Colorectal Cancer Screening Advisory Group

REVIEWING POPULATION SCREENING FOR COLORECTAL CANCER IN NEW ZEALAND

Report of the Colorectal Cancer Screening Advisory Group

FOREWORD

Colorectal cancer (cancers of the colon and rectum) is an important cause of morbidity and mortality in New Zealand. Each year approximately 2500 people develop colorectal cancer (CRC) and 1100 people die of the disease (Cancer Registrations and Deaths 2002, NZHIS 2006). These figures give New Zealand, along with Australia, one of the highest incidence rates of CRC in the world and, compared with other OECD countries, the highest death rate for colon cancer (Minister of Health, 2003).

Recent years have seen increasing interest in the potential of screening (the testing of people without symptoms to identify possible disease) to reduce the burden of colorectal cancer in New Zealand. This potential was highlighted in the late 1990s when a reduction in CRC mortality was demonstrated with faecal occult blood testing (FOBT) in two randomised controlled trials in Nottingham, England and Funen, Denmark.

In 1997, in response to these trial results, a working party was established by the National Health Committee to make recommendations on the advisability of introducing a publicly funded screening programme based on FOBT screening.

Having considered all available evidence and assessing its implications for New Zealand, the 1997 working party made the following recommendations (National Health Committee 1998).

1. 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 in New Zealand.

2. Population-based screening for colorectal cancer with other modalities, such as flexible sigmoidoscopy, colonoscopy or double-contract barium enema, is also not recommended as there is not yet evidence from randomised controlled trials that screening with any of these modalities reduces colorectal cancer mortality.

3. These decisions should be reviewed as evidence of benefit from new faecal occult blood tests and other screening modalities becomes available.

4. 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.

5. 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 (Working Party on Screening for Colorectal Cancer 1998).

In the intervening years, Guidelines on Surveillance and Management of Groups at Increased Risk of Colorectal Cancer (New Zealand Guidelines Group 2004) have been developed by a subcommittee of the original working party under the auspices of the New Zealand Guidelines Group. However, as documented in the report that follows, capacity constraints restrict the ability of large centre public hospitals to provide surveillance colonoscopy as recommended by the guidelines.

While no further randomised controlled trial evidence in relation to CRC screening by any modality has been published since 1998, recent evaluation reports of the colorectal cancer screening pilots in both the United Kingdom and Australia have stimulated renewed interest in the potential of screening using FOBT to reduce mortality from CRC. The availability of long-term follow-up data in relation to the Nottingham and Funen trials also provides an opportunity to review the advice of the initial working party.

Consequently in early 2005 the National Screening Unit (NSU) appointed a Colorectal Cancer Screening Advisory Group. The role of this advisory group is to provide the NSU with independent strategic advice and recommendations on population screening for CRC in New Zealand. The advice provided by the group does not necessarily reflect the views of the National Screening Unit.

This report provides the advisory group's advice and recommendations on screening and other issues in relation to colorectal cancer. It should be considered within the broader context of a range of activities offering potential improvement in the control of colorectal cancer in New Zealand.

CONTENTS

LIST OF ABBREVIATIONS

CAD	computer aided polyp detection system
CRC	colorectal cancer
CT colonography	computed tomographic colonography
DHB	District Health Board
FOBT	faecal occult blood testing
FOBTg	guaiac faecal occult blood testing
FOBTi	immunochemical faecal occult blood testing
FS	flexible sigmoidoscopy
FSA	first specialist assessment
GP	general practitioner
KPI	key performance indicator
NHC	National Health Committee
NHMRC	National Health and Medical Research Council
NSU	National Screening Unit
NZHTA	New Zealand Health Technology Assessment
PHO	Primary Health Organisation
QALYs	quality adjusted years of life saved
RCT	randomised controlled trial
VC	virtual colonoscopy

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EXECUTIVE SUMMARY

This report follows the report of the Working Party on Screening for Colorectal Cancer in 1998, which did not recommend population screening with faecal occult blood tests because of "the modest potential benefit, the commitment of health sector resources and the small but real potential for harm" (National Health Committee 1998). The 1998 report recommended that this decision be reviewed as new information became available. This is now the situation and a review of colorectal cancer screening in New Zealand is appropriate. To this end, in April 2005 the National Screening Unit (NSU) of the Ministry of Health established the Colorectal Screening Advisory Group and charged it with the following objective:

> *To provide the National Screening Unit with strategic advice and recommendations on the appropriateness and feasibility of a population colorectal cancer screening programme in New Zealand.*

The findings and recommendations of the Advisory Group are summarised below.

- Colorectal cancer (CRC) is a major cause of illness and death in New Zealand. Each year about 2500 people develop CRC and about 1100 people die of the disease. Colorectal cancer is clearly an important health issue in New Zealand. For this reason, a CRC screening programme merits consideration.

- The Advisory Group considered CRC screening using the New Zealand Criteria to Assess Screening Programmes (National Health Committee 2003).

- The Advisory Group's conclusions with regard to the assessment of CRC screening against the criteria are shown on page 16.

- Screening for CRC was considered for the following screening test options:

    - the guaiac faecal occult blood test (FOBTg)
    - the immunochemical faecal occult blood test (FOBTi)
    - flexible sigmoidoscopy
    - colonoscopy.

- The Advisory Group also considered the potential of other screening modalities, particularly CT colonography.

- The only screening test option for which quality evidence from randomised controlled trials is available is the guaiac faecal occult blood test (FOBTg), but this test has been shown to have limited sensitivity in detecting CRC and the mortality benefit remains modest.

- Immunochemical tests (FOBTi) have higher analytical sensitivity for detecting faecal blood and although there is no RCT evidence, they would be assumed to achieve an equal or even greater reduction in CRC mortality, compared

with FOBTg. An FOBTi based screening programme would be more resource intensive largely because of the higher colonoscopy demand following a positive test result.

- The FOBT test positivity in a New Zealand population (a key determinant of the potential benefit and the colonoscopy burden) is unknown.

- A screening programme based on one of the other screening modalities may be an option in future. Evidence of mortality reduction from screening based on flexible sigmoidoscopy or colonoscopy will not be available for many years.

- An effective CRC screening programme would require substantial workforce planning, expansion and capital investment so that the New Zealand health system could support it.

- This is crucial for colonoscopy services since all four screening modalities require colonoscopy either for follow-up diagnosis or first line screening.

- The results of a colonoscopy capacity survey in NZ in 2005 (see Appendix 4) have identified significant delays in the provision of colonoscopy, which may be affecting outcomes from colorectal cancer. This is despite the fact that the number of colonoscopies performed in the main centre public hospitals has almost doubled between 1997 and 2005. There is an immediate and urgent need to expand colonoscopy services within the public health sector.

- Existing public hospital colonoscopy capacity is insufficient to deliver timely diagnostic colonoscopy for individuals with symptoms suggestive of CRC. Based on the results of the 2005 colonoscopy capacity survey, nationally 930 patients in this category were estimated to have been waiting > 6 months for a diagnostic procedure.

- Existing public hospital colonoscopy capacity is insufficient to deliver timely surveillance procedures for those identified at increased risk of CRC as outlined in the *Surveillance and Management of Groups at Increased Risk of Colorectal Cancer* (New Zealand Guidelines Group 2004). Based on the results of the 2005 colonoscopy capacity survey, nationally, 2790 patients were estimated to have been waiting > 6months for a surveillance procedure.

- Preliminary considerations lead us to estimate that the total number of colonoscopies performed per annum within the public sector would need to increase by 10%-12% to ensure patients aged over 50 years with symptoms suggestive of CRC are offered a diagnostic colonoscopy within the 8 week time frame specified by the national colonoscopy referral guidelines (CPAC).

- Additionally it is estimated that the total number of colonoscopies performed per annum within the public sector would need to increase by a further 15% to ensure individuals identified at increased risk of CRC as outlined in the

Surveillance and Management of Groups at Increased Risk of Colorectal Cancer (New Zealand Guidelines Group 2004) are offered a surveillance colonoscopy within 6 months from the time of first referral or scheduled repeat date.

- To support the colonoscopy requirements of an FOBT based programme an additional increase in colonoscopy capacity, equivalent to an increase in public hospital capacity of approximately a further 30% for FOBTg and 65% for FOBTi, would be required to avoid displacement of diagnostic and surveillance services.

- In addition to workforce planning an effective CRC screening programme would need to: a) address social and ethical issues, such as delivering a safe programme that meets people's expectations whilst preventing any increase in inequalities through the programme and b) draw on models and frameworks developed specifically to take account of Māori needs and perspectives.

- The Advisory Group offers a number of recommendations that may assist the introduction of an effective CRC screening programme. A feasibility study of CRC screening using FOBTi (or FOBTg and FOBTi) should be considered and planning initiated. This would inform a decision on whether the New Zealand health system could support an FOBTi-based CRC screening programme that achieves high participation rates and is acceptable, effective and economically efficient.

- A feasibility study is an essential pre-requisite to a decision regarding a pilot study particularly in relationship to the provision of colonoscopy, given the current capacity constraints in New Zealand.

- The Advisory Group also makes some recommendations with regard to optimising the diagnosis and treatment of colorectal cancer. These should improve outcomes for CRC in New Zealand regardless of whether a screening programme is in place.

- In addition to the expansion of colonoscopy services there is an immediate need to ensure that throughout New Zealand the treatment of CRC, both surgical and oncological, is based on a multidisciplinary approach with audited outcomes meeting international standards.

RECOMMENDATIONS

A. Screening options
The Advisory Group offers the following recommendations in regard to the three screening options that show the most potential for screening programmes.

1. Screening using faecal occult blood tests

> **Recommendations**
> It is recommended that:
> - a feasibility study of CRC screening with 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 United Kingdom pilots.
> - a feasibility study is a pre-requisite to a decision regarding a pilot study.

See Appendix 6 for the recommended parameters for the feasibility study and the components of the screening pathway that should be monitored.

2. Screening using flexible sigmoidoscopy

> **Recommendations**
> It is recommended that:
> - any further consideration of screening for CRC by one-off flexible sigmoidoscopy be deferred until the results of the United Kingdom and Italian multicentre trials are available.
> - opportunities to contribute to further clinical trials in this area be pursued.

3. Screening using colonoscopy

> **Recommendations**
> It is recommended that:
> - any further consideration of screening for CRC by colonoscopy be deferred until the results of randomised control trials are available. No randomised control trials are currently in progress.
> - research opportunities addressing the potential of CRC screening by colonoscopy be pursued. In this regard, New Zealand has been invited to participate in the Nordic multicentre RCT, involving CRC screening by one-off colonoscopy, and this opportunity should be drawn to the attention of the Ministry of Health and the New Zealand Cancer Control Council.

B. Optimising diagnosis and treatment of colorectal cancer in New Zealand

Implementing the following recommendations will improve outcomes from colorectal cancer in New Zealand. In addition, their implementation is essential to the development of the infrastructure and processes that are needed for a successful CRC screening programme.

1. Colonoscopy capacity

Recommendations
It is recommended that:
- colonoscopy capacity be expanded with some urgency to ensure timely provision of diagnostic colonoscopy within the public health sector for people with symptoms suggestive of CRC.
- colonoscopy capacity be expanded with some urgency to facilitate the availability of surveillance procedures for those at increased risk of CRC as outlined in the Guidelines for *Surveillance and Management of Groups at Increased Risk of Colorectal Cancer* (New Zealand Guidelines Group 2004).

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2. Guideline for groups at increased risk of colorectal cancer

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Recommendation
- It is recommended that the implementation of the Guidelines for *Surveillance and Management of Groups at Increased Risk of Colorectal Cancer* (New Zealand Guidelines Group 2004) be monitored with regard to both education of medical practitioners and provision of adequate colonoscopy capacity.

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3. Referral guidelines for diagnostic colonoscopy

Recommendation
It is recommended that evidence-based guidelines identifying high- and low-risk symptoms for CRC be developed with the aim of optimising referral and improving utilisation of colonoscopy for diagnostic purposes.

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4. Quality assurance in colonoscopy

Recommendations
It is recommended that the relevant professional bodies in New Zealand develop and promote agreed quality parameters for the technical performance of colonoscopy and the continuous quality improvement process for colonoscopy. This work would include the development of and resourcing for structured and standardised training in colonoscopy. Recognition of training by the New Zealand Conjoint Committee for Recognition of Endoscopy Training (New Zealand Society of Gastroenterology, The NZ Committees of the The Royal Australasian College of Physicians and Royal Australasian College of Surgeons) should also be promoted as a prerequisite for independent practice.

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5. Treatment for CRC

Recommendations
It is recommended that:
- the treatment of CRC, both surgical and oncological, be based on a multidisciplinary approach with audited outcomes meeting international standards.
- the resources required to provide appropriate and timely colorectal cancer treatment services be considered as part of any work on CRC screening and surveillance.

6. Inequalities in CRC outcomes

Recommendations
It is recommended that factors identified as contributing to the increasing CRC mortality rates among Māori and Pacific peoples be investigated and addressed with urgency.

7. Cancer Registry information

Recommendations
It is recommended that current initiatives to expand the Cancer Registry to include clinical stage, survival and treatment modality for colorectal and other cancers are supported and progressed with some urgency. Such initiatives have implications that are broader than screening.

8. Pathology reporting for colorectal neoplasia

Recommendations
It is recommended that the relevant professional bodies reach a consensus on:
- the staging system to be used in reporting colorectal cancer to the Cancer Registry.
- the classification of and information required in reporting colorectal neoplasia.

9. Pathology workforce

Recommendation
It is recommended that the policy work on CRC screening and surveillance assesses the impact on the pathology workforce and identify specific actions that might be required.

C. Improving outcomes from CRC for Maori

Recommendations

It is recommended that in order to optimise outcomes for Māori, any CRC-control programme, including screening, should

- adopt a 'Hauora' model to address health & wellbeing.
- include the following features:
  - alliances with relevant Māori health organisations (such as the Māori Medical Practitioners Association, Māori Nurses Organisation, Māori development organisations and iwi/Māori groups)
  - mechanisms (including prioritisation, resources and performance incentives) to ensure Māori participation in the planning and provision of the programme
  - use of te reo Māori (in addition to English) in information, health promotion and other materials relating to the programme
  - complementary measures to determine the programme's success in Māori terms.

D. Ongoing programme of research into the control of colorectal cancer in New Zealand and factors driving inequalities

Recommendation

It is recommended that there is ongoing research on colorectal cancer screening that complements research across the cancer control continuum.

E. Review of recommendations

Recommendation

The above recommendations should be reviewed when results of a New Zealand FOBTi feasibility study, the United Kingdom and Italian multicentre randomised control trials on flexible sigmoidoscopy, and any new RCT-based research on other screening modalities become available.

National Health Committee Screening Criteria with regard to CRC: Conclusions of the Advisory Group

1. The condition is a suitable candidate for screening

Conclusion: CRC is a major cause of illness and death in New Zealand. Also, there is an early stage at which most CRC could be detected or prevented through screening. Therefore it is a suitable candidate for screening.

2. There is a suitable test.

Conclusion: There is a range of available tests but there are limitations to each one. Those with greatest potential at present are two faecal occult blood tests (FOBTg and FOBTi), flexible sigmoidoscopy and colonoscopy.

3. There is an effective and accessible treatment or intervention for the condition identified through early detection.

Conclusion: There is access to surgery (the primary treatment) for colorectal cancer throughout New Zealand, but outcomes may vary, especially for rectal cancer. For potentially curable but at-risk groups of patients with CRC, chemotherapy and radiotherapy used in conjunction with surgery improves outcomes and is available in N.Z.   The increase in CRC mortality rates for Maori between 1980 and 2001 could reflect both physical and cultural barriers to treatment. Early treatment of CRC identified at an early stage through screening can lead to a better outcome, provided that the health system has the capacity to support it and the programme is designed to minimise or avoid inequalities.

4. There is high quality evidence, ideally from randomized controlled trials, that a screening programme is effective in reducing mortality or morbidity.

Conclusion: The only modality for which there is RCT evidence is guaiac FOBT. However, there are limitations of this test; in particular 50% of cancers will be missed because of its low sensitivity. A separate shortcoming of guaiac FOBT is difficulty with interpretation and quality control. Comparisons between FOBTg and FOBTi have shown that FOBTi has a higher analytical sensitivity to detect faecal blood. It is therefore assumed that it will achieve at least the same or greater reduction in mortality within an organised screening programme, although no RCT data are available to test this assumption.   Further information from studies in progress is required before the appropriateness or feasibility of a flexible sigmoidoscopy screening programme could be considered in New Zealand.   Similarly, further consideration with regard to screening by colonoscopy should be deferred until the results of randomised controlled trials assessing participation, feasibility, safety and mortality reduction are available.

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

Conclusion: In the trials reported to date physical harms as a consequence of colonoscopy are less than were anticipated based on the data available to the previous working party; however this is dependent on ongoing rigorous quality control. Similarly, with regard to psychological harm, the data from the United Kingdom pilot has been reassuring.

6.   The health care system will be capable of supporting all necessary elements of the screening pathway, including diagnosis, follow-up and programme evaluation.

Conclusion: Screening is more than offering a test. Currently there is not the capacity for New Zealand to offer any CRC screening programme. The implications for colonoscopy and pathology services are of particular concern. This could be addressed by substantial workforce planning, expansion and capital investment.

7   There is consideration of social and ethical issues.

Conclusion: Potentially the social and ethical issues are profoundly complex and any CRC screening programme would need to be carefully planned, implemented and monitored to ensure that participants are well-informed of test limitations and to maximise benefit while minimising harms. The risk of increasing inequalities must also be taken into account so that the potential benefits of screening are distributed evenly among all population groups in New Zealand.

8   There is consideration of cost-benefit issues.

Conclusion: Compared with existing screening programmes, FOBTg CRC screening appears to be cost-effective; however, the benefits are at best modest. Other screening modalities (flexible sigmoidoscopy, colonoscopy and FOBTi) are expected to bring greater benefits, but supporting RCT evidence is not yet available. They are also more expensive, particularly with regard to set-up costs. If evidence of greater benefit becomes available, these higher cost options may in the end represent the best course of action. Evidence of cost-effectiveness of FOBTg is based on overseas populations. CRC incidence is higher in NZ and test positivity is unknown, consequently both costs and benefits may differ.

INTRODUCTION

Improving the control of colorectal cancer in New Zealand
Cancers of the colon and rectum are the second most common cause of cancer-related deaths in New Zealand (New Zealand Health Information Service 2006). Only lung and prostate cancer (in men) and breast and lung cancer (in women) are more frequent causes of cancer death in New Zealand.

As with all cancers, the control of colorectal cancer (CRC) requires a systematic and co-ordinated approach to all aspects, including primary prevention, early detection and screening, diagnosis, treatment and care (Cox and Sneyd 2005). *The New Zealand Cancer Control Strategy* (Minister of Health 2003) provides a mandate for such an approach, highlighting the need to identify priorities for action that are evidence-based and that will address the incidence, impact and inequalities with respect to cancer in New Zealand. Current research is also addressing inequalities in New Zealand, including reasons for CRC survival differences between Māori and non-Māori.

Screening for colorectal cancer
Screening is a process whereby people who have no symptoms are invited (directly and/or through publicity) to undergo a test or procedure, usually at regular intervals. The National Health Committee defines screening as:

> *"a health service in which members of a defined population, who do not necessarily perceive they are at risk of, or are already affected by, a disease or its complications, are asked a question or offered a test to identify those individuals who are more likely to be helped than harmed by further tests or treatments to reduce the risk of disease or its complications."* (National Health Committee 2003).

In some instances, the purpose of screening is to detect cancer at an early stage of development. In others, cancer screening identifies precursors of cancer, the treatment for which can reduce the risk of cancer developing.

Screening is a complex process that involves more than just a screening test. It involves a 'pathway' of screening activities that include identifying and inviting potential participants, fully informing them of what is involved, investigating abnormal results and treating disease that is detected. In screening programmes, all activities along the screening pathway are planned, co-ordinated, monitored and evaluated. In contrast, opportunistic screening lacks formal quality processes and no formal co-ordination, monitoring and evaluation; also, there is no assurance that the necessary follow-up diagnostic services are available.

Colorectal cancer usually develops within a pre-existing adenomatous polyp, typically over many years. The extent of spread of a cancer is known as its *stage*. There are various staging systems (Fielding et al 1991). Most are modifications of the Dukes' Staging System: stage A is cancer confined to the bowel wall; in stage B

it penetrates through the bowel wall; and in stage C cancer has invaded the regional lymph nodes. Stage D has been added to identify patients with cancer that has spread to other organs.

Cancers detected at an early stage have a better prognosis than cancers detected later.

The primary aim of screening for CRC is to detect CRC before symptoms develop. Screening also provides an opportunity to identify colorectal polyps that are likely to progress to cancer (thereby preventing development of the disease). Although various screening tests have been proposed for individuals at average risk of developing CRC, only guaiac faecal occult blood tests (FOBTg) have been shown in randomised controlled trials (RCTs) to result in a definite but modest reduction in CRC mortality.

Initial advice on screening for colorectal cancer in New Zealand
The Working Party on Screening for Colorectal Cancer convened by the National Health Committee in 1997 reviewed the published scientific evidence up to May 1998 and recommended the following:

1. 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 in New Zealand.

2. Population-based screening for colorectal cancer with other modalities, such as flexible sigmoidoscopy, colonoscopy or double-contract barium enema, is also not recommended as there is not yet evidence from randomised controlled trials that screening with any of these modalities reduces colorectal cancer mortality.

3. These decisions should be reviewed as evidence of benefit from new faecal occult blood tests and other screening modalities becomes available.

4. 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.

5. 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 (National Health Committee1998).

Surveillance recommendations for groups at increased risk
In response to recommendation 5 above, a subcommittee of the Working Party on Screening for Colorectal Cancer developed evidence-based surveillance recommendations for individuals identified to be at increased risk of developing CRC (New Zealand Guidelines Group 2004). This guideline, developed as a companion

document to the 1998 report, defines the major groups at increased risk for CRC as those individuals with:

- a personal history of
  - colorectal cancer
  - colorectal adenoma or
  - inflammatory bowel disease
- a family history of CRC (as determined by the number of affected first-degree relatives and the age at which they were diagnosed with CRC).

The guideline is intended for use by primary health care providers, and medical and surgical specialists, to facilitate consistency of advice and care for those individuals who are at increased risk of developing colorectal cancer.

Review of New Zealand decision on population screening for CRC
The initial report recommended that the decisions of the original working party be reviewed as evidence of benefit from new faecal occult blood tests and other screening modalities became available. Although there is no new RCT evidence relating to screening for CRC, several overseas initiatives are significant:

- Updated reports from the Nottingham and Funen biennial FOBT RCTs, after 3-6 and 9 screening rounds respectively, have also been published and pilot screening programmes using FOBT have been undertaken in the United Kingdom and Australia. On the basis of the results of these pilots both countries are now planning to gradually introduce population screening for CRC.
- Two parallel multicentre randomised controlled trials to measure the extent of reduction in CRC incidence and mortality by a single screening sigmoidoscopy examination at around the age of 60 years have been initiated in the United Kingdom and Italy. Both groups have reported their preliminary findings.
- Updated reports from the Nottingham and Funen biennial FOBT RCTs, after 3-6 and 9 screening rounds respectively, have also been published and pilot screening programmes using FOBT have been undertaken in the United Kingdom and Australia. On the basis of the results of these pilots both countries are now planning to gradually introduce population screening for CRC.
- In 2004, Finland also began establishing a population-based programme designed in the same way as a randomised controlled trial, involving expansion over a 10-year period of groups randomised into screening or control groups (Malila et al 2005).
- Countries such as the USA recommend screening by various modalities; however these are not within the context of a national organised screening programme.

Given this new information, a review of the New Zealand decision on population screening for CRC is appropriate.

Establishment of the Colorectal Cancer Screening Advisory Group

The Colorectal Screening Advisory Group was established in April 2005 by the National Screening Unit (NSU) of the Ministry of Health to support the NSU to achieve its vision, namely:

> *Saving lives, reducing inequalities, and building the Nation's health by leading the delivery of screening programmes, uncompromising in their quality and trusted by the communities we serve.*

In its **terms of reference**, the Advisory Group was advised to:
- involve key stakeholder groups, including consumers
- use the best available evidence to inform its work
- identify relevant linkages to the Treaty of Waitangi to inform its work
- have a strong focus on quality improvement and equity
- have a population health perspective with an understanding of the principles of screening programmes.

The **objective** of the Advisory Group:

> *To provide the National Screening Unit with strategic advice and recommendations on the appropriateness and feasibility of a population colorectal cancer screening programme in New Zealand.*
> *In developing its advice the Group should strive to achieve consensus in providing its advice to the NSU.*

The **key task** of the Advisory Group:

> *To report to the NSU regarding its advice on a population CRC screening programme in New Zealand.*

Composition and working arrangements

The Advisory Group comprised 14–16 members who were appointed for their particular expertise in matters relating to colorectal cancer and screening programmes. The NSU appointed members, after discussion with relevant stakeholders including providers, consumer groups and professional groups. Not all clinical specialist groups were represented on the Advisory Group but there was the opportunity to co-opt members and to obtain advice on areas outside the expertise of Advisory Group members. The NSU provided a secretariat and organisational support.

Membership included expertise and/or representation from:
- Association of General Surgeons of New Zealand
- Cancer Society of New Zealand
- Consumers
- Health economics
- Māori health
- New Zealand Committee of the Royal College of Pathologists of Australasia

- National Screening Advisory Committee
- New Zealand Committee of the Colorectal Surgical Society of Australasia
- New Zealand Society of Gastroenterologists
- Public health/epidemiology
- Royal New Zealand College of General Practitioners

Advisory Group's process for determining advice

In its deliberations, the Advisory Group used as its starting point the 1998 report and recommendations of the National Health Committee's Working Party on Population Screening for CRC (National Health Committee 1998).

The current report builds upon the evidence and recommendations of the 1998 report; the two reports should be considered alongside each other. In determining its advice on screening for CRC, the Advisory Group also considered other opportunities to improve outcomes of CRC in New Zealand, particularly with regard to diagnosis and treatment.

In formulating its recommendations the Advisory Group considered:
- an NZHTA literature review, commissioned by the NSU, focusing on published data since the 1998 report (Kerr et al 2005)
- additional literature as referenced in this report
- follow-up mortality data from the Nottingham and Funen RCT FOBT trials
- final report UK Colorectal Cancer Screening Pilot
- final report Australia Bowel Cancer Screening Pilot Programme
- baseline findings of a single flexible sigmoidoscopy screening to prevent colorectal cancer: UK and Italy multicentre randomised trial
- face-to-face visits of two members of the Advisory Group with those responsible for the UK pilot sites in Scotland
- *A Survey of Colonoscopy Capacity in New Zealand* (Yeoman and Parry 2005), commissioned by the NSU
- consumer acceptability research commissioned by the NSU
- presentations to meetings by members of the group, as well as by those external to the group with particular expertise – see Appendix 7.

Framework for advice: the National Health Committee criteria

The Advisory Group considered colorectal cancer screening against criteria for screening developed by the National Health Committee (2003). These criteria are based on accepted international criteria, including World Health Organization (WHO) principles for the introduction of population screening programmes, adapted for the New Zealand context. The WHO criteria were used by the 1998 working party to assess population screening for CRC in New Zealand. The National Health Committee criteria have been used in recent years to consider potential screening programmes for several conditions, including screening for prostate cancer, antenatal HIV infection and newborn hearing loss.

In the foreword to the criteria, the NHC chair acknowledges, 'screening is a complex process requiring careful consideration of clinical, social, ethical and economic

issues'. Furthermore, screening programmes should be 'based on good quality evidence that they do more good than harm, at reasonable cost, and they should be delivered within the context of an effective quality assurance programme' (National Health Committee 2003).

The eight criteria are designed to ensure that all the relevant information is available to people making a decision about whether or not to establish a screening programme. They are detailed below.

NHC criteria for assessing screening programmes

1. The condition is a suitable candidate for screening.
2. There is a suitable test.
3. There is an effective and accessible treatment or intervention for the condition identified through early detection.
4. There is high quality evidence, ideally from randomised controlled trials, that a screening programme is effective in reducing mortality or morbidity.
5. The potential benefit from the screening programme should outweigh the potential physical and psychological harm (caused by the test, diagnostic procedures and treatment).
6. The health care system will be capable of supporting all necessary elements of the screening pathway, including diagnosis, follow-up and programme evaluation.
7. There is consideration of social and ethical issues.
8. There is consideration of cost–benefit issues.

In applying the NHC criteria to screening for CRC, the Advisory Group has drawn upon the definitions and types of information identified by the NHC as relevant to each. In its deliberations the key issues identified by the 1998 working party were considered and noted accordingly. The report that follows is organised around these criteria, with a discussion of the relevant information and a concluding statement relating to each one.

1. IS CRC A SUITABLE CANDIDATE FOR SCREENING?

Criterion 1. The condition is a suitable candidate for screening.

The condition should be an important health problem. The epidemiology and natural history of the condition should be understood. The burden of the condition should be considered, including specifically for Maori (National Health Committee 2003).

Epidemiology of colorectal cancer in New Zealand

Colorectal cancer was identified in the previous colorectal cancer screening report as a major cause of illness and death in New Zealand (National Health Committee 1998). The epidemiology and natural history of the condition were also addressed in the report. CRC remains the second most common cause of cancer registration and the second most common cause of cancer death (Ministry of Health 2006). In 2002, the latest year for which data is available, there were 2588 registrations of colorectal cancer and 1135 deaths.

Comparisons of incidence and mortality

Comparisons by country
Table 1.1 shows that the age-standardised incidence of colorectal cancer in New Zealand is higher than in Australia and the United Kingdom (Ferlay et al 2004), ie, the two countries where pilot studies of FOBT screening for colorectal cancer have been undertaken, and also higher than Denmark, the US and the UK where randomised controlled trials of screening have been undertaken.

Table 1.1: Age-standardised incidence and mortality of CRC in NZ, Australia, Denmark, the US, and the UK in 2002

	Age-standardised (world) incidence per 100,000		Age-standardised (world) mortality per 100,000	
Country	Male	Female	Male	Female
New Zealand	53.0	42.2	23.2	18.6
Australia	47.4	35.9	18.7	13.3
United Kingdom	39.2	26.5	17.5	12.4
United States	44.6	33.1	15.2	11.6
Denmark	41.0	33.0	23.3	19.2

As Table 1.1 indicates, males have higher age-standardised incidence rates and mortality rates than females.

Comparisons by age group
Figure 1.1 shows the age-specific incidence (in five-year age groups) of colorectal cancer in New Zealand, derived from cancer registrations in New Zealand in 2001 (Ministry of Health 2005). As with most cancers, the incidence of colorectal cancer increases with age.

Figure 1.1: Age-specific incidence of colorectal cancer (male and female combined) in New Zealand 2001
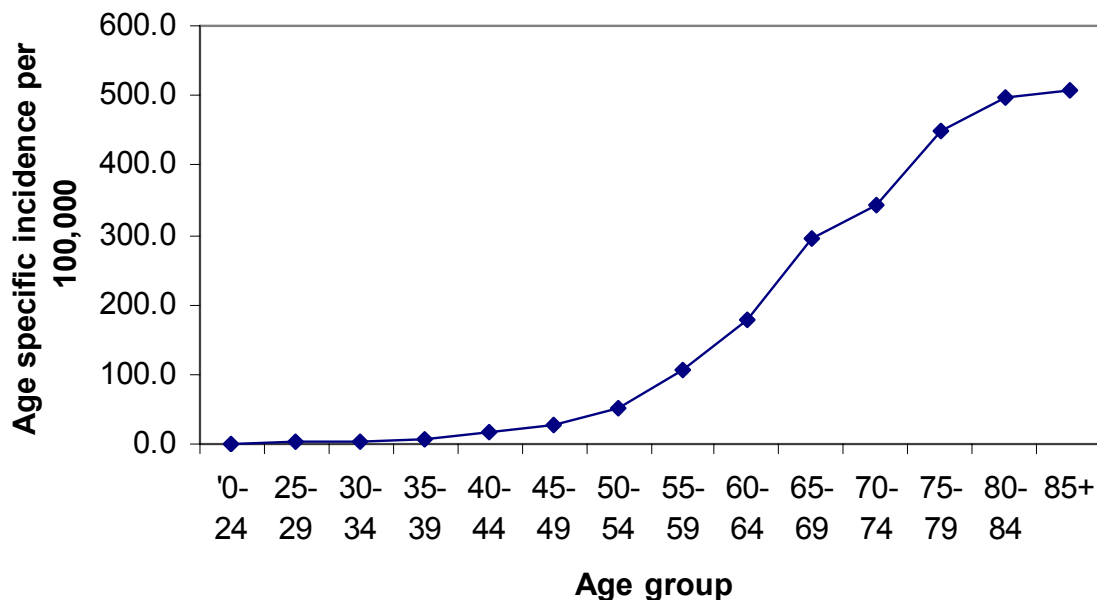
Comparisons over time

Age-standardised colorectal cancer incidence rates are forecast to decline in New Zealand, with a fall of 11% forecast for men from 1996 to 2011, and a fall of 21% forecast for women (Ministry of Health 2002). Figure 1.2 shows these projections.

Despite this, the absolute number of registrations is projected to increase, because the continuing growth in population size and the ageing population will more than offset the projected decline in incidence.

