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CME ARTICLE

Colorectal cancer screening

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55-year-old Mr Tan visited your clinic for a routine medical check-up. He had a history of well-controlled hyperlipidaemia and smoked 2–3 cigarettes per day. His uncle was diagnosed with colorectal cancer at 72 years of age. Mr Tan had no symptoms. You raised the issue of colorectal cancer screening during the consultation. He had heard many unpleasant stories about colonoscopy, including the bowel preparation protocol, and did not like the idea of having an instrument inserted into his colon. He had also heard that colonoscopy is a major procedure requiring general anaesthesia. Mr Tan said that he had sent his stool to the Health Promotion Board for a free test last year, and was told that it was normal. He felt that he was not at risk and there was no further need to screen for colorectal cancer.

HOW COMMON IS THIS IN MY PRACTICE?

Colorectal cancer (CRC) is an important health problem worldwide. It is the most common cancer in Singapore: 9,320 new cases of CRC were diagnosed between 2010 and 2014,[1] giving a crude incidence of 48.9 per 100,000. The incidence of CRC in Singapore is among the highest in the world. Risk factors for developing CRC are older age, male gender, family history, Chinese race, smoking and obesity.[2] Many patients with CRC are diagnosed at Stage III or later, which is associated with poor survival. CRC screening can help to detect and remove pre-malignant lesions, such as colonic adenoma, or diagnose early asymptomatic cancer to improve outcomes. However, a successful screening programme requires concerted efforts from family doctors, specialists and the government to improve uptake.

WHAT IS COLORECTAL CANCER SCREENING?

Screening is defined as the application of tests or procedures for the early detection of disease in asymptomatic people.[3] CRC can arise from colorectal adenomas, giving rise to the classic adenoma-carcinoma sequence of pathogenesis as depicted by Morson et al.[4,5] It can also arise from flat neoplasms and serrated adenomas. The average time taken for the evolution from small adenoma to cancer ('polyp dwell time') has not been established, but indirect evidence suggests that it takes an average of about ten years for an adenomatous polyp, particularly one that is < 1 cm in diameter, to develop into invasive cancer.[6] This long period of progression from polyp to cancer provides the rationale behind CRC screening: it allows detection and removal of adenomas (i.e. polypectomy) or early-stage CRC that is asymptomatic. Removal of the precursors of cancers can prevent CRC. CRC screening should begin at 50 years of age. This is supported by the updated Asia-Pacific consensus recommendations on colorectal cancer screening,[2] as well as the United States Preventive Services Task Force (USPSTF) recommendation statement,[7] as it has been shown that screening adults aged 50–75 years reduces CRC mortality.

Screening tests for CRC include stool-based and direct visualisation tests. Table I summarises the characteristics of each CRC screening strategy. It was demonstrated that any form of screening for colorectal cancer is cost-effective compared to no screening.

Stool-based tests

The three stool-based tests are: (a) guaiac-based faecal occult blood tests (gFOBT); (b) faecal immunochemical tests for haemoglobin (FIT); and (c) multitargeted stool DNA tests (FIT-DNA). Both gFOBT and FIT detect the presence of components of haemoglobin in faeces. Several randomised clinical trials (RCTs)[8-12] have shown that biennial or annual screening with gFOBT reduces colorectal cancer mortality. Biennial screening with Hemoccult II® resulted in a reduction in CRC-specific mortality, from 9% to 22% after 2–9 rounds of screening with 11–30 years of follow-up,[9-12] whereas annual screening with Hemoccult II, after 11 rounds of screening, resulted in a greater reduction of 32% in CRC-specific mortality than biennial screening at 30 years of follow-up.[8]

FIT uses antibodies raised against the globin moiety of human haemoglobin and has improved sensitivity compared to gFOBT for detecting colorectal cancer.[13] With a single stool specimen, its sensitivity and specificity for CRC was demonstrated to be 73%–88% and 91%–96%, respectively.[14,15] FIT-based screening programmes were associated with a 22% reduction in CRC mortality. Moreover, the advantages of FIT over gFOBT include: (a) it has increased specificity, as the antibodies bind only to human globin; (b) it is not confounded by blood loss proximal to the colon; (c) it is unlikely to be affected by antioxidants

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Table I. Characteristics of colorectal cancer screening strategies.[7]

