Colorectal cancer screening

Targeted population screening can help prevent colorectal cancer. Diagnosis of asymptomatic colorectal cancer and polypectomy to prevent cancer development are the goals of screening.

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Colorectal cancer is the most common internal malignancy in Australia and the second most common cause (after lung cancer) of cancer-related death. The incidence of colorectal cancer increases dramatically in patients over 50 years of age, and in 80 to 85% of cases there is no positive family history of the disease. If diagnosed early (Dukes stage A), over 90% of patients with the cancer survive five years, compared with only 8% of patients who present with metastatic disease (Figure 1).[1] However, many patients with the cancer have advanced disease by the time they present, and in NSW, for example, the overall five-year survival rate is about 65%.[2]

Screening strategies

Screening tests for the presence of a condition whereas surveillance monitors a known condition. The goal of cancer screening is to identify malignant or premalignant disease at an asymptomatic and potentially more favourable prognostic stage. Population screening for colorectal cancer is targeted at people without symptoms or personal or familial risk factors who may be at risk solely because of their age. Colorectal cancer is a good candidate for this type of strategy. An ideal screening test is simple, effective, inexpensive and widely accepted.

Almost all colorectal cancers are derived from colorectal adenomatous polyps, which are usually present for many years before a small percentage becomes malignant. The 'dwell time' for these adenomas represents a unique window of opportunity for the detection and subsequent prevention of colorectal cancer via adenomatous polyp removal (polypectomy). Prevention of the cancer by polypectomy and the diagnosis of asymptomatic cancer are the aims of colorectal cancer screening.

Screening is inappropriate for patients with symptoms of colorectal cancer, who should be assessed using colonoscopy (Figure 2). The signs and symptoms of colorectal cancer include rectal bleeding, anaemia (especially iron deficiency anaemia), recent change in bowel habit, new

IN SUMMARY

- **Colorectal cancer is common but highly preventable.**
- **Annual faecal occult blood testing (FOBT) is recommended for asymptomatic average risk individuals from the age of 50 years.**
- **Symptomatic patients, those with a moderate or high risk family history, and those with a personal history of inflammatory bowel disease, colorectal polyps or cancer should be evaluated by colonoscopy.**
- **The National Bowel Cancer Screening Program is a co-ordinated program currently being phased in to enhance the early detection of colorectal cancer through FOBT.**

onset abdominal pain and unintentional weight loss. Patients with a personal or family history of colorectal cancer, or a personal history of adenoma or inflammatory bowel disease, may have an increased risk of developing colorectal cancer. These patients require a screening program tailored to their circumstances, usually one utilising colonoscopy.

In a 50-year-old patient, the risk of developing colorectal cancer within the next five years is 1 in 300; by 60 years of age, the risk increases to 1 in 100 (Table 1). As the incidence of colorectal cancer is less than 10% in people under 50 years of age, screening in the absence of a known risk factor is not recommended for this population group. The screening therefore targets asymptomatic people, aged 50 years or more, who have no risk factors (average risk patients).