Figure 1.2: Trends and projections of age standardised rates, colorectal cancer. (Source: Ministry of Health. Cancer in New Zealand: trends and projections. Public Health Intelligence Occasional Bulletin No 15. Wellington: Ministry of Health, 2002)

(a) Male incidence rates

(b) Male mortality rates

(c) Female incidence rates

(d) Female mortality rates

Key:
- ● Observed
- — Fitted and projected
- -- Minimum and maximum estimates
- ▨ 90% Bayesian credible interval
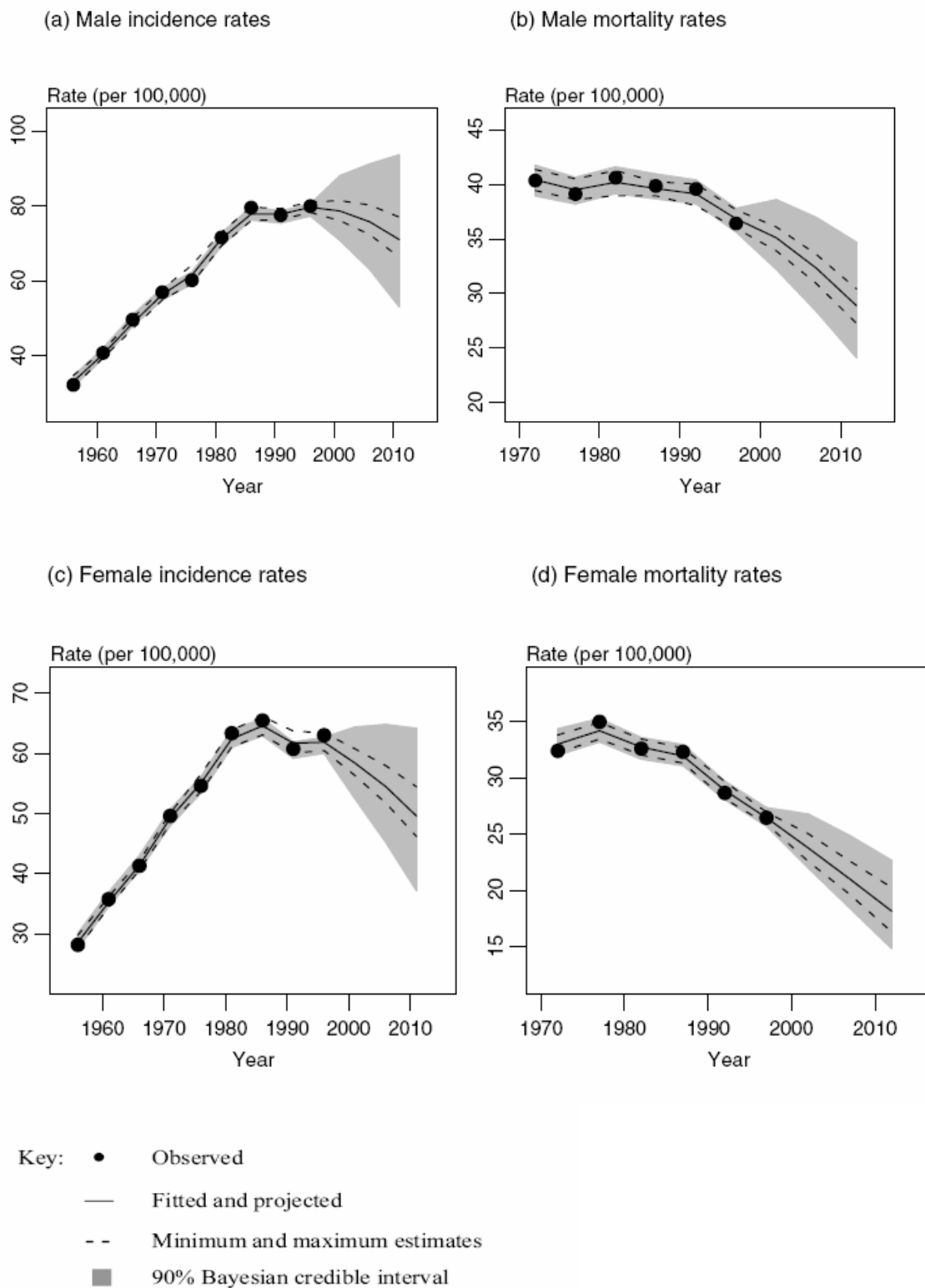
Figure 1.2 also shows that colorectal cancer mortality rates have been declining overall in New Zealand since the 1970s, and this decline is forecast to continue, reflecting the projected decline in incidence and improvements in survival (Ministry of Health 2002). However, Skegg and McCredie (2002) show that mortality from colorectal cancer is higher in New Zealand than in Australia, and suggest that this is partly due to the higher incidence of colorectal cancer in New Zealand but may also reflect poorer survival after diagnosis in New Zealand compared to Australia.

As identified in the initial report, the stage distribution of colorectal cancer recorded by the Cancer Registry continues to be consistent with a largely unscreened population (Keating et al 2003).

Table 1.2: Stage of CRC at diagnosis in screened and control patients

Modified Dukes' Stage	CRC detected by screening	All CRC in screening group	CRC in control group
A	41%	20%	11%
B	30%	32%	33%
C	21%	24%	31%
D	6%	22%	21%
Unknown	2%	2%	4%

Source: Hardcastle et al 1996

Incidence and Mortality for Māori
Age-standardised registration rates are lower for Māori than for non-Māori (New Zealand Health Information Service 2005). Colorectal cancer was the fourth most common cancer among Māori and the second most frequent among non-Māori during 1996 to 2001. On average, 85 Māori were diagnosed each year with colorectal cancer and around 50 died from the disease. Among non-Māori, there were 2400 registrations and 1080 deaths. The mortality:incidence ratio was 57% among Māori and 41% among non-Māori. The incidence of colorectal cancer increased with age, and was more common among males than females. Although, as noted above, colorectal cancer mortality rates have been declining overall in New Zealand since the 1970s, in contrast, Māori cancer mortality rates have increased between 1980 and 1999 (Blakeley et al 2004).

Figure 15.1: Age-standardised colorectal cancer incidence and mortality, 1996–2001
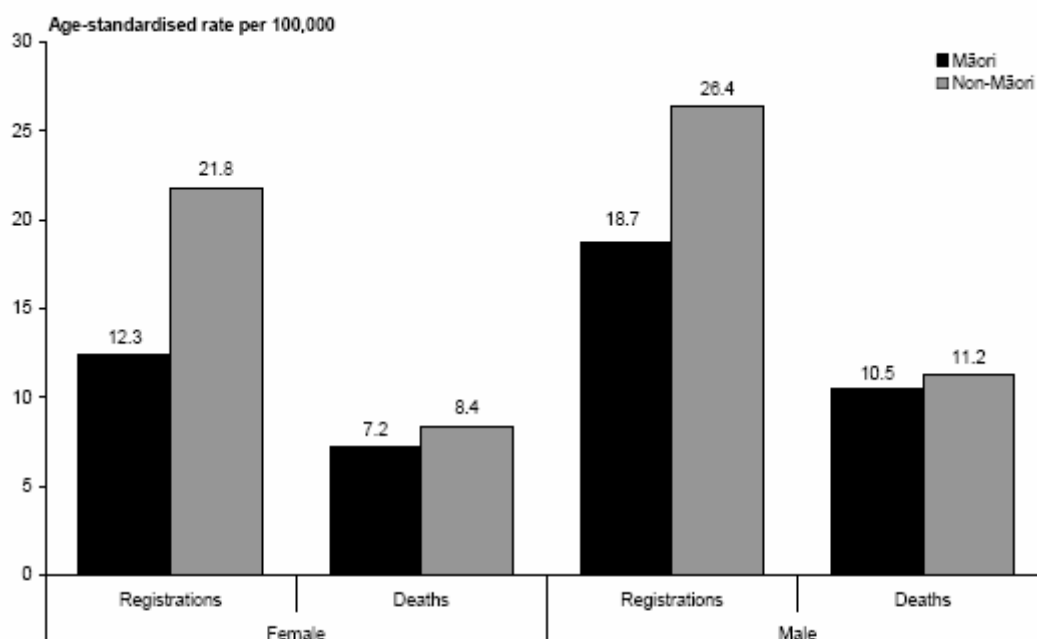
Table 15.1: Age-standardised colorectal cancer incidence and mortality, 1996–2001

		Māori		Non-Māori		Ratio (95% CI)	
		Number	Rate* (95% CI)	Number	Rate* (95% CI)		
Registrations	Total	514	15.5 (14.2–16.9)	14,410	24.1 (23.6–24.5)	0.64	(0.59–0.70)
	Female	221	12.3 (10.8–14.1)	7,149	21.8 (21.2–22.4)	0.57	(0.49–0.65)
	Male	293	18.7 (16.6–20.9)	7,261	26.4 (25.7–27.0)	0.71	(0.63–0.80)
Deaths	Total	292	8.8 (7.9–9.9)	6,502	9.8 (9.5–10.1)	0.90	(0.80–1.02)
	Female	129	7.2 (6.0–8.5)	3,177	8.4 (8.0–8.7)	0.86	(0.72–1.03)
	Male	163	10.5 (9.0–12.3)	3,325	11.2 (10.8–11.7)	0.94	(0.80–1.10)

* Rate per 100,000 standardised to Māori population.

(Robson et al 2006)

Colorectal cancer screening and Māori
Although Māori are not a population with elevated risk of CRC, prevalence has increased over time (and since our last report). Māori are, moreover, at risk of not accessing services at equitable rates and this risk is especially relevant to designing a responsive CRC screening programme.

How then could the health system ensure that Māori gain the maximum benefit from the screening programme? Two key documents/frameworks guide us in this endeavour: the Māori Health Strategy, together with its implementation plan (He Whakatataka 2002), and Te Pae Mahotanga – Durie's framework for health promotion/public health (Durie 1999).

He Korowai Oranga
The Māori Health Strategy and Implementation Plan (King and Turia, 2002; Minister of Health, 2002) identify the broad approach to Māori health for the health system.

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The following Kaupapa are given:

- **affirming Māori processes** - the strategy strongly supports Māori holistic models and wellness approaches to health and disability. It will also tautoko, or support, Māori in their desire to improve their own health. He Korowai Oranga seeks to support Māori-led initiatives to improve the health of whānau, hapū and iwi. The strategy recognises that the desire of Māori to have control over their future direction is a strong motivation for Māori to seek their own solutions and to manage their own services.
- **improving Māori outcomes** - achieving this will mean a gradual reorientation of the way that Māori health and disability services are planned, funded and delivered in New Zealand. Government, District Health Boards (DHBs) and the health and disability sector will continue to have a responsibility to deliver improved health services for Māori, which will improve Māori outcomes.

Four pathways for action are identified:
1. development of whānau, hapū, iwi and Māori communities
2. Māori participation in the health and disability sector
3. effective health and disability services
4. working across sectors.

While all of these pathways are important, pathways 2 and 3 are of particular relevance for CRC screening.

Te Pae Māhutonga
For effective implementation of a screening programme, Durie's Te Pae Mahutonga framework (Durie 1999) would provide a useful approach.

Te Pae Māhutonga is the name for the constellation of stars popularly referred to as the Southern Cross. Te Pae Māhutonga has long been used as a navigational aid and is closely associated with the discovery of Aotearoa and then New Zealand. The constellation has four central stars arranged in the form of a cross, and there are two stars arranged in a straight line which point towards the cross. They are known as the two pointers.

Because it is an icon of New Zealand, and because Te Pae Māhutonga has served as a guide for successive generations, it can also be used as a symbolic map for bringing together the significant components of health promotion, as they apply to Māori health, but as they might also apply to other New Zealanders.

The four central stars can be used to represent the four key tasks of health promotion and might be named according to reflect particular goals of health promotion: Mauriora, Waiora, Toiora, Te Oranga. The two pointers are Ngā Manukura and Te Mana Whakahaere.

Directions	Questions	Implications for Colorectal Cancer Screening Programme
Ngā Manukura – Leadership	Whose agenda are you working to	Do Māori have differential outcomes for colorectal cancer?
	What are the groups and organisations who will be allies	Māori medical practitioners Māori nurses Māori community health workers
Mauriora – access to te Ao Māori	Te reo Māori resources	Advertising, promotional and information resources in te reo Māori
Waiora – environmental protection	Somewhat less relevant for a screening programme	Responsible use of resources
Toiora – health lifestyles	Harm minimisation	Both the screening programme and its target need to result in reduced harm as measured in Māori terms
	Targeted	By Māori for Māori provision of services
	Culturally relevant	Use of a Hauora model, such as that represented by Te Whare Tapa Wha
Te Oranga – participation in society	Participation in the screening programme	Resources and incentives to ensure participation
Te Mana Whakahaere – autonomy	Control	Highly visible Māori leadership
	Sensible, Māori-centric measures of outcome	Development of measures of participation, acceptability and outcome

In conclusion, the implications for a screening programme for Māori health are:

- adoption of a Hauora model to represent health
- building alliances with relevant Māori health organisations (such as the Māori Medical Practitioners Association, Māori Nurses Organisation, and Māori Development Organisations)
- mechanisms (including prioritisation, resources and performance incentives) to ensure Māori participation in the planning and provision of the programme
- the use of te reo Māori in information, health promotion and other materials relating to the programme
- the development and use of measures of success for the programme in Māori terms, as complementary measures.

Conclusion: CRC is a major cause of illness and death in New Zealand. Also, there is an early stage at which most CRC, in theory, could be detected or prevented from developing through screening. Therefore it is a suitable candidate for screening.

2. IS THERE A SUITABLE CRC SCREENING TEST AVAILABLE?

Criterion 2. There is a suitable test.

There should be a suitable screening test, with specific consideration given to test characteristics (National Health Committee 2003)

The Advisory Group considered the following screening test options for CRC:
- two kinds of faecal occult blood tests (FOBT):
    - guaiac faecal occult blood testing (FOBTg)
    - immunochemical faecal occult blood testing (FOBTi)
- flexible sigmoidoscopy (FS) as first-line screening
- colonoscopy as first-line screening
- other potential screening modalities.

This section gives an overview and initial assessment of each of these options. In subsequent sections, there is more in-depth analysis of the effectiveness, available research findings and other implications of the four main modalities identified above.

Faecal occult blood tests

Test description
Faecal occult blood tests are tests for microscopic amounts of blood or breakdown products of blood in or on the stool with the presence of blood being used as an indicator of neoplasia (especially cancer and larger polyps) (Young et al 2002; Kerr et al 2005; Australian pilot study 2005). There is a normal loss of blood in the stool (Dybdahl 1984; Robertson 1987; Bird 1985) up to 1–2 ml per day (Crooke 2005; Dybdhal 1985; Young 1996). Cancers and larger polyps bleed intermittently with about two-thirds of cancers bleeding in the course of a week (Kerr et al 2005). These tests require the collection of faecal material which is then tested for blood.

Two main types of faecal occult blood tests are currently in use: (a) guaiac based tests (FOBTg) and (b) immunochemical based tests (FOBTi).

Guaiac faecal occult blood tests
Various types of FOBTg (notably Hemoccult and Hemoccult II) have been used in the major randomised control trials of population based screening studies to date (Kerr et al 2005). These tests are based on a chemical reaction in which the pseudoperoxidase activity of Haem (as haemoglobin or free Haem) converts colourless components in guaiac to blue coloured compounds (Young et al 2002). For guaiac tests two different sites on three separate successive faecal samples have been used in the major RCTs. Sticks or spatulas are used to collect the samples and smear them on to windows in the test card.

Simplicity/acceptability
Compared with other primary screening modalities (except FOBTi), this test is the simplest. It does however involve the self collection and sampling of three

successive stool samples with this process being carried out before the stool contacts water in the toilet. The smears of these samples need to be stored until all the samples have been collected and then sent to a processing centre usually by mail. Participation rates were in the range of 50-60% in the Nottingham RCT (Kerr et al 2005) and UK Colorectal Cancer Screening Pilot and somewhat higher in the Funen RCT (67% in the first screening round) (Kerr et al 2005).

Sensitivity of the test
In the Nottingham RCT using the hemoccult test (a test of only moderate analytical sensitivity) sensitivity for colorectal cancer was approximately 54%. Programme sensitivity for colorectal cancer was 59%. In the Funen RCT test, sensitivity for colorectal cancer was 51% (Kerr et al 2005).

Specificity of the test
In the Nottingham RCT test, specificity for colorectal cancer was estimated at between 96% and 98%. In the Funen RCT test, specificity for colorectal cancer was estimated at 98% (Kerr et al 2005).

Safety of the test
While no direct safety issues are known, there are concerns relating to hygiene at the time of sampling and test transportation.

Test limitations
Peroxidase activity which may lead to false positive tests is also present in haemoglobin/myoglobin of animal origin (especially in undercooked red meats) and in various plant foods (eg, turnip, cauliflower, broccoli, melons, radishes and spinach) (Blue Cross Blue Shield Assoc 2006; Sinatra et al 1999). Therapeutic drugs, especially aspirin and non-steroidal anti-inflammatory drugs, may lead to false positive tests by inducing gastro-intestinal bleeding (Young et al 1996, 2002). High dose vitamin C may lead to false negative tests (Young et al 2002; Jaffe et al 1975). Therefore dietary and therapeutic restrictions have generally been recommended in order to reduce the number of false positive and negative results (Young et al 2002; American College of Physicians 1997; Ransohoff and Lang 1997)

The need for these restrictions is debated and they may not be necessary in some populations (Young et al 2002; Ouyang et al 2005; Pignone et al 2001). Because vegetable peroxidase activity decays after the faecal smears have been made on the test cards, delayed testing of 72 hours or greater has been advocated (Ouyang et al 2005; Rozen et al 1999; Sinatra et al 1999). There appears to be no published studies on the effect of dietary/therapeutic restrictions on test positivity in the New Zealand situation.

Because the degradation products of Haem do not have peroxidase activity, FOBTg are more sensitive to colorectal bleeding than upper gastrointestinal bleeding (Blue Cross Blue Shield 2006; Young et al 1996) although relatively small amounts of ingested blood can still be detected (Rockey et al 1999). Analytical sensitivity (which may not equate to diagnostic sensitivity) varies in the numerous commercially available tests (Crooke 2005). Claimed analytical sensitivities include 10 mg

haemoglobin per gram of faeces (Helena Colisure), 50% positivity at 0.3 mg per gram of faeces and 100% positivity at 1 mg per gram (Hemoccult) and 0.3 mg per gram for Hemoccult SSENSA (Crooke 2005). Faecal smears on guaiac cards slowly dry out and should be tested within a defined period (7-12 days) (Bird et al 1985; Crooke 2005). The effects of drying may be countered by rehydrating the smear prior to testing. Rehydrating these tests increases sensitivity but reduces specificity and positive predictive value and is therefore not recommended (Kerr et al 2005; Young et al 2002; Winawer et al 2003; Smith 2005). In the USA these tests have been regarded as suitable for use outside of laboratories but increasingly quality control and documentation requirements as well as regulatory requirements for proficiency testing of those performing these tests are being enforced (Crooke 2005).

Major RCTs of screening have used a central screening site (laboratory) for the reception of the specimens, the carrying out of tests and the reporting of the tests. Applicable quality control systems can be implemented and monitored but are limited (Young et al 2002). The development of the blue colouration of a positive test may be transient and a definition and negative and positive tests has differed between programmes (Young et al 2002). The Nottingham RCT as well as English and Scottish pilots (NHS 2003) defined a positive result as 5 or more of the 6 smears giving a positive blue reaction. Weak positives were defined as 1-4 positive windows and were repeated after dietary/therapeutic restriction and if any smears were positive the test was then reported as positive. Recently it has been advocated that any positive smear should be reported as a positive result (Ransohoff and Lang 1997.

Other FOBTg tests have a greater analytical sensitivity and one of these hemoccult SENSA (analytical sensitivity of 0.3 mg haemoglobin/ g of faeces) has been the most extensively evaluated in screening populations (Young et al 2002)). The test has a more stable and readable colour change indicating a positive test. Positivity rates have varied from 5 to 16.7% (cf 2 to 5.1% for hemoccult). Dietary restriction and delay of test development for 72 hours may ensure positivity rates toward the lower end of the range (Young et al 2002). In one USA study specificity for neoplasia was relatively low (87.5%) although sensitivity for cancer was high (79.4%) (Levin et al 1997).

Two-test strategies using a cheap sensitive FOBTg followed, if positive, by a more expensive but more specific FOBTi on the same specimen has been investigated. In a study using HOSENSA/Heme Select specificity for colorectal neoplasia was high (97.9%) but sensitivity for cancer was only 65.2% cf HOSENSA alone (79.4%) (Young et al 2002; Allison et al 1996; Levin et al 1997)

Immunochemical faecal occult blood tests

Test description
Immunochemical faecal occult blood tests use antibodies to detect partial sequences of antigenic sites usually on the globin portion of the haemoglobin molecule. The antibodies do not react to non-human globins or with plant peroxidases thus

eliminating the need for dietary restrictions (Ouyang et al 2002). Because globin is degraded in the upper gastrointestinal tract, the test is not sensitive to upper gastrointestinal bleeding (Rockey et al 1999; Nakama et al 1996, 1998; McDonald et al 1984). Sample collection varies for different types of immunochemical tests. For example, two FOBTi tests were used in the recent Australian pilot study (2005). One test required the tip of a probe to be inserted into the stool and passed along the stool several times. The probe was then inserted into a collection tube. This test required collection from a stool separated from the toilet water by a biodegradable sheet placed above the water in the toilet. The other test used a brush to collect material from the surface of the stool within the toilet bowl water. The brush was then smeared onto a card.

The pilot studies in Australia used biennial testing. Studies carried out by Nakama et al (1997, 2000) concluded that for immunochemical occult blood screening sampling from two successive bowel motions was optimum. This has been adopted in the Australian pilot study (2005). Detection systems for immunochemical tests are varied and include chromatography, haemaglutination and gel filtration methodologies some of which are complex and may necessitate the test being carried out in a laboratory setting (Young et al 1996). The tests are more expensive than FOBTg tests (Ouyang et al 2005; Young et al 2002). The immunochemical tests however are capable of more sophisticated quality control, can be automated and calibrated allowing the analytical sensitivity (and test positivity rate) to be varied (Young et al 2002; Ouyang et al 2005; Smith et al 2004, Cole 2003). These tests generally show a greater analytical sensitivity than FOBTg tests. For example, a claimed detection limit of 0.03 mg of haemoglobin per gram of faeces (Ngaio Diagnostics Immunocare), through to 0.3 mg of haemoglobin per gram of faeces (haem select, immudia-haemSP) (Crooke 2005).

Simplicity/acceptability
These are the most simple of the primary screening tests for colorectal cancer. Because no dietary or therapeutic restrictions are required, participation rates are higher compared with FOBTg (by 13% in one study) (Young et al 2002; Cole 2001). Some of these tests use a sampling technique similar to that of FOBTg tests, ie, from a non-immersed stool, but one FOBTi uses a simple brush sampling from stool in the toilet water. This was shown to have a significant positive effect on participation rate in preliminary studies although this effect was not seen in the Australian pilot study. This pilot used biennial testing (as in most of the FOBTg studies) but only used one sample from two successive stools (cf 2 x 3 in FOBTg studies). Despite this much simpler testing procedure participation rates in the Australian pilot were 45.4% overall. There are many factors other than the nature of the test which impact on participation rates and are likely to have had an effect in this study.

Sensitivity of the test
As no population based RCTs of colorectal cancer screening using FOBTi exist, no sensitivity data from such studies are available. Studies comparing the performance of FOBTg against that of FOBTi have been carried out and reviewed (Kerr et al 2005). This review concluded that 'there is limited definitive evidence regarding superior immunochemical FOBT screening performance over the guaiac tests.

HemeSelect is the immunochemical test that compares most favourably with the guaiac tests.'

The Australian pilot study (2005) used Bayer Detect as one of the two FOBTi studied. This is a commercial evolution of HemeSelect. For each 1000 population screened, two cancers were confirmed in the Nottingham RCT and in the UK pilot whereas four (confirmed or suspected) cancers were found in the Australian pilot. It is difficult to interpret such comparisons, since the positivity of FOBTi can be "set" by predetermining the cut-off for a positive test.

Specificity of the test
There is a lack of data on the specificity of FOBTi (see sensitivity above.) In studies reviewed by Young et al (2002) one showed a specificity for colorectal neoplasia (cancer plus adenomas) of 95.2% using HemeSelect (Allison et al 1996). Again, sensitivity and specificity will vary depending on the cut-off used for a positive FOBTi result.

Safety of the test
While no direct safety issues are known there are concerns relating to hygiene at the time of sampling and test transportation

Test limitations
A consensus concerning the role of FOBTi in a screening situation has not been reached (Young et al 2002; Kerr et al 2005; Blue Cross Blue Shield Assoc 2006; Ouyang et al 2005). While the majority of studies reviewed by New Zealand Health Technology Assessment (NZHTA) (Kerr et al 2005) pointed to some benefit of FOBTi over FOBTg testing, the evidence base for this was not conclusive. Despite this the Australian pilot study (2005) which has just been concluded used two types of FOBTi and following evaluation has advocated a national programme using FOBTi. It is also of some interest that the English colorectal cancer screening pilot (2003) had as one of its conclusions:

> *The majority of test-positive results in the UK Pilot have come from repeat-testing; this has caused long screening histories in many participants, and may be overly-burdensome in a national programme. Consideration should be given to tests which provide more definitive results on the first round of screening (e.g., immunological tests) – these warrant further evaluation.*

These tests have not been demonstrated to save lives or reduce CRC mortality in an RCT. These tests are more expensive than FOBTg (Young et al 2002) and most require skilled staff to conduct the testing.

Flexible sigmoidoscopy as first-line screening

Test description
Flexible sigmoidoscopy refers to examination of the rectum and sigmoid colon by a fibre-optic endoscope designed to examine the distal 30–60 cm of the large bowel

(as opposed to the colonoscope designed to examine the entire large bowel). For screening purposes the longer 60cm instrument is usually chosen. During this procedure if bowel preparation has been adequate, bowel lesions including polyps may be biopsied or removed. FS can be used as a single one-off screening test or be repeated at regular intervals.

Simplicity/acceptability
Preparation for this examination is by enema only, which can be administered by the patient at home prior to the procedure. This is in marked contrast to the preparation for colonoscopy. In the UK FS one-off multicentre trial of 17,148 subjects assigned to the screening group, 9999 (58%) attended and 9911 were actually examined. Of the 9911 subjects who underwent FS, 94.8% completed the short questionnaire administered after the test. Of these 60.4% reported mild discomfort and 22.9% reported that they found the test to be less painful than expected. Only 5.1% of the screenees found the test more than mildly embarrassing. This proportion was similar for women and men (UK Flexible Sigmoidoscopy Screening Trial Investigators 2002). A New Zealand study suggested that colonoscopy was preferred to FS because sedation was used for the former and not the latter (Elwood Cancer Detect Prev 1995).

Sensitivity of the test
The majority of CRC (60-70%) occurs at or distal to the splenic flexure. Consequently the proportion of asymptomatic CRC within reach of a 60 cm flexible sigmoidoscope is considered to be 50-60% of the total. In practice it is likely that the proportion will be smaller as complete examination to the splenic flexure will not be achieved in all subjects. FS cannot detect cancers proximal to the splenic flexure but approximately 30% of patients with such cancers will have adenomas in the left colon (Dinning 1994). If all subjects with adenomas detected by FS screening were offered examination by colonoscopy, it is estimated that the detection of asymptomatic cancer would increase to 55-70%. FS screening detects adenomas in 10-25 percent of subjects and removal of high-risk adenomas (> 10mm in size, villous type or severe dysplasia on histological review) may reduce the subsequent risk of malignant change.

Specificity of the test
A diagnosis of cancer in the portion of bowel examined at flexible sigmoidoscopy can usually be accurately predicted from the visual appearance at the time of the examination and therefore the specificity for cancer is high. Polyps will be detected in up to 30% of examinations but only about half of these will be adenomas. Histological review is necessary to determine the nature of the removed lesions (Norfleet et al Dig Dis Sci 1988) and therefore the specificity of FS for adenomas is highly dependent on this histological follow-up. The identification of distal adenomas also determines which patients require follow-up colonoscopy as these can predict proximal colonic cancer.

Safety of the test
Flexible sigmoidoscopy is generally safe but as with any invasive procedure there can be complications. In the reported baseline findings of the UK multicentre

randomised trial among the 40,674 subjects who underwent sigmoidoscopy there was one perforation (0.1/100) relating to snare polypectomy and 12 were admitted to hospital for bleeding (eight after polypectomy) (Aitken 1998). Six people died within 30 days of FS, three relating to myocardial infarction at 6, 15 and 26 days and one case each of cardiomyopathy (next day), intracerebral haemorrhage (7 days) and lung cancer (18 days). In the 5% of subjects referred for colonoscopy because of high-risk distal polyps, there were 4 perforations, all associated with polypectomy, three requiring surgery. There was one death within 30 days of colonoscopy as a consequence of myocardial infarction. In the Italian trial among the 9911 subjects undergoing FS there was one perforation (0.1/1000) and among the 775 who underwent colonoscopy there was one perforation and one episode of bleeding post polypectomy (both 1.3/1000). These adverse events are further detailed in Appendix 2.

Test limitations
The chief limitation pertains to the fact that only the distal bowel is examined and the portion examined is influenced by both the adequacy of enema preparation and anatomical/technical factors that can vary between subjects. In the Italian multicentre FS trial the FS could be completed beyond the sigmoid descending junction under adequate bowel preparation on a single occasion in 7077 of 9999 attendees ie, 79.8%. Among the remaining 2022 subjects the examination was terminated because of pain or bowel adhesions in 749 subjects and unsatisfactory bowel preparation resulted in partial visualisation of the colonic mucosa in another 650. A further 623 subjects had bowel preparation that was so inadequate that no segment of the bowel mucosa could be visualised and a further test had to be offered. In addition cancers in the unexamined more proximal bowel will not be detected. The detection of distal adenomas is associated with the presence of a proximal cancer and follow-on colonoscopy for such subjects increases the number of CRCs detected but not all proximal cancers will have distal adenomas and 30-40% of cancers present at the time of the FS will still be missed.

Colonoscopy as first-line screening

Test description
Colonoscopy is a procedure in which a fibre-optic instrument containing a tiny video camera is inserted into the rectum and steered for about 70-100 cm around the colon until it reaches the end of the small intestine. The interior of the bowel is viewed on a video monitor for polyps or cancers. If polyps are discovered, they are removed by a diathermy current and sent for biopsy report. If cancers are discovered they are simply biopsied for confirmation of their cancerous nature and the patient is referred to a surgeon to discuss operative removal. Colonoscopy is done under conscious sedation using intravenous drugs. Prior to colonoscopy there is a period of dietary restriction (avoiding seeds and nuts) and liquids only are allowed on the day prior. Oral laxatives with lots of water to drink are given to cleanse the bowel prior to the procedure. After resting for an hour after the procedure and having some food, the majority of individuals feel well and are able to go home. Driving is not permitted for 8 hours after the procedure.

Simplicity/acceptability
No one would argue that colonoscopy is a simple screening procedure. It involves bowel preparation, conscious sedation, time off work and a small element of risk. In the last 5 years, however, colonoscopy has become increasingly popular as a primary screening test for CRC. This is because its accuracy as a once-only test is superior to all other testing modalities. Acceptability varies widely according to an individual's perception of personal risk. This in turn may be influenced by knowledge about CRC or experience of friends or relatives who have developed CRC. Acceptability increases after a positive faecal occult blood screening test or after radio or television programmes, especially those promoted by well-known celebrities (Cram et al 2003).

Sensitivity of the test
Sensitivity of colonoscopy for detection of CRC is > 95% (Eddy 1990) and for detection of advanced adenomas is about 90%. This compares with about 50% and 12% for CRC and adenoma detection by FOBTg and FOBTi tests (Ransohoff and Lang 1997). Flexible sigmoidoscopy (FS) and barium enema have intermediate sensitivities. CT colonography (see later) compares reasonably favourably with colonoscopy. Because colonoscopy has high sensitivity for polyp detection, it has the potential to reduce the incidence of CRC in the screened population rather than simply to detect cancers earlier. This would seem to be a major advantage of colonoscopy screening over the less invasive methods such as FOBTg and FOBTi.

Tandem colonoscopy studies (Hixon et al 1991, Rex et al 1997, van Rijn et al 2006) have shown that it is very unusual to miss significant pathology (cancers and large polyps). It is not always possible to visualise the caecum; and missed cancers may result if further investigations such as double contrast barium enema or CT colonography are not performed. Sensitivity is thus operator dependent. About 1 in 110 individuals with polyps who have had a clearing colonoscopy will develop CRC within 3 years. Causes include: missed polyps, missed depressed or flat adenomas, rapidly progressing new cancers, incomplete removal of polyps or a false negative biopsy result (Pabby et al 2005).

Specificity of the test
The specificity of colonoscopy approaches 100%. This can be compared with 96% for FOBTg tests (4% will have a positive FOBT and negative colonoscopy) and 88-96% for FOBTi (4-12% false positive tests) depending on the sensitivity settings of the laboratory test procedure (Young 1998).

Safety of the test
The safety of colonoscopy varies with operator experience and the acceptability of the risks associated with this procedure can vary depending on whether the procedure is performed for diagnostic purposes in patients with symptoms, or as part of a screening programme in asymptomatic individuals. Since there are no randomised trials of primary colonoscopy screening, complication rates for colonoscopy in a randomly selected screened population come from the three FOBT RCTs where colonoscopy was performed as the follow up investigation for those with a positive test. The death rate from colonoscopy was 1/14720. Bleeding and

perforation rates were 1/1143 and 1/1524 respectively. Population surveillance by colonoscopy in the Telemark polyp study (Thiis-Evensen et al 1999) reported no endoscopic complications in 788 colonoscopies including 1734 polypectomies. There were only two experienced endoscopists performing these procedures. In a large Japanese study (Morikawa et al 2005), there were no serious complications in over 21,000 colonoscopies, where no therapeutic procedures (polypectomies) were performed. Endoscopists in this study had each performed more than 3000 previous procedures. These figures for screening and surveillance colonoscopy contrast with meta-analyses of diagnostic and therapeutic colonoscopies reporting severe complications in 0.2% after diagnostic and 1-2% after therapeutic colonoscopy.

Test limitations
Apart from the potential risks of screening colonoscopy, the main disadvantages are the need for dietary restriction and bowel cleansing, time off work to undergo the procedure, the cost of the procedure and the lack of sufficient trained endoscopists and assistants to increase colonoscopy capacity to meet the requirements of a screening programme. Furthermore, more than one screening colonoscopy in a lifetime has been recommended.

Participants in FOBT screening programmes may also be subjected to the inconveniences and risks of colonoscopy as this is the follow-up diagnostic investigation for those identified to have a positive FOBT. Some individuals who adhere to regular FOBT testing starting at age 50 years, by age 85 may have undergone one or more colonoscopies because of false positive FOBTs (Winawer et al 1997).

The one-off performance of a screening test such as colonoscopy is not the only issue relevant to population screening. Annual or biennial FOBT testing may provide multiple chances to detect lesions, increasing overall programme sensitivity. If colonoscopy is only repeated 10 yearly, then fast growing cancers might be missed. These may be picked up by more frequent test procedures such as 5 yearly FS plus annual or biennial FOBT or even biennial FOBT alone. Some have argued that the absolute risk of dying from CRC by the age of 75 years (2%) would have to be markedly reduced by colonoscopy screening to offset the cumulative risks of repeated colonoscopy (Ransohoff 2005).

Quality issues in colonoscopy screening
Colonoscopy is the final common pathway for all screening modalities. The quality issues surrounding colonoscopy (Lieberman 2005) and the training of colonoscopists needs to be a priority for any agency charged with responsibility for CRC population screening.

Other potential modalities

Virtual colonoscopy
Test description
Virtual colonoscopy (VC) or computed tomographic (CT) colonography allows the creation of a two- or three-dimensional image of the colon enabling a 'fly through' moving picture, simulating conventional optical colonoscopy. The data is obtained from rapid helical CT scanning of the abdomen. Unlike conventional colonoscopy the data is able to be double read which increases sensitivity at no additional risk to the patient.

Simplicity/acceptability of the test
The procedure itself is quick, requires no IV sedation, and patients can return to regular activity directly after the scan is completed. It allows imaging of both the outside and inside of the bowel as well as providing images of neighbouring organs. Where conventional colonoscopy sometimes fails to examine the whole colon due to technical factors or obstruction, CT colonography still provides a complete examination. Patients must still undergo rigorous bowel preparation similar to that for conventional colonoscopy, have air pumped into the bowel, are exposed to radiation and if a lesion is detected must undergo conventional colonoscopy to biopsy or resect the lesion. This might be required in up to 20% of cases. Currently, CT colonography is less expensive than conventional colonoscopy and requires on average 15 minutes of radiologist's reporting time for each study. Double reporting advocated for screening procedures would increase costs. Acceptability would be improved if bowel preparation could be avoided. Early reports of successful imaging using faecal markers in unprepared bowel raise this prospect (Iannaconne 2004).

