NZ relevant information on any differences in participation related to the test type by different population groups. This approach would allow an evidence based decision about which FOBT to select for a national programme	Would increase complexity of study May require larger numbers (although this would need to be calculated) Would require infrastructure to support both types of tests

Note: other combinations are possible e.g. testing guaiac alone vs. a two-tier approach

This choice of screening test(s) for the feasibility study needs to be confirmed and then a tender process undertaken.

5.4.4.2 Mechanics of the test

If FOBTi is chosen there would need to be technical work to determine the actual positivity rate of the FOBTi. The positivity threshold may alter during the feasibility study,

as it did in Australia.^{xvi}[77-79] If FOBTg is used a positivity definition needs to be clarified as different definitions have been used in the pilots (see Table 3), with some countries using a weakly positive category. [38, 44] Dietary restriction is also an option for FOBTg, although not universally used (see Table 2).

Other issues that would need to be considered include the storage and handling of faecal specimens and the ability to send completed samples in the post. NZ Post currently decrees that:

“Perishable biological specimens and substances must only be sent if they are packaged correctly and sent by signature required courier”. [80]

5.4.5 Results delivery

Protocols around delivery of results need to be determined; Table 2 details the approaches other countries used. New Zealand experience from BSA and NCSP may also be relevant. Protocols around how follow-up is arranged at this point also need to be determined; this will depend on decisions made about how the screening programme is set up (e.g. programme hubs, role of primary care). Protocols that are equally effective for Maori and non-Maori need to be determined.

5.4.6 Diagnostic test

Colonoscopy is the first line investigation for positive screening tests. Protocol around how to access the test, acceptable waiting times, what constitutes a complete test and second line investigations (e.g. DCBE) need to be finalised.

^{xvi} The Inform test initially had a 12.6% positivity rate, this declined to 6% and then increased to 8% by the end of the pilot. Bayer Detect had a more stable positivity rate averaging 8.2%.

5.4.7 Recalling for ongoing screening

Assuming a population register is utilised, direct invitation for repeat screens will be issued from the programme. Decisions outlined in section 5.4.2 will be relevant to recall.

5.4.8 Safety net features

Consideration needs to be given to safety net protocols relating to the screening pathway. These protocols aim to ensure that back-up mechanisms are in place to identify and follow-up individual participants and groups of participants whose progress through the screening pathway falls significantly outside the expected norms. This will relate closely with the process of developing quality and monitoring standards for the screening pathway (section 5.4.11).

Consideration will need to be given to safety net features that identify when inequalities are occurring between different population groups, to allow rapid investigation and amelioration.

5.4.9 Treatment

The provision of high quality, timely and appropriate treatment to those who have cancers detected via the screening programme is an important part of the screening pathway.[64] The inclusion of treatment data on the screening register allows evaluation of the entire screening pathway, and a more complete understanding of the outcomes achieved from the screening programme. Moreover, the standardised methods of collecting diagnosis and treatment data which are required, such as synoptic pathology reports and pro-forma treatment records, provide better quality information for other users, such as the NZCR. [81]

A CRC screening programme would potentially provide an opportunity to improve quality of care for all patients with CRC in New Zealand, by encouraging best practice treatment. Recent audits suggest that New Zealand is not currently meeting international

best practice for CRC in terms of waiting times, investigations, or provision of adjuvant chemotherapy, [57, 82] There are currently no New Zealand guidelines for colorectal cancer management. The development of a local best practice guideline or the adoption of the recent guidelines produced in Australia or the United Kingdom, [83, 84] would be important for establishing standards for monitoring the pathway of care provided to patients with screen-detected CRC and important in being able to monitor equity of treatment between population groups.