Method	Frequency	Other considerations
Stool-based test		
gFOBT	Every yr	Does not require bowel preparation, sedation, or transportation to and from the screening examination (test is performed at home)
FIT	Every yr	Does not require bowel preparation, sedation, or transportation to and from the screening examination (test is performed at home)
FIT-DNA	Every 1 or 3 yr	Insufficient evidence about appropriate longitudinal follow-up of abnormal findings after a negative diagnostic colonoscopy; may potentially lead to overly intensive surveillance due to provider and patient concerns over the genetic component of test
Direct visualisation test		
Colonoscopy	Every 10 yr	Requires less frequent screening; screening and diagnostic/ therapeutic follow-up on positive findings can be performed during the same examination
CT colonography	Every 5 yr	Concerns remain over the potential harm that may be associated with overdiagnosis and overtreatment of incidental extracolonic findings, although overall evidence remains unclear
Flexible sigmoidoscopy	Every 5 yr	Mortality benefit is limited to distal colorectal cancer; preparation (2 small enemas 1 hr before the examination) is considered less onerous to patients
Flexible sigmoidoscopy with FIT	Every 10 yr (flexible sigmoidoscopy) Every yr (FIT)	Potentially attractive option for patients who want endoscopic screening but want to limit exposure to colonoscopy and full bowel preparation regime

CT: computed tomography; FIT: faecal immunochemical test; gFOBT: guaiac faecal occult blood test

such as vitamin C or vegetable peroxidases; (d) it requires fewer stool samples (one compared with three); and (e) analysis can be automated. FIT-DNA is an emerging screening technique that combines FIT with testing for altered DNA biomarkers in colorectal cancer cells shed into the stool. It has increased sensitivity but lower specificity than the use of FIT alone for detecting colorectal cancer.[16]

Direct visualisation tests

Flexible sigmoidoscopy

Flexible sigmoidoscopy examines the distal part (descending or left-sided) of the colon. Five randomised trials of screening sigmoidoscopy have shown a decrease in cancer incidence and colorectal cancer mortality.[17-21] Using Markov modelling analysis, Dan et al showed that performing single sigmoidoscopies on individuals in Singapore when they are 60 years of age is the cheapest screening strategy; it would reduce CRC incidence by 19% and mortality by 16%, compared with no screening.[22] It is important to emphasise, however, that all studies using flexible sigmoidoscopy showed no reduction in proximal CRC incidence, which is not surprising, as the examination is limited to the left colon. Flexible sigmoidoscopy combined with FIT has also been studied in a randomised controlled trial[17] and was found to reduce the CRC-specific mortality rate more than flexible sigmoidoscopy alone. It is potentially an attractive option for patients who want endoscopic screening but prefer limited exposure to colonoscopy and want to avoid the full bowel preparation regime.

Colonoscopy

Colonoscopy is considered the 'gold standard' test for CRC screening. There are no randomised controlled trials on the effectiveness of screening colonoscopy to reduce CRC incidence and mortality in average-risk patients. However, studies on flexible sigmoidoscopy provide indirect evidence that colonoscopy reduces CRC mortality. A prospective cohort study also found an association between self-reports from patients who were screened with colonoscopy and a lower CRC mortality rate.[23] Moreover, data from computed tomography (CT) colonography studies has enabled the sensitivity of colonoscopy to be estimated so that the results can be applied to community practice.[24-27] Compared with CT colonography or colonoscopy with CT colonography (e.g. segmental unblinding), the sensitivity of colonoscopy is 89%–98% for detecting adenomas ≥ 10 mm and 75%–93% for adenomas ≥ 6 mm.[24,25,27]

The diagnostic accuracy and therapeutic safety of colonoscopy depends, in part, on the quality of the colonic cleansing or preparation. Hence, it is important that patients are educated and engaged in the colonoscopy preparation process. Patient counselling, along with written instructions that are simple, easy to follow and in the patient's native language, should be provided.[28] Risks of colonoscopy include sedation-related adverse events, perforations (four in 10,000 procedures) and major bleeding (eight in 10,000 procedures).[7]

CT colonography

CT colonography, also known as virtual colonoscopy, is minimally invasive imaging of the entire colon and rectum. Its utility in screening for colorectal cancer has been studied. Based on seven studies of CT colonography with bowel preparation, the per-person sensitivity and specificity for detecting adenomas ≥ 10 mm were 67%–94% and 86%–98%, respectively. To detect adenomas ≥ 6 mm, the per-person sensitivity and

Table II. Risk categories for colorectal cancer (CRC).[31]