Sensitivity of the test
Early reports suggested high sensitivity for polyps > 1 cm in diameter (Fenlon 1999). Other studies report lower sensitivities around 46-59% (Johnson 2003). A comprehensive same day study shows comparable sensitivity and specificity for CTC and conventional colonoscopy (Pickhardt 2003). Most recently, in a large study of screening CT colonography in average risk individuals, using oral contrast to tag luminal contents and experienced radiologists using multi-detector CT scanners, sensitivities for polyps > 1cm was reported to be 94%, accuracy comparable to conventional colonoscopy. Furthermore the same authors developed a software program called CAD (computer aided polyp detection system) which had 89% sensitivity (Summers 2005). Sensitivities for polyps smaller than 1cm are generally much lower.

Specificity of the test
Specificities are reported to be 92% for polyps <6mm 97% for polyps >9mm in a meta-analysis (Mulhall 2005). However using the CAD system the false positive rate was 2.1 (95% CI, 2.0-2.2) for polyps >10mm and 6.7% for polyps <8mm (Summers 2005). Should computer reporting become established it would remain to be seen how "well" radiologists would reinterpret the computer hits, thereby maintaining high specificity.

Safety of the test

Aside from the radiation exposure, CT colonography is regarded as a very safe procedure without complications from sedation and the instrumentation aspects of optical colonoscopy. It can also be perfomed safely on anticoagulated patients. However, CT colonography identifies lesions outside the bowel in a significant proportion of studies (eg, liver and kidney cysts), that may require further expensive and sometimes invasive procedures to establish the benign nature of such lesions (most of which are benign). This is definitely a disadavantage when CTC is used as a screening test for bowel cancer and polyps.

Test limitations

Limitations of CT colonography include the lower sensitivity for detection of polyps < 5mm, the requirement for bowel preparation and possibly contrast ingestion and the need for follow-on optical colonoscopy in all those with positive findings, which could approach 20%. Most gastroenterologists prefer the option of direct screening with optical colonoscopy, which allows direct biopsy or resection of lesions at the same time as the procedure. CT colonography is regarded as a useful adjunct when colonoscopy is incomplete or impossible because of bowel obstruction. Since colonoscopy resources are limited however, CT colonography screening could increase overall screening capacity at a lower cost than conventional colonoscopy, and appropriate resources in terms of multislice CT scanners are already widely available in NZ.

Conclusions

CT colonography has the potential to become a viable option for primary or secondary (those with positive FOBT screening tests) colorectal cancer screening. It is now a recognised and proven technique but its niche in the diagnosis and screening of colorectal disease is still being established. It might increase screening compliance for some individuals who reject conventional colonoscopy. It is likely that its widespread use would lead to an increase in requirement for conventional colonoscopy resources to follow up those with positive findings (Bond 2005).

An independent report on CT colonography by the NZ branch of the Royal Australian and New Zealand College of Radiologists (RANZCR) is provided in Appendix 5.

DNA testing of stool for mutations of APC, K-ras, p53 and BAT-26 genes has also been studied, but the relatively poor sensitivity (52–74%) and high cost have made this modality impracticable at present (Ouyang 2005).

Conclusion: There is a range of available tests but there are limitations to each one. Those with greatest potential at present are two faecal occult blood tests (FOBTg and FOBTi), flexible sigmoidoscopy and colonoscopy.

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3. IS THERE AN EFFECTIVE AND ACCESSIBLE TREATMENT FOR CRC DETECTED AT AN EARLY STAGE?

Criterion 3. There is an effective and accessible treatment or intervention for the condition identified through early detection.

There should be evidence that early treatment leads to better outcomes than late treatment. There should be agreed evidence-based policies outlining which individuals should be offered treatment and the appropriate treatment to be offered (National Health Committee 2003).

The main forms of treatment for CRC are:
- surgery
- radiation and chemotherapy in conjunction with surgery (adjuvant therapy).

This section focuses on the effectiveness of these modalities and their current availability in New Zealand. Questions of accessibility are explored in more depth in Section 6, which addresses the capacity of the health system to support a CRC screening programme.

Surgery
The primary treatment of colorectal cancer is the surgical removal of the tumour with any regional spread. The outcome of this procedure is determined predominantly by the stage of the tumour at that time. Patients with early stage disease can expect long-term survival with surgery alone. At present there is access to surgery for colorectal cancer throughout New Zealand but outcomes especially for rectal cancer may vary. (McArdle 1991, Robinson 2005, Bissett 2000, Hoffmann 1997, The Lothian Large Bowel Cancer Project 1995). This is addressed in more detail in Section 6.

Radiation and chemotherapy
Radiation and chemotherapy are widely used both to improve quality-of-life-adjusted survival in patients who develop incurable disease and to increase the rate of cure in those with surgically curable cancers.

This discussion focuses on radiation and chemotherapy used in conjunction with surgery for potentially curable, but at-risk groups of patients (e.g., those with low-rectal cancers or with Dukes' stage B and C disease). This is referred to as **adjuvant** therapy.

Adjuvant radiation therapy
Based on the higher rates of local recurrence with rectal cancers and the low risk of local recurrence with colon cancers, adjuvant radiation therapy is generally used only in (selected) patients with rectal cancers. Historically, radiation was administered post-operatively to reduce the risk of local recurrence for high-risk (Dukes' B and C) tumours – recurrence being an outcome that is devastating in terms of pain management in the palliative setting. Despite the impact on local recurrence, post-

operative radiation has never been shown to increase survival (NHMRC CRC guideline chapter 16.8 p.178). With subsequent research suggesting that post-operative radiation impaired long-term rectal function, pre-operative administration of radiation was investigated and subsequently found to be as effective with less adverse effects than post-operative radiation (Sauer R, Becker H, Honenberger W, et al 2004).

On this background of research there has also been a significant improvement in surgical technique over the last 30 years such that local recurrence rates with surgery alone have generally declined from over 30% to under 10% (NHMRC CRC guideline; Chapter 12 page 125). Further research has indicated that those at greatest risk of local recurrence after modern surgery are those with low rectal tumours or where the tumour extends to the fascia propria on preoperative MRI (Bissett et al 2001; Adam et al 1994). Radiation is therefore indicated in these scenarios.

Adjuvant chemotherapy
Metastatic spread of cancer is the major cause of mortality in most common epithelial cancers including colorectal cancer. Approximately 20% of patients with colorectal cancer will have obvious metastatic disease at first presentation. Following curative surgery in those with no obvious secondary disease however, about 50% of Dukes' C and 25% of Dukes' B stage patients will still ultimately relapse.

Palliative chemotherapy for those who present with metastatic disease and for those who relapse after presentation with earlier stages of disease has been shown to improve survival (Damjanovic et al 2004). Drugs such as 5-fluorouracil, irinotecan and oxaliplatin are widely used in this setting with newer agents such as bevacizumab and cetuximab awaiting funding approval (Damjanovic et al 2004).

New chemotherapy agents are first tested in the palliative setting so there is an apparent lag in the use of these agents in the adjuvant setting. At present therefore only 5-fluorouracil (5FU) is widely used after curative surgery and it has been shown to reduce the risk of death from colon cancer such that for Dukes' C patients the 5 year survival rate increases from ~ 50% to ~ 60-65%. (Moertel et al 1990) Early reports of longer term follow-up of such studies show these survival differences are sustained and possibly increasing (O'Connell et al 2005).
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A recently reported large RCT has confirmed a survival benefit for patients with Dukes B disease given adjuvant 5-FU chemotherapy (Gray et al 2004). Current practice however would be to offer adjuvant chemotherapy to those with 'high-risk' Dukes' B tumours (e.g., obstruction or perforation at presentation; high proliferative index, insufficient lymph node harvest, etc) (NHMRC CRC Guidelines p.168).

Two recent RCTs have shown a further improvement in outcomes, with an increase in three-year disease-free survival (DFS) by adding a second chemotherapy agent oxaliplatin to 5FU (Andre et al 2004; Wolmark et al 2005). Oxaliplatin, while

approved for use in New Zealand, has not as yet been funded for this purpose.

In summary there is simple adjuvant chemotherapy available in New Zealand that makes a difference to outcomes following resection of colorectal cancer. The migration to lower-risk stages with a screening programme may reduce the number of Dukes C patients needing treatment although it is unclear what impact there will be on the number of high-risk Dukes B tumours requiring chemotherapy. In the future drugs such as oxaliplatin and newer drugs that show activity in the palliative setting (bevacizumab, cetuximab) may further improve survival for Dukes' B and C patients and their introduction should be anticipated.

Treatment outcomes for Māori
Whether treatment of CRC detected through a screening programme would lead to an improved outcome for Māori is a question that needs further analysis. Inequitable outcomes are indicated in a recent chartbook of Māori and non-Māori cancer statistics (Robson et al 2006) (see section1), which analyses differences in cancer incidence, mortality, stage at diagnosis and survival in Aotearoa/New Zealand, using national cancer registrations and mortality data for the six-year period 1996–2001 (inclusive).

Colorectal cancer was more common among non-Māori than Māori, but mortality rates were similar for both populations. Māori males had a lower likelihood of being diagnosed with CRC than non-Māori females but a higher risk of death from CRC.

Stage at diagnosis was unknown for a higher proportion of Māori colorectal cancer registrations (16%) compared with non-Māori (10%). Around 40% were diagnosed at a regional stage of disease spread. Māori were significantly less likely than non-Māori to be diagnosed at a localised stage. The odds of Māori being diagnosed when the disease had spread (distant stage) were two-thirds more than for non-Māori.

Once diagnosed with colorectal cancer, Māori were two-thirds more likely than non-Māori to die from their cancer. Half the survival disparity can be attributed to differences in stage at diagnosis. The higher risk of death was significant among those diagnosed at a localised or regional stage, and among those whose stage at diagnosis was not recorded.

In summary, non-Māori had excess rates of colorectal cancer but, once diagnosed, were less likely than Māori to die from their cancer. Non-Māori were more likely than Māori to be diagnosed at an earlier stage of disease spread, but significant survival disparities exist among those diagnosed at a localised and regional stage. Colorectal cancer is an important cancer for both Māori and non-Māori. The reasons for disparate outcomes should be investigated, including differential access to diagnostic and staging services, and treatment pathways.

Conclusion: CRC detected and treated at an early stage has an improved prognosis. There is access to surgery (the primary treatment) for colorectal cancer throughout New Zealand, but outcomes may vary, especially for rectal cancer. For potentially curable but at-risk groups of patients with CRC, chemotherapy and radiotherapy used in conjunction with surgery improves outcomes and is available in New Zealand. The increase in CRC mortality rates for Maori between 1980 and 2001 could reflect both physical and cultural barriers to treatment. Treatment of CRC identified at an early stage through screening can lead to a better outcome, provided that the health system has the capacity to support it and the programme is designed to minimise or avoid inequalities.

4. IS THERE HIGH QUALITY EVIDENCE FOR THE EFFECTIVENESS OF A CRC SCREENING PROGRAMME?

Criterion 4. There is high quality evidence, ideally from randomised controlled trials, that a screening programme is effective in reducing mortality or morbidity.

A high standard of evidence is needed because screening is actively promoted to healthy populations and has the potential for causing harm. The best level of evidence comes from randomised controlled trials (RCTs), which can control for critical potential biases (National Health Committee 2003).

This section reviews the evidence for the effectiveness of population-based screening programmes to reduce CRC mortality. It also includes information from pilot screening programmes which addresses whether a programme can be successfully implemented in practice. It focuses on the four viable screening tests identified in Section 2: guaiac faecal occult blood testing, immunochemical faecal blood testing, flexible sigmoidoscopy and colonoscopy. Of particular interest is evidence from randomised controlled trials but for many of the proposed screening tests this information is limited or not currently available.

Evidence for the effectiveness of guaiac faecal occult blood testing
The potential to reduce CRC mortality with faecal occult blood testing has been demonstrated in two randomised controlled trials in Nottingham, England and Funen, Denmark, which were considered by the working party in 1998. While no further randomised controlled trial evidence in relation to CRC screening by any modality has been published since 1998, follow-up data in relation to both trials are available (see Appendix 1) with a reported CRC mortality reduction of 13% in the Nottingham study (after 11.7 years and 3-6 screening rounds) and of 11% in the Funen study (after 17 years and 9 screening rounds).

The mortality reduction decreased slightly with time in the Nottingham trial (15% to 13%), but more so in the Funen trial (18% to 11%) where screening has continued to be offered. It is therefore unclear whether the magnitude of benefit shown by the trials can be maintained over time.

Reasons for declining numbers screened at each round in the Funen RCT
In the Funen RCT 67% of those invited attended the first screening round. Only these subjects were re-invited to subsequent rounds. By the 9th round only those subjects who had participated in all 8 previous rounds and had not been diagnosed with colorectal neoplasia were invited. The decline in numbers screened per round in the Funen trial (see Table 4.1 below) occurred for several reasons:

(a) Some people were out of the eligible age-range (in the 1st round the mean age was 59.8 years but by the 9th round the mean age was 73 years).
(b) Some people had died (by the 9th round, only 78% were still alive).
(c) Some people had been diagnosed with CRC (see Table 4.1 below).

(d) Some people were diagnosed with adenomas and therefore were referred for colonoscopic surveillance (see Table 4.1 below).

(e) Some people declined further invitations for screening. Only 67% participated initially. These people were re-invited to subsequent screening rounds, but by round 9, for the reasons outlined in (a) to (d) above, only 9,367 were invited and 8,558 (91%) participated.

Table 4.1: Participation and results of 9 rounds in Funen RCT

Round	Number screened	Mean age	Adenoma 10mm+ (rate per 1,000 screened)	CRC (rate per 1,000 screened)
1	20,672	58.8	68 (3.3)	37 (1.8)
2	18,781	60.5	61 (3.2)	13 (0.7)
3	17,279	62.2	41 (2.4)	24 (2.4)
4	15,845	63.8	44 (2.8)	21 (1.3)
5	14,203	65.2	56 (3.9)	23 (1.6)
6	12,533	66.6	70 (5.6)	25 (2.0)
7	11,058	68.0	29 (2.6)	13 (1.2)
8	9,774	69.3	23 (2.4)	21 (2.1)
9	8,558	70.7	27 (3.2)	20 (2.3)

Note that this table reports results for the Funen RCT, which was a *closed cohort*. In a population screening programme, new people would become eligible and be invited for screening, so the first two screening rounds may be similar to rounds 1 and 2 above, but subsequent rounds would be likely to resemble round 2 (the mean age and detection rates would not be expected to increase).
(Ref: Kronberg et al 2004)

The longer follow-up was reassuring in reporting low complication rates from colonoscopic follow-up of positive FOBT results.

A recent paper (Moayyedi and Achkar 2006) reports the results of a meta-analysis of the Minnesota (biennial screening results only), Funen and Nottingham RCTs, with the authors suggesting that FOBT screening has no impact on overall mortality as there is an increase in deaths from other causes. This analysis produced the following results (see Table 4.2):

Table 4.2

Outcome	Minnesota RR (95% CI)	Funen RR (95% CI)	Nottingham RR (95% CI)	Combined RR (95% CI)
CRC mortality	0.96 (0.75 to 1.24)	0.86 (0.73 to 1.00)	0.87 (0.78 to 0.97)	0.87 (0.80 to 0.95)
Non-CRC mortality	1.01 (0.96 to 1.05)	1.01 (0.98 to 1.03)	1.03 (1.01 to 1.05)	1.02 (1.00 to 1.04)
All-cause mortality	1.00 (0.96 to 1.05)	1.00 (0.98 to 1.03)	1.00 (0.99 to 1.02)	1.00 (0.99 to 1.02)

They provide three possible explanations assuming this is not a chance finding: (1) people whose deaths from CRC have been avoided die rapidly of other causes (the overall life-years saved are very modest), (2) the CRC mortality estimates are biased, leading to underestimation of CRC deaths and overestimation of deaths from other causes in the intervention group, (3) FOBT screening causes a real increase in non-CRC deaths.

There are some major limitations to this analysis, which mean that the conclusions drawn by Moayyedi and Achkar should be treated with caution. Most importantly, there is an error in the result for non-CRC mortality in this paper. The correct result for non-CRC mortality in the Nottingham RCT is RR = 1.01 (95% CI 0.99 - 1.02), in other words no statistically significant difference between the screening and control groups. When this error is corrected, the combined result for non-CRC mortality is RR = 1.01 (95% CI 0.99 - 1.02). The corrected result for the Nottingham trial is consistent with the published results from this trial which reported "no statistically significant difference in mortality from causes other than CRC between the intervention and control groups" (Scholefield et al 2002).

The issue of a significant reduction in CRC mortality but no reduction in all-cause mortality is not a new debate (Black et al 2002, Gail and Katki 2002, Weiss and Koepsell 2002, Begg and Bach 2002). Given the size of the trials, because CRC accounts for only about 3 to 4% of mortality overall in these trials, a reduction in CRC mortality could not be expected to produce a detectable reduction in all-cause mortality.

UK Colorectal Cancer Screening Pilot
The UK Colorectal Cancer Screening Pilot was established to determine the feasibility of screening for colorectal cancer in the UK using faecal occult blood testing. One of its key purposes was to determine whether outcomes achieved in the trial settings could be matched in population-based programmes (The UK CRC Screening Pilot Evaluation Team 2003).

The pilot had two sites, one in central England (two health authorities) and the other in Scotland (three health authorities). Evaluation of the first round of screening was undertaken by an independent, multi-disciplinary team which measured performance against benchmarks derived from the Nottingham trial. The evaluation also examined psychosocial and ethnicity issues related to acceptability and uptake of screening, the impact of screening on routine services, stakeholders' attitudes to screening, and the health economics of screening (The UK CRC Screening Pilot Group 2004). Details are provided in the final report of the evaluation group (The UK CRC Screening Pilot Evaluation Team 2003).

Key features and results of the pilot are presented in Appendix 1. Overall the results of the pilot compared favourably with the results of the Nottingham trial, leading evaluators to conclude that the benefits observed in the RCTs of FOBT screening are achievable in a national programme (The UK CRC Screening Pilot Evaluation Team 2003). Some of the key issues for a national roll-out identified by the screening team are:

- the need to reconsider the appropriate screening age range
- the likely impact of a screening programme on already overstretched endoscopy services
- the 10% participants with a positive result who did not have follow-up colonoscopy
- the 50% sensitivity of FOBT in a screening context, resulting in half of cancers being missed.

Following the pilot study results, England plans to introduce a national bowel cancer screening programme over three years for people aged 60-69 years. Once national coverage has been achieved the programme may be expanded to a wider age group. Scotland is planning roll-out of a national programme from 2007 onwards inviting all men and women aged 50-74 years registered with a GP.

Evidence for the effectiveness of immunochemical FOBT
The characteristics of FOBTi as a screening test for colorectal cancer have been described in Section 2. There has not been a randomised controlled trial of FOBTi screening for colorectal cancer, but because FOBTi is a type of faecal occult blood test, assumptions have been made based on the results of the randomised controlled trials that used FOBTg to screen for CRC. It has been assumed that since both screening tests detect colorectal cancer from the presence of blood in the faeces, FOBTi will be superior because it detects human blood specifically (rather than blood from ingested meat and peroxidases of ingested plant origin). This means that dietary restrictions are not required. Comparison studies have shown that in certain circumstances FOBTi can provide higher sensitivity than FOBTg, and has similar acceptability (see Section 2). For these reasons, it is assumed that FOBTi will produce a greater mortality reduction than FOBTg.

Australian Bowel Cancer Screening Pilot Programme
The Australian Bowel Cancer Screening Pilot Programme established in 2002 was designed to provide information about the feasibility, acceptability and cost effectiveness of bowel cancer among the Australian population in both rural and urban areas (Australian Govt Dept of Health and Ageing 2004 and 2005). The pilot also compared the performance of two types of immunochemical FOBTs – only one round of screening took place during the pilot. Its overall purpose was to inform decisions about the planning and introduction of a national bowel cancer screening programme in Australia.

Key documentation in relation to the pilot includes the final evaluation report (Australian Government 2005), the analysis of screening data routinely collected and stored in a Bowel Cancer Screening Pilot Register (Aust Govt 2004: Bowel Cancer Screening Pilot Monitoring and Evaluation Steering Committee) and a qualitative study to assess attitudes, opinions and behaviours that influenced participation and non-participation in the pilot (Aust Govt 2004: Bowel Cancer Screening Pilot Monitoring and Evaluation Steering Committee).

The pilot programme offered biennial screening with FOBTi (two types of FOBTi were used so that they could be compared) to people aged 55–74. Eligible people were identified using Medicare enrolment files (this was not a complete population register, but was called 'the register' for the purposes of the pilot), and were sent an invitation to participate in screening. The Medicare register identified most of the eligible people, but some invitations were sent to people who had died and some to people who already had colorectal cancer. It was suggested that the register should avoid this by matching against death records and cancer registries. The letter of invitation included information and an FOBTi kit. Those with symptoms and/or a family history of colorectal cancer were advised to visit their GPs. The remaining participants used the FOBTi and forwarded the completed tests directly to a pathology laboratory. The laboratories notified participants, the nominated GP, and the screening register of the results. Those with negative FOBTi results will be re-invited for FOBTi screening in 2 years. Those with positive results were asked to see their GPs for referral for further diagnostic investigation (colonoscopy). Not all patients with positive FOBTi results visited their GPs (62.1% visited their GPs following a positive FOBTi), or sought colonoscopy. Some people sought colonoscopy without seeing their GPs (although it is difficult to know how many because of missing data). The proportion of people proceeding to colonoscopy following referral by a GP was 65.1%. For those people, there was a median waiting time of 30 days between the GP consultation and a follow-up. Those with positive colonoscopy results were referred for appropriate treatment. Those with negative colonoscopy results will be re-invited for FOBTi screening in 5 years.

In this pilot, unlike that for the UK, general practitioners had an important role, which included advising patients who had received invitations, those who had positive FOBTi results, and those requiring colonoscopy. GPs favoured the use of electronic forms for collection and transfer of information to the register.

Key evaluation findings and implications for New Zealand are as follows:

- The overall participation rate was 45.4%.
- Participation according to age, gender and ethnic group may be different in New Zealand.
- Background rates of screening colonoscopy are higher in Australia than in New Zealand, and this may have affected participation in the pilot (a major reason for not taking part in the pilot was 'already had other bowel tests').
- The Australian pilot included only one screening round, so participation at re-screening is unknown.
- More information on health promotion and ways to increase participation would be useful.
- The invitation process and type of FOBTi were both acceptable.
- Of the correctly completed, valid FOBTis, 9% were positive.
- There was some pressure on colonoscopy services, which were generally well-managed.
- In the event of a national programme there remain questions about
  - the impact of large numbers of colonoscopies on current health system structures
  - how to achieve adequate quality assurance of colonoscopy performance and the number of appropriately skilled colonoscopists required.
- In light of the impact of the pilot on pathology services, it was suggested that greater use of electronic data transfer between laboratories and the screening register should be made.
- There was significant loss to follow-up with incomplete records for many pilot participants (Australian Govt Report 2005). Of concern, this meant the Australian pilot was unable to accurately report on invasive cancers detected.
- There were 'no routine quality control processes for data collection, except for reminder letters issued by the Register'.
- Appropriate information systems would be required for FOBT screening in New Zealand.

Evidence for the effectiveness of flexible sigmoidoscopy
Two parallel multicentre randomised controlled trials were undertaken in 14 centres in the United Kingdom and 6 centres in Italy. Their purpose was to measure the extent of reduction in CRC incidence and mortality by a single screening sigmoidoscopy examination at around the age of 60 years and to determine both the optimum age interval for screening and the duration of the protective effective of a single test (Segnan et al 2002). To increase compliance rates and the statistical power of the study potentially eligible individuals were enrolled in the trial and randomised only if they responded positively to a questionnaire asking if they would be likely to accept the offer of screening. This design impacts on the external validity of the study particularly with regard to anticipated participation rates when offered to the general population (see Appendix 1). The overall participation rate was 39%.

The recruitment and screening phases of the trial have been completed, with baseline results (summarised in Appendix 1) having been reported by both the UK

(UK Flexible Sigmoidoscopy Screening Trial Investigators 2002 - summarised in Appendix 1) and the Italian centres (Segnan et al 2002).

In the UK trial, of the 354,262 questionnaires apparently delivered, 262,841 (70%) replied and of these 194,726 (55%) responded that they were interested. After exclusions for ineligibility and numbers excess to study requirements 170,432 were randomised with 57,254 being invited for screening. Of these, 40,674 (71%) attended for screening and 2131 (5%) were identified to have high risk polyps (> or equal to 1cm in size, three or more adenomas, tubulovillous or villous histology, severe dysplasia or malignancy) and referred for colonoscopy. Overall, distal adenomas were detected in 4931 (12.1%) and distal cancer in 131 (0.3%). In those undergoing colonoscopy proximal adenomas were detected in 386 (18.8%) and proximal cancer in nine cases (0.4%). Of the cancers detected 62% were Dukes A or locally excised. An average number of 48 people were screened per week with two to three colonoscopy referrals per week.

These limited baseline results suggest that the screening regimen gives a high yield of neoplasia (3.5/1000 screened UK trial, 5.4/1000 screened Italian trial) and is acceptable and feasible. The neoplasia yield could be anticipated to reduce both the incidence and mortality of CRC in the group offered screening but it will be some years until the extent of reduction in CRC incidence and mortality can be measured. These results are required before the appropriateness or feasibility of screening flexible sigmoidoscopy for CRC in New Zealand could be considered.

Evidence for the effectiveness of colonoscopy
There is, as yet, no RCT evidence that a population-based programme of screening colonoscopy would reduce CRC mortality. RCTs of FS screening are in progress, and if substantial reductions in mortality are observed, it will be hard to argue that screening colonoscopy would not produce even more substantial benefit. However, if RCT evidence for efficacy is *sine qua non* for a population-based screening programme then colonoscopy as first-line screening could not be implemented for many years.

A randomised controlled trial of one-off colonoscopy is proposed in Scandinavia, but any information on mortality reduction will again be many years away (Hoff and Bretthauer 2006).

The Cleveland Clinic (Mehran et al 2003) reported the yield of lesions found at screening colonoscopy in average risk 50-59 year olds. Polyps were found in 58%, but only 2.2% were high grade and 2.2% were cancerous. Colonoscopy screening in asymptomatic US veterans reported point prevalence rates of 1%, 10.5% and 36.5% for CRC, advanced neoplasia and overall adenomas (Lieberman et al 2005). Another study (Imperiale et al 2002) reported a 4.1% incidence of advanced neoplasia in over 1500 screening colonoscopies in asymptomatic 40-49 year old persons. A more recent study from Israel of colorectal neoplasia detected by colonoscopy in average risk individuals aged 40-80 years report in the 50-75 age

group a prevalence rate of 1.2%, 6.7% and 20.9% for CRC, advanced neoplasia and overall adenomas (Strul et al 2006).

Colonoscopy was performed soon after a screening FOBTi test in a large Japanese study (Morikawa et al 2005) involving nearly 22,000 asymptomatic adults. Overall incidence of neoplasia was 19.8%, of advanced neoplasia was 3.33% and of invasive cancer was 0.36%. In those with a positive FOBTi the yields were 57.4%, 25% and 6.6% respectively. While the yields were much greater in those with a positive FOBTi, the sensitivities for one-off FOBTi were only 27.1% for advanced neoplasia and 65.8% for invasive cancer, with significantly lower sensitivity for proximal than distal lesions.

Table 4.3: Estimated benefits (colorectal cancer mortality reduction) with each modality

	FOBTg	FOBTi	Flexible sigmoidoscopy	Colonoscopy
RCT evidence of reduction in mortality	15%	n/a	n/a	n/a
Programme specification	45/50-74 yrs Biennial Not rehydrated	55-74 yrs Biennial (Australian pilot)	One-off flexible sigmoidoscopy for those aged 55-64 yrs	One-off colonoscopy at age 60 yrs
Expected participation	>60% (based on population RCTs)	> 45% (based on Australian pilot)	In multicentre RCT 55% agreed to randomisation and 71% participated (39%)	Unknown

Conclusion: The only modality for which there is RCT evidence is guaiac FOBT. However, there are limitations of this test; in particular 50% of cancers will be missed because of its low sensitivity. A separate shortcoming of guaiac FOBT is difficulty with interpretation and quality control. Comparisons between FOBTg and FOBTi have shown that FOBTi has a higher analytical sensitivity to detect faecal blood. It is therefore assumed that it will achieve at least the same or greater reduction in mortality within an organised screening programme, although no RCT data are available to test this assumption. Further evidence from studies in progress is required before the appropriateness or feasibility of a flexible sigmoidoscopy screening programme could be considered in New Zealand. Similarly, further consideration with regard to screening by colonoscopy should be deferred until the results of randomised controlled trials assessing participation, feasibility, safety and mortality reduction are available.

5. DOES THE POTENTIAL BENEFIT OF CRC SCREENING OUTWEIGH THE POTENTIAL HARM?

Criterion 5. The potential benefit from the screening programme should outweigh the potential physical and psychological harm (caused by the test, diagnostic procedures and treatment).

The screening programme should ensure that the benefit is maximised and the harm minimised. An assessment should be made of whether this is both a net benefit to the population and that individual participants can reasonably expect more benefit than harm from screening (National Health Committee 2003).

Screening differs from other health services, in that apparently healthy individuals are invited or encouraged to participate on the understanding that it can benefit them; in general, they have not approached the health system for help. Thus the health system has an obligation to minimise the potential physical and psychological harms associated with screening. Identifying and trying to quantify these harms is as important as calculating expected benefits (Kerr et al, 2005).

Section 4 has explored the benefits of a screening programme in terms of its effectiveness, and Section 8 conducts a more wide-ranging cost–benefit analysis. Both physical and psychological harms are discussed in this section.

Physical harm
A key concern of the 1998 working party was the potential harm associated with colonoscopy for investigation following a positive FOBT. At the time there was limited information available on the harms associated with screening (as compared with diagnostic) colonoscopy. Applying available data from the Nottingham and Funen trials, the 1998 working party estimated that of every 10 people proceeding to colonoscopy because of a positive FOBT, six would be investigated for false-positive results. These people would be exposed to the inconvenience and discomfort of a procedure with a perforation risk of 0.045 percent to 0.17 percent and a mortality rate of possibly 0.02 percent. The 1998 report also identified a range of potential positive and negative psychological consequences associated with screening for CRC. Based on the limited information available, the working party concluded that CRC screening using FOBTg had a 'small but real potential for harm'.

The Advisory Group has been reassured by the more recent available data from the UK pilots (i.e., in a healthy screened population) – in particular, the absence of colonoscopy-related deaths. Nevertheless, the group acknowledges that colonoscopy (and sigmoidoscopy) complication rates relating to perforation and haemorrhage with the rare but possible consequence of death will always be dependent on the level of expertise of the operator. Quality controls and workforce training therefore would have to be in place for any colonoscopy performed as part of a screening programme. This is even more so if flexible sigmoidoscopy or colonoscopy is used as the first-line screening modality.

Authors of the published baseline findings of the UK RCT using single flexible sigmoidoscopy note that in the UK, flexible sigmoidoscopy is judged a more suitable tool for population screening than colonoscopy, in part because it is safer (UK Flexible Sigmoidoscopy Screening Trial Investigators 2002). Adverse physical effects occurring within this trial are included in Appendix 1, which summarises information on physical harms associated with CRC screening using both flexible sigmoidoscopy and colonoscopy from trials or pilots of screening programmes published subsequent to the 1998 National Health Committee report. Physical harms associated with the Australian pilot programme are not included, as these have not been addressed in the final evaluation report. It should be noted that a considerable amount of literature from other studies also is available.

Psychological harm
The 1998 report also acknowledged the very limited availability of research specifically addressing the potential psychological harm associated with screening for colorectal cancer. In the main, the report relied upon research and the experience of other forms of screening, highlighting anxiety and apprehension associated with phases of the screening pathway.

Particular areas of concern identified were:
- for those with missed cancers, false reassurance by a negative test result that they did not have CRC
- for those proceeding to colonoscopy on the basis of a positive FOBT, unnecessary anxiety and potential negative influence on future compliance with follow-up investigations among those who have no significant abnormality detected.

More recent data, including an investigation of psychological morbidity associated with the Nottingham FOBT trial (Parker et al 2002), have been reassuring. In this trial, FOBT screening was found not to have caused increased or sustained anxiety or psychiatric morbidity. Although anxiety scores were highest in those notified of a positive result, these scores fell in participants with false-positive test results after colonoscopy (Parker et al 2002). In participants with false-positive results, 85 percent thought they would accept re-screening in two years if offered (Mant et al 1990).

Findings of a comprehensive survey of invitees to FOBT to the UK pilot eight months following the first invitation are also reassuring, with levels of anxiety and depression among participants not significantly different from population norms. While the pilot evaluation report acknowledged the likelihood of short-term anxiety, it concluded that provided the standard of information and other elements of the pilot could be replicated in a national programme, adverse psychological effects in the population would be minimised (The UK CRC Screening Pilot Evaluation Team 2003).

The final evaluation report of the Australian pilot programme does not refer specifically to assessment of psychological harm among participants. However, it notes that in regard to those requiring follow-up colonoscopy, some GPs reported

that their patients had told them of high levels of anxiety, and feared that there were not enough specialists to cope with the colonoscopy demand (Australian Govt Report 2005: Bowel Cancer Screening Pilot Monitoring and Evaluation Steering Committee).

Conclusion: In the trials reported to date physical harms as a consequence of colonoscopy are less than anticipated based on the data available to the previous working party; however this is dependent on ongoing rigorous quality control. Similarly, with regard to psychological harm, the data from the United Kingdom pilot has been reassuring.

6. COULD THE HEALTH CARE SYSTEM FULLY SUPPORT A CRC SCREENING PROGRAMME?

Criterion 6. The health care system will be capable of supporting all necessary elements of the screening pathway, including diagnosis, follow-up and programme evaluation.

To use RCT evidence of efficacy to justify a screening programme, essential programme elements must be in place to ensure screening practice will match the quality standards of the RCT. The programme elements will include population recruitment, systematic recall, linkage to follow-up assessment, dedicated assessment centres and continuous monitoring and evaluation. The screening programme should be integrated with existing health services, as far as practicable, with specific goals for Maori participation (National Health Committee 2003).

This section assesses the capacity of the New Zealand health system to support each of these key elements of the screening pathway for any CRC screening programme:
- identifying the appropriate population to be eligible for the screening programme
- providing information about the programme and inviting eligible people to participate
- undertaking the screening test and analysing the results
- conducting follow-on investigations, ie, colonoscopy, on the basis of test results
- managing and treating any cases of CRC that are identified through the programme
- co-ordinating, monitoring and evaluating the programme.

A requirement of all elements of the pathway is the need for the NZ health system to deliver the programme and its benefits to Māori. How to address this need is discussed in the final part of this section.

