NATIONAL CANCER PREVENTION POLICY

2004–06

Screening to detect cancer early

Bowel (colorectal) cancer

The Cancer Council Australia

Bowel (colorectal) cancer

The Cancer Council aims to reduce the burden of bowel cancer on the Australian community and ensure that an effective and efficient screening or early detection program for bowel cancer is conducted in Australia.

Bowel cancer in Australia

Bowel cancer, also known as colorectal or large bowel cancer, is a major health problem in the Australian community. One in twenty-one Australians is likely to develop the disease (AIHW & AACR 2003). In 2000, there were 12,405 new cases of bowel cancer—6863 reported in men and 5542 in women—representing 14.6% of all new cases of cancer (excluding non-melanoma skin cancer) (AIHW & AACR 2003). The incidence rate rises steadily with advancing age and most cases occur after the age of forty years. Between 1990 and 2000, the rate of new cases of bowel cancer registered for men and women increased slightly (AIHW & AACR 2003).

With the ageing of the Australian population, we can expect the total number of new cases of bowel cancer to increase substantially. Rates of bowel cancer are higher among people with a family history of this type of cancer and there are two specific syndromes which have a defined inherited genetic basis—familial adenomatous polyposis (FAP) and hereditary non-polyposis colorectal cancer (HNPCC). HNPCC is also associated with an excess of cancers at other sites, including the endometrium and ovary.

In 2000, there were 4718 deaths in Australia from bowel cancer: 2569 in men and 2149 in women. Bowel cancer was the third most common cause of death from cancer in men (after lung and prostate cancers) and the third most common in women (after breast and lung cancers). Between 1990 and 2000, the death rate for bowel cancer fell by 0.9% per year for men and by 1.4% for women (AIHW & AACR 2003). Despite the trend towards better survival, bowel cancer remains an important cause of premature death in Australia.

Can bowel cancer be prevented?

In recent decades, there has been considerable interest in identifying modifiable risk factors associated with bowel cancer. The main focus of research into preventable risk factors associated with bowel cancer has been in relation to diet (including nutritional supplements) and other lifestyle factors such as physical activity, intake of aspirin and other non-steroidal anti-inflammatory drugs, and smoking (NHMRC, COSA & ACN 1999).

A recent comprehensive overview of diet and cancer estimated that 66–75% of bowel cancer could be prevented by diet and physical activity (AICR & WCRF 1997). The National Health and Medical Research Council (NHMRC) noted that 'appropriate dietary changes, together with

regular physical activity and maintenance of healthy weight could, in time, substantially reduce the incidence of colorectal cancer' (NHMRC, COSA & ACN 1999 p. 18). (See the chapters on diet and physical activity for more information.)

A number of studies have shown that smoking is a risk factor for bowel cancer and precancerous adenomas (Chao et al. 2000; Limburg et al. 2003; Kune et al. 1992; Kikendall et al. 1989). The report from the Cancer Prevention Study II estimated that, in the USA, approximately 12% of deaths from bowel cancer among both men and women were attributable to smoking (Chao et al. 2000).

The use of aspirin has also been identified as a potential means of preventing bowel cancer. Findings from the Nurses' Health Study indicate that the benefit is not evident until after at least a decade, if not two decades, of regular aspirin consumption (Giovannucci et al. 1995). Adverse effects of aspirin include acute upper gastrointestinal bleeding (Weil et al. 1995). After reviewing research into the effects of aspirin and non-steroidal anti-inflammatory drugs, the NHMRC concluded that 'aspirin and non-steroidal anti-inflammatory drug chemoprevention is consistently protective in case–control and cohort studies, but is not recommended until the dosage and the balance between risk and benefit is evaluated in randomised controlled trials' (NHMRC, COSA & ACN 1999 p. 17).

Screening tests and programs for bowel cancer

Rationale

In conjunction with the preventive measures described above, there has been a focus on screening to reduce the impact of bowel cancer in the community.

Research into bowel cancer indicates that most bowel cancers develop from adenomatous polyps (adenomas); a small adenoma will grow into advanced cancer over an estimated ten years. It should be recognised that it is common for middle-aged or elderly people to have one or more adenomas; most (perhaps nineteen out of twenty) never progress to cancer. Adenomas are described as 'advanced' when certain features such as larger size (10 mm or more in diameter) are present, these features acting as markers of greater likelihood of progression to cancer. Once cancer has developed, growth may occur slowly over twelve to twenty-four months or even longer. While the cancer remains confined to the bowel wall, surgical resection gives cure rates around 90% (NHMRC, COSA & ACN 1999).

