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Screening for colorectal cancer: what fits best?

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Colorectal cancer (CRC) screening has been shown to be effective in reducing CRC incidence and mortality. There are currently a number of screening modalities available for implementation into a population-based CRC screening program. Each screening method offers different strengths but also possesses its own limitations as a population-based screening strategy. We review the current evidence base for accepted CRC screening tools and evaluate their merits alongside their challenges in fulfilling their role in the detection of CRC. We also aim to provide an outlook on the demands of a low-risk population-based CRC screening program with a view to providing insight as to which modality would best suit current and future needs.

KEYWORDS: colonoscopy • colorectal cancer • CT colonography • fecal blood test • screening • sigmoidoscopy

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Learning objectives

Upon completion of this activity, participants will be able to:

- Describe available stool-based modalities for CRC screening, based on a review
- Describe available structural examinations for CRC screening, based on a review
- Describe overall principles regarding CRC screening, based on a review

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Colorectal cancer (CRC) is an important health issue worldwide. It is the most common malignancy in Europe (excluding non-melanoma skin cancers) and the second most common in terms of cancer-related mortality [1]. Although decreasing in incidence, CRC remains the third most common cancer in the USA and is the third leading cause of cancer deaths [2]. By contrast, in Europe, there seems to be a trend of modest increase in incidence [1]. Survival and mortality from CRC has seen an improvement over the past 30 years [3]. This is in no small part due to earlier detection of the disease and also treatment advances in the management of CRC [4]. Despite this, the economic burden of this disease remains huge. Recent estimates from the National Cancer Institute have put the cost of CRC cancer care in the tune of US\$12.1 billion in 2006, second only to breast cancer and accounting for 12% of the total expenditure for cancer care every year [201]. This is in stark contrast to the US\$7.49 billion estimated in a previous study for CRC cancer care in 2000. In this study, projections based on trends at that time indicated that the total cost of CRC cancer care was set to increase by a further 89% by the year 2020 [5]. As the current updated figure has already increased by more than 60% in just 6 years since the year 2000, we are more than likely to see a healthcare bill in excess of the original US\$14 billion estimated for this disease. The reason for this dramatic increase is multifactorial, but its impact on the delivery of healthcare in developed countries, and indeed worldwide, is unarguably profound. There is therefore a compelling need to contain the spiraling cost of this disease. To achieve this, healthcare providers will need to reduce its incidence, optimize cancer care for cost efficiency and avert early mortality from cancer, which is estimated to result in an average 15 years of life lost per patient. All these points underpin the rationale for CRC, screening, and there is now a substantial

body of evidence to show screening does reduce the incidence and mortality of CRC [6]. However, there are controversies as to the modality that would best serve the purpose of screening in a general population. Different methods offer unique strengths and herein we review the most frequent modalities employed and their cost-effectiveness in an attempt to determine 'what fits best' as a general population screening tool (TABLE 1).

Role for CRC screening

CRC fulfills the WHO's criteria for screening through early detection of the disease and/or its precursors polyps [7]. Compared with other cancer screening programs, CRC screening has been shown to be cost effective [8]. There are a range of modalities for CRC screening, and the recent joint guideline from the American Cancer Society, the Multi-Society Task Force on Colorectal Cancer and the American College of Radiology broadly grouped tests into those that can primarily detect cancer early (stool-based tests) and structural tests that can detect cancer and also adenomatous polyps such as colonoscopy, flexible sigmoidoscopy (FS) and CT colonography [9]. Detection of adenomatous polyps has the potential to prevent future cancers via therapeutic measures such as polypectomy. This is particularly relevant for polyps that exhibit features that harbor significantly increased malignant potential, such as large size or the presence of high-grade dysplasia on histology. Polyps larger than 1 cm in size and/or display high-grade dysplasia on histology are often termed 'advanced adenomas.' The guideline did not recommend a single specific screening modality; rather it encouraged medical practitioners to fully appraise patients of the various options and to allow them to choose. However, they did emphasize that cancer prevention, rather than cancer detection, should be the primary goal [9].

Table 1. Summary of currently available screening modalities, their performance in detecting colorectal cancer and polyps, and their effect on colorectal cancer incidence and mortality.