Identification of eligible population
To reduce colorectal cancer mortality in the eligible population, a screening programme must correctly identify a high proportion of those with colorectal cancer (in other words, the sensitivity of screening must be high), and it must include enough people for the eligible population as a whole to benefit (i.e., coverage must be good). Both are important; high sensitivity cannot completely compensate for poor coverage, and vice versa. Screening programmes that do not have access to population registers have difficulty in achieving satisfactory coverage, as demonstrated in the Australian pilot (see below). This issue was also recognised by the European Commission in its guidelines for mammography screening:

> *Ideally each population to be screened should be derived from a population register. In the absence of such a register, a listing of women in the target population will need to be compiled. For the screening programme to have maximum effect it is essential that the screening register is both complete and accurate. The types of error which occur in registers relate to wrong address,*

wrong name, wrong date of birth, mistakes in other personal data, spelling and typing mistakes and wrong reference numbers. The register must be regularly updated as in some urban populations the mobility may amount to 20% per annum. Without a defined population, it is impossible to calculate accurately the attendance rate. The higher the attendance rate achieved, the greater the potential benefit to the target population. *(European Commission 1996)*

Providing information and inviting participation

Concern was expressed in 1998 about the absence of a population register to invite participants to take part in screening. Although such a register still has not been established, general practice registers are more up to date than they were and in July 2005 there were reported to be 81 Primary Health Organisations (PHOs) covering approximately 3.9 million New Zealanders (Ministry of Health Website Established Primary Health Organisations (PHOs) as at 1 April 2006 http://www.moh.govt.nz). Additionally, New Zealand has experience in establishing screening information systems – the critical importance of which has been highlighted by the Australian pilot.

Recruitment options for New Zealand include:
- centrally controlled invitations – eg, from a national database such as the electoral roll or National Health Index. At present the electoral roll cannot be used for this purpose (it can only be used for research). A change in legislation would be required before the electoral roll could be used as a register for screening.
- regionally controlled invitations – eg, people enrolled with a PHO.
- locally controlled invitations – eg, people registered with a general practice.

Implications for general practice

General practice had markedly different roles in the UK and Australian bowel cancer screening pilots (see Appendix 3). In both the Australian and Scottish pilots, recruitment was initiated centrally using a population database. Initially in Scotland a prior notification list was provided by GPs but this practice was considered unhelpful and subsequently stopped. In the Australian pilot, GPs participated in encouraging recruitment though the invitation was mailed from a central source. Although there was potential benefit from GP involvement in recruitment, this was not evident in the participation rates as reported. Recruitment in Australia was 45.4%, whereas in Scotland it was 55% in round 1 and 52% in round 2. However, this might be accounted for by the high level of opportunistic colonoscopy screening undertaken in Australia outside the screening pilot.

GPs in the Australian pilot were included in pilot education, in the reporting of test results and in clinical correspondence for those referred for colonoscopy whereas in Scotland there was much less GP involvement in the screening pilot which was limited to initial practice visits explaining the pilot, requests for prior notification lists which was subsequently discontinued, reporting to GPs only of positive screening results, and clinical correspondence following colonoscopy. A screening programme

in New Zealand might include pre-programme education, verification of recruitment lists, reporting of test results and clinical correspondence. The Australian and Scottish pilots highlighted a need for the development of criteria for checking recruitment lists, a process to ensure GP non-attendees are followed up, the use of electronic forms and electronic submission of forms related to the programme, education about the use of screening-related colonoscopy referrals to be restricted to those with positive results, and education and application of guidelines when considering referral of a participant with a negative FOBT result for colonoscopy.

Screening test volumes

In regard to actually screening for CRC and analysing the results, the support required from the health system would vary depending on the screening test that was used. The four main screening modalities identified in Section 2 are examined here in terms of their implications for the New Zealand health system.

FOBTg as the screening test

For a biennial FOBTg screening programme of people aged 50–74 with 60% participation, it would be necessary for 260,000 tests to be read – with this number increasing as the population ages (to around 330,000 by the 8th year of screening).

Several kinds of FOBTg are being used in clinical laboratories. Decisions would need to be made concerning:
(i) whether to use a medium analytical sensitivity test such as hemoccult or a high analytical sensitivity test such as hemoccult SENSA.
(ii) whether to process tests in general practices (not recommended), develop a stand alone testing facility within the programme or tender out to one or more diagnostic laboratory services.

For a national screening programme there would be no reason why access to any commercially available test could not be negotiated. In any case a contract to ensure continuity of test supply would be required. Key performance indicators (KPIs) would have to be developed for laboratories or offices performing the tests.

There would need to be a clear definition of responsibilities for reception and documentation of specimens, qualifications/training (accreditation) of staff reading the tests, responsibilities for reporting including turnaround time, methods of reporting and report distribution, responsibilities of follow-up of test results (including technically inadequate tests). A clear and agreed definition of inadequate/negative results would also need to be specified.

FOBTi as the screening test

For a biennial FOBTi screening programme of people aged 50–74 with 60% participation, it would be necessary for 260,000 tests to be read – with the number increasing as the population ages (to around 330,000 by the 8th year of screening).

Several kinds of FOBTi are being used in clinical laboratories in New Zealand. For a national screening programme there would be no reason why access to any commercially available test could not be negotiated.

The two kinds of FOBTi used in the Australian pilot study are able to be automated. For one of the Australian pilot FOBTi, a diagnostic laboratory was used to process the test, and for the other a pathology accredited laboratory run by the commercial supplier of the test was used. These tests require fully trained laboratory staff and are capable of being quality controlled in the same way as other diagnostic laboratory testing. No automated tests are currently in use in New Zealand but a single site should be capable of processing the workloads generated in a New Zealand programme.

Whatever the test(s) used, it would be important that contracting arrangements are entered into to ensure timely and accurate testing including continuity and certainty of supply of tests. There needs to be clearly defined responsibilities covering specimen reception, documentation and tracking of specimens, proper qualifications/training of staff reading tests, reporting of test results specifying turnaround time, reporting methodology and reporting distribution, documentation and verification of accreditation and quality control, and defined responsibilities relating to follow-up of results including technically inadequate tests. Suitable KPIs would need to be specified and audited. Arrangements for variation of analytical sensitivity/positive test rate may be required. In any case a clear and agreed definition of positive/inadequate/negative results would need to be established.

Flexible Sigmoidoscopy as the screening test
For a one-off FS screening programme at age 60 with 50% participation, it would be necessary for 18,000 procedures to be performed in the first year – with the number increasing as the population ages (to around 23,000 by the 8th year of screening).

A survey of colonoscopy capacity in New Zealand (see Appendix 4), conducted in 2005 (Yeoman and Parry 2005), established that the majority of endoscopy centres do not utilise FS; only 3 of 24 (13%) of public units and 6 of 12 (50%) of private units perform FS as a dedicated procedure (ie, using a flexible sigmoidoscope and not a colonoscope to conduct the examination).

In addition the three public units utilising FS report a combined total of approximately 600 procedures per annum (cf 2800 colonoscopies in the same units) with the six private centres performing a combined total of approximately 500 procedures per year (cf 2500 colonoscopies in those units).

The competence of nurse endoscopists (Maule et al 1994, Working Party British Soc Gastro 2005) has been established and their role is acceptable to patients. Within the United Kingdom there are over 200 nurse endoscopists but none are employed in New Zealand. In addition only 25% of public units and none of the private units surveyed in New Zealand would be willing to employ or train non-physician endoscopists to perform either FS or colonoscopy.

A decision to introduce screening for CRC utilising FS would therefore involve substantial investment and training – this could not be justified without evidence of mortality benefit in randomised controlled trials. The results of the UK multicentre single FS screening trial are therefore awaited.

Colonoscopy as the screening test
For a one-off colonoscopy screening programme at age 60 with 50% participation, it would be necessary for 18,000 procedures to be performed in the first year – with the number increasing as the population ages (to around 23,000 by the 8th year of screening).

The workforce resources and capacity to perform population-based colonoscopy screening are not currently available in New Zealand (or in any country, including the USA, Seaff et al 2004).

A decision to introduce screening for CRC utilising colonoscopy as the screening test would therefore involve substantial investment and training. This could not be justified without evidence of mortality benefit from randomised controlled trials. There is no such evidence at present and there are no RCTs in progress.

Follow-up Diagnostic investigation
Following on from analysis of test results from the initial screen is the crucial step of diagnostic investigation, when abnormal results are analysed and followed up with further tests as necessary. Following a positive test result from screening by FOBTg, FOBTi or FS, patients are referred for colonoscopy to obtain an accurate diagnosis. All four screening modalities also involve surveillance colonoscopy over time, for patients who have a cancer diagnosis or major polyps. The burden on colonoscopy services is detailed below.

Colonoscopy burden (including surveillance implications)
All four of the above CRC screening options involve colonoscopy. In order to assess the burden on colonoscopy services, some simple modelling of each screening option on the 2005 New Zealand population was undertaken. This is summarised in table 6.1. These figures include colonoscopies required following a positive test result for the first three options (to obtain an accurate diagnosis), the initial colonoscopy for one-off colonoscopy screening, and surveillance of large polyps for all options. Details are provided in the table footnotes.

Table 6.1 shows the number of colonoscopies in year 1 and year 8 of a screening programme, by which time colonoscopy surveillance for large polyps would be established.

FOBTg

The number of initial referrals to colonoscopy is highest in the first two years (i.e. the prevalence round), 5500 for each year, assuming test positivity of 2.1%. It then drops to 3200, (assuming test positivity of 1.2%) and increases only as the population increases. However surveillance begins in year 4. By year 8 total colonoscopies are over 7000, with surveillance colonoscopies forming 45% of the total.

FOBTi

The pattern of colonoscopy for FOBTi based screening is similar to FOBTg, but the overall load is much higher, with 13000 in the first two years and then a dip in year 3 to 8000. The level then rises due to surveillance colonoscopy and reaches 17000 by year 8. This assumes FOBTi test positivity of 5%.

The test positivity for FOBTi can be "set" by predetermining the cut-off for a positive test. This affects the sensitivity and specificity of the test and the resultant burden on colonoscopy services. Based on experience from the Australian pilot, a test positivity of 8% has been suggested for the first round of a screening programme (Graeme Young, personal communication).

If the test positivity was set to 8% for the first screen (reducing to 4.57% at subsequent screens), colonoscopy referrals would be 21000 for the first two years, drop to 13000 in year 3, then increase with the population to 15000 by year 8. Surveillance colonoscopy would begin at 6800 in year 4 increasing to 12000 by year 8. Total colonoscopies would reach 27000 by year 8. These volumes are similar to one-off colonoscopy screening at age 60.

Flexible sigmoidoscopy

The colonoscopy load from flexible sigmoidoscopy screening is modest, initially 1000 increasing to 4800. However FS is an endoscopic procedure and if used as a primary screening test would by itself substantially impact on endoscopic workloads, requiring 18000 procedures in the first year and increasing to 23000 by year 8. Surveillance of polyps, particularly of smaller adenomas, accounts for most of the colonoscopy. If participation were 40% (rather than 50%), then colonoscopy volumes would drop proportionately, ie, to 800 in year 1 and 3800 in year 8.

Colonoscopy screening

First line screening by colonoscopy would require 18000 colonoscopies in the first year increasing to 28000 by year 8 with surveillance colonoscopy then forming 16% of the total. If participation was 40% (rather than (50%), colonoscopy volumes would fall to 14000 in year 1, and 23000 in year 8.

The demand by average-risk individuals for screening colonoscopies is increasing. Resources are increasing in parallel to meet this demand, largely in the private sector. This means that some participants in a national FOBT screening programme would probably still opt for a colonoscopy at some time. This has already occurred

in the Australian FOBT pilot programme where some participants who did not have a positive FOBT still proceeded to colonoscopy.

Summary points

1. Surveillance colonoscopy is an important determinant of total colonoscopy burden. In the 4th year of a FOBTg or FOBTi programme, surveillance colonoscopies account for a third of the total; by the 8th year they account for nearly half.
2. FOBTi test positivity of 8% would lead to colonoscopy volumes equivalent to one-off colonoscopy screening at age 60.
3. The burden of FS based screening on colonoscopy is modest, but FS is itself an endoscopic procedure therefore would impact considerably on services.
4. Most of the colonoscopy following FS screening is for surveillance of small adenomas. Therefore guidelines on such surveillance would be required.
5. Screening by colonoscopy would involve considerable expansion of services.

Current colonoscopy capacity within the Public Health Sector
Concern about colonoscopy capacity was expressed by the 1998 working party, and the colonoscopy capacity survey (Yeoman and Parry 2005) has confirmed that this remains inadequate. The overall response rate for the colonoscopy capacity survey was 86% (100% for the 7 major centres and 81% for the smaller centres) and these units reported approximately 18,000 colonoscopies to be performed within New Zealand's public hospitals each year. If there had been a 100% response rate then it is estimated that approximately 20,000 colonoscopies are being performed each year in New Zealand's public health sector. The number of procedures performed each year within the four main population areas (Auckland, Wellington, Christchurch and Dunedin) has almost doubled since 1997 (8222 as against 4286). Despite this more than half of the major public centres and a third of small public centres are unable to deliver a diagnostic colonoscopy for patients with symptoms suggestive of CRC within a three month period.

The National Guidelines for colonoscopy referral currently advise an 8 week wait time for patients with symptoms suggestive of CRC. At the time of the survey 828 patients aged over 50 years in this category were reported to have been waiting > 6months for a diagnostic colonoscopy. The national estimate allowing for non responding units is 930 patients. An additional number of patients would have been waiting for between 3-6 months, also outside the guidelines, for a diagnostic procedure. Exact numbers in this group are not known and a further survey is required to determine this. Preliminary consideration of referral rates for diagnostic colonoscopy and comparison with service capacity lead us to estimate that the total number of colonoscopies performed per annum within the public sector would need to increase by 10%-12% in order to ensure patients aged over 50 years with symptoms suggestive of CRC are offered a diagnostic colonoscopy within the 8 week time frame specified by the national colonoscopy referral guidelines (CPAC). Further increases would be required to accommodate an ageing and increasing

population with additional capacity likely to be required to clear the current waiting list.

Evidence-based guidelines documenting high- and low-risk symptoms for CRC, as developed in the United Kingdom, could optimise referral and utilisation of diagnostic colonoscopy (Association of Coloproctology of GB and Ireland 2002; Thompson MR et al 2003)

Surveillance colonoscopy is recommended for individuals at increased risk of CRC (see Guidelines www.nzgg.org.nz) but in the majority of large centres only 20% of patients awaiting a surveillance procedure have been offered this within 6 months from the time of referral or advised repeat date. It is noted that in most cases, surveillance is given lower priority than diagnostic colonoscopy. Responding public hospitals reported approximately 2550 patients still waiting for a surveillance procedure 6 months after referral. The national estimate including non-responding units is 2790. To offer a surveillance colonoscopy within 6 months from the time of first referral or scheduled repeat date it is estimated that the total number of colonoscopies performed per annum within the public sector would need to increase by 15%. Further increases would be required to accommodate an ageing and increasing population. Additional capacity would be required to clear the existing backlog.

The estimates above are conservative and additional work needs to be done on monthly referrals for diagnostic and surveillance colonoscopies, and also for acute colonoscopies, which are given priority in the public hospital system and therefore displace patients in the other two categories.

Factors limiting provision of colonoscopy
A shortage of endoscopy nurses limits provision of colonoscopy for two thirds of public centres but an increase in the availability of endoscopists to perform additional sessions would increase colonoscopy provision in 50% of public hospitals. These factors currently result in approximately 95 unutilised half-day endoscopy sessions per week. If this situation were rectified within public hospitals and 5 colonoscopies were performed in one session then with current equipment and theatre capacity 475 additional colonoscopies could be performed each week.

Projected colonoscopy burden of proposed screening options
Given the projected colonoscopy burden of the proposed CRC screening options and allowing for natural growth in colonoscopy demand (as demonstrated by increase from 1997 to 2005) in addition to rectifying the current gap in service provision, a significant investment in infrastructure and training for colonoscopy would be mandated as outlined below. These figures do not allow for natural growth in colonoscopy demand.

Table 6.1 Colonoscopy burden of CRC screening options (year 1 → year 8)

	FOBTg	FOBTi	FS	Colonoscopy
Programme Specification	Biennial 50-74 years	Biennial 50-74 years	One-off test at age 60	One-off test at age 60
Participation	60%	60%	50%	50%
Screening test volumes (1)	260,000→330,000	260,000→330,000	18000→23000	18000→23000
BURDEN ON COLONOSCOPY				
Screening colonoscopy			Indirect burden (2)	18000→23000
Initial referral colonoscopy	5500 → 4000 (3,4)	13000→ 9500 (3,5)	1000 → 1200 (6)	Not applicable
Surveillance colonoscopy	0,0,0, 1800→ 3200 (7)	0,0,0, 4200 → 7300 (7, 8)	0,0,0, 800 → 3500 (9)	0,0,0 900 → 4300 (10)
Colonoscopy burden per year	5500 increasing to 7200	13000 increasing to 17000	1000 increasing to 4800	18,000 Increasing to 28,000
% INCREASE IN COLONOSCOPY CAPACITY REQUIRED				
To offer screening programme	28–36%	65-85%	5-25% (2)	90–140%
To also rectify current service gap for high risk and symptomatic patients	52-66%	90% - 115%	30%- 55% (2)	115- 170%

(1) These figures assume 95% of the eligible population can be identified.
(2) These figures do not take into account the impact of the FS procedure which is itself an endoscopic procedure therefore would put further pressure on endoscopic services; requirements are 18000 in year 1 increasing to 23000 in year 8.
(3) The volumes are higher in the first two years, the prevalence screen.
(4) Test positivity of 2.1% for the first screen then 1.2% for subsequent screens
(5) Test positivity of 5% for the first screen and 2.86% for subsequent screens.
(6) Assumes 5.3% are referred for colonoscopy
(7) Surveillance begins in year 4. Large polyps (32.6% in first round and 29.3% in subsequent rounds) are followed up at 3 and 6 years; Other adenomas (4.5% in the first round and 8.9% in subsequent rounds) are followed up after 5 years.
(8) The %age polyp yield for colonoscopy after FOBTi is assumed to equal that for colonoscopy after guaiac based FOBT
(9) Surveillance begins in year 4. Large polyps (found in 85% of colonoscopy referrals) are followed up at 3 and 6 years. Other adenomas found in 7.3% of those screened followed up at 5 years.
(10) Surveillance begins in year 4. High-risk adenomas (5%) are followed up after 3 and 6 years. Other adenomas (10%) followed up after 5 years.

Quality in colonoscopy
The required expansion of colonoscopy resource within the context of screening 'well' individuals would mandate quality assurance of colonoscopy performance to minimise both missed lesions and significant complications of the procedure. An acceptable completion rate to the caecum (> 90% all cases, > 95% in screening) minimises missed lesions but achieving this within the screening context is not always easy as demonstrated by the reported completion rates in the various screening trials or pilots – 89.9% UK FOBT pilot, 75.7% Italian SCORE trial. The sensitivity of colonoscopy for detecting colorectal neoplasia also varies between operators depending upon the specialty of the operator – i.e., gastroenterologists compared with non-gastroenterologists (Haseman et al 1997; Rex 1997). Different sensitivities between gastroenterologists for adenoma detection have also been described with one influencing factor being the quality of colonoscopic withdrawal technique (Rex 2001; Atkin et al 2001).

Complications as a consequence of colonoscopy arise as a result of sedation, cardiopulmonary events or the procedure itself and the interventions performed (NHC Report 1998 p.43). Complications associated with the procedure itself are largely confined to therapeutic procedures such as polypectomy but can occur during diagnostic investigations with inexperienced operators (NHC Report 1998 p.44).

The colonoscopy capacity survey (Appendix 4) revealed that currently two thirds of responding public centres were documenting morbidity and mortality as a consequence of colonoscopy, half were auditing completion rates to the caecum and a third were recording patient discomfort during procedures. Quality parameters for the technical performance of colonoscopy should be agreed upon and promoted by the relevant professional bodies in New Zealand. This would be mandated if CRC screening were to be implemented in New Zealand.

National continuous quality improvement targets for colonoscopy should also be established as recommended by the US Multi-Society Task Force on CRC (Rex 2002). Documentation of performance achievement for these targets should become routine practice within New Zealand endoscopy units. A number of units use a computer generated endoscopy reporting system and this allows crude documentation of some targets, eg, completion rate to caecum, polyp detection rate. Customised colonoscopy audits operate in some New Zealand centres (Haque, Parry, Gerred 2002, Czechowski et al 2005) and these allow more comprehensive documentation of performance.

The advent of CRC screening in New Zealand and expansion of the colonoscopy workforce would include the development of and resourcing for structured and standardised training in colonoscopy. An endoscopy training course has recently been established in New Zealand (Morris 2005).

Recognition of training in gastrointestinal endoscopy by the New Zealand Conjoint Committee (N.Z. Society of Gastroenterology, The Royal Australasian College of

Physicians and The Royal Australasian College of Surgeons) should also be promoted as a pre-requisite for independent practice.

Quality in endoscopy also requires adequate facilities and nursing staff to safely monitor sedated patients and to ensure appropriate infection control of both the instruments and environment (Rex 2002).

Histology reporting for colorectal neoplasia
An audit of the histopathology reports of rectal cancer resections submitted to the New Zealand Cancer Registry in 2000 (Keating et al 2003) showed fairly uniform and high reporting rates for tumour type, maximum depth of penetration of rectal wall, tumour diameter, tumour differentiation, distance to nearest margin and number of nodes examined (93-100%). Vascular invasion, circumferential margin involvement, macroscopic description of tumour site, position of positive nodes and perineural invasion were reported somewhat less frequently (37-75%).

It is likely that larger adenomatous polyps (>1cm) are fairly uniformly reported with architectural pattern (villous, tubulovillous and tubular) and degree of dysplasia (either high grade and low grade, or severe, moderate and mild dysplasia). It is less likely that small or diminutive lesions (<10mm) are so uniformly reported. Increasingly diminutive lesions are received for histologic assessment following surveillance and symptomatic colonoscopy. If a national consensus on the nomenclature of those lesions could be achieved, registration and even uniform synoptic reporting may be possible. It is noteworthy that only one laboratory in the year 2000 was using routine synoptic reporting for colorectal carcinomas. In particular, professional bodies representing pathologists, surgeons and gastroenterologists would need to confer and reach some agreement for this to happen. Minimum data sets and reporting pro-formas for colorectal cancer already exist (Royal College of Pathologists 2000). This has not preceded most screening trials reported to date and it is notable that in the Australian pilot study a proper assessment of pathologic findings has not been reported (Aust Govt Final Evaluation Report 2005).

At the very least a screening programme in addition to cancers would need to register significant polyps which would generate follow-up in their own right. Significant polyps would probably include:

- larger adenomatous polyps >10mm
- multiple adenomatous polyps > or equal to 3
- polyps with a significant villous component
- polyps with high grade dysplastic change

Most programmes have not centralised histopathology reporting for colonoscopy biopsies and surgical resections. The audit of New Zealand reporting of rectal cancers (Keating et al 2003) did not indicate significant differences in reporting between laboratory types. As long as there are nationally agreed reporting/staging

systems in place there appears to be no pressing reason to change to centralised reporting.

Pathology workforce issues
Little, if any, provision has been made in overseas programmes for increased histopathology workload. The English pilot study (UK (NHS) CRC Screening Pilot Evaluation Team 2003)) now acknowledges pathology workforce problems and has estimated the need for an extra 0.1 FTE pathologists for each 250,000 of total population. Australia has run a pilot and did not anticipate pathology workload difficulties but has had problems in compiling and receiving histology data.

In an FOBT programme nearly all positive tests should result in colonoscopy and those with cancer require biopsy and subsequent resection. Those found to have polyps and some other lesions also require biopsy. All biopsies and resections require histopathologic examination. Those that survive their cancer, as well as those with significant but benign polyps, will require further follow-up colonoscopies. A full-time equivalent histopathologist can examine approximately 5000 cases per annum. Although it is difficult to precisely predict the increase in workload for histopathologists, it is clear that the introduction of a programme would result in not only an immediate and initial increase in specimens, but also an ongoing increase in specimens from further surveillance. These increases would not be totally offset by any decrease in the subsequent numbers of cancers.

Accurate quantification will only be possible after we know the participation and positivity rates of a FOBT (or other testing modality if selected) in our population, the rate of detection of cancers and polyps requiring follow-up, the policy adopted for follow-up and the way the screening programme would be implemented to achieve full coverage of the relevant population. Based on the recommendations of the English pilot study (UK (NHS) 2003) New Zealand would require an increase of 1.6 FTE pathologists, although this is probably a minimum figure as test positivity rates may well be higher in New Zealand. New Zealand is estimated to be 63 full-time equivalent pathologists short by comparison to Australia which is in turn short compared to international standards. Fourteen of New Zealand's 93 histopathologists are >60 years of age. Each year for the last 3 years there has been a fall in the number of pathologists and full-time equivalents (RCPA 2005).

Management and treatment of disease
Section 3 outlined the main forms of treatment of CRC (surgery, adjuvant radiation therapy and adjuvant chemotherapy). In this section the potential impact of screening for CRC on treatment services for CRC is considered.

Surgery
In order to maximise the benefits of screening, surgery would need to be offered in a timely manner and be of appropriate quality to achieve good outcomes. Although there are no national figures for the time taken from diagnosis of CRC and assessment by a surgeon to surgery, it is estimated that at present this would occur within one month for most patients. Although the introduction of screening would be

expected to increase the number of patients with CRC presenting for surgery, this is expected to be a modest and temporary increase that should not overwhelm present services.

The question of the quality of the surgery must, however, also be addressed. Optimal treatment of rectal cancer is a special challenge for the surgeon as it requires careful clearance of the tumour from the pelvis while preserving the surrounding pelvic autonomic nerves and maintaining the intact anal sphincter (Hill 1998). Treatment also requires close co-ordination with those offering adjuvant therapies. In rectal cancer there are significant differences in outcome both in terms of local recurrence and survival between different surgeons depending on training and case volume (Porter 1998) and technique (Bissett 2000). Targeted training for surgeons operating on rectal cancer has been shown to improve national rectal cancer outcomes in the Netherlands (Kapiteijn et al 2002). In New Zealand there has been a recent increase in training posts for colorectal surgeons. Ongoing audit of surgeons and centres with adequate reference to case mix would be required to ensure adequate quality of surgery (Sagar 1994, Murray 1995). This may mean that rectal surgery is better performed in centres with a high volume and multidisciplinary teams.

The most recent NHMRC Guidelines recommend:

> *Elective surgery for rectal cancer should be carried out by a surgeon who has undergone a period of special exposure to this form of surgery during surgical training and who has maintained satisfactory experience in the surgical management of rectal cancer.*

Disease staging
A review of pathology reporting of rectal cancer in New Zealand was carried out in 2000 and has been published (Keating et al 2003). No significant variation was noted between laboratories in public, private and teaching institutions. Several staging systems were reported including Dukes (56%), Jass (21%), TNM (20%), Astler-Coller (14%), and ACPS (10%). Multiple staging systems were included in the report in 40% of reports. Although 31% of reports did not include a stage, the bulk of these reports were from a single major centre where by policy, all of the histopathological observations required for staging were contained in the reports. This allows the clinician to do the final staging with knowledge of the relevant clinical information. Reports of colorectal cancer population screening programmes referring to staging have in the main used the Dukes system.

Medical oncology services
In evaluating the impact of a CRC screening programme on medical oncology services in New Zealand, it is helpful to note that the current key determinant in the decision to refer for adjuvant chemotherapy is the stage of the disease.

The impact of a screening programme on stage of disease at presentation is therefore important. The shift in tumour stage seen in the Nottingham and Funen

studies (Hardcastle et al 1996; Kronborg et al 1996) resulted in an increase in the percentage of Dukes' A (11% to 20-22%) and a decrease in Dukes' C (23–31% to 19–24%) patients with little change in Dukes' B (33–37% to 32–34%) or Dukes' 'D' (21–24% to 20–22%) patients.

If a screening programme was introduced now there may be a net reduction in the use of adjuvant chemotherapy due to the reduced number of patients having Dukes' C tumours and increased numbers of those having low risk Dukes' A tumours (which do not require chemotherapy). The percentage of Dukes' B patients classified as high risk and those of them who receive chemotherapy at present is not quantifiable due to the lack of accurate data systems in place. Similarly it is difficult to tease out the shift of high risk B tumours to low risk B or A, and the shift of C tumours to B (high or low risk) when screening is introduced.

Although not reflected in changes in stage at presentation, the overall impact of a screening programme is to reduce CRC mortality, which will result in fewer patients requiring palliative chemotherapy. This would have a positive impact on the services as these treatments are generally given for longer and often in sequence rather than combination, so are more time and resource consuming. In particular the reduced use of some of the newer more expensive drugs would favourably impact on the cost of running the oncology services (although this may be offset by their imminent use in the adjuvant setting).

The current state of access to treatment in some cancer centres has been less than ideal although access has improved dramatically in other centres with better staffing levels.

An email survey of the six medical oncology services was conducted in November 2005 for the purposes of informing this report on the issue of waiting times for first specialist assessments (FSA) by a medical oncologist and time to treatment. Unlike the radiation waiting times (published on the Ministry of Health website), the medical oncology waiting time data collection is not standardised and is not able to determine the time from surgery to commencement of adjuvant chemotherapy. For context it should be noted that the RCT evidence is based on commencement of chemotherapy within 5 to 7 weeks of surgery. The results of the survey are presented in Table 6.2.

Table 6.2: Medical Oncology Waiting Times Survey – November 2005

Cancer Centre	Referral to FSA (wks)	FSA to Treat (wks)	Data source	Comments
Auckland	Average: 1.57 Min: 0 Max: 4.6	Average: 1.7 Min: 0 Max: 11	Database	Data are for colorectal ca – priority B (adjuvant) and are from period Dec 04 to Nov05
Waikato	1-2	1-2	Estimate	Now fully staffed. Waiting times for FSA > 12 wks in past
Palmerston North	PN: 2-3 Regions: up to 6-8	PN: 4 Regions: 1-2	Estimate	All Dukes' C Colons seen within 3 weeks. 23% increase in new patients this year – anticipating increase in waiting times. Losing 1 FTE Med Onc June '06 – big problem if unable to replace.
Wellington	3	Mainly 3-4 (increasing)	Estimate	Audit December '04 ref to FSA 9 days, but steady increase since.
Christchurch	'Most within 2'	'Most within 1-2'	Not stated	Adjuvant patients by negotiation sometimes delayed if surgical recovery time slow.
Dunedin	DN: 2-3 Southland: 4-6	DN: 1 Southland: 1	Estimate	Dependent on staffing levels

It would seem from the data collected that many patients could expect timely treatment although a more formal examination of the time from surgery to commencement of chemotherapy would be required to better predict the risk of screen detected patients failing to get timely access to anticipated treatments.

Radiation oncology services

Unlike prescribing chemotherapy for resected colon cancer, in rectal cancer tumour stage is not the only parameter used to determine the use of radiation. In particular this treatment is prescribed in low-rectal tumours or in tumours that appear to invade the fascia propria on pre-operative MRI, a relatively small percentage of patients with colorectal cancer.

Stage shifts in rectal cancer with screening appear to be less evident than for colon cancer. It is therefore unlikely that there would be a large impact of a screening programme on radiation services. The radiation waiting times which previously exceeded guidelines have been less problematic in recent months (www.moh.govt.nz/) but still have the potential to vary according to staffing levels and technology upgrade status.

New knowledge

Clinical trials research is also constantly refining the duration and access criteria for the use of adjuvant therapy for CRC such that evidence for treating early stage disease may change, duration of radiation or chemotherapy schedules may shorten, etc.

The field of oncology is on the verge of a new era where the molecular profiles of tumours will enable better prediction of outcomes and more effective use of therapies. This may ultimately supplant the present treatment-by-stage paradigm. Predicting when this will become mainstream in colorectal cancer is difficult although it is conceivable it will be within the next decade if local infrastructure is in place to study this in New Zealand. This era should provide a more rational use of treatment resources – both for screen-detected and other patients.

Programme co-ordination, monitoring and evaluation
The purpose of monitoring and evaluation is to ensure that a programme is efficient and effective (Miller 1985; Miller 1992). There is also an ethical obligation on those responsible for a screening programme to ensure that the programme is appropriately evaluated. This ethical obligation arises because screening is offered with the understanding that it is beneficial.

> *We believe that there is an ethical difference between everyday medical practice and screening. If a patient asks a medical practitioner for help, the doctor does the best he [or she] can. He [or she] is not responsible for defects in medical knowledge. If, however, the practitioner initiates screening procedures he [or she] is in a very different situation. He [or she] should, in our view, have conclusive evidence that screening can alter the natural history of the disease in a significant proportion of those screened.*
> (Cochrane and Holland 1971).

This raises two extremely important issues: (1) there must be clear evidence that colorectal cancer screening is beneficial before a national screening programme is offered, and (2) once the programme is established, the programme must be monitored to ensure that it can deliver the promised benefit.

The National Screening Unit (NSU) was established in July 2001 within the Ministry of Health with responsibility for both the national operational function in cancer screening and programme co-ordination, monitoring and evaluation. The current cancer screening programmes are the National Cervical Screening Programme (NCSP) and the national breast screening programme, BreastScreen Aotearoa (BSA). In 2004 the NSU's role has expanded to the provision of leadership across non-cancer screening programmes, eg, the newborn metabolic screening programme.

The NSU has led recent work to assess potential new screening programmes – universal newborn hearing screening and antenatal HIV screening – and is also undertaking policy work on screening for several other conditions.

Both the NCSP and BSA have explicit quality and policy standards in place. The monitoring of both programmes includes independent monitoring of key programme indicators on a quarterly (NCSP) or biannual (BSA) basis. Should a colorectal

cancer screening programme be established in New Zealand, appropriate monitoring across the screening pathway would be essential, including independent monitoring similar to that currently undertaken for the NCSP and BSA.

Thus New Zealand has a well-defined and resourced organisation dedicated to ensuring that new programmes are established properly in the first place and accountable for the ongoing co-ordination, monitoring and evaluation of screening programmes. This provides a sound platform on which to base decisions about colorectal cancer screening, and to ensure that any programme is monitored appropriately to ensure that it is delivering the promised health benefits.

Conclusion: Screening is more than offering a test. Currently there is not the capacity for New Zealand to offer any CRC screening programme. The implications for colonoscopy and pathology services are of particular concern. This could be addressed by substantial workforce planning, expansion and capital investment.

7. WHAT ARE THE SOCIAL AND ETHICAL ISSUES IN RELATION TO CRC SCREENING?

Criterion 7. There should be consideration of social and ethical issues.

There should be evidence that the complete screening programme is clinically, socially and ethically understood and acceptable to health professionals and the wider public. Potential participants should be given information that allows them to weigh up probable benefit and harms. Culturally appropriate, evidence-based information should be available for people offered screening to assist in making an informed choice (National Health Committee 2003).