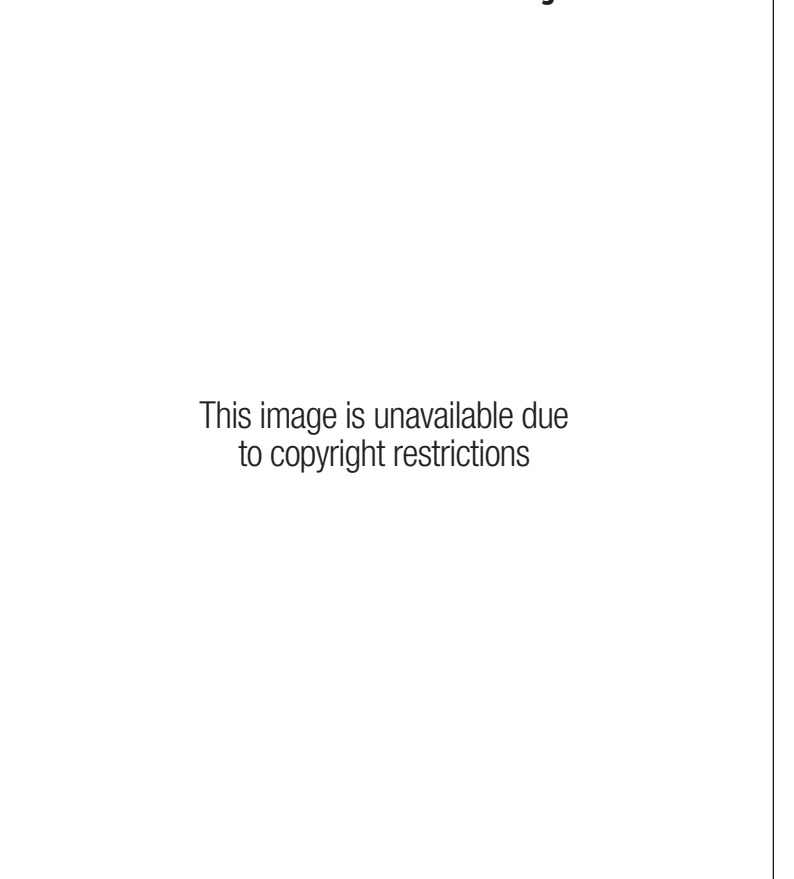
Role of faecal occult blood testing

There is now Level 1 evidence from randomised controlled trials showing faecal occult blood testing (FOBT) in colorectal cancer screening reduces mortality. FOBT is the cheapest and least invasive colorectal cancer screening tool available. The test is undertaken at home and then mailed to a laboratory for analysis.

Screening using FOBT has resulted in tumours being identified at an earlier stage, offering the benefits of less intensive therapy and an improved prognosis. It has been shown that with screening, 36% of cancers were diagnosed in Dukes stage A, compared with 11% of controls.[3] It has also been shown that the relative risk of dying from colorectal cancer was reduced by 33% in screened populations, and that there was a 47% reduction in the number of patients presenting with Dukes stage D cancer when FOBT was performed annually.[4]

The two forms of FOBT are faecal immunochemical tests such as InSure (previously !nform) and Detect, and chemical (guaiac) tests like Hemoccult II SENSA. Unlike the chemical tests, the immunochemical tests are not affected by diet or medications. A recent Australian study[5] showed that InSure was a more sensitive detector of colorectal cancer and advanced adenomas than Hemoccult II SENSA. In a screening population, InSure had an overall positive rate of 6.7% and a 3.4% false positive rate. The specificity was 96.6% and had an estimated true sensitivity of 75% for cancer and 27% for significant adenoma. False negatives may occur due to uneven distribution of blood in the faeces or if bleeding is intermittent.

Colorectal cancer screening



Colorectal cancer is a frequent cause of morbidity and mortality in Australia. Screening by annual faecal occult blood testing is recommended for people at average risk for the cancer and who have no symptoms. People at higher risk or with symptoms should be evaluated by colonoscopy. A national bowel cancer screening program is currently being phased in by the Federal Government to enhance the early detection of colorectal cancer.

Alternatives to faecal occult blood testing

There are alternatives to FOBT for primary screening of patients of average risk. In addition to annual or biennial FOBT, the NHMRC approved guidelines suggest consideration of flexible sigmoidoscopy every five years.[6] Even though colonoscopy is the gold standard for diagnosis of