Screening modality	Approach to screening	Recommended interval	Test sensitivity for CRC (%)	Test specificity for CRC (%)	Test sensitivity for advanced adenoma (%)	Test specificity for advanced adenoma (%)	Incidence reduction CRC (%)	Mortality reduction CRC (%)	Ref.
<i>Stool-based examinations</i>									
gFOBT	Two step	Annual or biennial	12.9–85	80–97.7	4–33	>80		16	[6,19,28,98]
FIT	Two step	Annual or biennial	81.8–100	87.5–96.9	27–56.8	91.4–97.3			[33–38]
Fecal DNA	Two step	Uncertain	25–86	73–96	15–57	84–96			[97]
<i>Colon examinations</i>									
Colonoscopy	One step	10 year	95		88–98		67–76	50–65	[39,40,53]
Sigmoidoscopy	Two step	5 year	95		83	59.6	31–33	38–43	[53,64,67]
CT colonography	Two step	5 year	96		90 [†] 78–90 [‡]	86–89 [†] 86–89 [‡]			[72,74,99]

[†]Performance of CT colonography for detection of adenomas ≥10 mm in size.

[‡]Performance of CT colonography for detection of adenomas 6–9 mm in size.

CRC: Colorectal cancer; CT: Computed tomography; FIT: Fecal immunological test; gFOBT: Guaiac-based fecal occult blood test.

Different screening modalities

Stool-based tests

CRC screening with stool tests typically involves a two-stage approach, with patients positive for the test being referred for colonoscopy. Traditional guaiac-based stool tests (guaiac-based fecal occult blood test [gFOBT]) and immunochemical-based tests (fecal immunological test [FIT]) both check for the presence of occult blood in the stool, which is associated with advanced colorectal neoplasia and cancer. A newer stool DNA test checks for the presence of mutations associated with colorectal neoplasia. However, this test is not widely available, and the results are still not very further accurate or reliable enough and, as such, are not discussed further in this review [10,11].

Guaiac-based fecal occult blood tests

gFOBT is the earliest stool-based test developed for CRC screening. Based on the peroxidase activity of heme reacting together with hydrogen peroxide and a resin found in guaiac to give off a blue color, it is still one of the most widely used screening modalities worldwide [12,13]. Its efficacy has been confirmed in major prospective trials, with patients undergoing regular gFOBT testing having a reduction of 16% in relative risk for CRC mortality [6]. It is cheap to perform and can be carried out conveniently in a physician's office.

However, there are several technical issues with its use, such as the qualitative color change, which can be difficult to interpret, necessitating formal training of personnel to avoid misreading of the result [14]. Dietary restrictions are encouraged prior to gFOBT testing to minimize the effects of a heme-rich diet (red meats and liver) and of plant peroxidases on the specificity of the test [15–17]. Medications such as aspirin and NSAIDs known to induce

gastrointestinal bleeding have also to be withheld as the detection of heme in the stool does not differentiate between an upper or lower gastrointestinal source, therefore generating false-positive results [18]. Usually stool samples are tested from three separate bowel movements collected by patients. Testing of gFOBT on stool samples obtained in the physician's clinic during a digital rectal examination is not very sensitive and is not recommended, although it is widely practiced [9].

Overall, one-time sensitivity for detecting CRC using gFOBT is low, ranging from 12.9 to 50% although a study using a more sensitive gFOBT (Hemoccult® SENSE®, Beckman Coulter, Inc., CA, USA) has reported a sensitivity of 85.7% [19]. When used repeatedly in the setting of an annual or biennial CRC screening program, the overall sensitivity of gFOBT for detecting CRC is between 51.1 and 72.2%, with a positive-predictive value ranging from 8.0 to 17% [19]. A study using Hemoccult SENSE in this setting has reported sensitivity as high as 100% but with a lower positive-predictive value range of 2.4–5.5% [20]. It is important to note that the performance of gFOBT is highly dependent on patient compliance with repeated testing, and there could be selection bias confounding the results in these studies, meaning its actual performance in the real world could well be lower than currently observed [9,21]. It is also to be noted that the US Preventive Services Task Force no longer recommend the use of traditional gFOBT because of its poor sensitivity, in preference for gFOBT with higher sensitivity such as Hemoccult SENSE for guaiac-based fecal testing for CRC.