5.4.10 High risk people identified through screening

A certain number of individuals who participate in screening will be determined after this event to be at “high risk” of CRC, due to an adenoma or polyp cancer being detected through screening. For these individuals best practice guidelines outline how they should be monitored on an ongoing basis, mostly with surveillance colonoscopy at specified intervals. [69] The exact colonoscopy requirements are not clear, but in the UK pilot 1388 adenomas were detected in addition to 552 cancers. [40]

A decision needs to be made about whether the ongoing colonoscopy surveillance needs of these individuals will be incorporated within the programme. We would argue that the screening programme has an ethical obligation to these individuals to ensure that they have best practice follow-up, given that they were invited to participate. A decision has been made to include the ongoing surveillance requirements of similar individuals with adenomas within the screening programme in England. [73]

5.4.11 Quality and monitoring standards for screening pathway

Quality standards need to be set for every step along the screening pathway and an appropriate monitoring framework is required to determine if the standards are being met. Standards will apply at a number of levels: to procedures; individuals; teams; institutions and overall systems.[59] These standards, and their monitoring, are an essential ethical requirement for all screening programmes, to ensure that harms are minimised and benefits are maximised for participants.

Generic information on this subject is available in the Improving Quality report by the National Screening Unit, and there is detailed policy and quality documentation for BSA and NCSP. [59, 85, 86] Determining quality and monitoring standards for colorectal cancer screening is a large and iterative piece of work and it may be that only key aspects are in place for a feasibility study. Any key aspects would need to focus on areas of inequality in order to provide information to allow evaluation of the aims and objectives of the feasibility study. As a general point monitoring for a CRC screening programme is likely to be as intensive, if not more so, than breast cancer screening due to the fine balance of harms and benefits.

5.4.12 High risk people not eligible for population-based screening

As discussed in section 5.2 individuals and groups who are already at high risk of CRC have specific surveillance and management guidelines, and would be suitable for FOBT screening.[69] What happens to these individuals during a feasibility study and a national screening programme is of concern, as it already appears that there is not currently sufficient capacity in the system to manage their surveillance requirements.[57]

It needs to be considered (early in the process) whether a register and information system for a population –based programme can also incorporate the needs of individuals at high risk to ensure that they receive best practice care. In addition, planning for a feasibility study and population based screening programme needs to encompass what is required to implement the high risk guidelines (e.g. workforce).

Chapter 6 Evaluation of a study

This chapter briefly touches on evaluation of the feasibility study and considers 'success' criteria in more detail.

Chapter 6 Summary and Recommendations

- Evaluation is an essential part of the feasibility study.
- Setting predetermined success criteria for a feasibility study is problematic. There are two ways of thinking of success criteria; minimum success levels and more ideal/aspirational targets.
- We have been unable to find any precedent for setting minimum success criteria for a feasibility study. In addition there are a number of problems setting them, such as a lack of evidence to support them, the need for many criteria to be based on value judgements and the international trend that no pilot or feasibility study has concluded that population screening is not feasible.
- Setting ideal/aspirational targets for the feasibility study will be a useful exercise as it would set targets for the pilot sites, facilitate meaningful evaluation and provide information on where extra resources would need to be delivered in a screening programme.

We recommend that:

- There is independent, on-going, multi-disciplinary evaluation, conducted by a group with relevant expertise (including in Maori health), planned as part of the study, and that it covers the four areas of effectiveness, safety and acceptability, equity and economics.
- Ideal/aspirational targets for the study be developed with the input of the implementation group and pilot sites, once the screening pathway has been finalised.

A detailed discussion of the evaluation process is beyond the scope of this report. In general, however, the evaluation is part of the feasibility study process. Ideally it would be conducted by a group independent of the planning and delivery of the feasibility study; be on-going throughout the study period and beyond; and involve a multidisciplinary

team, including those with expertise in evaluation, quantitative and qualitative research, Maori health, measuring inequalities, health economics, screening, primary care, and specialist secondary care services.

