3. Screening colonoscopy: rationale and performance

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Synopsis

Colorectal cancer (CRC) is the second leading cause of cancer death in North America and Western Europe [1]. As populations live longer due to advances in medicine and public health, rates of CRC are likely to increase. The biology of CRC offers an opportunity for both early detection and prevention. Most cancers evolve from premalignant adenomas over a period of many years; spread of malignancy from the colon to sites outside the colon likewise occurs over years. Screening of asymptomatic populations has demonstrated that cancers can be detected at early, more curable stages, compared to unscreened controls. Furthermore, studies have demonstrated that detection and removal of premalignant adenomas can prevent incident cancers [2,3]. Therefore, if screening tests could identify patients with high-risk adenomas, many cancers could be prevented, mortality reduced, and the burden of caring for patients with cancer diminished. If the target of screening is the advanced adenoma, we should ask: how effectively do screening tests identify patients with advanced adenomas?

Higher risk subjects

There is consensus that colonoscopy should be the preferred screening test for individuals known to have higher than average risk [4]. Higher risk categories include individuals with familial hereditary syndromes (familial polyposis, hereditary nonpolyposis colorectal cancer syndrome), chronic colitis due to ulcerative colitis or Crohn’s disease, and a family history of colorectal cancer in a first degree relative. Patients with a personal history of adenoma or cancer should receive colonoscopic surveillance, and are not considered part of a screening cohort.

Average-risk subjects

Recent studies [5,6] have raised questions about whether colonoscopy should also be a preferred screening test in average-risk individuals. The performance characteristics of several screening modalities in average-risk populations have been scrutinized by the United States Preventive Services Task Force (USPSTF) and by expert multidisciplinary panels [4,7–10]. All of the expert panels strongly recommend that population screening should begin for average-risk individuals at age 50 years. They have noted that colonoscopy is more effective than other screening tests for polyp detection. Although some experts have argued that colonoscopy itself should be the preferred screening test [8], others have argued that it should be one of several screening options [4,7,9].

This chapter will review the rationale for considering colonoscopy as a primary screening test in average-risk populations and discuss implementation issues including compliance, resources, and cost.

Rationale for screening

Screening with colonoscopy should be considered in the context of other screening tests. For each test we should ask:

- What is the likelihood that the test will detect the target lesion (advanced adenoma or early cancer)?
- Are there programmatic issues, such as need for repeat testing, which impact
effectiveness?

- What are the potential harms?

**Fecal occult blood test (FOBT) ▲ ▲**

Three randomized, controlled trials have compared population screening with FOBT to no screening \[11–13\]. Although there were differences in study methods, the findings are consistent across all of the studies. Cancers are detected at earlier stages in screened compared to unscreened subjects, and this translates into significant mortality reduction of 15–33% over time \[11–13\]. Rehydration of FOBT slides increases sensitivity, but reduces specificity, so that many more patients will receive colonoscopy for false positive results over time. In the Minnesota study \[11\], 38% of subjects in the FOBT arm received colonoscopy during the first 13 years of the study. One analysis has suggested that some of the benefit of the FOBT test could be explained by random assignment to screening colonoscopy \[14\].

In the Veterans Affairs (VA) Cooperative Study \[15\], average-risk subjects \( n = 2885 \) had both one-time rehydrated FOBT and screening colonoscopy. FOBT was positive in 50% of patients with cancer, consistent with other studies \[16,17\]. However, among patients with advanced neoplasia without invasive cancer (defined as adenoma with high-grade dysplasia or villous histology, or tubular adenoma \( \geq 1 \) cm), the FOBT was positive in only 21.6%. Moreover, it is likely that if rehydration had not been used, the positive rate would have been lower. These results suggest that one-time FOBT has serious limitations for detection of high-risk adenomas. If FOBT is to be used for screening, a program of repeat screening must be developed. Compliance with repeat screening is poor. There is some concern that patients may be falsely reassured after a negative test, and not return for repeat testing \[7\]. If the FOBT is positive, there is consensus that patients should undergo complete colonoscopy. This represents a second step in which compliance can break down.

These studies support the hypothesis that population screening of average-risk subjects could reduce CRC mortality. FOBT is a poor test for detection of advanced adenomas. Although there is some evidence \[3\] that screening with FOBT can lead to reduction in cancer incidence (due to polyp detection and removal), this incidence reduction is modest. The need for frequent repeat testing, and appropriate follow-up of positive tests with colonoscopy, represent important program limitations.