Most people with advanced adenomas and many with early stage cancer experience none of the symptoms that would alert them or their doctor to the presence of disease. For people diagnosed with bowel cancer, the stage of development of the tumour at the time of diagnosis, as well as the treatments that follow, will affect their prognosis. Survival rates for bowel cancer are strongly related to early diagnosis, with five-year case survival rates found in South Australia to be:

- 88% for Stage A, when the cancer is contained within the bowel wall
- 70% for Stage B, when the cancer has extended through the bowel wall
- 43% for Stage C, when the cancer is present in the lymph nodes
- 7% for Stage D, when the cancer cannot be removed by surgery or has spread to other areas of the body (NHMRC, COSA & ACN 1999).

The two objectives of screening are to prevent cancer by identifying and removing precancerous advanced adenomas and to diagnose and treat early stage curable cancer. The evidence on screening for bowel cancer was reviewed in a report for the Australian Health Technology Advisory Committee (AHTAC 1997). The report concluded that the efficacy of screening based on the faecal occult blood test (FOBT) had been demonstrated, but that the best approach to mass screening of the Australian population required definition, and pilot studies were warranted. In 1999, guidelines for the prevention, early detection and management of bowel cancer were developed (NHMRC, COSA & ACN 1999). The guidelines incorporated the AHTAC recommendations on screening and were endorsed and published in 1999 by the NHMRC. A second edition is due to be released by the NHMRC in 2004.

Three screening tools for the early detection of bowel cancer have been proposed: the FOBT, sigmoidoscopy and colonoscopy (NHMRC, COSA & ACN 1999). Two other tools—computerised tomographic colonography and faecal DNA testing—may have a future role in screening but are still undergoing evaluation (Winawer et al. 2003; Pineau et al. 2003; Johnson, Harmsen et al. 2003; Johnson, Toledano et al. 2003; Ginnerup Pedersen et al. 2003).

Faecal occult blood test (FOBT)

Cancers in the large bowel have a tendency to produce low-grade bleeding (Macrae & St John 1982; St John et al. 1992). The detection of blood in small (but not visible) concentrations in the faeces provides the basis for use of FOBT in screening for bowel cancer. With FOBT, blood can be detected through the chemical or immunochemical properties of haem and haemoglobin. The chemical tests, most of which use guaiac-impregnated slides as the test system, depend on detection of the chemical activity of haem. Certain foods and medications have the potential to interfere with test results. The immunochemical tests utilise antibodies to human globin and are not affected by diet or medications. (For further discussion of the properties of the tests refer to Young, Macrae & St John 1996 and Young et al. 2002.)

FOBT is done at home. Depending on the particular test, samples are collected from either two or three bowel actions. The samples are then sent to a laboratory for analysis to check for the presence of blood. With the chemical tests, dietary modification may be required—essentially this involves avoiding red meat and vitamin C supplements for several days.

As bleeding may be intermittent, the finding of blood in one or more samples should be investigated by colonoscopy (see below). Bowel cancer will be identified in 5–10% of those with a positive FOBT, an adenoma will be identified in another 35–40%, and bleeding will be due to a non-neoplastic cause such as haemorrhoids in the remainder. However, as shown by the FOBT-based randomised controlled trials and other large studies, the likelihood of finding bowel cancer is twelve to forty times greater in a person with a positive FOBT than in someone whose test shows no evidence of bleeding (Mandel et al. 1993; Mandel et al. 1999; Alexander & Weller 2003).

A false negative result from the FOBT (i.e. no bleeding detected in a person who actually has bowel cancer or an advanced adenoma) may occur because of intermittent blood loss or uneven distribution of blood in the faeces or, in the case of chemical tests, because of intake of vitamin C supplements (Young, Macrae & St John 1996). The choice of test also affects false negative rates, as many FOBTs have different thresholds for detection of blood, and therefore for cancer. The chemical test used in the European randomised controlled trials had a sensitivity for cancer of only 50% (Hardcastle et al. 1996; Kronborg et al. 1996) whereas many newer chemical and immunochemical tests have a sensitivity for cancer in the range 70–90% (Allison et al. 1996).

Periodic testing is recommended, as a normal (i.e. negative) result does not rule out the possibility of future development of bowel cancer.

Evidence from the European randomised controlled trials, which used a low sensitivity test repeated two-yearly for ten years, suggests that this approach would lead to a reduction of 15–18% in mortality from bowel cancer among those offered screening (Hardcastle et al. 1996; Kronborg et al. 1996). The reduction in mortality was estimated to be 30–40% among those who actually perform the test (Scholefield et al. 2002; Jorgensen, Kronborg & Fenger 2002).

Sigmoidoscopy

Sigmoidoscopy involves tube examination of the rectum and the lower part of the colon (i.e. the section of large bowel closest to the anus). The sigmoidoscope may be rigid (best suited for examining the rectum) or flexible (reaching into the lower part but unable to examine the upper part of the colon). Flexible sigmoidoscopy allows examination of the area where 55–60% of bowel cancers and advanced adenomas occur (AHTAC 1997). When abnormalities are detected, a tissue sample (a biopsy) can be collected for pathological examination.