Evaluation would cover the four areas of effectiveness, safety and acceptability, equity and economics. The specific evaluation questions would be directly related to the aims and objectives of the feasibility study (see section 4.2). These would need to be agreed between the implementation group and evaluators. A mix of process and impact evaluation will be required and a variety of methods would also be needed e.g. focus groups, surveys, and epidemiological analysis. Ideally the evaluation would be iterative, with early results feeding in to the continuing screening process to improve processes and outcomes.

6.1 Success criteria and targets

The Ministry of Health is particularly interested in success criteria for a New Zealand feasibility study. Success criteria can be thought of as either a series of minimum levels that a feasibility study must achieve in order to be deemed successful (and presumably be implemented as a national programme) or as ideal/aspirational targets that it should strive for. [87] The implications of these two approaches are quite different.

We were unable to find evidence of any minimum level criteria being explicitly stated prior to any CRC screening pilot/ feasibility study in other country, but the UK had some specified targets that it hoped to achieve (see section 2.2.3). We have been unable to find any definitive statement on what would have happened if the targets were not achieved.

In New Zealand, an expert advisory group developed criteria (called performance targets) for the breast screening pilot studies which formed the basis for the Interim National Quality Standards. [88] These standards were largely met, [89] however again it was not clear what the process would have been if some, or all of the targets were not achieved.

The following sections explore minimum targets and ideal/aspirational targets in more detail.

6.1.1 Setting minimum levels

As can be seen by the lack of any examples, setting and, more importantly justifying, minimum criteria to predetermine 'success' of a feasibility study would be difficult. This is for a number of reasons:

- A lack of applicable evidence to underpin the criteria e.g. the available epidemiological evidence around participation and test positivity would only apply to FOBTg screening programmes. Modelling would need to be done to answer such questions as: at what level of participation would population mortality benefits no longer accrue? Inevitably this would involve assumptions which could limit the usefulness of the modelling.
- For other important criteria such as safety and acceptability, equity and economic efficiency criteria would be based on ethical and value judgements. For example it would need to be determined what is considered a cost effective intervention in New Zealand. In addition accepting a level of inequality would be ethically unacceptable in the authors' opinion.
- Setting predetermined decision rules would be difficult e.g. what would happen if one minimum level was met but not another?
- In order for such criteria to be acceptable they would have to have considerable stakeholder, and probably public buy-in and agreement. Reaching consensus on some of these issues would be problematic, if not impossible.
- Setting minimum levels might potentially contradict other research. For example
 - The Catalonian pilot study concluded it was feasible to implement CRC screening with 17% participation. [38]
 - A paper has been published suggesting that high levels of participation are not necessary for a cost effective screening programme.[90]

6.1.2 An ideal targets approach

A process of setting more aspirational/ ideal performance targets for each stage of the screening process for a CRC feasibility study would undoubtedly be useful. The study could be evaluated against these targets, to optimise the probability of a quality screening process (in terms of effectiveness, safety, equity and economic efficiency). This would provide information on where efforts needed to be expended during programme implementation. However a decision would need to be made about what would happen if targets were not achieved.

Any targets would need to be agreed to by the implementation group and the pilot sites would need to have input into this process, to ensure that practicalities were considered. Table 10 gives a list of some of the targets that could be considered. This is an indicative list only, and some of it is dependent on the finalisation of the screening pathway.

Table 10 Areas for possible targets for a CRC screening feasibility study

Area	Potential targets
Effectiveness	Percent of eligible population who participate in screening (probably minimum of 60% based on RCT evidence) % of adequately completed tests Test positivity -% of tests % of those testing positive going on to have diagnostic investigations Colonoscopy waiting times PPV -cancer and neoplasia
Safety and Acceptability	Percent of people who intend to screen again A quality measure of FOBT Colonoscopy completion and/or caecal intubation rate, as a percent of colonoscopies attempted/performed Colonoscopy adverse events, as a percent of colonoscopies performed
Equity	Differences in participation rates between key population groups (no difference) Differences in measures of acceptability between key population groups
Economic	Cost per person screened Cost per cancer detected (Cost per year of life saved-modelled Cost per QALY- modelled)

Chapter 7 Timeframes

This section looks at the time frames required to develop and deliver a feasibility study.