**Flexible sigmoidoscopy ▲ ▲**

There is evidence from two case control studies \[18,19\] that exposure to sigmoidoscopy is associated with a reduction in colon cancer mortality, in that portion of the colon examined. In these studies, patients with death due to CRC were ascertained, and an age-matched control group without CRC was used for comparison. Selby et al. \[18\] compared 261 patients with fatal rectosigmoid cancers (within reach of the sigmoidoscope) to 868 age and sex matched controls: 8.8% of cases had sigmoidoscopy compared to 24.2% of controls, suggesting that endoscopic sigmoid screening could reduce the risk of fatal cancers within the range of the sigmoidoscope (odds ratio 0.41). Moreover, the benefit remained strong even when the most recent exam was 9–10 years earlier. Newcomb et al. \[19\] had similar results.

Both studies did not find that sigmoidoscopy reduced the likelihood of fatal cancers of the right colon, perhaps because such tumors would not be readily detected with sigmoidoscopy. Muller and Sonnenberg \[20\] reported another case control study in a VA population to determine the impact of either sigmoidoscopy or colonoscopy on CRC risk. Compared to controls, patients with CRC were less likely to have had prior endoscopic exams of the colon (odds ratio 0.51 for colon cancer; 0.55 for rectal cancer). Two ongoing, randomized trials using flexible sigmoidoscopy will report findings in the next
few years [21,22].

Limitations of screening by flexible sigmoidoscopy

These case control data provide compelling evidence that screening sigmoidoscopy could substantially reduce CRC mortality, particularly from tumors in the distal colon. An important limitation is that a large portion of the colon is not examined at sigmoidoscopy. If most patients with advanced neoplasia in the proximal colon, had index adenomas in the distal colon, which would lead to complete colonoscopy, then sigmoidoscopy would be a sensitive screening test.

Two screening colonoscopy studies reported the findings of complete colonoscopy, and estimated the potential findings of screening sigmoidoscopy in average-risk subjects [5,6]. Advanced neoplasia was more likely to be found in the distal colon (55% in Indiana study; 53% in the VA study). Both studies found that more than 50% of patients with advanced proximal neoplasia (beyond the reach of the sigmoidoscope) would not have been identified with sigmoidoscopy, even assuming that any index adenoma would lead to colonoscopy. In addition, both studies found that as average-risk subjects get older, they are more likely to harbour advanced proximal neoplasia, and that these are less likely to be identified with sigmoidoscopy alone.

Sigmoidoscopy is able to detect advanced adenomas and early cancers in the area examined. The key limitation of sigmoidoscopy is that a large portion of the colon is not examined; some patients with advanced proximal neoplasia would go undetected. There is also concern that with increasing age, sigmoidoscopy may be less effective.

Combined flexible sigmoidoscopy and FOBT

The American Cancer Society has long recommended screening with both FOBT and FS beginning at age 50 [9], among other options. Intuitively, this combined approach should have a greater impact on CRC mortality than either test alone. In one study [23], patients were offered sigmoidoscopy with or without FOBT. Although the patients were not randomly assigned to groups, the groups were comparable. Follow-up was irregular and compliance with follow-up testing poor. During the 9-year follow-up, 144 cases of CRC were found, but only 28 were actually detected through screening. The major finding was that patients screened with both FOBT and sigmoidoscopy had better long-term survival after detection of cancer compared with controls suggesting a benefit from evaluation of positive screening tests. The overall mortality rate of the two groups was similar.

In the VA Cooperative Study [15], combined screening with one-time FOBT and sigmoidoscopy would have identified 76% of patients with advanced neoplasia, only slightly better than sigmoidoscopy alone (70%). With increasing age, there was a trend for decreasing efficacy of the combined screening approach. Modelling [24–26] has suggested that the combined approach could be more effective and less costly than other screening approaches, if tests are performed programmatically, on a regular basis as is recommended (annual FOBT and sigmoidoscopy every 5 years). However, the models require assumptions about compliance with initial testing and follow-up colonoscopy after positive tests, which may not be realistic in clinical practice.

Radiographic colon imaging with barium, CT, or MRI

No large studies have evaluated colon imaging with barium in an average-risk population. The USPSTF rates barium as ‘unknown’ with regard to effectiveness in reducing incidence and mortality from CRC, and only ‘fair’ with regard to ability to detect cancer and advanced neoplasia. The National Polyp Study
found that the sensitivity of barium studies for detection of polyps larger than 1 cm was 48% [27].