Risk category	Description
Average	• Aged ≥ 50 yr • No family history of CRC • No personal history of adenoma, sessile serrated polyps, CRC or IBD
Increased	• Personal history of adenomatous polyps, sessile serrated polyps, CRC or IBD • Family history: (a) 1 first-degree relative with CRC aged < 60 yr or 2 first-degree relatives with CRC at any age (b) First-degree relative with confirmed advanced adenoma(s) (i.e. high-grade dysplasia, lesions ≥ 1 cm, villous/tubulovillous histology) (c) First-degree relative with CRC aged ≥ 60 yr (d) 1 second-degree relative with CRC aged < 50 yr
High	• Presence of high-risk syndromes such as hereditary nonpolyposis CRC and polyposis syndrome (e.g. familial adenomatous polyposis)

IBD: inflammatory bowel disease

specificity were 73%–98% and 80%–93%, respectively.[7] Incidental extracolonic findings are common, occurring in about 40%–70% of screening examinations. Between 5% and 37% of these findings result in diagnostic follow-up, and about 3% require definitive treatment, indicating potential overdiagnosis and overtreatment from CT colonography.[7] Radiation risk is a relative disadvantage of CT colonography; nonetheless, with new developments in technique, the risk of ionising radiation from CT colonography is extremely low and likely to be negligible.[29]

WHAT CAN I DO IN MY PRACTICE?

Despite advancements in screening modalities, treatment of pre-neoplastic adenomas and treatment options for CRC, the incidence of CRC in Singapore continues to rise rapidly. A major reason may be poor screening uptake, which is where primary care providers can play an important role. In addition to creating awareness by actively discussing CRC screening among suitable individuals, primary care providers can also address certain specific concerns and fears about screening modalities with their patients. In a local, nationwide, representative household survey, Wong et al[30] reported that both patient and physician factors were barriers to CRC screening. The study demonstrated the impact of the physician in advocating screening, with screening uptake showing a positive association with the physician's recommendation. In particular, screening in women was positively associated with attending a public talk on CRC. However, only 22.6% of the patients in the study were advised by their physicians to undergo screening.[30] Addressing both patient and physician barriers to CRC screening is a crucial step in overcoming poor patient understanding of CRC as a fatal disease; the inability to identify symptoms of CRC; and a lack of awareness that screening is an important tool against cancer development.

Like all screening programmes, CRC screening should be considered for all appropriate individuals at both acute and chronic consultations. The primary care physician can proactively screen at-risk individuals in the community for CRC by first assessing individual risk before making specific recommendations for CRC screening. History-taking is important and should emphasise risk factors for colorectal cancer, including age, smoking history, personal history of colorectal adenomas and inflammatory bowel disease (IBD), and family history (age of onset, number of affected family members and degree of consanguinity). Individuals can then be stratified according to their risk factors into average, increased and high risk groups (Table II).

For average-risk individuals, the USPSTF guidelines emphasise shared decision-making, a process in which the physician and patient share information, then reach a shared medical decision about the screening test that is best for the patient. Table I shows the recommended screening intervals for CRC.

Individuals with increased risk of CRC should have personalised screening strategies. In particular, for those who have an affected first-degree relative diagnosed before 60 years of age or two first-degree relatives with CRC at any age, colonoscopy is recommended every five years, beginning ten years prior to the earliest diagnosis in the family or at 40 years of age at the latest.[31] Individuals who have a first-degree relative with a confirmed history of advanced adenoma(s) (i.e. high-grade dysplasia with lesions ≥ 1 cm and villous/tubulovillous histology) should undergo colonoscopy at the relative's age of onset of adenoma, or by 50 years of age at the latest.[31] For those with one affected first-degree relative diagnosed at 60 years of age or older, or one second-degree relative diagnosed prior to 50 years of age, colonoscopy should begin at 50 years of age. High-risk individuals with a family history of familial adenomatous polyposis or hereditary nonpolyposis colorectal cancer, or those who have IBD must be referred and co-managed by a gastroenterologist, colorectal surgeon and/or cancer geneticist for regular and active surveillance of CRC.[32,33]

In Singapore, citizens and permanent residents aged ≥ 50 years are invited to screen for colorectal cancer annually using free FIT kits from Community Health Assist Scheme general practice clinics under the Integrated Screening Programme. In addition, the free FIT kit is available for collection at the Singapore Cancer Society and selected retail pharmacy outlets. However, more can be done to encourage screening uptake. Both patient and physician factors must be identified and addressed.

WHEN SHOULD I REFER TO A SPECIALIST?

Specialist referral is indicated if patients have a positive faecal occult blood test or prefer other screening modalities such as colonoscopy or CT colonography. In addition, primary care providers can refer individuals found to have increased or high risk of CRC to specialist care. In such cases, colonoscopy is the preferred screening or surveillance modality.