The Advisory Group considered a range of social and ethical issues, some of which were covered in the 1998 report of the previous working party and some of which are affected by evidence available since the 1998 report. These issues may be summarised as follows.

- **Information and consent**: There is a need for informed consent about the implications of participating in a screening programme as well as consent for individual procedures.
- **Acceptability and participation**: There is uncertainty regarding the acceptability of CRC screening to New Zealanders. This is important because it influences participation.
- **Impact of screening**: There is the question of whether an effective screening programme can be established and sustained.
- **Cultural issues**: A screening programme must be as effective for Māori as it is for non-Māori (as noted in the 1998 report).
- **Inequalities**: There is the potential for CRC screening to increase inequalities - the UK and Australian pilots reported lower participation levels by those in lower socio-economic groups.

These issues are addressed in more detail in this section. In addition, there is an ethical obligation on those funding and providing a screening programme to ensure that it is effective and that the potential for benefit significantly outweighs the risk of harm. This issue is addressed in Section 8.

Information and consent

There is a significant difference between everyday clinical practice and population screening (Cochrane and Holland 1971). Unlike treatment and assistance to patients seeking help, a screening programme systematically invites people with no symptoms or signs of the disease to take part in an intervention that most would not have considered and that will only benefit a few. Indeed, the success of a screening programme relies on the participation of large numbers of people who will not benefit directly from it, and who risk being harmed.

> *Adverse consequences are common to any cancer screening programme. However, they must be recognised (by both the medical profession and more*

importantly by the population as a whole) as being implicit to a programme whose overall effect is beneficial. They must also be minimised (and be seen to be minimised) by close attention to quality control and audit. Only then will public confidence, essential to the success of any cancer screening programme, be maintained. The importance of this area needs considerable emphasis (Robinson et al 1999).

Historically, screening to detect or prevent disease at an early stage has been considered a positive initiative that has been enthusiastically promoted. More recently, there has been a greater recognition of the limitations and risks of screening and the tension between communicating these and achieving high participation rates so that disease incidence and mortality are reduced (Duffy et al 2001). It is important that the distinction between a screening programme and clinical practice is well recognised and understood along with the particular duty of care that is required of providers when inviting people to take part in something that could harm them (Medical Council of New Zealand 2002; General Medical Council 1998; Grimes and Schulz 2002). This duty includes being able to respond to positive screening results in a timely and professional way that ensures high standards are met.

Although the statistics show that CRC is a significant problem in New Zealand, consumers and practitioners would need to be satisfied that screening for this cancer will be of benefit. They would also need to know that there is a good screening test that can be relied upon to give credible results. There is a responsibility to effectively communicate all relevant information to people who are invited to participate in a screening programme so they are able to make an informed decision about whether to take part. This legal duty is described in the Code of Health and Disability Services Consumers' Rights 1996[1].

People need to understand that they are consenting to both the screening test and to taking part in a screening programme. Because high participation levels are needed to achieve the benefits of population screening, past practice has tended to focus on only obtaining consent for the screening test.

Information provided for participants in a screening programme needs to describe the risks, limitations and possible harms of screening including the likelihood of false positive and negative results from the screening test that may prompt the need for follow-up procedures such as colonoscopy or long-term surveillance. Within the Australian pilot, for example, participants with a nominated GP who tested positive were advised to consult their GP; however, no timeframe was specified. Without a date specified, many felt the referral must not have been too important, while others were prone to put off the visit to a later date, only to forget to visit their GP at all (Aust Govt Final Evaluation Report: Bowel Cancer Screening Pilot Monitoring and Evaluation Steering Committee 2005).

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[1] Health and Disability Commissioner Act 1994

It should be emphasised that any colorectal cancer screening programme, through the detection of adenomas, will generate a substantial number of follow-up surveillance colonoscopies. Although there was no reported mortality resulting from colonoscopy in the Nottingham RCT, morbidity information does highlight the need for careful auditing of colonoscopy performance, particularly where national screening is introduced (Robinson et al 1999).

This is reinforced by reported failings in the national cervical screening programme in the United Kingdom, which parallel New Zealand's experience. Inquiries in relation to both programmes have highlighted the need to emphasise four areas:
1. the aim of the screening test (cervical screening is not a test for cancer but for abnormal cells that might lead to cancer)
2. the fallibility of the test (it is not 100% accurate)
3. the need for reporting symptoms irrespective of the result of the screening test (abnormal bleeding)
4. the effectiveness of a screening programme in preventing deaths (in the UK, estimated as 3900 deaths per year).

As highlighted by those who assessed the risks associated with the Nottingham RCT, any future national colorectal cancer screening programme would need to address and emphasise these same four issues (Robinson et al 1999).

People also need to be made aware of other implications of participating in cancer screening, eg, any significant medical, social or financial implications of the condition for which the screening is done (Medical Council of New Zealand 2002). This could include employer screening procedures and insurance policies where participation in screening could be a disadvantage.

Providing balanced information is a particular challenge of screening programmes. Studies have shown that the active promotion of a cancer screening programme results in people significantly overestimating their risk of having or getting the disease. The greater the concern about personal risk, the greater the use of CRC screening procedures (Vernon 1997).

Acceptability and participation
The level of acceptability, and thus the level of participation, in a CRC screening programme will be affected by the kind of screening test chosen. As the 1998 working party report noted, a considerable amount of programme resource is required for recruitment strategies to achieve adequate levels of participation. It also noted the differing levels of acceptability about screening interventions and possible adverse effects between people who consider themselves at high risk, or who have had a personal experience with cancer and those who have no recognised risk factors. Here we consider the issues in relation to the four main screening modalities introduced in Section 2.

Acceptability and participation levels with faecal occult blood tests
Although mortality benefits of CRC screening using the FOBTg have been demonstrated, these are modest and have been achieved over a long period of time under ideal study conditions. We do not know if a screening programme with FOBTg in New Zealand could achieve the same results. In addition, whilst people may be persuaded to accept an initial offer of screening, many may opt not to participate in subsequent screening rounds or follow-up procedures for abnormal results.

Concerns over effectiveness of FOBTg
There are varying views on whether it is acceptable to promote FOBTg when it is generally expected to detect only 50% of the cancers. In addition, overseas studies and pilots reveal a modest uptake (with 60% in the United Kingdom and 45.4% in Australia). On the basis of the higher rate, FOBTg screening will only detect 3 out of every 10 cancers. This is because only 6 out of every 10 people with cancer will participate and only 3 of those 6 will have their cancer detected.

It is relevant to note that New Zealand general practitioners are likely to raise ethical concerns about offering the FOBTg, partly because they are not able to reassure patients that the test will detect a majority of the cancers.

NSU survey in New Zealand
A recent consumer study of acceptability and knowledge of CRC screening was commissioned by the NSU (Health Outcomes International 2006). A series of 10 focus groups was conducted with consumers from around New Zealand. There were equal numbers of men and women between the ages of 50-74 as well as specific focus groups for Māori, Pacific peoples and those from rural areas. The focus of the report was on knowledge, barriers and enablers and what would be needed to achieve satisfactory testing compliance levels for the introduction of screening – rather than on consumer acceptability of the limitations of screening. The research provides useful information on consumer views about FOBT as a screening test but not their views on the various limitations of a screening programme, the possibility of needing ongoing surveillance of abnormalities or the potential impact on services for people with symptoms of colorectal cancer who may have to wait longer.

The participants were not asked about the importance of certainty or, for example, how they would weigh up a one-off highly intrusive but very accurate test (screening colonoscopy) against a less intrusive but not so accurate test (screening flexible sigmoidoscopy) or the FOBT which is self administered but not very sensitive.

The study did show low levels of knowledge about CRC and the limited information participants had was usually the result of knowing someone with the disease. Women had a greater awareness of screening programmes. Pacific women disclosed that the subjects of cancer and private parts of the body were avoided in day-to-day conversations. The participants suggested that when the focus is on the screening test being non-invasive and painless, people could overcome their embarrassment and reluctance to handle faeces. They identified a need for a considerable amount of information and education to address these issues.

Overseas studies have observed hygiene issues relating to the handling of faecal material as a source of anxiety, inconvenience and embarrassment (Myers et al 1991; Harris and Byles 1997). Participants in the New Zealand study were invited to comment on the FOBT kit and carrying out the test. Storage, hygiene, labelling and difficulties using the test kit were amongst the problems identified. Although the participants were accepting of the need for a colonoscopy to check any positive FOBT results, those who had had a previous bowel investigation stated they were reluctant to go through it again. This reaction was consistent across all ethnic groups and raises a question about participation levels for subsequent screening rounds.

The participants unanimously agreed that the cost of CRC screening to consumers would be a critical determinant in whether people would take part in a screening programme. It was suggested that this was likely to be a particular issue for older people. Overall, participants stated their doctor would be the person most likely to influence them to take the test. Māori participants said they would be more likely to consider the test if it were recommended to them by their local Māori health provider, GP, community worker or nurse.

Overseas findings
It is also important to note that although the UK pilot achieved close to its target uptake of 60%, there were important sub-groups in which uptake was low (The UK CRC Screening Pilot Evaluation Team 2003). FOBTg appeared less acceptable to men, to younger people and, as already indicated, to those from materially deprived areas and belonging to certain ethnic sub-groups. Uptake was also lower in Scotland, which may have been a reflection of the relatively dispersed and rural population (although this cannot be concluded with certainty). Uptake among ethnic minority groups was influenced by GP attributes, including religion and language of the practitioner. The UK evaluation team recommended that special efforts, including tailored recruitment strategies, would be needed to improve uptake in these groups.

The most important factors affecting FOBTg response in the UK pilot were those relating to the ease or difficulty of completing the kit, with non-responders significantly less confident than responders. These included physical (e.g., bowel movement irregularities, storage difficulties) as well as perceived psychological barriers (e.g., embarrassment, disgust and prospect of having unpleasant treatment). The evaluation team concluded that while CRC was considered to be a serious disease to which people consider themselves susceptible, practical issues such as ease of completion of a FOBT will still influence their decisions to participate in screening (The UK CRC Screening Pilot Evaluation Team 2003).

Quantitative and qualitative research conducted as part of the evaluation of the Australian pilot programme (focusing on knowledge, attitudes and satisfaction with service delivery among those invited to participate with the principle aim of assisting in planning of a possible national programme) found that those likely to participate in the pilot had:
- a biological family history of bowel cancer

- greater awareness of bowel cancer and the need for screening, and
- experience with other screening or testing programmes (Bowel Cancer Screening Pilot Monitoring and Evaluation Steering Committee 2005).

Among pilot participants, 90.6% indicated that they were either very likely or likely to participate in an FOBT based screening programme in the future.

The major reasons reported for not taking part in the pilot were having 'already had other bowel tests' and having a 'lack of symptoms' or 'feeling well'. Non-participants were usually less aware of the screening process and, therefore, less likely to consider participating.

A number of factors contributed to lower participation among Aboriginal and Torres Strait Islander people and for non-English speakers. They included language barriers around the complexity of the testing procedure, cultural barriers (in relation to tests involving the bowel), and practical barriers (eg, difficulty with postal contact).

Acceptability and participation levels with flexible sigmoidoscopy
In the UK FS trial the overall participation was 39%. A study assessing the acceptability of flexible sigmoidoscopy within the context of the UK flexible sigmoidoscopy trial emphasises the importance of analysing satisfaction with the test as well as looking at medical end points (Sutton et al 2000). Results of the study indicated a high level of acceptability, with 99% having been glad they had the test. The authors highlight the need for such assessment as part of the evaluation of screening as populations may respond differently because of cultural differences.

Acceptability and participation levels with colonoscopy
Colonoscopy is not a simple procedure. Although some recent reports have started to recommend colonoscopy as a primary screening test (Morikawa et al 2005), to date there appears to be limited literature on its acceptability as a primary test and no RCT evidence comparable to screening using FOBT.

Analysis of data from the UK FOBT trial found that colonoscopy uptake following a positive FOBT was 87%, with the main reason for non-uptake appearing to be 'unwillingness' (The UK CRC Screening Pilot Evaluation Team 2003). The need for further psychosocial research to understand specific beliefs associated with non-uptake was noted.

Impact of a screening programme

Promotion
Historically, the promotion of a screening programme has raised people's expectations of its capabilities, and results may appear to fall short of these expectations. The active promotion of any cancer screening programme results in people significantly overestimating their risk of developing the disease and encourages large numbers of people to have a preoccupation and anxiety with finding something wrong. CRC screening also has the ability to detect abnormalities

(adenomas) that may never actually be a problem. Screening can put people on a treadmill of unnecessary tests, interventions and ongoing surveillance (New Zealand Guidelines Group 2004). Care needs to be taken to avoid generating increased levels of anxiety about disease and cancer in particular.

Credibility:
The credibility of a screening programme can be undermined if the screening test is considered unreliable and this could be the situation with FOBTg because of its disappointing sensitivity (misses half the cancers). A lack of confidence in one programme could also spread to other screening programmes. In addition, for an individual participant reassurance from a false negative test could result in symptoms being ignored as well as delays in diagnosis and treatment.

Sustainability:
The New Zealand public would want to be assured that New Zealand could sustain the demands of another cancer screening programme and that a CRC screening programme would only be set up if it could realistically achieve its objectives. It would need to be properly co-ordinated and monitored and would need to ensure equitable access so people would not be discriminated against on the basis of their ethnicity, where they live, the cost to participate or the language they speak.

The public would also want to know that CRC screening programme would be a good use of limited resources and that there would not be an undesirable impact on existing screening programmes and other health services eg, displacement of diagnostic and treatment services for individuals with symptoms suggestive of CRC.

Conclusion
Although screening for CRC offers the potential for a mortality reduction in those screened, a test such as FOBTg with its limited ability to detect cancer has the potential to increase anxiety and create ambiguity. This can place a burden on existing services and allocated resources. Caution is therefore required in considering a CRC screening programme.

Cultural issues for Māori
New information since the previous report of the CRC Advisory Group suggests that the incidence of CRC in Māori may be higher than was initially thought, paralleling the rates for Pākehā. In addition, the evidence shows that the outcome for Māori who get CRC is worse than for non-Māori, probably due to differential access to services (Jeffries et al 2005). Further research is needed to establish whether a systematic approach to CRC screening has the potential to reduce these statistics. Specific health models and frameworks (Durie 1999; King and Turia 2002)[2] [3]have been developed to make sure Māori perspectives are taken into account. It is

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[2] Te Pae Mahutonga (Durie 1999)
[3] Māori Health Strategy (He Korowai Oranga) and Implementation Plan (Whakatataka) (King and Turia 2002)

important that these are used in any screening, pilot, feasibility or other research activities where there is an intention to include Māori people. (See Section 6 for a discussion of the application of these models to colorectal cancer screening for Māori).

Although a recent New Zealand study of consumer acceptability revealed that Māori participants considered they were at high risk of developing and dying from CRC, there is no new information on other aspects of CRC screening (Health Outcomes International 2006). For instance, there is no information on how Māori perceive the screening pathway, being involved in a CRC screening programme or how they view the risks and limitations of screening. There is also no information about Māori views on CRC screening in relation to other cancer control initiatives or health services generally.

Inequalities

The potential for screening programmes to increase inequalities also needs to be acknowledged. In the UK, for example, the CRC pilot showed that the uptake and acceptability of screening was lower among people from areas of higher social deprivation and ethnic sub-groups. Yet in some cases, non-responders reported a number of health behaviours which could put them at increased risk of CRC (The UK CRC Screening Pilot Evaluation Team 2003). In the Australian pilot, participation was higher for the two least disadvantaged quartiles. It also tended to be lower for Aboriginal and Torres Strait Island people compared to the general eligible population and for people who spoke a language other than English (Aust Govt Report: Bowel Cancer Screening Pilot Monitoring and Evaluation Steering Committee 2004). In both the UK and Australian pilots, participation was higher among women than men.

Existing screening programmes in New Zealand have a lower proportion of Māori, Pacific and older participants. This means that the potential benefits of screening are less likely to be seen in these groups. As a result, particular attention has been placed on identification and invitation procedures, as well as improving support systems to help improve access and reduce barriers to screening[4]. The pressure to establish and extend screening programmes creates a risk that the effort to achieve these, lessens the ability to focus on groups where participation levels are low.

Conclusion: Potentially the social and ethical issues are profoundly complex and any CRC screening programme would need to be carefully planned, implemented and monitored to ensure that participants are well-informed of test limitations and to maximise benefit while minimising harms. The risk of increasing inequalities must also be taken into account so that the potential benefits of screening are distributed evenly among all population groups in New Zealand.

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[4] Approximately 14% ($5.6m) of the Breastscreen Aotearoa budget is spent on activities to encourage consumer participation.

8. WHAT IS THE BALANCE BETWEEN THE COSTS AND THE BENEFITS OF A CRC SCREENING PROGRAMME?

Criterion 8. There should be consideration of cost–benefit issues.

There needs to be scrutiny of the cost–benefit of screening programmes, as they are resource intensive. Other options for minimising the morbidity and mortality of the condition should be considered to ensure screening is the most cost-effective way of obtaining health gains (NHC, 2003).

Effectiveness

The task of weighing up costs and benefits depends heavily on the quality of evidence of the benefit, ie, effectiveness, of screening. The best evidence is from population-based RCTs. Therefore, absence of RCT evidence on screening by FOBTi, flexible sigmoidoscopy and colonoscopy is problematic. Even for FOBTg, where there is RCT evidence, the benefit for a population is an estimate and the confidence interval around the estimate of mortality reduction needs to be taken into account.

In this section, several approaches to the question of the relative costs and benefits of a CRC screening programme are considered:

* cost-effectiveness analysis
* estimates of the financial cost of a programme
* an assessment of total costs and total benefits.

Where there may be differences depending on the kind of screening test used in the programme, these are explored.

Cost-effectiveness
Cost-effectiveness analysis is one way of balancing costs and benefits. The cost effectiveness ratio is defined as:

> <u>Increase in cost when screening compared to no screening</u>
> Increase in benefit when screening compared to no screening

The usual measure of benefit from screening programmes is the years of life saved, or sometimes the quality adjusted years of life saved (QALYs), where the years gained are adjusted for the quality of life enjoyed.[5]

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[5] Even if screening detects a cancer and treatment is successful, life afterwards may not have 'full' quality (weighted as 1). The quality weight after diagnosis of colorectal cancer has been estimated at 0.96.

Within the analysis, comparisons can be made of cost-effectiveness of variations to a screening programme, for example different age ranges, and screening intervals. This information can be helpful to policy makers.

The 1998 report reviewed the evidence of the cost-effectiveness of colorectal cancer screening by FOBT, FS and colonoscopy (NHC 1998 Ch.8). This is summarised below and the main studies are referenced again, together with updates since the 1998 report. The analyses are in three broad categories:
1. economic analyses conducted alongside the RCTs.
2. application of RCT results to other countries.
3. simulation exercises.

Only FOBTg screening has analysis in the first two categories. Cost-effectiveness of screening by other modalities is based on simulations, in which a model is constructed assuming cancer detection rates, and cure rates dependent on stage at diagnosis. Unit costs of procedures are then applied.

Even for FOBT, not all information required for a cost-effectiveness analysis is available (for example the mortality reduction is limited to that observed over the life of the trial and would not be exactly determined until all trial participants had died). Actual costs are not always known. Therefore all studies involve some element of modelling and parameter estimation. Almost all studies undertake some sensitivity analysis to predict the effect on the cost-effectiveness ratio of changes in key variables eg, unit costs, mortality reduction, and the participation rate.

It is important that all relevant costs are included in a cost-effectiveness analysis (Drummond et al 1997). For a screening programme this includes the major cost-elements on the screening pathway, from identification and recruitment of the eligible population, through to testing and diagnosis. A mechanism to recall people for screening is often required. There are likely to be consequential changes to treatment costs, due to screening identifying cancers at an earlier stage, and this may need to be considered. Finally there can be considerable set-up costs and staff training to cope with the expected volume of tests and procedures.

The 1998 report found that:

> *No published cost-effectiveness analyses include the full health services costs of a screening programme, in particular health promotion, recall systems, administrative overheads, set-up costs and training* (NHC, 1998).

Therefore the Advisory Group paid particular attention to this aspect when reviewing recent literature.

FOBTg
The 1998 report focused on publications based on population RCTs. Early results of an economic evaluation alongside the Nottingham RCT of biennial FOBT screening for people aged 50-74 in the UK (Whynes et al 1998) reported favourable cost-

effectiveness ratios compared with mammography screening. Similarly a simulation analysis based on the Funen RCT (biennial screening 45-75 years) in Denmark (Gryd-Hansen et al 1998) found lower cost-effectiveness ratios than for breast screening and cervical screening.

However the UK study did not include the infrastructural costs of a programme (including administration, register and computerised recall system) and neither study included health promotion costs or set-up costs for expanded colonoscopy services (including capital costs and staff training). Therefore the cost-effectiveness would be somewhat overstated by these studies (and the costs to mount a programme would be underestimated).

Results on the most cost-effective age range for FOBT screening were not definitive. The Danish study showed better cost-effectiveness for older age groups. The UK study showed little difference in the cost-effectiveness ratio by age range, but results were more favourable for women (£4951 per QALY saved) than for men (£5685) (1996 prices). Only 8 years of screening on average had been undertaken in the UK trial. Simulations projecting the mortality reductions forward for further screening rounds produced lower cost-effectiveness ratios (£2047 per QALY gained for men and £1371 for women).

A more recent study (Whynes 2004), based on further data from the Nottingham trial (13 years of screening), has confirmed that the cost-effectiveness ratio for biennial FOBT screening is acceptable. The cost per quality adjusted year of life saved was £1584 (CI: 717, 8612) (2002 prices), much lower than the original estimates. Again, though, the analysis does not include the costs of administration, a register, health promotion or colonoscopy expansion, including workforce training.

A more comprehensive costing was undertaken by Stone et al (2004) in a study applying RCT results to Australia. The cost per disability adjusted life year gained for biennial FOBT screening for people aged 55-69 was $A17,000 (CI: 13,000-52,000) (1996 prices). This included the costs of recruitment, a register and recall system. No set-up costs for further endoscopy services were included, on the assumption that existing capacity was sufficient.

This study (Stone 2004) also estimated the costs of a biennial FOBTg national programme for Australia. For people aged 55-69 the annual cost was estimated at $A55M (CI: 46, 96) (1996 prices). It was postulated that a screening programme could bring savings in a number of areas including from a reduction in 'de facto screening colonoscopies' and less expensive treatment due to a shift in stage at diagnosis. Extending the programme down to people aged 50 would add $A22M to the cost; extending up to age 74 would add $A13M.

Compared with existing screening programmes, FOBTg CRC screening appears to be cost-effective in overseas populations. The incidence of CRC is higher in New Zealand and this could affect the test positivity, demand for colonoscopy, cancer

detection rate and mortality reduction. Cost structures may also differ. The cost-effectiveness ratio may therefore be different for New Zealand.

Flexible sigmoidoscopy and colonoscopy
The 1998 report found that the results of cost-effectiveness studies of screening by other modalities (flexible sigmoidoscopy and colonoscopy) to be limited due to the lack of RCT evidence of benefit (mortality reduction). This is still the case. Moreover, participation in these programmes is usually low; recent results from the UK flexible sigmoidoscopy trial bear this out with a participation rate of 39% (UK (NHS) FS trial, *Lancet*, 2002)

Modelling exercises have been undertaken, for one-off flexible sigmoidoscopy and also colonoscopy, assuming mortality reductions based on cure rates for treatments of the cancers at various stages, which it is hoped would be found by screening. O'Leary (2004) modelled one-off screening of average-risk people aged 55-74 in Western Australia, with 42% participation. The model predicted 21% mortality reduction per year for screening by flexible sigmoidoscopy and 31% for colonoscopy screening. The estimated *additional cost* per *additional* life year saved, *compared to the status quo* was $A16,801 for flexible sigmoidoscopy and $A19,285 for one-off colonoscopy (at 2001 prices). The status quo in Australia involves significant colonoscopy (1 in 20 in this age group). Therefore these results may not be transferable to New Zealand. In the absence of RCTs, the expected mortality reductions are speculative, as are the cost-effectiveness ratios.

Immunochemical faecal occult blood tests
Estimation of cost-effectiveness of screening using the new immunochemical faecal occult tests cannot be accurately determined due to the absence of RCT data on their benefits. It is thought that the benefit should be higher than when using FOBTg due to the greater sensitivity of FOBTi, but the associated decrease in specificity of the test would lead to a higher number of colonoscopies and hence higher costs. The test itself is also more expensive. The effect on the cost-effectiveness ratio (of increases in both the numerator and denominator) is not accurately known but sensitivity analyses of FOBT screening showed the ratio to be highly sensitive to both the mortality reduction and the test specificity.

Costs of a screening programme in New Zealand
At the time of the 1998 report, no country had a colorectal screening programme. The published cost-effectiveness analyses did not address the estimation of the costs to mount a programme. As mentioned above, major cost components were omitted from these studies, and it was acknowledged that these would need to be taken into account for a national programme (Whynes 1998).

The 1998 report presented estimates of the likely cost of biennial FOBTg screening in New Zealand, based on the results from the Nottingham RCT and factoring in some of the omitted costs (health promotion, administration and a register for recall)

based on New Zealand experience with the cervical screening programme. Set-up costs for additional colonoscopy services were not included.

Costs were estimated at $24 million (1997 prices, excluding GST) for the first screening round for people aged 50-74, assuming 54% participation (60% of the 90% of the population who could be identified at that time and thus invited to be screened). A significant proportion ($6.25 million) of this cost was for colonoscopies following positive FOBTg results.

The costs of a FOBTg-based programme have now been updated, to take into account, firstly, increased unit costs and, secondly, the higher participation (now 60% rather than 54%) that might be expected as health services develop their ability to identify the population to be screened (assumed now to be 95% compared to 90% previously). Costs have been estimated for the first eight years of a screening programme using the 2005 population as the base year (Department of Statistics), then allowing sub-groups to age in and out. Costs are in 2005 dollars. Table 8.1 shows the costs for the first year and the numbers of people undergoing each procedure.

Estimates are also shown for year 8 by which time full surveillance will be in place. Cost estimates are also shown for other screening modalities (FOBTi, flexible sigmoidoscopy and colonoscopy). These estimates are for the ongoing costs of screening programmes.

The estimates do not include important set-up costs, notably for the expansion of colonoscopy services (including equipment and staff training), policy development, quality assurance, a national media campaign, and the development of a screening register. Changes in treatment costs due to earlier stage at diagnosis are not included.

The estimates include estimates of administration costs, health promotion and the operational costs of a screening register.

The main purpose of this modelling was to identify the level of services required for each screening option. The actual costs would depend on how a programme is delivered and on factors which are unknown at present, including consumer participation, method of recruitment, positivity of FOB tests, and negotiated prices for services.

There has been no attempt to estimate cost per life year saved, since there is no RCT evidence of benefit for many of the screening modalities.

The NSU has commissioned a separate costing and economic evaluation of various screening options which draws on the NSU's experience in funding and operating other screening programmes.

Table 8.1: Estimated Resources and Costs of screening by different modalities
Year 1→Year 8
2005 prices

	FOBTg	FOBTi (5% positivity)	FS	Colonoscopy
Programme specification	Biennial 50-74 years	Biennial 50-74 years	One-off test at age 60	One-off test at age 60
Initial target population (1)	934,590	934,590	38,174	38,174
Identified population (2)	870,103	870,103	36,266	36,266
Participation	60%	60%	50%	50%
VOLUMES	**Year 1→Year 8**	**Year 1→Year 8**	**Year 1→Year 8**	**Year 1→Year 8**
Screened population (3)	260,000→330,000	260,000 → 330,000	18,000 → 23,000	18,000 → 23,000
Follow-up (4) Colonoscopy	5500 → 7200	13000 → 17000	1000 → 4800	0 → 4300
Histology	2600 → 2736	6100 → 6519	815 → 2406	2770→4168
COSTS				
Health promotion (5)	$3.07M →$3.89M	$3.07M→$3.89M	$0.26M→$0.33M	$0.26M→$0.33M
Identification invitation (5, 6)	$3.51M→$4.44M	$3.51M→$4.44M	$0.29M→$0.38M	$0.29M→$0.38M
Screening Test (7)	$1.82M→$2.30M	$5.12→$6.48M	$9.52M→ $12.30M	$14.27M→ $18.44M
GP referral (8)	$0.27M→$0.20M	$0.65M→$0.47M	$.05M→$0.06M	ZERO→ZERO
Follow-up Colonoscopy (4)	$ 4.87M→$6.36M	$11.59M→$15.15M	$0.85M→$4.24M	ZERO→$3.86M
Histology	$0.16M→$0.17M	$0.38M→$0.40M	$.05M→$0.15M	$0.17M→$0.26M
Administration (5)	$1.49M→$1.89M	$1.49M→$1.89M	$0.12M→$0.16M	$0.12M→$0.16M
Information system (5, 9)	$1.45M→$1.84M	$1.45M→$1.84M	$0.10M→$0.16M	$0.10M→$0.17M
Total estimated ongoing costs	$16.64M increasing to $21.08M	$27.26M increasing to $34.56M	$11.24M increasing to $17.78M	$15.21M increasing to $23.60M
Costs not estimated	Register set-up Media campaign Expansion of colonoscopy Quality assurance	Register set-up Media campaign Expansion of colonoscopy; Quality assurance	Media campaign Expansion of colonoscopy Quality assurance	Media campaign Expansion of colonoscopy Quality assurance

(1) Year 2005; excludes those with existing CRC diagnosis (2% aged 50-74; 1% aged 60)
(2) Assumes 95% of eligible population can be identified
(3) FOBTg and FOBTi screening are biennial, hence 50% of participating population are screened each year; For FS and colonoscopy screening a new group aged 60 are screened each year.
(4) For FOBTg, FOBTi, FS includes referral after +ve test, and polyp surveillance; for colonoscopy includes polyp surveillance, which begins in year 4 (see Table 6.1 Ch. 6 for details)

(5) Updated from the 1998 report using the consumer price index; estimated pro rata for the population eligible for screening
(6) Identification by GPs; invitation by letter
(7) Cost of test kit, test reading and reporting is $6.04 for FOBTg and $16 for FOBTi. Cost of FS is assumed to be $525 (based on O'Leary 2004) converted to New Zealand dollars and updated by CPI. It is assumed large polyps are removed at colonoscopy. Cost of routine colonoscopy is $754 and $1423 with polypectomy (MOH prices paid to DHBs).
(8) GP consultation for referral for colonoscopy following positive screening test (FOBTg, FOBTi or FS screening only); $50 per visit assumed.
(9) The costs of an information system for FS and colonoscopy would probably exceed the estimates shown, since the method of estimation is more appropriate to a larger database. Actual costs would depend on how the programme was delivered.

For each screening modality the estimated costs rise over time, firstly because of the ageing population, and secondly because of colonoscopy surveillance following removal of large polyps (over 10 cm).

It is possible that there may be some savings due to less costly treatment arising from a stage shift at diagnosis by screening, but it is not known when such savings would occur. Therefore they have not been included here.

Cost of FOBTg screening programme
The estimated cost of a biennial FOBTg based programme for people aged 50-74 is $16.64 million in the first year (and also in the second year), increasing to $21.08 million in year 8.

As mentioned above, the test positivity could differ in New Zealand, compared to that observed in the RCTs, due to the higher prevalence of the disease. Diet may also have an effect. This could translate into a higher colonoscopy burden and higher costs.

Cost of FOBTi screening programme
Estimated costs for a biennial FOBTi based programme screening people aged 50-74 are $27.3 million for the first and second years, much higher than FOBTg at $16.6 million. These higher costs can be attributed to the higher cost of the test itself (compared to FOBTg) and also the higher volume of colonoscopies resulting from the higher positivity rate.

By year 8 the costs (in 2005 prices) reach $34.55 million. Over 40% of this is for colonoscopy, including $8.39 million for initial referrals and $6.76 million for surveillance colonoscopy.

If the positivity rate were set at 8% (rather than 5%), then the cost in the first (and second) year would be $34.83 million. Over half of this ($18.54 million) would be for colonoscopy. Year 8 costs would be over $44 million, with colonoscopy accounting for $24 million.

Cost of FS programme
The estimated cost of one-off screening by flexible sigmoidoscopy at age 60 is $11.24 million for the first year, increasing to $17.78 million by year 8. Most of the cost, especially in the early years, is for the screening test itself. This procedure is not generally undertaken in the public hospital system, and no price was available. The estimate used ($525) is based on a conversion from an Australian study (O'Leary 2004). If this screening modality were chosen, there would be considerable set-up costs involved. The unit price could be higher. Current charges in the New Zealand private sector are around $900.

Colonoscopy for surveillance of adenomas reaches 3500 by year 8. By then the cost of colonoscopy including initial referrals amounts to $4.24 million.

These figures are for 50% participation in screening. If the rate drops to 40%, consistent with the UK RCT (UK (NHS) Pilot, *Lancet* 2004), the costs are $9.11 million in year 1 rising to $14.4 million in year 8.

Cost of colonoscopy screening programme
The estimated cost of one-off screening by colonoscopy at age 60 is $15.21 million for the first year, increasing to $23.60 million by year 8. Most of the cost is for the screening test itself (the initial colonoscopy). In the first year over 18000 colonoscopies would be performed. By year 8 this rises to almost 28,000, including for polyp surveillance.
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These figures are for 50% participation in screening. Participation could be lower, due to the preparation required for the test, and also because of the inconvenience and cost of travel (Frew et al 1999) since the procedure may not be offered in smaller centres. The cost for 40% participation is estimated at $12.30 million in year 1, rising to $19.43 million in year 8.

An assessment of total costs and total benefits
In considering cost–benefit issues in relation to a population screening programme, it is important to consider total benefit to the population as well as total cost. High participation in screening and high quality of all services on the screening pathway, are paramount in achieving full benefits for the population.

Total benefit to the population
This depends on the age range chosen for screening, the prevalence of the disease in that age range, the test sensitivity, the quality of diagnostic services and treatment, and the level of participation in screening.

Total cost
This also depends on the age range, the prevalence of the disease, the test sensitivity and specificity, the quality of diagnostic services and treatment, and the level of participation in screening.

Participation

Both total benefit and total cost are affected by the level of participation. It has been argued that the cost-effectiveness ratio is not materially affected by low participation (Howard et al 2005). Whether this is so depends on the relative size of fixed and variable costs of a programme, and the perspective of the cost analysis ie, who bears the cost. But more importantly low participation means lost opportunity to benefit and it is highly likely that this loss would be sustained by particular subgroups (low socioeconomic groups) thus leading to inequity.

Health promotion to ensure high participation and (in the case of FOBTg and FOBTi) to retain participation is essential and needs to be planned and funded.

Quality

High quality of all services on the screening pathway and for treatment services is required in order to achieve the potential benefits. A major issue is assuring quality of colonoscopy, given the expansion of colonoscopy services required for population screening.