Fecal immunological test

FIT, in turn, detects the protein globin that is unique to the human species by utilizing monoclonal antibodies raised against them. As

globin is destroyed by proteases during transit through the small intestine, its presence in stool highly suggests blood from a colonic origin [22,23]. FIT is not dependent on peroxidase activity, and there is no need to undergo any dietary or medication restrictions as there is with gFOBT. Unlike gFOBT, the readings from FIT are quantitative, with measurements of the amount of globin being read by enzyme-linked immunosorbent assay and a numerical value produced as output [24]. The quantitative nature of the test removes ambiguity once a cutoff limit for positivity is set. The cutoff limit can also be adjusted to optimize the detection of advanced adenomas and cancers in different local population groups [25,26]. It also has a lower detection limit for occult blood and has been shown in several studies to have increased sensitivity and specificity compared with gFOBT [27,28]. Less stool sample requirements (one or two stool samples for FIT) and ease of use of the collection kit can improve patient adherence with screening [29]. As it is a newer test, its effectiveness in reducing CRC incidence and mortality has not been proven in any direct study to be superior to gFOBT. Furthermore, the performance between different commercially available FITs can vary, and regular assessment of its sensitivity and specificity will be needed as the technology develops [30]. There are also technical issues such as false-negative results because of delayed processing of the sample. This occurs as a result of globin degradation and is a temperature-dependent process based on *in vitro* studies [31]. This has a detrimental impact on the reliability of the test in practice, with one Italian study noting reduced test positivity during the summer months for a regional CRC screening program [32]. Therefore, logistical issues are of significance and should be given particular consideration for any national CRC screening program.

Overall, the sensitivity of FIT for the detection of CRC is reported to range from 81.8 to 100% and from 27 to 56.8% for the detection of advanced adenomas. The specificities for detecting CRC and advanced adenomas were 87.5–96.9% and 91.4–97.3%, respectively [33–38].

Colon examinations

Colonoscopy

Colonoscopy is one of the most common screening modalities employed for CRC screening in the USA and has several advantages. It allows for direct visualization of the colonic mucosa and the whole colon can be assessed. Polyps discovered during the procedure can be readily removed by polypectomy. There is evidence from observational and case-controlled studies that polypectomy can reduce the incidence of CRC [39,40]. Prospective randomized trials looking into this effect are currently underway [202,203]. Colonoscopy is the only method that offers a one-step approach to CRC screening: all the other CRC screening tests have to further refer subjects who test positive for full colonic evaluation with colonoscopy. This one-step approach streamlines the workflow, reduces the number of visits subjects have to attend and may even enhance patient compliance with CRC screening guidelines because of the extended recommended interval between retesting: 10 years for a negative screening colonoscopy [41]. However, colonoscopy is an invasive procedure and carries with it an inherent risk, although the risk is low. Studies reported an overall complication rate of 2.9–5 per 1000 endoscopies

and a perforation rate of 0.9–1.8 per 1000 endoscopies [42,43]. A screening colonoscopy program also reported a complication rate of 0.1% [44]. Subjects have to undergo the arduous task of having to take bowel preparation to cleanse the bowel prior to colonoscopy and the procedure itself can often be uncomfortable and poorly tolerated. Sedation is commonly used to improve patient comfort and compliance during the procedure but this has its own inherent risks and drawbacks [45]. Newer technologies such as the use of CO₂ insufflation instead of air during procedure may help to decrease patient discomfort, leading to better patient satisfaction and attendance [46].

Colonoscopy as a screening modality is also heavily operator dependent. Competency with this procedure is absolutely vital, so that the whole colonic mucosa is visualized (cecal intubation) and lesions are properly identified (adenoma detection) with minimal patient discomfort (patient satisfaction) and complications. These all have an sequential impact on the ability to detect CRC, and there is evidence that expertise is a risk factor for missed CRCs during colonoscopy [47]. It is therefore of paramount importance that the quality of the screening colonoscopy is ensured to achieve the maximal efficacy from this modality. Training of specialist personnel and the regular auditing of key performance indicators in a colonoscopy-based screening program will help to standardize clinical practice and upkeep the requirements for implementing this strategy [48]. Of the quality indicators for screening colonoscopies, adenoma detection rate (ADR) merits particular mention. Kaminski *et al.* showed that the only two factors that determined the risk of interval cancer were the patient's age and the endoscopist's ADR. A total of 42 interval CRC were identified during a period of 188,788 person-years. The hazard ratio between endoscopists who had an ADR greater than 20% and those with an ADR less than 20% was over 10.75 for the development of interval CRC [49].