TAKE HOME MESSAGES

1. CRC is the leading cancer in Singapore.
2. CRC screening and polypectomy can prevent CRC.
3. Screening tests for CRC include stool-based tests (i.e. gFOBT, FIT and FIT-DNA) and direct visualisation tests (i.e. flexible sigmoidoscopy, alone or combined with FIT, colonoscopy and CT colonography).
4. Physicians should discuss appropriate screening modalities with patients.

Mr Tan eventually opted for an annual faecal immunochemical test for haemoglobin to screen for colorectal cancer (CRC). The result was positive and you referred him to a gastroenterologist. Six months later, he visited your clinic for a routine review. He mentioned that he underwent a colonoscopy five months ago. It revealed a small, 6-mm benign polyp (tubular adenoma with low-grade dysplasia) in his sigmoid colon, which was successfully removed during the colonoscopy. His gastroenterologist had since discharged him with a memo and Mr Tan was well. You advised him to undergo a surveillance colonoscopy in five years' time if all goes well. He was glad to have heeded your recommendation to undergo CRC screening.

ABSTRACT Colorectal cancer, which is the leading cancer in Singapore, can be prevented by increased use of screening and polypectomy. A range of screening strategies such as stool-based tests, flexible sigmoidoscopy, colonoscopy and computed tomography colonography are available, each with different strengths and limitations. Primary care physicians should discuss appropriate screening modalities with their patients, tailored to their individual needs. Physicians, patients and the government should work in partnership to improve uptake of colorectal cancer screening to reduce the morbidity and mortality from colorectal cancer.

Keywords: colorectal cancer, polypectomy, screening

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SINGAPORE MEDICAL COUNCIL CATEGORY 3B CME PROGRAMME

(Code SMJ 201701A)

		True	False
1.	Colorectal cancer (CRC) is the most common cancer in Singapore.	☐	☐
2.	Risk factors for developing CRC are older age, male gender, family history, smoking and obesity.	☐	☐
3.	Screening is defined as the application of tests or procedures for the early detection of disease in symptomatic people.	☐	☐
4.	Evidence shows that CRC screening in adults aged 50–75 years reduces CRC mortality.	☐	☐
5.	Screening methods for CRC include stool-based tests and direct visualisation tests.	☐	☐
6.	Stool-based tests require bowel preparation and sedation before the tests.	☐	☐
7.	Both guaiac-based faecal occult blood test (gFOBT) and faecal immunochemical test (FIT) can detect the presence of components of haemoglobin in faeces.	☐	☐
8.	gFOBT can be confounded by blood loss proximal to the colon.	☐	☐
9.	Results of FIT can be affected by antioxidants such as vitamin C or vegetable peroxidases.	☐	☐
10.	Multitargeted stool DNA testing has both higher sensitivity and specificity than the use of FIT alone for detecting CRC.	☐	☐
11.	Studies on flexible sigmoidoscopy showed no reduction in proximal CRC incidence.	☐	☐
12.	Colonoscopy is considered the 'gold standard' test for CRC screening.	☐	☐
13.	Risks of colonoscopy include sedation-related adverse events, perforations and major bleeding.	☐	☐
14.	CT colonography is invasive testing of the entire colon and rectum.	☐	☐
15.	It is common to have incidental extracolonic findings during CT colonography.	☐	☐
16.	Radiation risk is a relative disadvantage of CT colonography.	☐	☐
17.	An individual at average risk for CRC is someone who has a family history of CRC.	☐	☐
18.	An individual at high risk for CRC is someone who has a hereditary or genetic predisposition for CRC.	☐	☐
19.	For individuals with an affected first-degree relative diagnosed before 60 years of age or two first-degree relatives with CRC at any age, colonoscopy is recommended every five years, beginning ten years prior to the earliest diagnosis in the family or at 40 years of age at the latest.	☐	☐
20.	Specialist referral is indicated if patients have a positive faecal occult blood test.	☐	☐

Doctor's particulars:

Name in full : _____

MCR number : _____ Specialty: _____

Email address : _____

SUBMISSION INSTRUCTIONS:

(1) Visit the SMJ website: http://www.smj.org.sg/current-issue and select the appropriate set of questions. (2) Provide your name, email address and MCR number. (3) Select your answers and click "Submit".

RESULTS:

(1) Answers will be published online in the SMJ March 2017 issue. (2) The MCR numbers of successful candidates will be posted online at the SMJ website by 3 March 2017. (3) Passing mark is 60%. No mark will be deducted for incorrect answers. (4) The SMJ editorial office will submit the list of successful candidates to the Singapore Medical Council. (5) One CME point is awarded for successful candidates.

Deadline for submission: (January 2017 SMJ 3B CME programme): 12 noon, 24 February 2017.