Weighing up the costs and benefits

Table 8.2 presents four screening purchasing options, showing the likely benefit and cost of each. These are based on the four screening modalities. Costs and benefits could be altered by changing the screening parameters eg, age range for screening.
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Table 8.2: Screening Purchasing options- value for money

	FOBTg (biennial)	FOBTi (biennial)	FS (one-off)	Colonoscopy (one off)
Age range	50-74	50-74	60	60
Mortality reduction (1)	**15% RCT**	>15% Assumed	Unknown	Unknown
Participation	**60% RCT**	60% Assumed	50% Assumed	50% Assumed
Annual screened population (2)	260000→ 330000	260000→ 330000	18000→ 23000	18000→ 23000
Test availability	Good	Good	Limited (as dedicated FS procedure)	Required capacity not currently available
Pathology: Test reading Availability	Available; problem of quality control; (3)	Non-automated available; Automated needs to be set-up;	n/a	n/a
Pathology: quality control	Limited (3)	Good quality control possible (especially if automated)	n/a	n/a
Histology	Histology reading of biopsies/resections is available but will require workforce expansion (especially pathologists) for all options			
Annual colonoscopies Year 1→year 8	5500→7200	13000→17000	1000→5000	18000→28000
% increase in colonoscopy required (4)	28% → 36%	65%→85%	5%→25%	90%→140%
Ongoing annual Cost by year 8 (5)	$21M	$35M	$18M	$23M
Risk (due to colonoscopy) (6)	Low - provided high quality colonoscopy	Tight quality control required over expanded workforce	Low - provided high quality colonoscopy	Tight quality control required over expanded workforce

(1) Averaged over those **invited** to be screened
(2) Year 1 → year 8
(3) Because of limited quality control and difficulties with interpretation, FOBTg testing is not well supported by pathologists

(4) All options require increase in trained colonoscopists
(5) By year 8 polyp surveillance will be established.
(6) All options require high quality colonoscopy to reduce the risk

In summary the options are:

- **FOBTg**: modest gains for moderate cost but problem of quality control; substantial increase in colonoscopy required with associated set-up costs
- **FOBTi**: no RCT evidence, but an expectation of higher gains than FOBTg with higher ongoing costs; a doubling of growth of colonoscopy services compared to FOBTg with associated high set-up costs
- **FS**: no RCT evidence but expectation of moderate gains; large start-up cost to establish flexible sigmoidoscopy services; manageable colonoscopy load)
- **Colonoscopy**: no RCT evidence but greatest expected gains; high colonoscopy burden requiring rapid expansion and associated high set-up costs; also need to ensure participation.

Conclusion: Compared with existing screening programmes, FOBTg CRC screening appears to be cost-effective; however, the benefits are at best modest. Other screening modalities (flexible sigmoidoscopy, colonoscopy and FOBTi) are expected to bring greater benefits, but supporting RCT evidence is not yet available. They are also more expensive, particularly with regard to set-up costs. If evidence of greater benefit becomes available, these higher cost options may in the end represent the best course of action.

Evidence of cost-effectiveness of FOBTg is based on overseas populations. CRC incidence is higher in NZ and test positivity is unknown, consequently both costs and benefits may differ.

CONCLUSIONS

Table 9.1 below summarises the pros and cons of each kind of screening test that this report has examined in detail. The key considerations regarding each one are then highlighted in terms of their implications for a CRC screening programme in New Zealand.

Table 9.1: Pros and cons of the different screening tests for CRC:
FOBTg, FOBTi, flexible sigmoidoscopy and colonoscopy

Screening Criteria	FOBTg		FOBTi		Flexible sigmoidoscopy (FS)		Colonoscopy	
	Pros	**Cons**	**Pros**	**Cons**	**Pros**	**Cons**	**Pros**	**Cons**
Suitable Test	Presence of microscopic blood in stool used as an indicator of neoplasia		Tests for microscopic amounts of blood in the stool using antibodies to human haemoglobin		Examination distal colon allows visual detection cancer		Entire colon examined	
		Poor sensitivity-up to 50% of CRC in those screened will be missed.	Higher sensitivity than FOBTg Potential to identify a higher proportion of CRC than with FOBTg	Some CRC will still be missed	Sensitivity CRC estimated 50-60%	Will miss CRC in proximal colon	Best sensitivity (95%) and specificity for CRC.	
		Less specific for bleeding from large intestine	More specific for bleeding from large intestine	Lower specificity than FOBT, so more people will undergo unnecessary colonoscopy.	Can detect adenomas (pre-cancer) as well as invasive CRC		Can detect adenomas (pre-cancer) as well as invasive CRC	
				No consensus on which FOBTi for screening	May decrease incidence as well as mortality by removal adenomatous polyps in portion bowel examined		May decrease incidence as well as mortality	

Screening Criteria	FOBTg		FOBTi		Flexible sigmoidoscopy (FS)		Colonoscopy	
	Pros	**Cons**	**Pros**	**Cons**	**Pros**	**Cons**	**Pros**	**Cons**
	Non invasive		Non invasive		Single test	More invasive than FOBT Travel time for test	Single test	More invasive than FOBTg, FOBTi, or FS Travel time for test
	Self collected		Self collected					
	Less expensive than FOBTi			More expensive than FOBTg				
		Dietary restrictions	No need for dietary restrictions		Less bowel preparation than for colonoscopy No sedation	Requires enema preparation		Full bowel preparation
		3 samples needed	Less samples required.					Sedation for procedure
		Messy sampling technique	Simpler sampling techniques		Less time off work			More time off work
		Manual reading	Can be automated	Higher skill level cf FOBTg required for staff processing the test New laboratory equipment required		Procedure associated risks		Larger number of people exposed to risks of procedure ie bowel perforation and bleeding .
		Difficulty in definition positive test and reading weakly positive tests						
		Analytical sensitivity cannot be adjusted	Analytical sensitivity Can be adjusted			5% will need follow-up colonoscopy.		

Screening Criteria	FOBTg		FOBTi		Flexible sigmoidoscopy (FS)		Colonoscopy	
	Pros	**Cons**	**Pros**	**Cons**	**Pros**	**Cons**	**Pros**	**Cons**
		QA difficult	QA easier					
Evidence that screening is effective	**RCT evidence of 15% CRC mortality reduction over a significant period of time and a number of screening rounds**	Mortality reduction declined with longer follow-up.	Assumed reduction (based on comparison with FOBT)	**No RCT evidence.**	Multicentre RCTs in progress (UK and Italy), but not population-based	**No RCT evidence yet (mortality results due after 2005)**	Multicentre RCT in Scandinavia proposed	**No RCT evidence**
Potential benefit outweighs harm	Reassuring results from RCTs		Assumed similar to FOBT		Unknown	Unknown	Unknown	Unknown
Capacity of healthcare system	Requires 30-40% increase over current colonoscopy numbers performed within public health sector		Greater (65-85%) % increase in colonoscopy numbers than for FOBTg but positivity can be adjusted to manage the FU (but benefit may reduce)			Not in widespread use in New Zealand as a dedicated test. Equipment and workforce required	Already used as primary screening test for those at increased risk CRC	Impact on workforce.- potential to overwhelm New equipment required

Screening Criteria	FOBTg		FOBTi		Flexible sigmoidoscopy (FS)		Colonoscopy	
	Pros	**Cons**	**Pros**	**Cons**	**Pros**	**Cons**	**Pros**	**Cons**
Social and ethical issues		Biennial. Impact of missed cancers Acceptability of handling and storage of faecal material Some people falsely reassured Poor sensitivity may impact on the level of confidence and on other screening programmes		Biennial. Acceptability of handling and storage of faecal material	Single screening test may be more acceptable Procedure risks less than colonoscopy	Training and QA essential Less reassurance than for colonoscopy (only part of colon screened) Invasive Potential for procedure related complications	Single screening test may be more acceptable Provides high level reassurance as entire colon examined	Training and QA essential Invasive Potential for serious procedure related risks
Economic issues	Cost effective compared to other screening programmes	Substantial set-up cost for colonoscopy	Potential to be as cost-effective as FOBTg	Much higher costs, than FOBTg, (both ongoing and set-up)	Moderate costs once established	Set-up cost of FS services	Moderate costs once established	Very high set-up costs to expand colonoscopy services

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Implications of CRC screening test options for New Zealand

FOBTg and FOBTi
The potential to reduce CRC mortality with biennial FOBTg has been demonstrated in two randomised controlled trials in Nottingham, England and Funen, Denmark. The reported CRC mortality reduction was 13% in the Nottingham study (after 11.7 years and 3–6 screening rounds) and 11% in the Funen study (after 17 years and 9 screening rounds). The mortality reduction decreased slightly with time in the Nottingham trial (15% to 13%) but more so in the Funen trial (18% to 11%), where screening has continued to be offered. It is therefore unclear whether the magnitude of benefit shown by the trials can be maintained over time.

The longer study was reassuring in reporting low complication rates from colonoscopic follow-up of positive FOBT results. Similarly, with regard to long-term psychological harm, the data from the UK pilot has been reassuring.

Participation in the UK pilot study mirrored that in the RCT, indicating that FOBT is acceptable to the general population. Although the New Zealand acceptability study indicated that most would proceed with FOBT if offered it, we still do not know if a screening programme in New Zealand could achieve the same results.

The poor sensitivity of FOBTg (it will miss 50% of cancers) raises additional questions as to its acceptability as a screening procedure to health professionals, notably general practitioners. A separate shortcoming of FOBTg is the subjective nature of the interpretation of the test result, which causes difficulty for quality control.

FOBTi can involve methods of stool collection that are more acceptable to consumers than the methods for FOBTg, and it does not involve dietary restrictions prior to the test.

There has not been a randomised controlled trial of FOBTi screening for colorectal cancer, but because FOBTi is a type of faecal occult blood test, assumptions have been made based on the results from the randomised controlled trials of FOBTg screening. It has been assumed that since both screening tests detect colorectal cancer from the presence of blood in the faeces, FOBTi will be superior because it detects human blood specifically. Comparison studies have shown that in certain circumstances FOBTi can provide higher sensitivity than FOBTg, and has similar acceptability (see Section 2). For these reasons, it is assumed that screening using FOBTi will produce a greater mortality reduction than FOBT screening using FOBTg.

A consensus of the role of FOBTi in a screening programme has not been reached (Young et al 2002; Kerr et al 2005 [NZHTA]; Blue Cross Blue Shield Assoc 2006; Ouyang et al 2005). While the majority of studies reviewed by NZHTA pointed to some benefit of FOBTi over FOBTg testing the evidence base for this was not conclusive. Despite this the Australian pilot study which has just concluded (Aust Govt Report 2005) used two types of FOBTi and

following evaluation has advocated a national programme using FOBTi. It is also of some interest that the English colorectal cancer screening pilot (UK (NHS) 2003) had as one of its conclusions:

> *the majority of test-positive results in the UK Pilot have come from repeat-testing; this has caused long screening histories in many participants, and may be overly-burdensome in a national programme. Consideration should be given to tests which provide more definitive results on the first round of screening (e.g., immunological tests) – these warrant further evaluation.*

Colonoscopy capacity for both diagnostic and surveillance procedures remains constrained. The introduction of population screening for CRC using either FOBT would require significant workforce planning and capital investment.

Compared with existing screening programmes, FOBT CRC screening appears to be cost-effective in overseas populations. The incidence of CRC is higher in New Zealand and it is not known how this will affect the test positivity and demand for colonoscopy, and in turn the effect on the cancer detection rate, mortality reduction and thus cost-effectiveness.

Conclusion
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.

The Advisory Group recommends a feasibility study rather than a pilot study for the following reasons:

a) To clarify the purpose of the study. People differ in their interpretation of the purpose of a pilot study; some regarding a pilot study as determining how an actual programme would be run (after the decision to implement a national programme has been made), while others regard a pilot programme as providing essential information before a decision about a national programme can be made.

b) Currently NZ has insufficient colonoscopy capacity to appropriately assess people with symptoms of CRC and those at increased risk of CRC. The implications for provision of colonoscopy should be fully assessed as part of a feasibility study before a decision regarding a pilot study/ national programme is made.

c) New Zealand's capacity to provide many other components of CRC screening (including the ability to provide and interpret FOBTs, and pathology capacity for diagnostic purposes) is also uncertain, as are aspects of a CRC screening programme relating to potential benefit (for instance the positivity rate for FOBTg and FOBTi in New Zealand, and acceptability to the eligible population and health professionals). A feasibility study designed to address these uncertainties can provide the information required to make a decision regarding a pilot study/ national programme.

Flexible sigmoidoscopy
Flexible sigmoidoscopy while being a more invasive test and requiring enema bowel preparation does allow direct examination of the distal colon and the risk appears to be lower than for colonoscopy.

The majority of CRCs occur distal to the splenic flexure and therefore FS provides the opportunity to both detect CRC (3.5 /1000 screened UK Trial, 5.4/1000 screened Italy Trial) and also potentially reduce the future incidence of CRC in the area of bowel examined as a consequence of removing adenomatous polyps during the procedure.

Given the nature of the test participation is likely to be less than that for FOBT (on basis UK FS trial 39%) but a mortality reduction from CRC intermediate between that of FOBT and Colonoscopy is anticipated. Baseline findings of the UK and Italian multicentre trials have been reported but the mortality data is not anticipated for a number of years.

In New Zealand the majority of endoscopy centres do not utilise FS with only 3 of 24(13%) of public units and 6 of 12 (50%) of private units performing this as a dedicated procedure (i.e., using a flexible sigmoidoscope and not a colonoscope to conduct the examination) (Yeoman and Parry 2005).

In addition the three public units utilising FS report a combined total of approximately 600 procedures per annum (cf 2800 colonoscopies in the same units) with the six private centres performing a combined total of approximately 500 procedures per year (cf 2500 colonoscopies in those units).

The competence of nurse endoscopists (Maule et al 1994, Working Party British Soc Gastro 2005) has been established and their role is acceptable to patients but none are employed in New Zealand and only 25% of public units and none of the private units surveyed would be willing to employ or train non-physician endoscopists to perform either FS or colonoscopy.

A decision to introduce screening for CRC utilising FS would therefore involve substantial investment and training which could not be justified without evidence of mortality benefit in randomised controlled trials.

Conclusion
Further consideration with respect to screening for CRC by one-off flexible sigmoidoscopy in New Zealand should be deferred until the results of the UK and Italian multicentre trials are available.

Colonoscopy
Colonoscopy allows direct visualisation of the entire colon and is currently the gold standard investigation for detecting colonic pathology. It has been shown to detect more than 95% of CRC and 90% of advanced adenomas. Consequently it has the potential to offer a mortality benefit that is superior to any of the other proposed screening tests for CRC. In addition, as for FS, there is the potential to reduce the future incidence of CRC by the detection and removal of adenomatous polyps at the time of the procedure.

Nonetheless, it is not possible to draw firm conclusions on its effectiveness as the first-line test in a screening programme because no RCT evidence is available. Currently there is a Nordic initiative to conduct a randomised multicentre trial of screening for CRC by offering one- off colonoscopy to individuals aged 55-65 years of age but the results cannot be expected for many years.

Colonoscopy requires full bowel preparation and is an invasive test with the attendant risks of bowel perforation and bleeding chiefly relating to polypectomy. These aspects of the test reduce consumer acceptability. In any screening programme there would be a requirement for rigorous quality control of colonoscopy performance to minimise harms.
.
Primary surveillance colonoscopy is already recommended in New Zealand for surveillance in individuals with a moderate to high increase in their risk of developing CRC.

Colonoscopy is resource intensive and currently in New Zealand there is a significant shortfall in capacity within the public health sector for both diagnostic and surveillance procedures. The workforce resources and capacity to perform population based colonoscopy screening are not currently available in any country, including the U.S.A. (Seaff et al 2004) and if introduced in New Zealand would require a huge investment in training, workforce and equipment.

Conclusion
Further consideration with respect to screening for CRC by colonoscopy should be deferred until the results of randomised controlled trials assessing participation, feasibility, safety and mortality reduction, are available.

Research opportunities addressing the potential of CRC screening by colonoscopy should be pursued. New Zealand should consider accepting the recently extended invitation to participate in the Nordic colonoscopy trial.

SUMMARY

Colorectal cancer is a major health issue in New Zealand and it is a suitable candidate for a screening programme.

The Advisory Group offers a number of recommendations that may assist the introduction of an effective CRC screening programme. A feasibility study of CRC screening using FOBTi (or FOBTg and FOBTi) should be considered and planning initiated. This would inform a decision on whether the New Zealand health system could support an FOBTi-based CRC screening programme that achieves high participation rates and that is acceptable, effective and economically efficient.

The Advisory Group also makes some recommendations with regard to optimising the diagnosis and treatment of colorectal cancer that should improve outcomes, regardless of whether a screening programme is in place. In particular, there is an immediate and urgent need to expand colonoscopy services within the public health sector. There is also an immediate need to ensure that throughout NZ the treatment of CRC, both surgical and oncological, is based on a multidisciplinary approach with audited outcomes meeting international standards.

APPENDIX 1: RANDOMISED CONTROL TRIALS

TABLE A1.1: Funen and Nottingham randomised controlled trials of screening for CRC using FOBT (results published in 1996)

	Funen [1]	Nottingham [2]
Eligible population	Population based (Danish population register)	Population based (GP registers)
Size	2 groups of 31,000	2 groups of 76,000
Age range	45-75	50-74 (45-74 in pilot study)
Screening method	biennial FOBT (Hemoccult II)	biennial FOBT (Haemoccult)
Dietary restrictions	Yes	No (except for re-tests after positive FOB test results)
Participation at first screen	67%	53% [3]
Mean follow-up	10 years	7.8 years
Sensitivity (%) [4]	51	53.6
Specificity (%) [5]	98	96
PPV (%)	9 –17	12
Colonoscopy rate	4.3%	4%
Mortality rate in the control group	89 per 100,000 PY	70 per 100,000 PY
Mortality rate in the intervention group	73 per 100,000 PY	60 per 100,000 PY
Relative risk (95% CI)	0.82 (0.68 to 0.99)	0.85 (0.74 to 0.98)
CRC mortality reduction	18%	15%
ARR	16 per 100,000 PY	10 per 100,000 PY

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

2. *Hardcastle JD, Chamberlain JO, Robinson MHE, et al., Randomised controlled trial of faecal-occult-blood screening for colorectal cancer. Lancet 1996; 348: 1472-7.*

3. *The entire intervention group was invited at each round (including those who had not participated in the first round), and 60% participated in at least one screening round.*

4. *Sensitivity is calculated as true positive tests divided by the sum of true positive tests and interval cancers in the first year after a negative FOBT.*

5. *Specificity is estimated from all negatives divided by the sum of all negative plus false positive tests. This is a good estimate of specificity since false negative tests are a very small proportion of all negative tests.*

TABLE A1.2: Latest results from Funen and Nottingham trials

	Funen [1]	Nottingham [2]
Recruitment	1985	1981-1991
Screening rounds	9	3-6
Median follow-up	17 years	11.7 years
Screening	Continues (2004 report)	Finished in 1995
Participation (initial round) (final round)	67% 28% [3]	53% (60% at least once)
Non-attendees invited to subsequent rounds	No	Yes (from September 1990)
Mean age (initial round) (final round)	59.8 years 73.0 years	
Person-years (intervention)	431,190	844,419
Person-years (control)	430,755	843,463
CRC mortality Relative risk (95% CI)	0.89 (0.78 to 1.01)[4] 0.84 (0.73 to 0.96)	0.87 (0.78 to 0.97)
CRC mortality reduction	11%	13%
Percentage undergoing at least one colonoscopy	5.3%	1.9% [5]
Serious complications arising from colonoscopy	?	0.5% [6]
Colonoscopy-related mortality	Nil [7]	Nil [2]

1. Kronborg O, Jorgensen OD, Fenger C, Rasmussen M. *Randomized study of biennial screening with a faecal occult blood teat: results after nine screening rounds. Scand J Gastroenterol 2004; 39: 846-51.*

2. Scholefield JH, Moss S, Sufi F, mangham CM, Hardcastle JD. *Effect of faecal occult blood screening on mortality from colorectal cancer: results from a randomised controlled trial. Gut 2002; 50: 840-44.*

3. *Of the non-attendees at the final screening round, one third had other severe disease, and 6% thought they were too old to be screened.*

4. *CRC mortality including complications from treatment.*

5. *Some patients were referred for barium enema rather than colonoscopy (0.7% underwent barium enema). This was a clinical decision based on coexisting cardiovascular or respiratory disease. It is not clear how the percentage undergoing at least one colonoscopy could have dropped from 4% in the earlier report (unless 1.9% is the percentage for the second time-period, from 7.8 years to 11.7 years median follow-up).*

6. Robinson MHE, Hardcastle JD, Moss SM et al., *The risks of screening: data from the Nottingham randomised controlled trial of faecal occult blood screening for colorectal cancer. Gut 1999; 45: 588-92.*

7. Jorgensen OD, Kronborg O, Fenger C. *A randomised study of screening for colorectal cancer using faecal occult blood testing: results after 13 years and seven biennial screening rounds. Gut 2002; 50: 29-32.*

UK Colorectal Cancer Screening Pilot

Table A1:3
Aim: To test the feasibility of a national screening programme
- Demonstration pilot (based on Nottingham RCT)
- 2 English and 3 Scottish health authorities
- 2 year period

Choice of Test	FOBTg	- 2 samples@3 stools - Repeat test if weak positive test result
Recruitment	All residents 50-69	Test kit by mail; with information on false +ve, false –ve, adverse events
Analysis	2 laboratories	Accredited
Follow-up procedures After +ve FOBT	1. colonoscopy 2. DC barium enema	Quality Assurance programme
Histopathology	Specialist histopathologists	Quality Assurance
Uptake of FOBT	56.8%	Higher for women
positivity	1.9%	Higher for men, and by age
Colonoscopy uptake	81.5%	
Morbidity ex colonoscopy	Bleeding/pain 10 (0.24%) admit overnight 13 (0.32%) readmitted	2 perforations (.05%)
Positive predictive value	10.9% invasive cancer 35% adenoma	Higher for men
Stage distribution (16.6% invasive polyp)	48% A (26% + 22% polyp) 25% B 28% C 1% D	
Cancer detection rate	1.62 per 1000 screened	(6.91 for cancers+adenoma)

CONCLUSION: Pilot areas did as well as the Nottingham RCT

Table A1:4

Issues

Age range	Should it be up to 75 years?
Uptake of FOBT	Over 40% declined to participate
Uptake of colonoscopy after +ve FOBT	10.87% declined colonoscopy
Colonoscopy	The 5 pilot areas selected because had high standard; training required to meet demands of national programme; nurse colonoscopy?
Need to involve primary care	Letters of invitation
Sensitivity/specificity of FOBT	50 % sensitivity (misses half the cancers); Over half colonoscopies find no neoplasia (cancers/ adenomas)

CONCLUSION: FOBT screening is viable, but would put pressure on overstretched system; improvements in provision of services required.

Australian FOBT Pilot Programme

Table A1:5

Eligible population	56,907 eligible men and women from 3 pilot sites (one rural and two urban) were invited to participate in the pilot
Recruitment	2002-2004
Age range	Men and women aged 55-74 years on 1 January 2003.
Invitation method	Mailed invitations with FOBT kits included
Screening method	Self-administered immunochemical FOBT (two types; *Bayer Direct* FOBT and *Inform* FOBT)
Screening interval	Biennial screening
Screening rounds	Only one screening round (the prevalence screen) was undertaken during the pilot
Participation	25,840 (45.4%) overall 47.2% for *Bayer Direct* FOBT 43.6% for *Inform* FOBT
Positivity rate	2,308 (9.0%) of correctly completed FOBTs were positive (10.5% for men, and 7.7% for women)
Colonoscopy following positive FOBT	1,273 (54%) attended for colonoscopy#
Colonoscopy following negative FOBT	525 attended colonoscopy
High risk lesions detected in screened group	
Cancers detected following positive FOBT	67 (1.17 per 1,000 screened)*
Cancers detected in screened group	69 (1.21 per 1,000 screened)*

Because of incomplete data, it is likely that this is an underestimate, and that more people attended colonoscopy following a positive FOBT

* Because of problems with data quality and completeness in the Australian pilot, 'suspected' cancers were reported, rather than confirmed cancers. Of 67 suspected cancers detected following positive FOBT and colonoscopy, 20 had been confirmed at the time of the pilot programme evaluation.

(Ref: Australian Government Dept of Health and Ageing: Final evaluation report 2005)

Comments on the multicentre randomised controlled trial of screening for colorectal cancer using flexible sigmoidoscopy.

Study design

This is a multicentre randomised controlled trial undertaken in 14 centres in the UK and 6 centres in Italy.[1-3] Baseline findings from the UK centres of this multicentre trial have been published and are summarised below.

Eligible population

Initially general practices were approached to mail out a questionnaire to patients in the 55-64 year age-range. Of the 574 practices approached, 505 (88%) agreed. General practitioners excluded people according to the following exclusion criteria: inability to provide informed consent, history of CRC, adenomas or inflammatory bowel disease, severe or terminal disease, life expectancy less than 5 years, or sigmoidoscopy or colonoscopy within the previous 3 years. The remaining people were mailed a questionnaire and those who responded that they would attend for flexible sigmoidoscopy screening if they were invited, were entered into the trial.

Randomisation

Allocation to groups was by household (similar to the Nottingham FOBT Trial), rather than individual randomisation. Those individuals with a strong family history of bowel cancer or suspicious symptoms were not randomised (but were assessed outside the trial). People in the control group were not contacted.

Screening method

Single flexible sigmoidoscopy (FS). Small polyps were removed during this examination. Those with high-risk polyps (diameter 1cm or larger, 3 or more adenomas, tubulovillus or villous histology, severe dysplasia or malignancy, and 20 or more hyperplastic polyps above the distal rectum) were referred for colonoscopy. A very small percentage (0.1%) of people was referred directly for surgery following FS.

Assessment of people with positive screening results

Those with high-risk polyps identified at FS were referred for colonoscopy. As a result of colonoscopy people were discharged, invited to attend surveillance colonoscopy, or referred for surgery.

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Follow-up

Primary endpoints were incidence of CRC and death. Follow-up information was obtained from the National Health Service Central Registry database, and the Office of Population Censuses and Surveys.

Internal validity

This multicentre trial was designed to detect a 40% difference in the incidence of CRC at 10 years and in mortality at 15 years in each of two main subgroups (age less than 60, age 60 and over) with 90% power and a 5% level of significance. The required sample size was 195,000 (130,000 controls and 65,000 in the intervention group).

An intention to treat analysis is planned (to maintain control of confounding and avoid selection bias).

External validity

This multicentre trial was not population-based. Initially general practices were approached to mail out a questionnaire to patients in the 55-64 year age-range. Of the 574 practices approached, 505 (88%) agreed. Of the 375,744 people aged 55-64 registered with these practices, 7,602 were identified by their GPs as ineligible (however practices ranged from excluding 0 to 144 patients per practice). Of those sent questionnaires (excluding those returned undelivered) only 55% responded positively, and 8,280 were excluded as ineligible.

The main reason for designing the trial this way was to try to maintain high participation in the intervention group. The limitation is that those who took part in the trial may differ from the wider population in their views about screening in general, flexible sigmoidoscopy, and possibly in their risk of CRC. This means that certain results from this trial may not be generalisable to a wider population. These are listed below:

Acceptance of an invitation for FS screening;
Acceptance to a recommendation for colonoscopy;
Views obtained from acceptability surveys about FS or colonoscopy;
Polyp detection rates;
Cancer detection rates.

The results from the paper on acceptability of FS screening should be read with these limitations in mind (the authors address these issues in the discussion).
Differences in outcome between the intervention group and control group should be valid however, since the two groups should be similar at baseline (due to randomisation). It is important to note however, that no comparison between the intervention and control group has been provided in the report on baseline findings. Although the trial participants are a highly selected group, the trial investigators maintain there is no biological reason to expect FS

screening to produce a different effect on CRC incidence or mortality in the group of people who took part in the trial compared with a wider population. (This is the argument that is used to justify generalising the results from the British Doctors' Study about the effects of smoking to populations other than doctors).

Table A1:6 Randomised controlled trial of screening for colorectal cancer using flexible sigmoidoscopy baseline findings (UK centres only)

Eligible population	354,262 people sent initial questionnaire (via GP) to gauge interest in FS screening. 194,726 (55%) who responded positively were entered into the trial and randomised.
Recruitment	October 1996 to March 1999
Randomised	170,432 (57,254 invited for screening, 113,178 controls)
Age range	55-64 years
Screening method	Single FS screen, with removal of small polyps.
Attendance	40,674 (71%)
Discharged after single FS	38,525
Colonoscopy	2,131 referred to colonoscopy (2,051 accepted)
Surgery	37 referred straight to surgery after FS 157 referred to surgery after colonoscopy
Surveillance	1,745 (with 'high risk' polyps) referred for 2 further colonoscopies at 3-year intervals
High risk lesions detected in screened group	1,905 (4.7%)
Cancers detected in screened group	131 (0.3% of those screened)
Follow-up	Passive follow-up (through NHS Central Register and Office of National Statistics)
Primary Endpoints	Incidence of CRC Death
Secondary Endpoints	Adverse events associated with any aspect of the screening procedure

APPENDIX 2: PHYSICAL HARMS ASSOCIATED WITH CRC SCREENING

The following tables prepared by the National Screening Unit (Dr Carolyn Shaw, Public Health Registrar) cover literature from trials or pilots of screening programmes published subsequent to the 1998 National Health Committee discussion document. It should be noted that a considerable amount of literature from other studies is also available.

Physical harms

The harms that could potentially occur from a screening programme that uses either faecal occult blood testing or flexible sigmoidoscopy (FS) as the screening test, followed by diagnostic colonoscopy are outlined in Table A2.1.

Table A2.1 Potential harms on the CRC screening pathway

Where harm sustained in screening pathway.	Harms
Screening test-FOBT	The screening test itself is unlikely to cause physical harm
Screening test-flexible sigmoidoscopy	Perforation Post procedure surgery Haemorrhage Death
Diagnostic procedure-colonoscopy	Perforation Post procedure surgery Haemorrhage Death
Treatment-surgery, radiotherapy, chemotherapy	Death after surgery Chemotherapy related deaths? Radiotherapy related deaths?

Flexible sigmoidoscopy screening complication rates

Table A2.2 summarises the published harms from screening trials using flexible sigmoidoscopy. Harms are also possible from endoscopy instruments that are not sterilised adequately between procedures.

Table A2.2 Harms following screening with flexible sigmoidoscopy

Trial/Pilot	Moderate or severe pain	Vagal reactions (nausea/vomiting /dizziness)	Number of perforations	Haemorrhage rate	Surgery required post FS	Deaths
UK FS Trial (1) (2)	18%	3-4%	1 (out of 40674 procedures) (all occurred after snare polypectomy)	12 people required admission to hospital	3 people required surgery after perforation during colonoscopy or FS	6 in 30 days post FS (3xMI, intra-cranial bleed, lung cancer and cardiomyopathy)
SCORE Trial (Italy) (3)	8 (9911 procedures)	0.4%	1 (9911 procedures)	Nil	Not commented on (assume none)	Not commented on (assume none)
Telemark Polyp Study (4, 5)	Nil					
PLCO trial (USA)	Baseline data (including harms) not yet reported (due to be published July 2005 in JNCI)					

MI= myocardial infarction

There were also 2 non fatal cardiac events within 3 days of screening using flexible sigmoidoscopy reported in the UK FS trial (2). Other complications reported include gluteraldehyde colitis, latex allergy seizures (in individuals with epilepsy), and mild self limited bleeding (2, 3). Overall mild self-limited complications after FS were reported in 0.6% of individuals in the SCORE trial (3).

Colonoscopy complication rates

Table A2.3 summarises the published harms from screening trials using diagnostic colonoscopy after screening with either flexible sigmoidoscopy or faecal occult blood tests. Harms are also possible from colonoscopy instruments that are not sterilised adequately between procedures.

Table A2.3 Harms following diagnostic colonoscopy in screened population

Trial/Pilot	Perforations	Haemorrhages	Surgery required due to complications from colonoscopy	Other morbidity post colonoscopy	Number of deaths
Nottingham (6) (7)	5 (1474 procedures)	1 (1474 procedures)	6 (1474 procedures)	1 snare entrapment	Nil deaths Non significant increase in mortality from IHD in screened group
Funen (8)	Not reported				None
Minnesota (11)	No new evidence about harms published since 1997				
UK Pilot (9)	2 (3600 procedures)	23 admitted with post procedure bleeding or pain (3600 procedures)		Not stated	1 (of unrelated condition)
Australian Pilot	Not available				
UK FS Trial (1) (2)	4 (2377 procedures) (all occurred after snare polypectomy)	9 (2377 procedures)	3 people required surgery after perforation during colonoscopy or FS	Not stated	1 (MI)
SCORE trial (Italy) (3)	1 (775 procedures)	1 (775 procedures)	Not reported (assume none)	Not stated	Not reported (assume none)
Telemark Polyp Study (4, 5)	Nil				

MI= myocardial infarction

Harms from treatment

The harms from treatment are also included in the harms of a screening programme. Limited data are available on these harms (see Table A2.4).

Table A2.4 Harms following treatment

Trial/Pilot	Deaths within 30 days of surgery for cancer or adenoma diagnosed by screening	Over diagnosis[6]	Oncology related deaths
Nottingham(6)	5 (MI, PEx2, anastomotic leak and carcinomatosis)	6 cases (of about 45000 screened)	Not stated
Funen (8)	Numbers not reported, although there were comments about post operative deaths		Not stated
Minnesota(11)	No new evidence about harms published since 1997		
UK Pilot (9)	3 deaths post surgery (time frame not specified)	Not stated	Not stated
UK FS Trial (1) (2)	4 (2xMI, 1 respiratory causes and 1 septicaemia)	Not stated	Not stated
SCORE trial (Italy)	Not stated		
Telemark Polyp Study (4, 5)	Nil reported		

MI= myocardial infarction PE= pulmonary embolus

Other harms
No reported increase in mortality from suicide in screened group in Nottingham trial (10)

References

1.   Atkin WS et al. Uptake, yield of neoplasia, and adverse effects of flexible sigmoidoscopy screening. Gut 1998; 42(4): 560-55.

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5.   Thiis-Evensen E, et al. The effect of attending a flexible sigmoidoscopic screening program on the prevalence of colorectal adenomas at 13-year follow-up. American Journal of Gastroenterology 2001; 96(6):1901-7.

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[6] Defined as death from an unrelated cause (NOT CRC) between 30 days and 2 years post surgery for an adenoma or Duke's A cancer

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11   Mandel JS, Bond JH, Church TR, et al. 1993. Reducing mortality from colorectal cancer by screening for fecal occult blood. N Engl J Med 328:1365-71.

APPENDIX 3: ROLE OF GENERAL PRACTITIONERS IN UK AND AUSTRALIAN COLORECTAL CANCER SCREENING PILOTS

General Practice had markedly different roles in the UK and Australian bowel cancer screening pilots.

Role of general practice in Scottish pilot

The Scottish pilot and planned programme is centrally managed without significant GP involvement. During the initial pilot screening rounds, GPs had questions themselves and from their patients about the programme which were addressed by the screening nurse visiting practices. Subsequently there was little regular contact with practices and clinical information about patients with positive tests was primarily obtained from hospital rather than GP records.