Colonoscopy is often used as the 'gold standard' for the detection of CRC and adenomatous polyps with which other tests are compared. There are no studies that actually define the 'true' performance of this procedure but it is estimated to have sensitivity and specificity of 95% and 88–98%, respectively [21]. However, a study using back-to-back colonoscopy reported a significant adenoma miss rate of 6% for lesions more than 1 cm in size, whereas a study comparing colonoscopy with CT colonography (CTC) suggested that this miss rate could be as high as 12% [50,51]. A population-based study looking at right-sided CRC has indicated that approximately 4% of right-sided CRC are missed on colonoscopy [52].

There are several lines of evidence that have shown the efficacy of colonoscopy in the reduction in CRC incidence and CRC-related mortality [53]. More controversially, a recent population-based study verified the protective effect for distal colonic neoplasia but no effect on the prevalence of proximal disease. The reason for this is unclear but missing lesions in the proximal colon during colonoscopy cannot be ruled out [54,55].

Flexible sigmoidoscopy

In contrast to colonoscopy, FS only inspects the left side of the colon for neoplasia. The rationale behind using FS as a screening

tool in CRC hinges on observations that distal CRC are more common than proximal CRC; sigmoidoscopy and polypectomy prevent the development of distal CRC; and proximal colonic lesions are frequently associated with advanced distal disease [56–58]. Its usage is usually in a two-stage model, with FS used in conjunction with colonoscopy for initial FS-positive patients. FS is safe, quick and can be performed without sedation, negating the need for admission to the day ward for prolonged observation, unlike colonoscopy which is commonly performed with conscious sedation. Nonphysician healthcare workers, such as nurses and physician assistants, can also be trained in this relatively straightforward procedure, which improves capacity and accessibility as a CRC screening program [59]. Favorable patient factors supporting FS as a screening tool include the relative ease of use and tolerability of bowel enema, rather than the large volume oral preparations required for colonoscopy, resulting in better patient acceptability and uptake rates [60].

However, there are issues that pose a challenge with the use of FS as a screening tool. While the strategy of FS with follow-up colonoscopy may actually identify up to 80% of all advanced neoplasias, there are specific issues regarding proximal colonic lesions. Previous studies have shown that around 50% of proximal colonic neoplasia will be missed if the decision to proceed with full colonoscopy is based on distal colonic pathology alone [61,62]. Furthermore, the incidence of proximal colonic pathology increases with age, and there is evidence to show that performing FS for screening in women would result in a higher proximal colonic lesion miss rate than observed for a matched male cohort [63]. These have given rise to concerns that FS as a modality may not be suitable as a screening tool for certain subgroups of the population at average risk for developing CRC [63]. It is also interesting that Atkin *et al.* only reported a modest decrease in the incidence of proximal CRC in their study [64]. Another limitation of FS is the lack of consensus as to what a 'full' sigmoidoscopy constitutes. This is in part because of the lack of a reliable anatomical landmark by which to reference the length of colonic mucosa examined. There is therefore a significant potential for heterogeneity in clinical practice, which will impact performance. To address this, the US Multi-Society Task Force on Colorectal Cancer have recommended insertion of FS beyond 40 cm as a quality measure in FS [9]. While this guideline is helpful in clinical practice, using an absolute length of endoscope to determine the adequacy of colonic inspection is arbitrary at best and does not take into account other variables such as patient size and the presence of diverticular disease. Like colonoscopy, FS has also been shown to be heavily dependent on the operator for its efficacy and hence there is a need for implementation of a robust quality-assurance program alongside the screening strategy [65].

The efficacy of FS in detecting colonic neoplasia and reducing in CRC mortality has been proven in several case-controlled and cohort studies [66]. A study using a combination of CTC and colonoscopy as a gold standard has reported a sensitivity rate of 83.3% for FS in detecting advanced colonic neoplasia [67]. There are several randomized trials ongoing to further assess the impact of a CRC screening strategy with FS. One such trial in Norway failed to show a significant reduction in incidence of CRC with FS after a follow-up of 7 years [68]. More recently, however, Atkin

et al. reported the results of a multicenter randomized controlled trial (UK Flexible Sigmoidoscopy Trial), and the group was able to demonstrate a decrease in the incidence of CRC by 23% in the intervention group coupled with a reduction in CRC-related mortality by 31% after a median follow-up of 11.2 years. A borderline significant decrease in overall mortality was also observed in this study [64]. Segnan *et al.* similarly showed that in an Italian randomized controlled trial involving 34,272 subjects, the incidence and mortality of CRC were reduced by 31 and 38%, respectively, with FS over a median follow-up of 10.5 years [69]. Overall, the results looked promising and one explanation for the lack of observed benefit in the Norwegian study could be the brevity of the follow-up period.