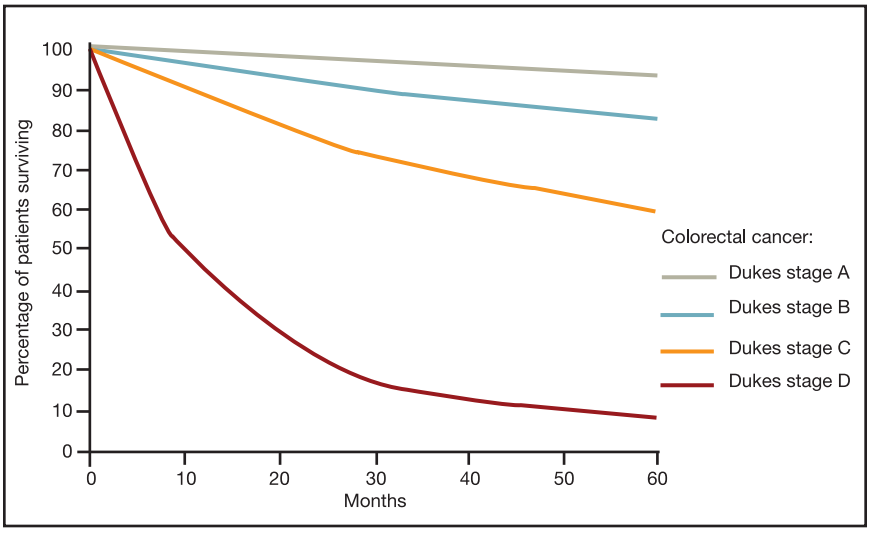
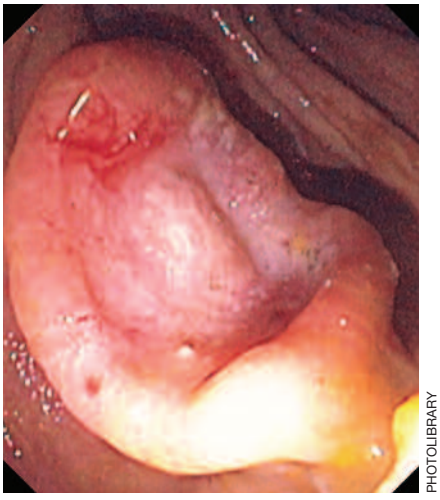


Figure 1. Survival of patients with colorectal cancer according to Dukes classification.



PHOTOLIBRARY

Figure 2. Colonoscope view of a colorectal cancer.

colorectal lesions, it is not suitable for population screening. The procedure is costly and has small but significant risks associated with it (about 1 in 500 patients have significant bleeding, 1 in 1000 have bowel perforation, and 1 in 10,000 risk death).[7] In addition, availability of the procedure is limited. Table 2 compares the limitations of the available colorectal cancer screening tests.

National Bowel Cancer Screening Program

Recently, the Federal Government supported a pilot program for screening average risk individuals for colorectal cancer using FOBT. Three centres participated in the pilot study, which included patients from diverse ethnic and socioeconomic backgrounds. A total of 25,840 patients participated (patient participation rate, 45%) and the overall rate of positive FOBT was 9%. Of the patients with a positive FOBT, 1273 (65%) had colonoscopy information available, which revealed 67 colorectal cancers and 259 adenomas. The positive predictive value of a positive FOBT for colorectal cancer and all types of adenoma was 25.6%. This is significantly higher than the positive predictive value of 7.5% for a significant family history.[8]

Following the success of the pilot program, the Federal Government allocated $43.4 million over a three-year period (which began in August 2006) to phase in a co-ordinated national screening program. Initially, FOBT screening is being offered to Australians turning 55 or 65 years of age between 1 May 2006 and 30 June 2008. By 2016, it is expected that biennial FOBT will be offered to all Australians between 55 and 74 years of age.

The National Bowel Cancer Screening Program is offering FOBT to all people based on age alone, with no knowledge of their comorbidities. GPs play a pivotal role in assessing patients' comorbidities and, in some instances, recommending nonparticipation in the program if life expectancy is limited or other reasons preclude investigation or treatment for a positive result.[9] Patients with symptoms or who have an increased risk of developing colorectal cancer should not participate in the program but should be referred to a specialist instead.

There are several issues regarding the National Bowel Cancer Screening Program that are worthy of further

Table 1. Absolute risk of colorectal cancer in people with no known risk factors

Age (years)	Risk of colorectal cancer within a time period			
	5 years	10 years	15 years	20 years
30	1 in 7000	1 in 2000	1 in 700	1 in 350
40	1 in 1200	1 in 400	1 in 200	1 in 90
50	1 in 300	1 in 100	1 in 50	1 in 30
60	1 in 100	1 in 50	1 in 30	1 in 20
70	1 in 65	1 in 30	1 in 20	1 in 15
80	1 in 50	1 in 25	–	–

Table 2. Limitations of colorectal cancer screening tests

Faecal occult blood test

Non-bleeding polyps or cancers will not be detected

False positive rate of 3%

Colonoscopy

Expensive

Limited resource

Requires patient preparation

Risks related to sedation, bleeding and perforation

False negative rate (missed lesions) of 5 to 10%, depending on lesion size

CT colonography

Expensive

Requires patient preparation

Exposure to radiation

Not established as a screening modality

Positive tests need to be followed up with colonoscopy

Colorectal cancer risk stratification according to family history[6]

Category 1

Patients who are at risk or have a slightly above average risk of developing colorectal cancer (up to twofold increased risk). Patients have one first- or second-degree relative with colorectal cancer who was aged 55 years or older when the cancer was diagnosed.