The initial checking of mail-out lists (prior notification lists) at GP practices has been stopped at the conclusion of the pilot phase as it contributed little of benefit. Checking prior notification lists was done by practices as a goodwill activity, the quality was considered patchy, and it was found that not only were GP-held patient addresses often incorrect (especially for men) but even clinical information was incomplete. Further, some GPs felt they were in a position of having to make decisions about who should be screened which was not the intention of the exercise (which was limited to checking accuracy of addresses, and excluding patients on clinical grounds eg, no colon, or patients who had died or who were considered to be receiving terminal care).

GP involvement was actively reduced by attending to alternative management of any issues that might impact on general practice. These included the following:

- The Screening Unit maintaining a high public profile and identifying itself as the contact centre for information
- No specific role for GPs boosting participation
- Positive FOBTs are managed by a designated screening nurse without practice involvement
- Notification to GPs of positive but not negative screening results
- Ensuring the programme was not used for symptomatic patients
- Hospital clinic management and ongoing surveillance of all colonoscopy findings
- Reporting negative colonoscopy results to GP with advice no further investigations required for asymptomatic patients.

There has not been any planned GP education on management of symptoms suggestive of colorectal cancer but patients receiving notification of negative screening results are advised about specific colorectal symptoms to report to their GP.

Role of general practice in Australian pilot

In the Australian pilot, people were invited to participate from a central register and both positive and negative results were notified to a GP who was responsible for arranging appropriate management. Most GP consultations resulting from the Pilot occurred after the laboratory had sent participants' FOBT results.

Role of GPs in the Pilot

GP involvement in the pilots (and planned programme) has been actively encouraged. GPs had both clinical and administrative roles to perform. When returning their completed FOBT, participants were asked to nominate the GP to whom their test results were to be sent. Participants were also encouraged to visit their GP prior to completing their FOBT, if they wished to discuss symptoms, family history, the meaning of a positive FOBT result, or any concerns about the appropriateness of screening. In cases where GPs were visited by a patient still considering whether to complete their FOBT, GPs were asked to explain the Pilot's objectives and provide information on bowel cancer and screening and how to complete the FOBT. The pathology laboratories were required to send the FOBT test results to the participant, their nominated GP and the Register within two weeks of receiving the FOBT. Pilot participants with a positive FOBT result were then advised to visit their GP. In these cases the GP was expected to refer the person for further assessment as appropriate. GPs were asked to provide information to the Register about consultations with Pilot participants using *GP Assessment* forms. GPs who returned the Pilot forms received an information payment from the Register.

Communication with GPs

Effective communication with GPs was critical given their central role in follow-up of participants, co-ordination with pathology laboratories, assessment of patients by colonoscopists and feedback to the Register. Communication with GPs was managed by each of the Divisions of General Practice in the Pilot sites, which provided GPs with information and support at the local level. Division activities included orientation evenings, information workshops, visits to GP practices, preparation of local information material, presentations at conferences and updates in GP newsletters.

Most GPs saw the Pilot as valuable. GPs also felt that the Pilot had been well designed and implemented, and commented positively that:

• workload and administration was not unduly burdensome;
• communication with them about the Pilot was good;
• their duty of care responsibilities were well defined; and
• the FOBTs were effective.

The general view was that, while there were a few components of the Pilot that could be improved, overall the Pilot had worked well. The increased workload as a result of the Pilot was not seen as onerous. GPs were also quite comfortable with the administration involved as it was part of a programme they saw as meaningful and important. In addition, the payment for completing forms and returning them to the Register was seen as an incentive for participation.

The invitation process

Although feedback suggests that some GPs were involved in encouraging people to participate, data from the Register suggests that this was not a major imposition on their time. It should be noted that for non-participants in the Pilot, a higher number would be more likely to participate in a future FOBT based screening programme for bowel cancer if their GP advised them to. GPs considered that it was impractical for them to provide initial reminders to encourage the target population to complete the FOBT in the first place, unless patients made an appointment to come into the practice. GPs were generally unaware of when the kits were received and they did

not necessarily know if a patient had nominated them as their GP. Furthermore, most felt that it carried more weight if the Register followed up invitations with no response – they considered that patients would feel more obliged to respond than if the call was from a GP.

GPs generally found patient reactions to the programme were positive. GPs involved in the qualitative research noted that, while some patients had been initially reluctant to participate, they had responded more positively after talking with existing participants, and finding out how easy the kits were to use.

Responding to positive FOBTs

GPs performed an important role in the operations of the Pilot once a participant received a positive FOBT result. The Register data indicated that only 62.1% of participants visited their GPs after a positive FOBT, which suggests that either:
• a significant number of participants who had a positive FOBT did not visit their GP; and/or
• a high proportion of participants did not have their *GP Assessment* forms returned.

The median waiting time between a positive FOBT result being sent to a participant and a GP consultation was nine days. This suggests that most GPs had relatively efficient processes for follow-up once a patient received a positive result.

GPs clearly saw that the Register would have the ultimate responsibility for reminders because the Register had access to all the necessary information to undertake the follow-up and there was a risk that those people without a nominated GP would 'fall though the net'. However, many saw it as good practice to follow-up their patients once there was a positive test result. Most GPs were comfortable with their duty of care responsibilities in the Pilot. Their view was that the duty of care remained with the Register until a patient consulted them regarding a positive result or a symptom. However, some changes were suggested to further clarify responsibilities. These centred around the programme communications encouraging patients to consult their GP, or a GP if they did not have a regular doctor. Firstly, patients receiving positive FOBT results who had not nominated a GP should be encouraged to consult a GP. Secondly, while patients with a nominated GP who tested positive were advised to consult their GP, a timeframe was not specified. A timeframe of two weeks was suggested as appropriate.

The colonoscopy referral process

The proportion of people with a positive FOBT who were referred for colonoscopy did not vary significantly by Pilot site, age, or sex. There was no significant variation in referral rates by quartile of socioeconomic status or whether or not the person spoke a language other than English.

Some patients with negative FOBT were referred for colonoscopy because of family history and/or symptoms of bowel cancer. Some GPs stated that the waiting times for colonoscopies had been too long during the Pilot (mean 30 days) and there had been insufficient specialists to deal with the numbers coming through the Pilot. They commented that this generated anxiety for patients. As a result, there were concerns expressed as to whether there would be enough specialists to cope with the increased demand for colonoscopies generated by a potential national programme.

It was suggested that better measurement and prioritisation of urgent cases would improve queuing times. Others believed this was less of a problem because they

had been able to prioritise urgent patients if a patient had other indicators of bowel cancer in addition to a positive FOBT result, such as family history or other clinical signs. The GPs that experienced this were reasonably comfortable with the waiting times as they felt they were able to manage their patients' expectations by letting those who had to wait for longer know that the risk that their positive test result meant bowel cancer was low. Others also noted that despite the issues with waiting times, the Pilot had provided better access to colonoscopies through the public system than had previously been available.

There were concerns over whose responsibility it was to ensure the completion of the referral process. Some GPs believed that there was no system in place to confirm when referrals for colonoscopies had been received. GPs said they would be more comfortable if the referral process included some form of check so they would know that a referral had been received, rather than the Register following up when no colonoscopy occurs within a pre-determined period.

The GP education programme

There were mixed reactions to the information that GPs received regarding the Pilot from the Register and the Divisions. There was a common perception that too much information had been provided on the programme prior to its commencement. This related to both the workings of the Pilot and bowel cancer generally. In relation to the former, a number of GPs had been concerned about their role in the programme and the time involved, after attending an information session. They talked about having received a 'huge' file of information to read which gave them the impression that the administration would be highly complicated. It was only after the Pilot started that they realised that the administration was in fact not difficult or overly involved. Some recommended that the information packs given to GPs be greatly reduced with only one or two pages outlining the process. Many found general education on bowel cancer to be unnecessary as this was basic information that they had learned in medical school.

Although many GPs believed that in general they had received too much information prior to the Pilot, there was one aspect of the education that they had found particularly useful – the efficacy of the FOBTs used. Perceptions of the tests depended on 'what articles they had read'. They therefore felt that education from the Divisions early in the Pilot on the effectiveness of the tests being used in detecting cases of cancer and reducing bowel cancer mortality was important. A number also found feedback during the Pilot on how the programme was working and how many cases had been picked up was useful in reinforcing the value of the FOBT as a screening test.

Opportunities to improve GP administration processes

Most GPs felt that effort had been taken in the development of processes and forms to make the administration as easy as possible. Furthermore, most felt that, as their dealings with patients regarding the Pilot had been spread over an extended period, they were not overloaded with too many patients at any one time.

GPs suggested there were a number of opportunities for improvement in the programme's operations. Almost all interviewed for the qualitative evaluation mentioned that the forms lacked a participant number, despite there being a box for insertion of these details on the GP forms. Initially, a number of GPs had spent time trying to find out this number when completing the forms. Eventually, they tended to leave this field blank, so it was seen to be an unnecessary item. Some GPs were

worried that failing to complete this item meant they would not receive payment as they had not filled in the form correctly.

Another issue identified with the forms was the difficulty in telling the *Referral* and *Nonreferral* forms apart. Many GPs suggested that the forms should be colour coded to overcome this confusion, or simply be combined with the option to tick a box to indicate whether the participant under consideration was for referral or non-referral. In addition, it was recommended that the forms should include a section with additional space where GPs could provide information deemed necessary, such as medication history and notes from the medical examination.

Another recommendation for form design was that the contact details of the Register and the Helpline should be included on the forms to save GPs from having to look elsewhere for this information. GPs were in favour of the use of electronic forms for collection and transfer of patient information. Most GPs felt that this would be much easier and consistent with the way they were doing the rest of their practice administration, but they noted that the forms would have to be compatible with their practice software in order to prevent double handling.

Some GPs reported being confused by the system of payments in the Pilot. They found it difficult to reconcile payments. Specific item numbers were offered as a suggestion to overcome this problem.

General Practice Quality Assurance

Proportion of participants with a positive FOBT visiting their GP
The data, as recorded in the Register, suggested that a significant number of participants that had a positive FOBT did not visit their GP.

GP referral rate for follow-up colonoscopy without a positive FOBT
The Register data indicated that there were patients referred for follow-up examination without a positive FOBT. The majority of these participants were referred for a family history and/or symptoms of bowel cancer.

Areas for possible further work
• Explore the possibility of electronic forms and electronic submission of forms to the Register.
• Promotion of the application of the NHMRC Guidelines when considering referral of a participant with a negative FOBT result for colonoscopy.

References:
Evaluation of the UK Colorectal Cancer Screening Pilot Final Report (February 2003, revised May 2003) UK CRC Screening Pilot Evaluation Team

Australia's Bowel Cancer Screening Pilot and Beyond Final Evaluation Report

Bowel Cancer Screening Pilot Monitoring and Evaluation Steering Committee
October 2005 © Commonwealth of Australia 2005

APPENDIX 4: A SURVEY OF COLONOSCOPY CAPACITY IN NEW ZEALAND

Yeoman, A and Parry, S 2005. *A Survey of Colonoscopy Capacity in New Zealand*. Report commissioned by the National Screening Unit.

Introduction

Current indications for colonoscopy in the New Zealand public health system include diagnostic procedures in symptomatic patients and surveillance of individuals at increased risk of developing Colorectal Cancer (CRC).
Guidelines for the Surveillance and Management of Groups at Increased Risk of CRC were released by the New Zealand Guidelines Group in May 2004.[1]

The introduction of population screening for CRC would increase the demand for colonoscopy and, as this is now being considered, an estimate of the current colonoscopy capacity in New Zealand is required.

Prior to this survey limited information was available with regard to both the number of colonoscopies being performed each year for diagnostic and surveillance purposes and any demand/supply gap in provision of this service.

Quality assurance for procedures such as colonoscopy is increasingly being accepted as the norm and is fundamental to any screening programme. However the extent to which this is practised in New Zealand's endoscopy units remains to be established as does the number of units offering training in colonoscopy.

While the prime focus of this survey is colonoscopy capacity within public hospitals, private facilities offering colonoscopy were included in the survey because spare capacity that could be utilised for screening or surveillance of CRC may reside in this sector.

Survey Aims

Colonoscopy is a procedure that is integral to the diagnosis of and surveillance for CRC.

This survey was performed with the aims of determining:

- The number of colonoscopies performed on an annual basis within New Zealand's public hospitals

- The existing gap between provision and demand for:

  - diagnostic colonoscopy in patients with symptoms suggestive of colorectal cancer
  - surveillance colonoscopy for individuals at increased risk of developing colorectal cancer as defined in the published guideline[1]

- Factors currently limiting provision of colonoscopy particularly in the public sector

- Number of endoscopy centres:

  - providing training for colonoscopy and
  - performing audit of colonoscopy performance

Survey Conclusion

In New Zealand's public hospitals a significant gap exists between colonoscopy demand and provision for both diagnostic and surveillance procedures related to colorectal cancer.

This gap in provision is more apparent in the main centre public hospitals.

If population screening for CRC were to be implemented a significant increase in colonoscopy resource would be necessary to ensure waiting times for symptomatic patients did not increase.

This conclusion is substantiated by the survey results outlined in the Executive Summary

Executive Summary

- The survey was base on the National USA Survey of Endoscopic Capacity (SECAP)[2] but modified for the New Zealand situation.

- The final survey questionnaire posed 39 questions and was dispatched to all public endoscopy units and private facilities identified as performing colonoscopy.

- The survey response rate for large centre public hospitals (Auckland, Hamilton, Wellington, Christchurch and Dunedin) was 100% and for small centres was 81% (17/21).

- The response rate for private institutions was 67% (12/18).

- The overall response rate of 78% compares favourably with the SECAP study (70%).[2]

- The number of colonoscopies performed annually in the public hospital centres responding to the survey is 18,139.

- The total number of colonoscopies performed in the 4 main population centres (Auckland, Wellington, Christchurch and Dunedin) is 8,222 compared to 4,286 in 1997.

- Despite this increase in colonoscopy provision:

    o more than half of large public centres and a third of small public centres at the time of the survey are unable to deliver diagnostic colonoscopy within a suitable time frame (within 3 months) for patients with symptoms suggestive of colorectal cancer.

- The responding public hospital endoscopy units reported 828 patients aged over 50 years with symptoms suggestive of colorectal cancer to have been waiting >6 months for a diagnostic colonoscopy.

- Surveillance colonoscopy is recommended for individuals at increased risk of colorectal cancer (www.nzgg.org.nz). In the majority of large centres only 20% of patients awaiting a surveillance colonoscopy have been offered the procedure within 6 months from the time of referral or advised repeat date.

- Surveillance colonoscopy is advised for individuals with a moderate increase in risk for developing CRC on the basis of family history of CRC but only 57% of large public centres and 65% of small public centres offer colonoscopy to this group.

- The responding public hospital endoscopy units reported 2550 patients still waiting for a surveillance procedure 6 months after referral.

- A shortage of endoscopy nurses limits provision of colonoscopy for two thirds of public centres.

- An increase in the availability of endoscopists to perform additional endoscopy sessions per week would increase colonoscopy provision in 50% of public hospitals.

- These factors result in a maximum of 94.5 unutilised half day endoscopy sessions per week within the responding public hospital units.

- All responding public centres offer training in colonoscopy but there is little information on what constitutes "training".

- Two thirds of responding public units currently audit colonoscopic morbidity and mortality, half audit completion rates to the caecum and only a third audit patient discomfort scores.

- Currently no non-medical endoscopists are employed by endoscopy units in New Zealand and only 25% of public units and no private units are willing to do so.

Survey Method

The survey was based on the National USA Survey of Endoscopic Capacity (SECAP) questionnaire commissioned by the Center for Disease Control (CDC) and published in Gastroenterology.[2]

Permission was obtained from the authors to utilise the published framework and modifications were made in keeping with local practices and infrastructures.
Extensive consultation was undertaken involving the NZ Gastroenterology Society Executive and the National Screening Unit Colorectal Cancer Advisory Group. This led to a revised questionnaire which was piloted within the Auckland metropolitan area.

The final survey questionnaire, incorporating changes suggested in the pilot survey, posed 39 questions.
The survey was dispatched with postage paid envelopes to all public endoscopy units and all private facilities identified as performing colonoscopy within New Zealand. If no reply was received within 6 weeks a follow up letter was sent.

In total 46 surveys were dispatched, 28 to public units and 18 to private institutions.
The responses were analysed by large and small centres.
Large centres relate to the five major population centres within New Zealand: Auckland, Hamilton, Wellington, Christchurch and Dunedin. These cities cover 52% of the New Zealand population based on data published in the 2001 census.

Small centre refers to all other public hospital units.
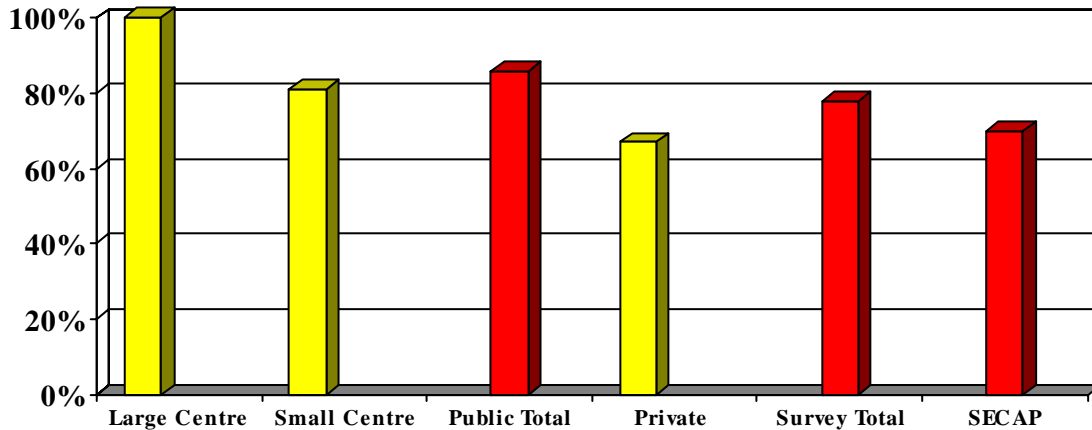
Survey: Results and Analysis

Response Rate
Public Hospitals: 100% for large centres (7/7) and 81% for small centres (17/21) providing an aggregate public system response rate of 86% (24/28).

Private institutions: 67% (12/18).

Overall: 78% (36/48). This compares favourably with the SECAP study response rate of 70%.

Response Rate

Number of Colonoscopy procedures performed (per annum)

Within the public system 18,139 colonoscopies were performed in the last year by responding centres with a further 13,066 procedures undertaken by responding private institutions.

The total number of colonoscopies performed in responding the public endoscopy units (18,139) was 20% greater than the total number expected/planned for (15,075) by their respective District Health Boards.

Annual Number of Colonoscopies
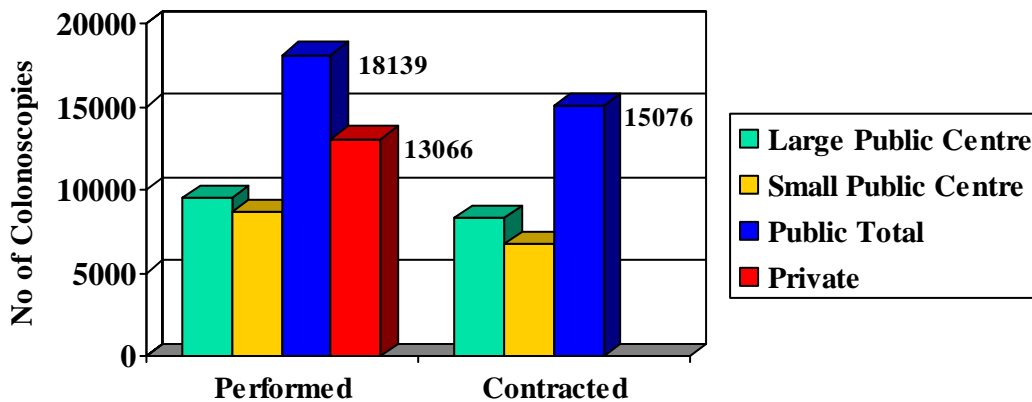
Comparison of current colonoscopy provision data with that collected in 1997 for New Zealand's four main population centres (Auckland, Wellington, Christchurch and Dunedin) demonstrates a 92% increase in colonoscopy provision over this time.

Increase in Colonoscopy Provision in Main Centres:
**Auckland, Wellington, Christchurch, Dunedin**
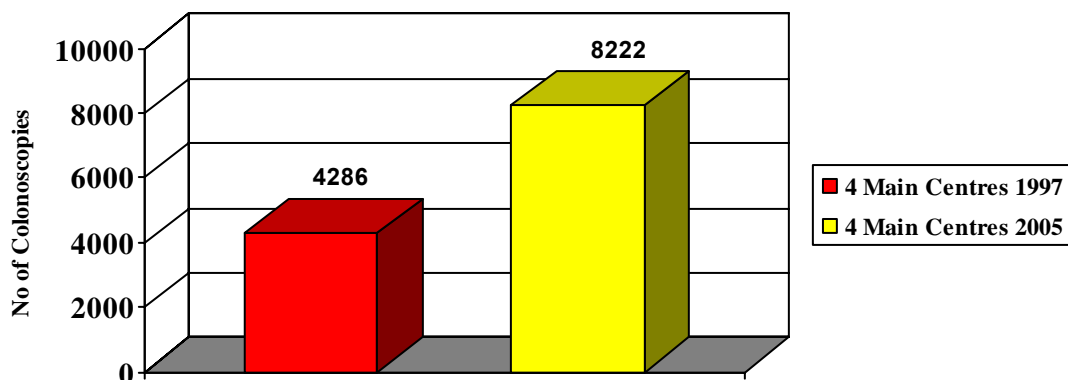
Number of Consultant Colonoscopists

Among responding public centres 123 consultant Colonoscopists are employed comprising, by specialty: Gastroenterology 59, General Surgery 48 and Colorectal Surgery 14.

When analysing the number of Colonoscopists in the private sector it is important to recognise that a significant proportion will also be contracted to the public health system.

Number of Colonoscopists by Specialty
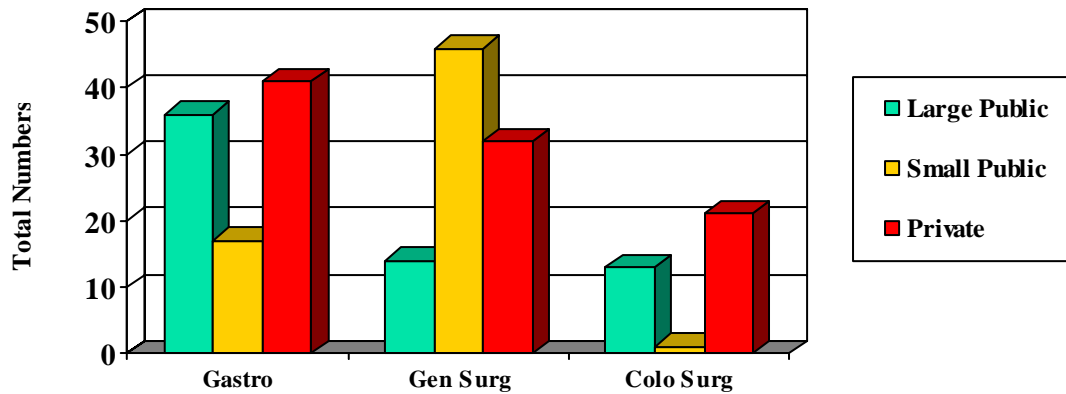
**Waiting times for colonoscopy**

Diagnostic procedures for patients with symptoms suggestive of Colorectal Cancer

Waiting times for colonoscopy depend on the clinical indication for the procedure.

For patients with symptoms suggestive of CRC (rectal bleeding, altered bowel habit) but without alarm symptoms (weight loss, anaemia or abdominal mass) the National Endoscopy Referral Guidelines[3] recommend a wait of up to 8 weeks for this category of patient.

Currently 60% of large public centres are unable to provide this service within 3 months compared with 35% for small public centres.

Average Wait for Colonoscopy in Symptomatic Patients
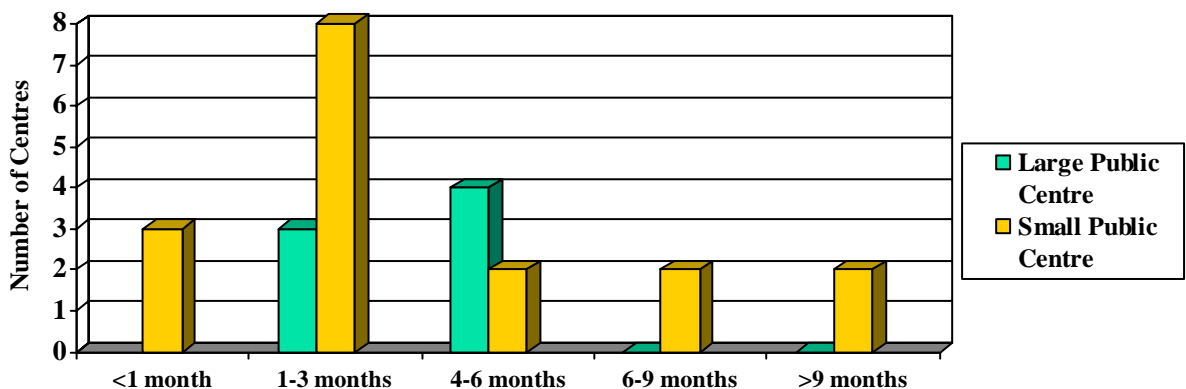
The responding public hospital endoscopy units reported 828 patients (798 collected data, 30 estimated data) aged over 50 years with symptoms suggestive of colorectal cancer to have been waiting >6 months for a diagnostic colonoscopy.

Patients Waiting > 6 months for a Diagnostic Colonoscopy
n = 828
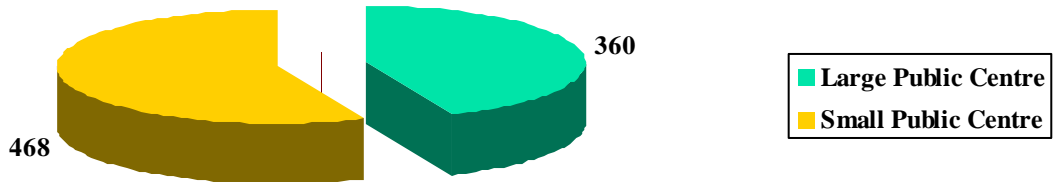
Surveillance Procedure for Individuals at Increased Risk of CRC

The New Zealand Guidelines for surveillance in those at increased risk of developing CRC advise surveillance colonoscopy for certain risk groups.[1] Unfortunately not all public hospitals are able to offer this – in particular, only 50% of large centres and 65% of small centres are currently able to offer surveillance colonoscopy for individuals with a moderate increase in CRC risk based on family history.

Percentage of Centres Offering Surveillance Colonoscopy
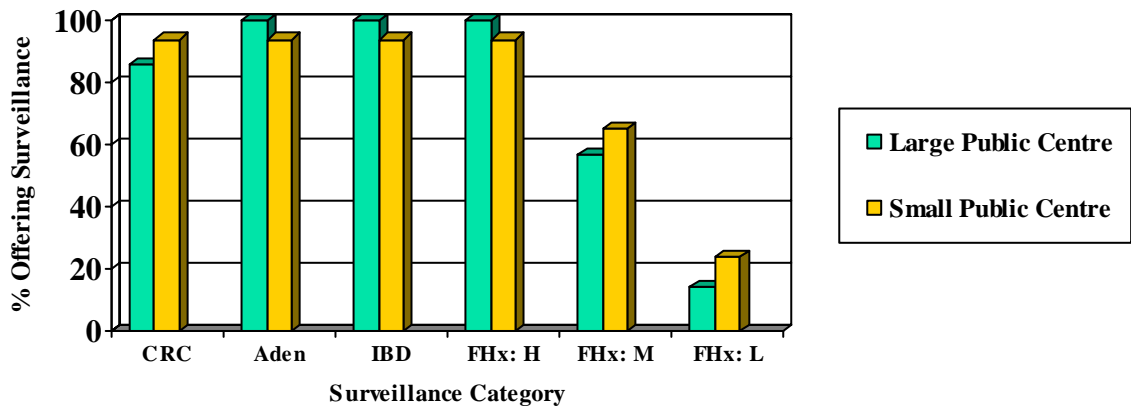
Of relevance if implementation of CRC screening is being considered is not just whether public endoscopy centres are able to offer colonoscopy but whether they are able to deliver a service within an appropriate time frame.

The public system is not currently able to offer surveillance colonoscopy to all patients within 6 months of referral. In particular large centres are only able to offer a minority of patients a procedure within this time frame.

Delivery of Surveillance Colonoscopy in Large Public Centres
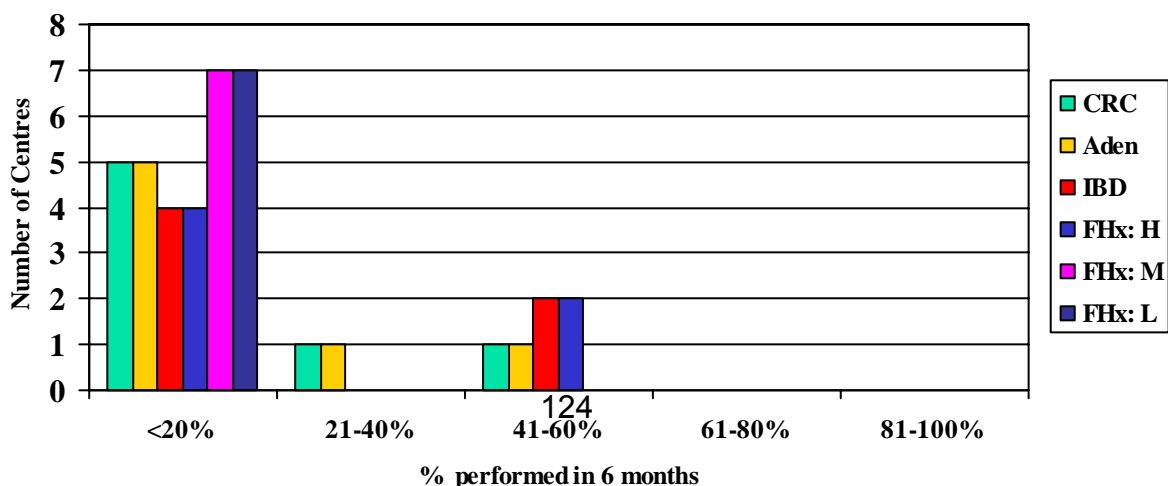
Delivery of Surveillance Colonoscopy in Small Public Centres
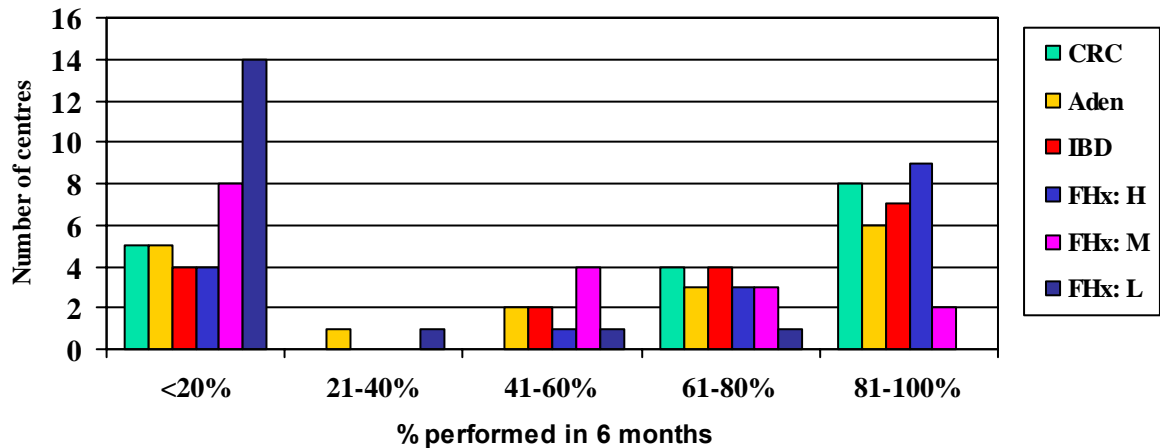
For surveillance purposes the majority of large centres are able to offer less than 20% of patients a colonoscopy within 6 months. Small centres are currently better placed with the majority offering surveillance colonoscopy to more than 80% of patients within 6 months.

Based on collected figures, responding public centres report 1550 patients
still waiting for colonoscopy 6 months from the time of referral. Another 1000 patients are estimated to still be waiting for their procedure 6 months from the time of referral.

Patients Waiting > 6 months for Surveillance Colonoscopy
n = 2550

Factors Identified to Limit Provision of Colonoscopy:

A shortage of trained nursing staff and non-availability of endoscopists to perform procedures in free endoscopy unit sessions are the major factors currently limiting colonoscopy capacity in the public system. Lack of space or equipment play only a minor role in limiting current colonoscopy capacity amongst responding centres.
Lack of nursing staff also hinders a third of responding private units but, in contrast to the public system, available theatre time and demand play a much greater role in limiting capacity.

Factors Limiting Provision of Colonoscopy
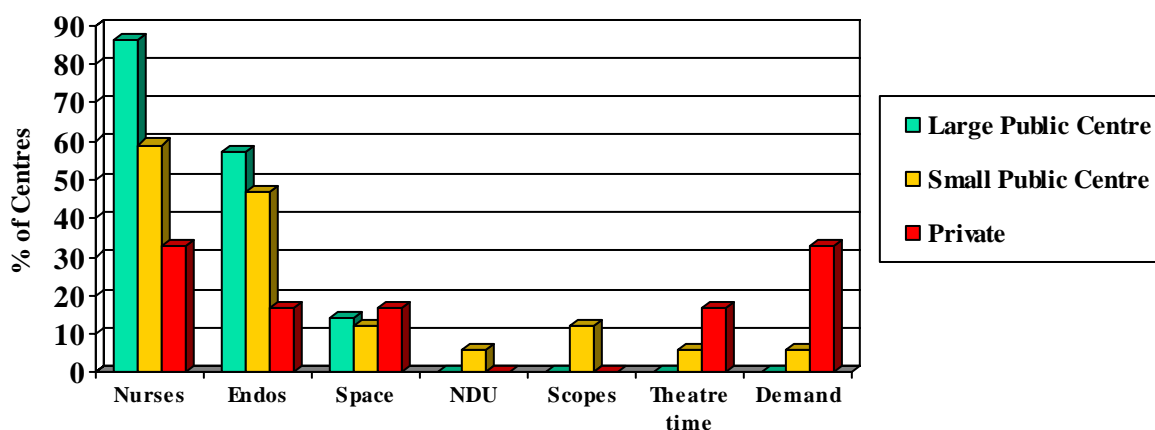
As a consequence of these deficiencies there are a maximum of 94.5 unutilised half days every week in the public system and 22 in the private system.

To fully utilise this unused capacity responding large public centres report a need for an average of 2.6 Full Time Equivalent (FTE) nurses and 1.2 FTE endoscopists. For small public centres this was reported as an average of 2.1 FTE nurses and 0.75 endoscopists.