CT colonography

CTC involves the imaging of the colon using low-dose ionizing radiation. Subjects undergoing CTC take oral bowel preparation similar to colonoscopy. During the procedure, a rectal catheter is inserted for insufflation to achieve colonic distention, which may be uncomfortable, although less so when using CO₂ insufflation rather than air. The procedure is quick and requires no sedation. It is minimally invasive and very safe, with a reported overall complication rate of 0.02% and perforation rate of 0.009% [70]. Subjects found to be positive for polyps on CTC would in turn proceed to colonoscopy for confirmation of diagnosis and therapy. Recent advances in this technology, such as multidetector CT and 3D reconstruction imaging, enable high-quality imaging of the mucosa to be acquired for polyp detection [71].

Pickhardt *et al.* performed CTC and colonoscopy on the same day on a cohort of asymptomatic subjects and were able to demonstrate a sensitivity rate of 93.9% for polyps at least 10 mm in size, whereas sensitivity for colonoscopy was 87.5% for detection of similar-sized polyps [72]. Specificity for the detection of lesions more than 10 mm in size was 96% in the study. Increased polyp size has been shown to be associated with increased risk of advanced histology such as carcinoma and this is reflected by the ability of CTC to detect CRC accurately. A recent meta-analysis of CTC in the detection of CRC involving 11,151 patients reported a sensitivity rate of 96.1%, comparable to that of colonoscopy, which had a sensitivity of 94.7% for the detection of CRC [73].

While the detection of CRC and large polyps is highly accurate with CTC, there are issues regarding the detection of smaller polyps that are less than 1 cm in size. It was shown in studies that the sensitivity for detection of polyps with CTC drops with decreasing polyp size to 59% for polyps ≥ 5 mm [74]. Current American College of Radiology guidelines have recommended not reporting polyps smaller than 6 mm based on the fact that the risk of advanced histology in these diminutive polyps is low, but there is still a lack of consensus among the multiple disciplines over this controversial statement [75,76]. Based on these criteria, it is estimated that approximately 12.2–30% of all screening CTCs will be referred for colonoscopy [72,74]. Another issue of CRC screening with CTC is the detection of extracolonic findings, which can be present in up to 70% of subjects being screened [77,78]. Additional resources

will have to be deployed for further evaluation of these findings, which may involve exposing asymptomatic subjects to invasive procedures such as tissue sampling, thereby having an overall impact on patient safety, patient anxiety and cost-effectiveness [79]. There are also safety concerns regarding radiation with the use of CTC but the amount of ionizing radiation used in CTC, is considered to be low and would be further minimized with the development of a low-dose regimen [80].

Cost-effectiveness analysis

With the mounting evidence to show that screening for CRC has a positive impact on the incidence of CRC and CRC-related mortality, the impetus for rolling out a national CRC screening strategy is compelling. With a menu of screening options to choose from, several other factors vital to a successful roll out would have to be considered, of which cost-effectiveness is one important aspect. This involves quantifying the benefits and risks for each modality under consideration. Benefits are usually calculated as the number of life years or quality-adjusted life years (QALYs) gained, whereas risks are commonly represented by the costs. Cost-effectiveness is measured by looking at the cost per additional life-year gained or cost per additional QALY gained (US\$/QALY). It is generally accepted that measures costing <US\$50,000/QALY are considered to be cost effective in developed countries.

Several cost effective analyses have clearly shown the superiority of screening over a no-screening strategy [81–83]. Even when compared with other screening programs, such as those for breast and cervical cancer, CRC screening remains a cost-effective measure [8].

As to which test is the most cost effective in terms of CRC screening is a subject that is hotly debated, with evidence supporting

each of the aforementioned modalities [84–89]. Cost-effectiveness analysis is mainly carried out by modeling, and heterogeneity in the comparative research methodology employed in different studies makes it difficult to draw comparisons and to decipher the 'true' cost-effectiveness between different screening strategies. Furthermore, cost-effectiveness analysis in a given healthcare delivery structure may not be generalizable to other healthcare structures. For example, there are studies to suggest that FIT is a less cost-effective strategy when compared with gFOBT for CRC screening [90,91]. By contrast, a health technology assessment of a population-based CRC screening program in Ireland found that biennial FIT screening at 55–74 years of age is the most cost-effective measure when compared with biennial gFOBT for the same age group and with for screening using FS [92]. Based on these findings, a population-based CRC screening program is currently being rolled out in Ireland using FIT in a two-stage screening strategy [204].