The data on CT or MRI imaging of the colon are preliminary, and the technology is still evolving. The range of sensitivity for large polyps is 40–96%, suggesting wide variation in either skill or technique. Currently, no review panel has recommended screening with these modalities, although they have captured the attention of the public.

The potential for genetic testing ▲▼

There are other screening modalities which show promise. When specific gene mutations were identified in patients with familial polyposis (adenomatous polyposis coli gene on chromosome 5) and hereditary nonpolyposis colorectal cancer syndrome (mismatch repair gene mutations), there was great hope that molecular genetics would provide a simple blood test to risk-stratify otherwise average-risk subjects. Such screening was touted to the public in the New York Times in the 1990s.

The reality of genetic testing to date has been sobering, but there has been recent progress. Several groups have identified genetic mutations in stool samples. If tumors slough cells with genetic mutations into the bowel lumen, and if these mutations can be identified, it may be possible to select individuals for colonoscopy based on the stool profile. This ‘needle in a haystack’ approach is complicated by the fact that there is no single mutation which identifies all high-risk patient.

New tests which search for several of the most common genetic alterations associated with CRC are under study [28]. With the development of the human genome project, has come the science of proteomics—and understanding of the relationship of a gene mutation to specific protein product. If altered protein products are circulating in the blood, it may be possible to screen patients with blood tests.

The case for screening with colonoscopy ▲▼

Colonoscopy can examine the entire colon in more than 90–95% of procedures, if performed by a fully trained endoscopist. Polypectomy can be performed at the same time. Given these obvious advantages, we should ask: why not perform screening colonoscopy?

Arguments against screening with colonoscopy ▲▼

General criteria for screening tests applied to the population are summarized in Fig. 1.

Colonoscopy is an invasive and expensive test. The risk of perforation, serious bleeding, and cardiopulmonary events is low when performed by experienced endoscopists (0.3–0.5%), but if applied to the general population, could account for considerable morbidity [29]. If only 5–6% of the adult population will develop colorectal cancer during life, most patients will not benefit from colonoscopy. Ideal screening would target colonoscopy at the patients most likely to have advanced neoplasia or cancer, and would not employ an expensive, invasive test to populations with a relatively low pretest probability of disease. However, the ideal simple test has been elusive. Lacking the perfectly sensitive, and adequately specific non-invasive screening test, screening with colonoscopy is now recommended as a screening option by all expert panels in the United States, though not in Canada, Europe, or Australia.
Arguments for screening with colonoscopy

Relative to other screening tests, there is substantial evidence that colonoscopy is very accurate for detection of significant neoplasia. In two tandem colonoscopy studies, in which patients had two colonoscopies performed. During the same session, the miss rate for polyps greater than 1 cm was less than 10% [30,31]. Since these studies were performed by experts, it is possible that in clinical practice, more lesions are missed by less expert endoscopists. Specificity for detection of neoplasia approaches 100%, because biopsies are usually obtained which confirm the histologic presence of neoplasia.

Does screening colonoscopy reduce mortality?

The ability to prevent incident cancers or reduce mortality with primary screening colonoscopy has never been tested in a clinical trial. However, there are several lines of indirect evidence which endorse the potential effectiveness of colonoscopy.

First, the FOBT trials all recommended colonoscopy as the followup test after a positive FOBT. It was colonoscopy which identified the early cancers that led to a survival advantage in screened populations. Ransohoff and Lang [14] performed a posthoc analysis of the Minnesota FOBT study, in which 38% of subjects in the screened group received colonoscopy over 13 years of study. They attributed much of the mortality reduction to high rates of colonoscopy, with only a portion of benefit derived from performance of the FOBT. In the follow-up of the Minnesota study, the subsequent incidence of CRC was reduced in patients who had been screened—a benefit attributed to colonoscopy with polypectomy by the authors [3].