Category 2

Patients who have a moderately increased risk of developing colorectal cancer (three- to sixfold increased risk). Patients have one first-degree relative with colorectal cancer who was diagnosed before 55 years of age or two first- or second-degree relatives on the same side of the family who were diagnosed with colorectal cancer at any age.

Category 3

Patients who are potentially high risk for developing colorectal cancer (lifetime risk approached 1 in 2).

- Patients with a suspected hereditary non-polyposis colorectal cancer pedigree (three or more first- or second-degree relatives on the same side of the family who developed colorectal cancer over two generations where one relative was the first-degree relative of two of the other relatives and where one was diagnosed with the cancer under the age of 50 years).
- Patients with suspected familial adenomatous polyposis pedigree
- Patients with a family history of known genetic mutations (APC or MMR genes)
- Any person from category 2 with the following additional high risk features:
  - a family member with multiple colorectal cancers
  - colorectal cancer before 50 years of age
  - at least one relative with endometrial or ovarian cancer.

comment. Firstly, 35% of people with positive FOBT results did not proceed to colonoscopy, especially if they were non-English speaking. Secondly, despite the NHMRC approved recommendation for screening all people over the age of 50 years, the federally funded screening program will only be available initially to people aged 55 to 74 due to cost-effectiveness reasons. People aged 50 to 54 years or any age not included by the roll out will have to purchase their kits. Thirdly, 23% of people aged 50 to 74 years in an American study were found to be unsuitable for inclusion in a population-based screening program due to above average personal or familial risk, symptoms or recent colonoscopy.[10] Finally, until specifically engaged by the patient, GPs may not be in a position to assess suitability for subsequent colonoscopy. This can result in the difficult situation of a patient who should not have been screened because of comorbid disease presenting with a positive FOBT result.

Family history and cancer risk

As mentioned earlier, asymptomatic people aged 50 years or more with no special risk factors are classified as being at average risk of developing colorectal cancer.

Having a family history of colorectal cancer or adenomatous polyps increases this risk of developing colorectal cancer in the future. There is some evidence that a large adenomatous polyp or multiple adenomas in a first-degree relative conveys the same risk as a history of colorectal cancer in a relative.[11]

The increase in colorectal cancer risk to an individual with a positive family history is related to the age of the affected relative at diagnosis and the closeness of the relationship, the number of affected relatives and the side of the family of these relatives. The categorisation of patients according to familial risk is shown in the box above.

Patients with a slightly above average risk

For people who have one first- or second-degree relative aged 55 years or older with colorectal cancer, the risk of developing the cancer increases up to twofold. This includes approximately 8 to 10% of middle-aged people in Australia.[12] The NHMRC approved guidelines recommend annual screening with FOBT for

Table 3. Surveillance based on personal risk factor history[6]

Personal risk factor history	Surveillance colonoscopy
Colorectal adenomatous polyps	
Polyp incompletely excised, removed piecemeal or proven to be malignant	Repeat colonoscopy in three months, then subsequent interval dictated by polyp histology, size and number For some malignant polyps, surgery may be necessary
Multiple adenomas, or Incomplete/inadequate colonoscopy	Repeat colonoscopy within one year, then subsequent interval dictated by polyp histology, size and number
Adenoma >1 cm in size or three or more adenomas, or High grade dysplasia or villous change, or Patient >60 years old with a first-degree relative with colorectal cancer	Repeat colonoscopy in three years, then subsequent interval dictated by polyp histology, size and number
One or two small tubular adenomas (<1 cm) with low grade dysplasia	Repeat colonoscopy in five to ten years
Hyperplastic polyps	As per average risk screening protocol except in patients with hyperplastic polyposis syndrome
Previous colorectal cancer	First colonoscopy between three and five years' post resection, then repeat colonoscopy every five years +/- annual faecal occult blood testing
Ulcerative colitis	Begin colonoscopy eight to 10 years after onset of symptoms, then repeat every one or two years If primary sclerosing cholangitis present, start surveillance from time of diagnosis
Crohn's disease	Begin colonoscopy eight to 10 years after symptom onset, then repeat every one or two years

patients in this category, with consideration of flexible sigmoidoscopy every five years.[6] Guidelines from the USA also support colonoscopy in this setting.[13] It is still being debated whether the risk and expense of periodic colonoscopy is justified in this patient group compared with the less invasive screening methods.