A combination of screening modalities, such as gFOBT alternating with FS, has also been shown to be potentially very cost effective [82]. On the other hand, CTC was found to be costly in comparison with other screening strategies, such as colonoscopy, in the US healthcare setting. This enabled decision-makers to conclude that CTC is not a cost-effective measure for CRC screening, and the Centers for Medicare and Medicaid Services has denied coverage of CTC for CRC screening (TABLE 2).

Conclusion & future directions

CRC screening is effective, with supportive evidence available from several long-term analyses of national programs, including the UK and USA. The screening programs in both countries

Table 2. Summary of cost-effectiveness analysis of each colorectal cancer screening strategy for healthcare systems in different countries.

Screening strategy, interval	Knudsen <i>et al.</i> , USA [91]		Heitman <i>et al.</i> , Canada [100]		HTA-HIQA Report, Ireland [92]	
	Life-years gained per 1000 subjects (vs no screening)	Cost per life-year gained (US\$)	QALYs gained per 1000 subjects (vs no screening)	Cost per QALY gained (CAN\$)	QALYs gained per 1000 subjects (vs no screening)	Cost per QALY gained (€)
gFOBT, yearly	81.1 [†]	10 [†]	12 [†]	15,991 [†]		
gFOBT, biennial					7.6	4428
FIT, yearly	80.1	800	12 [†]	2219 [†]		
FIT, biennial					23.7	1696
Colonoscopy, 10 yearly	86.7	2200	41	4870		
Sigmoidoscopy, 5 yearly	75	1400	36	10,008		
Sigmoidoscopy, once-off					5.8	589
CT colonography, 5 yearly	85.3	8900	41	12,500		

[†]Cost analysis based on high-performance version of gFOBT.

[†]Cost analysis based on high-performance version of gFOBT and FIT.

FIT: Fecal immunological test; gFOBT: Guaiac-based fecal occult blood test; HTA -HIQA: Health technology assessment – Health Information and Quality Authority; QALY: Quality-adjusted life year.

vary, but both are beginning to show a trend of reduced CRC mortality and incidence [1,4,93]. There are a number of acceptable tools by which CRC screening can be carried out, as evident in this review. However, the test of choice is still a question that is yet to be answered. While the recommendation by the US Preventative Task Force of making the patient aware of the full range of options available empowers the patient to make his/her own choice and allows for degrees of freedom for the physicians [94], having a single CRC screening strategy for a population-based CRC screening program is likely to be preferable to ensure homogeneity, equitable access and arguably efficiency in a resource-finite setting. It is also likely that no one single test is going to be the most suitable for CRC screening in different low-risk population groups and healthcare systems, in particular when patient acceptance and preference are taken into account. Our initial experience of a pilot study of population based CRC screening using FIT has demonstrated a good uptake rate for screening in the target population and efficacy in the detection of CRC and advanced polyps [95]. Several studies have also suggested good patient acceptance and uptake with FIT [29]. These patient factors, along with reliability, accessibility and ease of use, together with positive data from cost-effectiveness studies, position FIT very strongly as the test of choice for future CRC screening programs. However, as further research into enhancing the performance of existing technologies and further development of newer alternative methods such as fecal DNA tests and colonic capsule endoscopy come to light, the pendulum may well swing in their favor in the near future [96,97,202]. Several ongoing comparison studies are awaited and may also help to clarify this matter.

So, in conclusion, current evidence supports all aforementioned modalities as effective screening tools. FIT is one of the best currently available strategies for the introduction of a population-based CRC screening program. However, as technology advances and indeed the epidemiology of CRC changes, healthcare providers will need to adapt strategies and should

be prepared to review the performance of a program regularly to ensure that the process employed is the best fit for their population at any given time.

Most importantly, it is clearer than ever that not screening is no longer a befitting proposition, and ways to optimize adherence to CRC screening will be the way forward for the general population.