Evidence from several case–control studies indicates that screening by flexible sigmoidoscopy should lead to a substantial reduction in the death rate from bowel cancer (Selby et al. 1992; Newcomb et al. 1992). Major randomised controlled trials using flexible sigmoidoscopy for screening are currently underway in the US, UK and Italy (Gohagan et al. 2000; UKFSSTI 2002; Segnan et al. 2002). Progress results from the three trials show the screening procedure to be feasible, safe and well accepted (Weissfeld et al. 2002; Sutton et al. 2000; McCaffery et al. 2002; Segnan et al. 2002).

The AHTAC report suggested that 'the evidence is sufficient to warrant consideration of sigmoidoscopic screening as an alternative (or a complement) to FOBT screening' but noted that mortality data from the randomised controlled trials will not be available for several more years (AHTAC 1997 p. 66).

Colonoscopy

A colonoscope is similar to a flexible sigmoidoscope but is much longer. Interest in using colonoscopy as a screening tool relates to its ability to detect a very high proportion of bowel cancers and advanced adenomas by examination of the entire length of the large bowel. It allows biopsies to be taken from any suspected abnormalities as well as enabling most adenomas and some polypoid cancers to be completely removed during the examination.

Colonoscopy is the recommended follow-up test for those with positive findings at FOBT or screening sigmoidoscopy. It is also recommended as the primary tool for cancer surveillance in people with an increased risk for bowel cancer. These situations include a personal history of previous bowel cancer, advanced adenoma, chronic inflammatory bowel disease or a strong family history of bowel cancer (NHMRC, COSA & ACN 1999).

The place of colonoscopy as the primary tool in population screening is much less certain. Acceptability of the procedure is limited by its invasive nature and the need for vigorous bowel preparation and sedation. The feasibility of providing colonoscopy for the five million Australians at average risk is also doubtful, given the high cost of the procedure, workforce and other logistic issues, and diversion of resources away from other health services.

Of even greater importance, there is no high level evidence to support use of colonoscopy in population screening (NHMRC, COSA & ACN 1999). In 2001, the Canadian Task Force on Preventive Health Care stated that there was insufficient evidence to include or exclude colonoscopy as an initial screening test in people at average risk (CTFPHC 2001). Similarly, in 2002, the US Preventive Services Task Force was unable to find direct evidence that screening colonoscopy was effective in reducing the bowel cancer mortality rate (USPSTF 2002).

The policy context

In line with the AHTAC and NHMRC recommendations, the National Cancer Control Initiative developed a proposal for a feasibility study for bowel cancer screening in the general population (NCCI 1999). The recommendations were formulated by an expert group that included representatives of the cancer councils. In response to this proposal, funds were set aside in the May 2000 federal budget to mount a four-year national feasibility study based on biennial screening using immunochemical FOBTs (see section below on screening tests). Further funds were allocated in the May 2004 Federal Budget to complete the pilot.

The Population Screening Section of the Department of Health and Ageing assumed responsibility for planning the National Bowel Cancer Screening Pilot Study. The Health Insurance Commission, the cancer councils, and all other interested groups participated in the planning process. Three pilot sites—Mackay in Queensland, and defined suburbs in Adelaide and Melbourne—were chosen for the feasibility study. Screening using FOBT commenced in November 2002 in Mackay, February 2003 in Adelaide, and March 2003 in Melbourne.

The Cancer Council enthusiastically endorses the action of the Australian Government in funding a feasibility study into bowel cancer screening using faecal occult blood testing.

The feasibility study addresses the following recommendation of the 1997 AHTAC report (p.104):

- Given the uncertainties relating to the most effective means of implementing such a program and to the feasibility, acceptability and cost-effectiveness of such a program in the Australian setting, the program should commence with preliminary testing involving a number of pilot and feasibility studies.

The Cancer Council fully supports this study as the initial intervention which should guide and inform future policy on bowel cancer screening in Australia. The Cancer Council further supports the related recommendation of the 1997 AHTAC report (p. 104):

- On the basis of published evidence, and subject to favourable preliminary testing, it is recommended that Australia develop a program for the introduction of population screening for bowel cancer by faecal occult blood testing for the average risk population (well population aged over fifty).

What are the potential benefits of screening for bowel cancer?

Monitoring systems in South Australia found that only 15% of bowel cancers were detected at the earliest point, Stage A (AHTAC 1997). Thus an important potential benefit of screening the general well population is to improve the survival rate of people with bowel cancer by the detection of curable, early stage cancer (NHMRC, COSA & ACN 1999).