Chapter 7 Summary and Recommendations

Planning, delivering and evaluating a study addressing the feasibility of CRC screening in New Zealand is complex and will require a realistic timeframe.

We recommend that:

- A minimum of two years is allowed for planning, and preparation before screening is initiated at study sites.

7.1 International experience

Planning, delivering and evaluating a study is a prolonged process. Table 11 and Table 12 outline the key dates for the UK and Australian pilot studies respectively. In both countries it took about two years to commence actual screening from initiation of the project, reflecting the substantial amount of planning that is required. The prevalence round of screening is a two years process with evaluations being published subsequently.

Table 11 Key dates of UK CRC screening pilot and programme implementation

Date	Event [41, 49, 73, 74]
1997- mid 1998	Consideration of CRC screening against WHO screening programme criteria. Feasibility/pilot study recommended and basic parameters decided
September 1998	Expressions of interest called for from health authorities to be pilot sites
February 1999	Pilot sites announced
March 2000	First screening round commences at Scottish site
September 2000	First screening round commences at English site
March-September 2002	First screening round finishes
May 2003	Evaluation of first screening round published
November 2004	Announcement of national programme by UK Government
2006-2009	Phased roll out of national screening programme for ages 60-69 in England and 50-74 in Scotland

Table 12 Key dates of Australian CRC screening pilot and programme implementation

Date	Event [14, 15]
1997	Australian Health Technology Advisory Assessment Committee reviewed the evidence for CRC screening and concluded it had been demonstrated to be effective. Pilot study recommended.
2000	Funding for pilot studies announced in Australian Government budget
April 2001	Bowel Cancer Screening Pilot Implementation Committee announced to provide advice on design and implementation of the pilot. Specific Task Groups to support this work also established.
October 2001	Pilot site locations announced in Melbourne, Adelaide and Mackay (rural Queensland)
November 2002	First screening round commences at pilot sites
June 2004	First screening round finishes at pilot sites
October 2004	Commitment to implement a national programme by Australian Government
October 2005	Final evaluation of first screening round published
2006	Screening commenced for national programme
Unknown	Full implementation of a national programme

7.2 Previous New Zealand experience

Table 13 outlines the experience of implementing pilot studies and then a programme for breast cancer screening in New Zealand.

Table 13 Timeframes to implement breast cancer screening in New Zealand.

Date	Event [55, 60, 61, 70, 89]
1987/88	Recommendation to pilot breast cancer screening in New Zealand.
1991	Pilots commence in Otago-Southland and Waikato.
1995	Waikato evaluation published. Decision to implement a national programme made.
1996	Otago-Southland evaluation published. Planned date of commencement of national breast screening programme.
1999	Actual date of commencement of BSA.

7.3 Proposed New Zealand timeframes

Despite being in a good position to learn from other countries New Zealand would still need to do a huge amount of work to gear up for any sort of CRC screening activity. Indicative timeframes are shown in Table 14.

Table 14 Projected timeline for NZ feasibility/pilot study

Date	Event
Year 1	Funding secured. Project staff recruited to commence planning. Process for decision making established, including stakeholder engagement. Specific incorporation of eliminating inequalities focus within the process, planning and delivery of feasibility study. Pilot site(s) selected.
Year 2	Detailed project planning including: Finalising screening pathway. Quality parameters and measures. Development of communications and education strategy and material. Monitoring and evaluation parameters and criteria to be set. Infrastructure projects such as Information Systems, development of Population Register etc.
Year 3	First (prevalence) round of screening commences.
Year 4	First round of screening continues. Interim evaluation report.
Year 5	First round of screening completed. Second (incidence) round of screening commences. Final evaluation of prevalence round of screening published.
Year 6	Second round of screening continues.
Year 7	Second round of screening completed. Final evaluation of incidence round of screening published.

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