Expert commentary

The evidence for CRC screening in detecting and preventing CRC is mounting. This serves as an impetus for the introduction of population-based CRC screening programs, both to save lives and as a means of 'bending the curve' in the ever-rising cost of cancer care. This review highlights the currently available modalities of screening and reviewed the pros and cons of each for their inclusion in a population-based screening strategy. Current evidence favors FIT as one of the best modalities in a two-step CRC screening strategy. Although colonoscopy remains the gold-standard test for CRC, access, availability and the potential for harm continue to hinder its widespread acceptance as an upfront population screening tool.

Five-year view

Countries that had introduced CRC screening decades ago are now observing a trend of reduced CRC incidence and mortality. CRC screening is also gaining momentum in many countries and it is envisaged that in 5 years time, the number of subjects being screened worldwide will be greatly increased. We hope to see the favorable impact of reduced CRC incidence and mortality worldwide in the next 20–30 years. In addition, as emerging technologies and screening methods boast of ever-increasing efficacy, it is important to note that they will be only as good as the patient actually undergoing the test and, therefore, patient education and optimization of patient adherence to screening should be an integral part of any population-based CRC screening strategy.

Key issues

- The incidence of colorectal cancer (CRC) is increasing worldwide and its economic burden is huge. It is estimated that in 2006, CRC cancer care cost US\$12.1 billion in the USA. CRC screening is one of the ways to contain this spiraling cost.
- There are currently several CRC screening modalities available and these are either stool-based (guaiac-based fecal occult blood test [gFOBT], fecal immunological test and fecal DNA test) or structural examinations (colonoscopy, sigmoidoscopy, computed tomography [CT] colonography and colonic capsule endoscopy).
- gFOBT is the oldest available stool-based CRC screening test and has been shown to reduce CRC incidence and mortality in a two-step approach to CRC screening. Fecal immunological test has demonstrated better performance than gFOBT and is likely to supersede gFOBT as the first-choice stool-based screening modality.
- Colonoscopy is the only one-step approach to CRC screening. It is also the 'gold standard' with which other screening modalities are compared.
- There is increasing evidence that flexible sigmoidoscopy is highly effective in CRC screening, with reduced CRC incidence and mortality noted in two randomized controlled trials. This effect is particularly observed for distal lesions, while only a modest effect was noted for proximal CRCs.
- CT colonography is highly accurate in detecting CRC and large polyps over 10 mm in size; however, its performance decreases with smaller polyps and there is still controversy in the management of lesions <5 mm in size detected on CT colonography.

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Screening for colorectal cancer: what fits best?

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Activity Evaluation

Where 1 is strongly disagree and 5 is strongly agree

	1	2	3	4	5
1. The activity supported the learning objectives.					
2. The material was organized clearly for learning to occur.					
3. The content learned from this activity will impact my practice.					
4. The activity was presented objectively and free of commercial bias.					

1. You are considering starting a colorectal cancer (CRC) screening program in your health maintenance organization (HMO). Based on the review by Dr. Lee and colleagues, which of the following statements about stool-based modalities available for CRC screening is **most likely** correct?

- ☐ A Stool tests are sufficient for complete CRC screening
- ☐ B Guaiac fecal occult blood tests (gFOBT) and fecal immunochemical tests (FIT) detect very early stage colorectal neoplasia and cancer
- ☐ C A genetic stool DNA test is widely available and highly accurate
- ☐ D FIT has better diagnostic performance than gFOBT

2. Based on the review by Dr. Lee and colleagues, which of the following statements about structural examinations available for CRC screening is **most likely** correct?

- ☐ A Colonoscopy is the only 1-step approach to CRC screening, and it is the "gold standard" for other screening modalities
- ☐ B Flexible sigmoidoscopy is highly effective in detecting proximal CRCs
- ☐ C CT colonography is highly accurate in detecting CRC and polyps over 5 mm in size
- ☐ D The management of lesions <5 mm detected on CT colonography is well established

3. Based on the review by Dr. Lee and colleagues, which of the following statements about overall principles regarding CRC screening would **most likely** be correct?

- ☐ A There is no evidence that screening programs reduce CRC mortality or incidence
- ☐ B The screening test of choice is clearly determined
- ☐ C For a population-based CRC screening program, it is best to have multiple CRC screening strategies
- ☐ D FIT is one of the best strategies currently available for a population-based CRC screening program, but this may change with advancing technology and changes in CRC epidemiology