A screening program also has the potential to detect advanced adenomas, allowing them to be removed before progressing to bowel cancer.

Potential adverse effects

Bowel cancer screening may have adverse psychological effects. Of particular concern is increased anxiety experienced as a result of false positive results. The potential negative psychological and physical effects associated with a false positive test include anxiety induced by fear of being diagnosed with bowel cancer, physical effects of the performance of invasive diagnostic procedures (specifically colonoscopy), and the diagnosis of non-lethal lesions. In a study by Lindholm et al. (1997), anxiety due to positive test results was shown to decrease after investigation of the cause and no adverse effects were evident twelve months later.

The most significant adverse effect is the potential for physical harm linked to exposure to colonoscopy. Colonoscopy is performed as a day-case procedure and usually requires sedation. Colonoscopy can produce severe complications such as perforation, haemorrhage or death and carries a remote risk of transmitting infections. In a review of six prospective studies of colonoscopy, about 1 in 1000 patients suffered perforation, 3 in 1000 suffered major haemorrhage, and between 1 and 3 in 10,000 died as a result of the procedure (Winawer et al. 1997). In two more recent studies, the findings were similar, overall morbidity being 0.4% (Dafnis et al. 2001; Gatto et al. 2003). A review of a large Australian hospital series supported the conclusions of these other studies and reported a mortality rate of 0.004% in outpatients having the procedure (Viiala et al. 2003).

Who should be screened?

The incidence rate for bowel cancer rises steadily with advancing age. Australian health authorities recommend that, when introduced as a national program, men and women having no special risk factors other than their age should commence FOBT-based screening at the age of fifty years (NHMRC, COSA & ACN 1999). Anyone with relevant bowel symptoms should be encouraged to undergo diagnostic investigations rather than having screening and all those considering screening should be aware of the risks involved.

No upper age limit has been set for screening. Decisions about continued participation by the elderly are likely to be based on their personal preference and general state of health, and the perceived balance between benefits of screening and harms related to the follow-up investigations required in those with positive screening tests.

Screening people at increased risk for bowel cancer

The AHTAC report on colorectal cancer screening noted that a national approach to population screening for people without symptoms would need to be complemented by a national policy for groups potentially at increased risk for bowel cancer: individuals with a family history of bowel cancer, or a personal history of bowel adenoma, bowel cancer or inflammatory bowel disease (AHTAC 1997).

The NHMRC *Guidelines for the prevention, early detection and management of colorectal cancer* defines three categories of people in relation to risk for bowel cancer based on their family history of the disease. In the first category, people who have just one first-degree relative with bowel cancer are advised to have the same screening as those at average risk, provided their relative was diagnosed with cancer at or over the age of fifty-five years.

The second category includes people with two or more close relatives with bowel cancer or one first-degree relative diagnosed under the age of fifty-five years. Because of their greater risk for cancer, screening is generally based on periodic (usually every five years) colonoscopy. The third category covers members of families with definite or suspected FAP or HNPCC. People with FAP usually have hundreds of small polyps throughout their bowel, which become malignant if not removed. HNPCC does not produce polyps, but like FAP, is caused by an inherited change in a gene. The place of genetic testing, endoscopic and other methods of surveillance, and prophylactic surgery are described in Chapter 7 of the NHMRC guidelines (NHMRC, COSA & ACN 1997).

Detailed recommendations for surveillance by colonoscopy in those with past bowel cancer, adenoma or chronic inflammatory bowel disease are also in the NHMRC guidelines.

> The Cancer Council supports the implementation of a national bowel cancer screening program. In the meantime, men and women over fifty years should talk to their doctor about having an FOBT every two years.

Aims

The Cancer Council's aims are to:

- reduce the burden of bowel cancer on the Australian community
- ensure that an effective and efficient screening or early detection program for bowel cancer is conducted in Australia.

What we want to achieve	How we will do this
Screen the well population	Participate in and contribute to the evaluation of all aspects of the feasibility study Participate in and contribute to the development and implementation of community education and recruitment strategies relating to the feasibility study Identify recruitment strategies which will maximise participation of Aboriginal and Torres Strait Islander peoples Identify recruitment strategies which will maximise participation of culturally and linguistically diverse populations Liaise with policy-makers and funding bodies on the workforce, quality control and resource issues identified by the pilot programs to ensure that recommendations can be implemented Liaise with policy-makers and funding bodies on the establishment of centralised support for registration, recall, monitoring and evaluation to complement the running of a pilot program and to facilitate the expansion of screening programs Participate in the analysis of the pilot program outcomes and advise government on applying findings to the whole population Provide interim advice for the general public outside pilot areas
Identify high risk populations	Participate in the development and coordination of programs and registers for the population at high risk for bowel cancer

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Bowel cancer

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