Patients with a moderately increased risk

People who are at moderate risk for developing colorectal cancer (three- to sixfold increase) are those with one first-degree relative with the cancer who was diagnosed before the age of 55 years, or those who have two relatives on the same side of the family with the cancer who were diagnosed at any age. Although between 70 and 90% of patients in this category will never develop colorectal cancer, colonoscopy starting at 50 years of age or at an age 10 years younger than the youngest affected relative (whichever comes first) is recommended. In the absence of any positive findings, colonoscopy should be repeated at five-yearly intervals. Positive findings will require follow up with surveillance colonoscopy. The interval between colonoscopies will be determined by the polyp histology, size and number.

Patients at high risk

Patients with familial adenomatous polyposis syndrome and confirmed or suspected hereditary nonpolyposis colon cancer syndrome have a high risk of developing colorectal and other cancers. The patient and their families should be referred for genetic counselling and testing and for ongoing specialist management. They should also be registered with a familial cancer registry.

Personal history and cancer risk

Individuals with a history of longstanding extensive ulcerative colitis (or to a lesser degree Crohn's disease), previous adenomatous polyps, or colorectal cancer are at risk of developing colorectal cancer in the future. These patients need ongoing specialist surveillance, usually utilising colonoscopy (Table 3).

Colorectal adenomatous polyps

Surveillance programs in patients with colorectal adenomatous polyps will almost always involve colonoscopy; there is no role for FOBT alone in such programs. Table 3 summarises the suggested frequency of colonoscopy according to the history and current clinical status of the patient.

Previous colorectal cancer

Patients with previous colorectal cancer are followed up with colonoscopy for the detection of metachronous polyps or cancers (Table 3). Colonoscopy is performed between three and five years post resection (assuming the whole colon was examined for synchronous lesions at the time of the resection). Annual FOBT is recommended in the intervening years. Serum carcinoembryonic antigen levels can be used to assist post resection monitoring. This test has no role in the screening of patients without a previous diagnosis of colorectal cancer.

Screening for colorectal cancer: frequently asked questions

At what age should colorectal cancer screening start for individuals in the population who have an average risk status?
For people who have no known risk factors for the cancer, screening for colorectal cancer should begin at age 50 years.

Which test is recommended?
The recommended test for colorectal cancer screening is an immunochemical faecal occult blood test (FOBT) every one or two years.

How is the test completed?
Faecal occult blood testing is carried out at home using a specialised test kit that is then posted to a laboratory for analysis.

What is the National Bowel Cancer Screening Program?
The National Bowel Cancer Screening Program is a Federal Government initiative, inviting Australians turning 55 or 65 years of age between 1 May 2006 and 30 June 2008 to undertake a FOBT. The program will be extended to all Australians aged between 55 and 74 years by 2016.

How can a test be obtained?
FOBT kits can be purchased through some general practices and chemists or directly from the manufacturers.

Do patients need to change their diet or medication before undertaking this test?
No dietary or medication changes are required for the immunological FOBTs.
Diet and medication changes are necessary for the guaiac FOBTs.

What if the patient's FOBT result is positive?
If a patient's test result is positive, he or she should be referred for colonoscopy.

Up to what age should screening continue?
As a general guide, patients who are 75 years or older or who have significant comorbidities should not be screened.

Inflammatory bowel disease

The risk of colorectal cancer is increased in patients with long-standing inflammatory bowel disease and is associated with the extent of disease. It is reasonable to perform surveillance colonoscopy in a patient every year or two years (with multiple random biopsies to detect dysplastic changes) if the patient has been experiencing pancolitis for eight to 10 years or left sided colitis for 15 years.[14] A Cochrane review showed that this strategy was able to detect the cancer earlier and was therefore likely to improve prognosis.[15] Patients with primary sclerosing cholangitis also have an increased risk of colorectal cancer and surveillance should begin at the time of diagnosis.