Potential to Increase Colonoscopy Capacity

Improved Staffing

Improving this underutilisation of resources due to manpower shortages could significantly increase colonoscopy capacity. Survey respondents estimated that a predicted maximum of 27,400 colonoscopies could be performed each year in the public system. This equates to a 49% increase in capacity.

Within the private sector, respondents estimate a potential increase in the numbers of colonoscopies being performed per annum from 13,066 to 23,000, an increase of 76%.

Out of Hours Services

The utilisation of evening (after 5pm Monday to Friday) and weekend (Saturday and Sunday) sessions is one potential solution to increase current colonoscopy capacity.
Currently no public centres run a regular "out of hours" service for non urgent colonoscopy however 57% of large centres and 35% of small centres consider the provision of such a service to be possible if there was a significant increase in demand for colonoscopy.

Flexible Sigmoidoscopy

Flexible sigmoidoscopy is usually used as a follow-up procedure to assess the site of previously removed distal colonic lesions. However it has also been proposed as a screening test for colorectal cancer and consequently it is important to know if flexible sigmoidoscopy is being performed as a dedicated procedure in New Zealand.

At present the majority of centres do not utilise flexible sigmoidoscopy with only 3/24 (13%) public units and 6/12 (50%) of private units undertaking flexible sigmoidoscopy as a dedicated procedure (i.e. using a flexible sigmoidoscope and not a colonoscope to do an examination of the distal bowel).

In addition the three public units utilising flexible sigmoidoscopy report a combined total of only approximately 600 procedures per year (compared to 2,800 colonoscopies in the same

units) with the six private centres performing a combined total of approximately 500 procedures per year (versus 2,500 colonoscopies in those units).

Non-Medical Endoscopists

Nurse endoscopists have been utilised in other countries to combat the ever increasing demands on endoscopy services. There are now over 200 employed with the United Kingdom and they have been found to be competent and their role is acceptable to patients.[4, 5]
Currently no endoscopy unit in New Zealand employs non medical endoscopists with only 25% of public units and no private units willing to do so. Furthermore only 2 large centres would be willing to employ or train non-physicians to perform colonoscopy or flexible sigmoidoscopy.

Quality Assurance in Colonoscopy

Quality in the provision of colonoscopy is essential[6] and is of particular importance in the context of CRC screening as procedures are performed in otherwise well individuals.

Training

A pre-requisite for colonoscopists participating in a CRC screening programme would be high quality, standardised training. Currently endoscopy training is not nationally standardised although an endoscopy course has recently been established.[7]

There are 49 trainee colonoscopists in public centres comprising by specialty: Gastroenterology 11, General Surgery 33 and Colorectal Surgery 5. Large centres account for all Gastroenterology and Colorectal Surgical trainees while all trainees in small centres are in General Surgery. All respondents state that trainees receive formal training in colonoscopy however little information is available on what constitutes such "training".

Colonoscopy Audit

Audit is an essential part of clinical care when procedures that may cause harm are being performed. Quality assurance in colonoscopy requires organisations and Senior Medical officers to accept that audit of colonoscopy performance, with feedback, is integral to this process.

Morbidity and mortality occurring as a consequence of colonoscopy is clearly an important component of monitoring quality but at least 50% of public hospital centres do not document this and patient discomfort during colonoscopy is monitored by only a third of units.

Colonoscopy Audit

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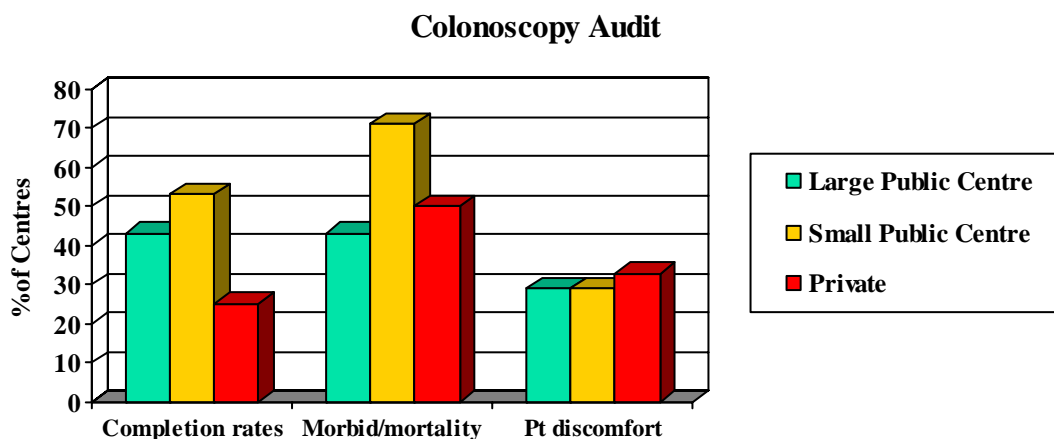
Colonoscopy Completion Rates

Another outcome measure for colonoscopy is the frequency with which the endoscopist examines the entire colon. This is usually determined by confirmation that the caecum has been r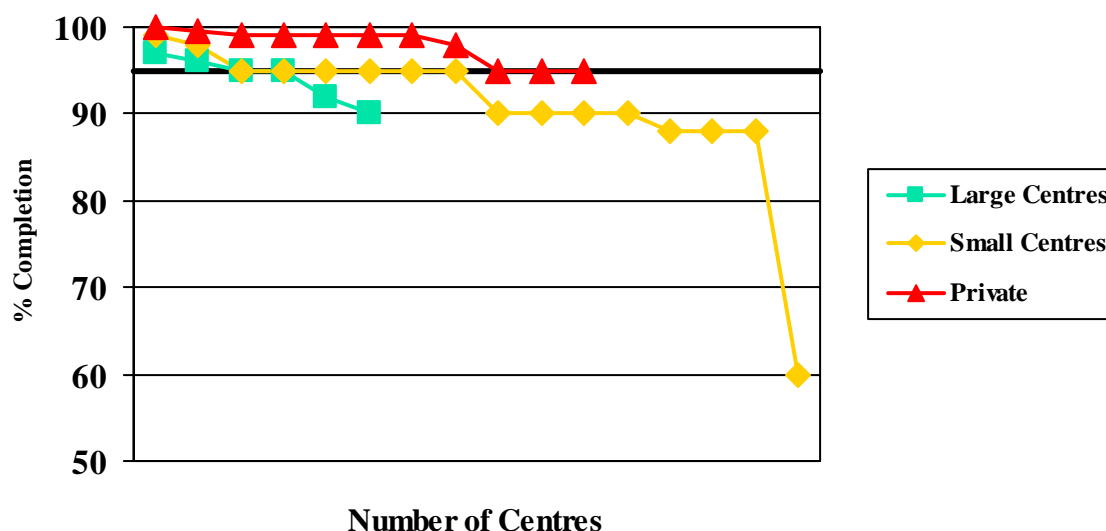eached and is referred to as the caecal intubation rate. It is recommended that independent practitioners are able to reach the caecum in 90-95% of cases. This figure, whilst not a guarantee of quality, is frequently used as a measure of basic competence in the practice of colonoscopy.

Caecal Intubation Rate by Unit

At present 10/24 (42%) of public centres fall below the recommended caecal intubation rate of 95%. However these figures are not controlled for by the presence of trainee colonoscopists.

The survey clearly demonstrates that audit of completion rates is not universal and this will need to be encouraged.

Conclusion

In New Zealand's public hospitals a significant gap exists between demand and provision for both diagnostic and surveillance procedures related to colorectal cancer. At the time of the survey responding public centres reported over 800 patients waiting more than six months for a diagnostic procedure and over 2,500 for a surveillance procedure. This is despite the fact that public hospital units are performing twenty percent more procedures than required of them by their respective District Health Boards.

This gap in provision is more apparent in the main centre public hospitals.

If population screening for CRC were to be implemented a significant increase in colonoscopy resource would be necessary to ensure waiting times for symptomatic patients did not increase.

Lack of nursing staff and available endoscopists are the chief factors limiting colonoscopy capacity in the public system at the current time.

Evening or weekend sessions are not currently available to make up the shortfall in colonoscopy provision and only 40% of public units report that they would be able to offer such services should demand increase.

Increasing colonoscopy capacity will highlight the need for quality assurance in colonoscopy. Colonoscopy training will need to be standardised and audit of colonoscopy practice, which at present is not universal, will need to be encouraged.

These conclusions are substantiated by the survey results outlined in the Executive Summary.

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1. Surveillance and Management of Groups at Increased Risk of Colorectal Cancer. New Zealand Guidelines Group. May 2004. Available at: www.nzgg.org.nz

2. Is there endoscopic capacity to provide colorectal cancer screening to the unscreened population in the United States? Seaff, L et al Gastroenterology 2004;127:1670-1677

3. Clinical Priority Assessment Criteria for Colonoscopy (CPAC). Available at www.electiveservices.govt.nz

4. Screening for Colorectal Cancer by Nurse Endoscopists. Maule WF. N Eng J Med 1994;330(3):214-8

5. Non Medical Endoscopists. Working Party Report for the British Society of Gastroenterology August 2005. Available at www.bsg.org.uk/clinical_prac/guidelines

6. ESGE Recommendations for Quality Control in Gastrointestinal Endoscopy: Guidelines for Image Documentation in Upper and Lower GI Endoscopy.

7. J.-F. Rey,R. Lambert. E.S.G.E. Guidelines. Available at www.esge.com

8. Endoscopy Training at an Advanced Surgical Skills Centre. Morris D. Abstract New Zealand Society of Gastroenterology Annual Scientific Meeting, 3 November 2005.

Colonoscopy Resource and Capacity in New Zealand: Survey

The National Screening Unit (NSU) has commissioned a nationwide research study involving a survey to determine the current endoscopic capacity of both the public and private N.Z. health care sector with regards to diagnosis, surveillance and screening for Colorectal Cancer. The survey is based on the CDC National Survey of Endoscopic Capacity (SECAP) conducted in the USA and reported in Gastroenterology 2004;**127**:1670-1677.

The survey will only be sent to the Clinician in charge or Charge nurse/Manager of each endoscopy unit.

The results of the survey will be used to identify deficits and shortcomings in the current medical infrastructure (including workforce), as well as to provide critical baseline information for use in planning potential national initiatives aimed at increasing colorectal cancer screening/surveillance.

All information that you provide will be kept private to the extent allowed by law, and the NSU does not plan to disclose identifiable data to anyone but the researchers conducting the study. Responses will be reported only in summary form along with information from the other facilities that participate in the survey. No personal identifiers will be included in either oral or written presentation of the study results.

If you have any questions regarding this survey please contact Dr Andrew Yeoman on 09-2760000 Pager 8301 or 0210722885.

When you have completed the survey, please return it in the enclosed postage-paid envelope to:

> Dr. Andrew Yeoman
> Research Fellow
> Gastroenterology Department
> Middlemore Hospital
> Private Bag 93311
> Otahuhu
> Auckland 6

Thank you for your participation in this important study.

Dr Susan Parry
Gastroenterologist/ Clinical Head of Department, Middlemore Hospital.
Chair NSU Colorectal Cancer Advisory Group

Colonoscopy Resource and Capacity in New Zealand: Practice site survey

Practice site refers to the specific site where the survey was received. In a hospital setting this will refer to a specific department, clinic or endoscopy suite. Responses should reflect only those procedures performed at your particular site or, if in a hospital setting, all procedures performed by your department, unless you are answering for all Departments performing endoscopy in your hospital.

If you are unable to answer any question please feel free to consult with others in your practice that may have access to this information.

1. Which of the following categories best describes the practice site where this survey was received? **(Circle one response)**

Hospital (DHB)	**1 ➔ GO TO QUESTION 2**
Private Hospital	**2 ➔ SKIP TO QUESTION 4**

2. Please indicate where endoscopy is routinely performed at your hospital/unit. **(Circle all applicable responses)**

	YES	NO
a) Dedicated endoscopy suite	1	2
b) Operating Theatre	1	2
c) Satellite clinic	1	2
d) Other (please specify)	1	2

3. Are your endoscopy services co-ordinated /delivered by one department? (**Please circle one response**)

YES➔ GO TO QUESTION 4

NO ➔ SKIP TO QUESTION 5

4. If endoscopy services are delivered by one department, which department is responsible for this service? (**Please circle one response**)

a) Gastroenterology	**1**
b) General Surgery	**2**
c) Colorectal Surgery	**3**
d) General Medicine	**4**
e) Other (Please specify)	**5**

5. If separate endoscopy services exist in your hospital, which departments deliver this service? **(Please circle applicable responses)**

a) Gastroenterology	**1**
b) General Surgery	**2**
c) Colorectal Surgery	**3**
d) General Medicine	**4**
e) Other (please specify)	**5**

6. Are you answering this questionnaire for all departments delivering endoscopy in your hospital? (**Please circle one)**

YES	**1➔**	*SKIP TO QUESTION 8*
NO	**2➔**	*GO TO QUESTION 7*

7. If providing information for one department only, which department do you represent?

a) Gastroenterology	**1**
b) General Surgery	**2**
c) Colorectal Surgery	**3**
d) General Medicine	**4**
e) Other (please specify)	**5**

8. How many **consultant endoscopists** work at your practice site?

Number of **consultant endoscopists:**

9. What are the sub-specialties of the **consultant endoscopists** at your practice site? **(Please provide numbers for each group)**

a) Gastroenterology

b) General Surgery

c) Colorectal Surgery

d) General Medicine

e) Other (please specify)

…………………..

10. How many **consultant endoscopists** in your practice site perform **COLONOSCOPY**? **(Please provide numbers)**

Number of consultant colonoscopists:

11. How many trainees (registrars and research fellows) work at your practice site?

Number of trainees:

12. Do trainees (registrars and research fellows) receive **colonoscopy** training at your practice site? **(Please circle one answer)**

YES	**1**
NO	**2**

13. What are the sub-specialties of the trainee <u>**colonoscopy trainees**</u> at your practice site? **Please provide numbers for each group.**

a. Gastroenterology

b. General Surgery

c. Colorectal Surgery

d. General Medicine

e. Other (please specify)

……………………

14. How many of the following does your practice site own or lease?

a. Video colonoscopes

b. Video sigmoidoscopes

c. Fibre optic sigmoid/colonoscopes

15. During a typical <u>**year**</u>, approximately how many **outpatient** and how many **inpatient** colonoscopies are performed at your practice site?

Outpatient | | **Inpatient** | |

16. What is your contracted volume of **outpatient** colonoscopies per year?
   (Please provide a number)

Contracted number of
outpatient colonoscopies:

17. Of the total number of **colonoscopies** performed at your practice site during a typical week, what **percentage** is provided by the following specialties?
   (**Please provide your best estimate**)

Percentage

a. Gastroenterology
b. General Surgery
c. Colorectal Surgery
d. General Medicine
e. Other (please specify)
……………………..

18. Regarding waiting times: **If you are responding on behalf of a public hospital service,** what would be your typical waiting time for an appointment for a **colonoscopy** for an individual aged > 50 years with symptoms suggestive of colorectal cancer but without alarm symptoms, i.e. unexplained weight loss, anaemia, abdominal mass or severe pain)?

(This presumes that referrals for patients in this category are not automatically returned to the referrer if they remain on the waiting list after 6 months)
(Please circle one response)

Within 1 month	**1**
1-3 month	**2**
4-6 months	**3**
6-9 months	**4**
> 9 months	**5**

To help gauge the gap between colonoscopy demand and capacity within the public hospital system, can you advise the number of patients in the above category who are **currently** still waiting for colonoscopy 6 months after the time of referral.

Number still waiting
at 6 months:

Is this number based on collected data: **YES**   **NO**
(Please circle)

19. Given your current colonoscopy capacity, are you able to offer outpatient surveillance colonoscopy as defined in the guidelines for the Surveillance and Management of Groups at Increased Risk of Colorectal Cancer, www.nzgg.org.nz, for individuals with the following:
(Please circle for each part.)

		YES	NO
i) Personal history of colorectal cancer		1	2
ii) Personal history of colorectal adenoma		1	2
iii) Personal history of inflammatory bowel disease		1	2
iv) Family history of colorectal cancer:	High Risk	1	2
	Moderate Risk	1	2
	Low Risk	1	2

20. If you are able to offer surveillance colonoscopy for these groups in your unit, **over the past year,** for approximately what percentage of patients in each category would a surveillance procedure have been offered at or before 6 months from the time of first referral (or from scheduled recall time):

i) Personal history of colorectal cancer ....

ii) Personal history of colorectal adenoma ....

iii) Personal history of inflammatory bowel disease ....

iv) Family history of colorectal cancer: High Risk ....

Moderate Risk ....

Low Risk ....

21. Approximately what **percentage** of your **total** number of outpatient colonoscopies/year are **surveillance procedures performed for the above groups?**

Percentage of total outpatient colonoscopies performed for surveillance:

To help gauge the gap between colonoscopy demand and capacity, can you advise the number of patients in the above category who are **currently** still waiting for a surveillance colonoscopy (for any of the indications in Q19) 6 months after the time of referral or from scheduled time of recall :

Number still waiting at 6 months:

Is this number based on collected data**: YES NO
(Please circle)**

22. Regarding colonoscopy capacity, are there any half days during the working week (Monday to Friday) that your endoscopy theatre is currently unused? **(Please Circle)**

<div align="center">

YES   **NO**

</div>

If yes, how many half days are unused per week?

Number of unused half days per week:

23. If the demand for colonoscopy was increased as a result of the guidelines for surveillance of those at increased risk or as a consequence of population screening for CRC, what is the **maximum** number of **colonoscopies, per week** that could be provided at your practice site with current staffing and equipment**?** Please provide your best estimate.

Number per week:

How many colonoscopies are you currently performing in your unit each week?

Current number per week

What are the main factors currently limiting your ability to increase the number of colonoscopies performed in your unit each week?

24. If the demands for surveillance colonoscopy were to exceed your current capacity and all available endoscopy theatre sessions were used during the working week, what staff increases would be required?

a. Nursing staff (FTE)   **Number:……**

b. Consultant endoscopists (FTE)   **Number:……**

c. Other   **Number:…….**

25. At your practice site do you currently perform colonoscopy during:
(Please circle)

a. Evening sessions (after 6pm)   **YES**   **NO**

b. Weekend sessions   **YES**   **NO**

c.

26. If the demands for surveillance colonoscopy were to exceed your current capacity despite staff increases during the working week, would evening or weekend sessions be a possibility?
(Please circle)

a) Evening sessions (after 6pm)   **YES**   **NO**

b) Weekend sessions   **YES**   **NO**

27. What other steps would be necessary to exceed your current colonoscopy capacity? **(Please circle all applicable answers)**

    a) Increase proportion working week consultant
         endoscopists allocate to procedures   **1**

    b) Increase or hire non physician endoscopists   **2**

    c) Expand your current unit   **3**

    d) Purchase more equipment   **4**

    e) Refer work to another unit   **5**

    f) Other (please specify)   **6**

        …………………...

28. Regarding delivery of colonoscopy in your centre, how much room time is allocated for a colonoscopy? **(Please circle one)**

    Less than 30 minutes………   **1**
    30 minutes……….   **2**
    30-45 minutes……….   **3**
    More than 45 minutes……….   **4**

29. Does your practice continuously/intermittently audit colonoscopic performance for:
(Please circle for each part)

	Yes	No
i) Colonoscopy completion rates	**1**	**2**
ii) Morbidity/ mortality	**1**	**2**
iii) Patient discomfort	**1**	**2**

30. At your practice site, approximately what percentages of colonoscopies performed in a week are incomplete?

Percentage of Incomplete Colonoscopies:

31. What is the **primary reason** for an incomplete colonoscopy? **Circle one response.**

    Poor bowel preparation……………   **1**
    Patient discomfort or pain………….   **2**
    Patient anatomy…………………….   **3**
    Pathology encountered……………..   **4**
    Other (Please specify)………………   **5**

32. Regarding the cost of colonoscopy, please estimate your average cost for the following **outpatient** procedures. Please exclude all costs other than that involving the procedure itself.

Colonoscopy **without** biopsy $

Colonoscopy **with** biopsy $

Flexible Sigmoidoscopy

33. Do any physician or non-physician endoscopists in this practice site perform flexible sigmoidoscopy as a dedicated procedure (ie rather than a colonoscopy to follow up previous pathology)?
   (Please circle one)

   YES   1
   NO   2 ➔ *SKIP TO QUESTION 37*

34. During a typical week, how many flexible sigmoidoscopies are performed by all physician and non-physician endoscopists at this practice site?
   (Please provide your best estimate)

   Total number of sigmoidoscopies:

35. Approximately what **percentage** of all flexible sigmoidoscopies are performed for colorectal cancer screening?
   (Please provide your best estimate)

   Percent performed for
   colorectal cancer screening:

36. Of the total number of **flexible sigmoidoscopies** performed during a typical week, what **percentage** is performed by the following types of providers?
   (Please provide your best estimate)

   Percentage

   a. Gastroenterologists

   b. General Surgeons

   c. Colorectal Surgeons

   d. General Physician

   e. Other (please specify)

Non- Physician Endoscopists

37. *Does your practice site employ non physician endoscopists (general practitioners/nursing staff) to perform:*
   (Please circle)

   Colonoscopy: *YES*   *NO*
   Flexible Sidgmoidoscopy: *YES*   *NO*

38. Would your practice site be willing to employ non specialist endoscopists to perform:
(Please circle)

Colonoscopy: **YES** **NO**

Flexible Sigmoidoscopy: **YES** **NO**

39. Would your practice site be willing to train non specialist endoscopists eg General Practitioners /nursing staff in:
(Please circle)

Colonoscopy: **YES** **NO**

Flexible Sigmoidoscopy: **YES** **NO**

<u>Comments</u>

If you have additional information on the number of patients waiting for a colonoscopy, or the time they have been waiting for this procedure please provide in this comments section.

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APPENDIX 5: COMPUTED TOMOGRAPHY COLONOGRAPHY (CTC) INDEPENDENT REPORT NZ BRANCH OF THE ROYAL AUSTRALIAN AND NEW ZEALAND COLLEGE OF RADIOLOGISTS

Independent report on CT colonography by Dr Mark Osborne for the NZ branch of the Royal Australian and New Zealand College of Radiologists.

Computed Tomography Colonography (CTC) is now an established technique widely used in the investigation of and screening for Colorectal Malignancy. It fulfils the criteria for a screening test in that it is minimally invasive and of relatively low cost. (Pickhardt 2003) It should therefore be viewed as a screening test similar to mammography which can be used to identify high risk patients within the screening population and not compared to conventional colonoscopy which is an invasive, time consuming (for both patient and Gastroenterologist) and expensive test but is the appropriate investigation for high risk patients who can be treated (biopsied) at the same time. It is estimated that up to 20% of patients may require referral; this of course means that at least 80% can be spared the cost and relative risk of conventional colonoscopy.

Simplicity/ Acceptability of CTC

In a study of 1233 patients who underwent both CTC and conventional colonoscopy on the same day (Pickhardt et al 2003) 68% rated CTC as more acceptable than conventional colonoscopy as compared to 24.5% who felt conventional colonoscopy was more acceptable and a majority of patients preferred CTC for future screening. In this study the average time the patient required for CTC was 15 minutes as opposed to 96 minutes for conventional colonoscopy (this included procedure time of 32 minutes and recovery time after sedation of 64 minutes). No patients undergoing CTC required sedation, average reporting time for CTC was 18 minutes.

Currently patients undergoing CTC are subjected to cathartic bowel preparation similar to conventional colonoscopy. More recent studies are now indicating that this may not be necessary and that similar sensitivity levels can be achieved without the use of laxatives. (Iannacconne 2004)

Sensitivity of the Test

Early reports have suggested a high sensitivity for Polyps of >1cm (Fenlon 1999) and this initial optimism has been reinforced by numerous subsequent articles (Pickhardt et al 2003; Halligan 2005; Summers 2005) with overall sensitivities for 7mm or greater polyps being of the order of 90-95% comparable to conventional colonoscopy. The introduction of CAD can be expected to lead to an overall improvement in this area by providing an effective second read of the data and also acting as a prompt to the reading radiologist. A number of other reports have appeared reporting lower

sensitivities (Cotton 2004; Johnson 2003). These studies are of questionable relevance in that they compare state of the art colonoscopy with substandard CTC, performed by inexperienced radiologists using old equipment, inadequate protocols and suboptimal software. Their findings do underline the need for good quality studies on state of the art CT equipment interpreted by experienced radiologists.

Specificity of the test

Specificities reported in series using state of the art equipment and experienced operators are consistently above 90% with a recent meta-analysis reporting specificities of 92% for polyps <6mm and 97% for polyps >9mm (Mulhall 2005). With the use of Computer Aided Diagnosis (CAD) other workers have shown even better results with a false positive rate of 2.1% for >10mm and 6.7% for <8mm (Summers 2005). Currently CAD systems are still at a developmental stage and are expensive to install but as the technology matures result such as those above indicate they will yield an incremental improvement in accuracy of CTC.

Studies have indicated that the vast majority of polyps smaller than 9mm are hyperplastic lesions which regress with time and as a consequence can be treated expectantly. Biopsy of these lesions at colonoscopy is unnecessary and increases the risk to the patient from the procedure

Safety of the test

CTC requires the use of ionizing radiation, using low dose techniques the dosage can be reduced by up to 50% compared to a conventional abdominal CT with no significant loss in accuracy.(Hara 1997) This aside it is regarded as a safe procedure with no significant risk of perforation and no need for sedation. Because the study also includes abdominal contents outside the bowel, incidental abnormalities will be discovered in up to 20% of cases. Many of these are benign eg, hepatic/renal cysts and require no further investigation. On occasion a significant abnormality will be demonstrated. A recently published study (Gleuker 2003) identified that only 1.3 % of these required medical or surgical intervention.

Advantages/limitations of the test

CTC fits the criterion for a screening test; it is a low cost test which is acceptable to the patients. It is low risk with accuracy rates comparable to conventional colonoscopy. It is less time consuming for the patient and the relevant medical specialists than conventional colonoscopy.   Recent advances suggest it may maintain a high level of accuracy without the need for cathartic bowel preparation further increasing its acceptability with patients. The equipment required is widely available in NZ.

CTC should not be viewed as a test which competes with conventional colonography. The latter is an invasive and time consuming test which enables simultaneous biopsy of suspicious lesions, Depending on the size threshold used these will be detected in 5-20% of CTC studies. Although widely available at present its capacity to investigate anything beyond the high risk population is extremely limited. As such it is an ideal complement to CTC being best fitted to investigate high risk individuals and follow-up abnormalities discovered at CTC of the screening population.

Conclusion

"CTC (Virtual Colonoscopy) has passed the development stage and is now at the stage of widespread availability, able to be performed on any multi – detector CT with uniformly good quality if standard protocols are followed. It is... currently a credible alternative screening method and should be considered as a reasonable alternative to other CRC screening tests when a patient is unable or unwilling to undergo conventional colonoscopy..." Consensus statement from the Virtual Colonoscopy Working Group. (Pickhardt 2005)

Whether the widespread introduction of CTC will lead to the need for an increase in requirement for conventional colonoscopy as claimed (Bond 2005) is open to question. It seems likely that interventional colonoscopy i.e. procedures during which polypectomy and/or biopsy are performed will increase but the need for screening with conventional colonography should decrease.

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APPENDIX 6: PROPOSED FEASIBILITY STUDY OF COLORECTAL CANCER SCREENING WITH IMMUNOCHEMICAL FAECAL OCCULT BLOOD TESTING IN NEW ZEALAND

The purpose of a feasibility study is to determine whether the New Zealand health system could support a national CRC screening programme using immunochemical faecal occult blood testing, which would be acceptable, effective and economically efficient. An outline describing the features that would need to be considered before a feasibility study could be implemented is provided below.

1.1 Feasibility study design: screening pathway components

The key issues to be addressed in the feasibility study design at each stage of the screening pathway are outlined in sections 1-9 as follows:

1. **Identification of eligible population**
   - Methods to identify the target population and establish a screening register.
   - Experience gained from BreastScreen Aotearoa and the National Cervical Screening Programme will be relevant.

2. **Information and invitation**
   - Eligibility and exclusion criteria for invitation
   - Source of invitation (central versus GP invitation)
   - Development of effective ways to invite participants
   - Information needs and how information will be provided
   - Appropriate informed consent process
   - Participation (including the test and follow-up), including participation by different groups (ethnic, age, socio-economic)
   - Participants' understanding of participants of information, including potential benefit and harms
   - Cultural appropriateness of information and cultural responsiveness of service delivery

3. **Testing and return of tests by participants**
   - How participants receive the test
   - Instructions for use of test
   - Stool sampling techniques
   - Information about those who do not complete the test and why
   - How tests will be sent to the laboratory

4. **Analysis of tests and notification of results**
   - Positivity rate
   - Recall for inadequate tests
   - Number of correctly completed tests received by laboratory
   - Rate of technically inadequate tests

- Time frame for tests to be received by laboratory
- Time frame for analysis of tests
- Time frame for reporting results
- Responsibility for reporting results and to whom (GP or central)

5. **Referral of participants with positive results**
- Responsibility for referral for colonoscopy
- Colonoscopy uptake
- Information about those who had/did not have investigation/follow-up and why/why not

6. **Diagnostic investigation**
- Waiting times for colonoscopy
- Impact on workforce/facility/service delivery. This will include the impact of screening on colonoscopy services for symptomatic patients as well as referral for those with positive FOBT results.
- Quality of colonoscopy performed
- Detection rates for high and low risk colorectal adenoma including site in colon ie proximal or distal.
- Detection rates for colorectal cancer (including site in colon) and stage distribution
- Protocols regarding
    size of polyps to be biopsied
    polypectomy technique for small polyps
    referral for ongoing surveillance colonoscopy
- Histologic reporting for colorectal adenoma and colorectal cancer
- adverse sequelae of colonoscopy
- Verification by pathology and collection of data
- Reporting and referral (noting difficulties in Australian pilot regarding reporting and referral).

7. **Management and treatment for those with CRC detected by screening**
- Ensure optimal treatment outcome for those diagnosed with CRC during screening by
    o establishment of multi-disciplinary assessment centres
    o timely surgery plus or minus radiation therapy and chemotherapy
    o uniform histologic reporting(including stage) for CRC
    o monitor impact of screening on access to treatment and treatment services
    o subsequent colonoscopy surveillance.

8. **Re-invitation (those not previously screened) and re-screening of those with negative tests and those with a previous negative colonoscopy**
- Re-invitation process
- Re-screen for those who test negative
- What is drop off? (participation at re-screening)

- Effective process (eg, constraints re re-invitation, no addresses, itinerant population, etc).

9. Monitoring and evaluation of all phases/components
- Performance indicators need to be developed
- Acceptability of screening process (including identification, invitation, screening, reporting results, referral for colonoscopy, colonoscopy procedure, provision of results, management for those with CRC diagnosed) for eligible population and health professionals
- Uptake of screening and reasons for those who decline (assess potential to increase inequalities)
- Referral rate to colonoscopy
- Colonoscopy acceptance
- Biopsy rate
- Colonoscopy adverse events
- Impact on services over time, eg, waiting times for colonoscopy (for screening participants and those with symptoms) and for treatment
- CRC detection rate
- Adenoma detection rate (number, size in mm, number and histological features – villous, high grade dyplasia)
- Will GPs/primary health care workers be able to manage what happens in invitation/referral process and what is the outcome for a national programme?

1.2 Economic efficiency of screening
- Unit costs and total costs of all services provided along screening pathway: identification, invitation, testing, diagnosis, re-invitation, monitoring (see 1-9 in section 1.1 above)
- Patient volumes at each step of the screening pathway
- Cost per eligible member of the population, at each step
- Cost per person invited
- Cost per person screened
- Cost per cancer detected
- Identification of differences in unit costs between regions of feasibility study and nationally.
- Provisional estimates of funding required for a national programme (optional).

1.3 Determining the appropriate FOBT

- determine positivity rate of FOBTg and impact of dietary/therapeutic restriction and time of test reading on this
- determine positivity rate of FOBTi(s) at manufactures specification and measure effects of lowering analytical sensitivity on positivity rate
- compare participation rates for FOBTg, FOBTi requiring dry stool sampling and FOBTi using brush sampling of wet stool FOBTi types.

1.4 Recommended parameters of feasibility study

- **Eligible population** New Zealand males and females aged 55-74 years (exclusion criteria = previously diagnosed CRC, already in colonoscopy surveillance programme, undergoing treatment for CRC)
- **Type of test:** FOBTi (FOBTi and type of FOBTi to be determined by scoping study)
- **Screening interval:** Two years
- **Location:** Multicentre (minimum of two centres, eg, one urban and one rural/provincial); location where capacity and colonoscopy quality can be assured
- **Number to be invited:** Sufficient to ensure adequate number of cancers detected and harms avoided; sufficient Māori to establish Māori participation (at screening and at re-screening)
- **Measures:** Coverage, participation rate, positivity rate, technical repeat rate, colonoscopy referral rate, adverse events following colonoscopy, false positive rate, adenoma detection rate, CRC detection rate, size distribution of adenomas detected, stage distribution of cancers detected, time taken to provide results (screening, colonoscopy, pathology), time from diagnosis of CRC to treatment, costs associated with screening
- **Duration of study:** Three years as a minimum, involving one complete (prevalence) round and one partial (incidence) round. Interim progress report after round one.
- **Evaluation of results and assessment:** independent evaluation and assessment at all stages (formatively and summatively), including economic evaluation
- **Criteria for termination:** circumstances under which study would end and decision made not to proceed to a national programme, or for modifying the screening process (for a national programme) would need to be determined in advance. Criteria for termination would relate primarily to safety/quality; an acceptable level of adverse events for colonoscopy would need to be determined
- **Information systems/data capture:** adequately resourced management system
- **Study targets:** could be based on early characteristics of the randomised control trials of CRC screening (surrogate measures as used in the evaluation of the pilot breast cancer screening programmes).

APPENDIX 7: LIST OF EXTERNAL CONTRIBUTORS

The Advisory Group wishes to acknowledge and thank the contributors listed below for their presentations and the contribution they made to the deliberations of the Group.

Dr Michael Crooke, Chemical Pathologist, Capital Coast District Health Board:
"Faecal Occult Blood Tests"

Dr Diana Sarfati, Senior Research Fellow and Public Health Physician, Wellington School of Medicine:
"Inequalities in CRC Treatment"

Dr Caroline Shaw, Public Health Medicine Registrar, National Screening Unit, Ministry of Health:
"Consumer Acceptability of CRC Screening"
"Epidemiology of CRC in New Zealand"

Dr Martin Tobias, Public Health Physician and Technical Specialist, Public Health Intelligence Unit, Ministry of Health:
"Mortality Projections for CRC in New Zealand"

Dr Andrew Yeoman, Research Fellow, Gastroenterology Department, Middlemore Hospital:
"Interim results from colonoscopy survey"

Professor Graeme P Young, Head of Gastroenterology, Flinders University:
"Sensitivity Immunochemical FOBTs for CRC"
"The Australian FOBTi Pilot Studies"

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