The risk of colorectal cancer is also increased in Crohn's colitis but, because the disease process tends to be patchy, it has been more difficult to develop surveillance guidelines. Nonetheless, it is reasonable to offer these patients surveillance every year or two years after 10 years of extensive disease (Table 3). A longer interval may be possible in patients with limited disease.

Conclusion

Colorectal cancer is a frequent cause of morbidity and mortality in Australia. The Federal Government's FOBT based screening program has the potential to detect asymptomatic cancers at an earlier, more treatable stage. Bowel cancer prevention should now be incorporated into the health maintenance plans of all patients aged 50 years and above.

There are well characterised groups of people at increased risk for colon cancer. For these patients, colonoscopic screening is justified on a risk to benefit basis. The aim of this strategy is to identify and remove premalignant lesions such as polyps. Some questions that patients may ask regarding colorectal cancer screening are discussed in the box on this page. MT

References

1. O'Connell J, Maggard MA, Ko CY. Colon cancer survival rates with the New American Joint Committee on Cancer sixth edition staging. J Natl Cancer Inst 2004; 96: 1420-1425.
2. Tracey EA, Chen S, Baker D, Bishop J, Jelfs P. Cancer in New South Wales: incidence and mortality report 2004. Sydney: Cancer Institute NSW; 2006.
3. Kronborg O, Jorgensen OD, Fenger C, Rasmussen M. Randomised study of biennial screening with a faecal occult blood test: results after nine screening rounds. Scand J Gastroenterol 2004; 39: 846-851.
4. Mandel J, Church TR, Ederer F, Bond JH. Colorectal cancer mortality: effectiveness of biennial screening for faecal occult blood. J Natl Cancer Inst 1999; 91: 434-437.
5. Smith A, Young GP, Cole SR, Bampton P. Comparison of a brush-sampling faecal immunochemical test for haemoglobin with a sensitive guaiac-based faecal occult blood test in detection of colorectal neoplasia. Cancer 2006; 107: 2152-2159.
6. Australian Cancer Network Colorectal Cancer Guidelines Revision Committee. Guidelines for the prevention, early detection and management of colorectal cancer. Sydney: The Cancer Council Australia and Australian Cancer Network; 2005. Available online: www.cancer.org.au/guidelines and www.nhmrc.gov.au (accessed May 2007).
7. Viiala CH, Zimmerman M, Cullen DJ, Hoffman NE. Complications rates of colonoscopy in an Australian teaching hospital environment. Intern Med J 2003; 33: 355-359.

8. The Australian Bowel Cancer Screening Pilot Program: analysis of routinely collected screening data, November 2004. Canberra: Australian Government Department of Health and Ageing; 2004.
9. Macrae FA. Providing colonoscopy services for the National Bowel Cancer Screening Program. Med J Aust 2007; 186: 280-281.
10. Worthley DL, Smith A, Bampton PA, Cole SR, Young GP. Many participants in fecal occult blood test population screening have a higher-than-average risk for colorectal cancer. Eur J Gastroenterol Hepatol 2006; 18: 1079-1083.
11. Ahsan H, Neugut AI, Garbowski GC, et al. Family history of colorectal adenomatous polyps and increased risk for colorectal cancer. Ann Intern Med 1998; 128: 900-905.
12. Digestive Health Foundation. Early detection, screening and surveillance for bowel cancer. Sydney: Gastroenterological Society of Australia and the Australian Cancer Society; 2006.
13. Winawer SJ, Fletcher R, Rex D, et al. Colorectal cancer screening and surveillance: clinical guidelines and rationale – update based on new evidence. Gastroenterology 2003; 124: 544-560.
14. American Society for Gastrointestinal Endoscopy. Colonoscopy in the screening and surveillance of individuals at increased risk of colorectal cancer. Gastrointest Endosc 1998; 48: 676-678.
15. Collins PD, Mpofu C, Watson AJ, Rhodes JM. Strategies for detecting colon cancer and/or dysplasia in patients with inflammatory bowel disease. Cochrane Database, Syst Rev 2006; 2: CD000279.

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