The second line of evidence is extrapolated from the case-control studies of sigmoidoscopy. These studies found a significant reduction in fatal colon cancers in that portion of the colon examined. There was no reduction in mortality from proximal colon cancers [18]. It is logical to assume that if more colon is examined, the benefit could be extended to as much of the colon as can be examined. The third line of evidence comes from the National Polyp Study [2], in which patients underwent complete colonoscopy with polypectomy and were followed over the next 5 years. When compared to reference populations, the incident rates of CRC were reduced by 76–90% in the study subjects. Although the comparison groups differed from the study subjects, the marked reduction in expected incidence is compelling. Finally, a case-control study in the VA population found that patients diagnosed with CRC were less likely to have had prior colonoscopy, compared to patients without CRC [20]. The risk reduction of 53% for colon cancer, and 39% for rectal cancer was significant. These studies provide compelling indirect evidence that screening colonoscopy could be effective; i.e. reduce colon cancer mortality and incidence.

Several investigators have modelled colon cancer screening, and evaluated a broad range of assumptions regarding accuracy, compliance, and harms. The conclusion of the most recent analyses is that colon cancer incidence could be reduced by 58–86%, and that CRC mortality could be reduced by 64–90% [32].

Patient acceptance of colonoscopy screening

Patient acceptance of colonoscopy as a screening test is unknown. Colonoscopy is well-accepted when recommended for evaluation of other positive screening tests and other gastrointestinal symptoms. In the VA Cooperative Study, nearly two-thirds of eligible subjects who were offered colonoscopy, completed the examination. The VA population may not be generalizable, but this study does demonstrate that good compliance can be obtained when procedures are fully explained. Acceptance of
sigmoidoscopy is estimated to be 25–50% [33]. Although acceptance of one-time FOBT may exceed 75%, compliance with repeat FOBT testing is poor. A colonoscopy screening program may require only one or two exams in a lifetime—a factor which may enhance program performance compared to other programs requiring frequent repeat testing and colonoscopic follow-up of positive screening tests.

**Potential harm from colonoscopy**

The largest study to report complications of colonoscopy is the VA Cooperative Study # 380 [29]. Serious complications, definitely attributed to colonoscopy, occurred in 0.3% of patients receiving screening colonoscopy. The most common serious complications were serious bleeding and myocardial infarction or serious arrhythmia. Most of the serious complications occurred in association with polypectomy. The serious complication rate of a diagnostic colonoscopy was 0.1%. Less serious complications were common—including vasovagal events (5.4%), transient oxygen desaturation (4.4%), abdominal pain requiring termination of the procedure (0.9%), and minor GI bleeding which did not require hospitalization or intervention (0.2%). Since these procedures were performed by experts, it is not known if complications would be more common in community practice. Studies are currently underway to measure 30 day complication rates in diverse clinical practice settings.

**Resources for screening colonoscopy**

The algorithm of every CRC screening program eventually leads to colonoscopy to evaluate positive tests. Public and provider awareness of the benefits of colon screening has increased over the past few years.

A Gallup poll in 1998, indicated that nearly 90% of the public was aware of potential benefits of colon screening. In March, 2000, a prominent television personality, had a screening colonoscopy performed on her program, with the goal of diminishing public fear of the test. An aggressive public education campaign followed the program. Despite this increased public awareness, compliance with screening has been poor—only 30–40% of the age-eligible population have had the recommended screening. However, there are indications that this may improve over the next few years.

In 1998, the Department of Health and Human Services added colon screening with FOBT or sigmoidoscopy as a Medicare benefit for average-risk individuals, and colonoscopy for individuals with a positive family history.

In July, 2001, the federal government extended the benefit to include colonoscopy screening for all. Health care systems such as the Department of Veterans Affairs have initiated annual reminders to primary providers to encourage fecal occult blood testing. Health maintenance organizations like Kaiser have enrolled all age-eligible patients into flexible sigmoidoscopy screening programs. The National Cancer Institute and the Centers for Disease Control are dedicating resources to study strategies which will improve compliance.

By 2000, most GI practices in the United States were confronted with increased demand for colonoscopy services. During this same time period of the late 1990s, there was a decline in the number of GI fellowship positions in the United States. The shifting demand for colonoscopy and the decline in newly trained endoscopists, has raised concerns about whether there are sufficient resources to provide colonoscopy screening to the general population.

Rex and Lieberman [34] examined some of the assumptions which underlie the demand for services. They assumed that some patients would have comorbid conditions which would preclude screening,
some would have examinations to evaluate symptoms, and a large number would be non-compliant. In a ‘best-case’ scenario, 60% of the population would be compliant with screening. Therefore, rather than a stampede to screening colonoscopy, the demand may more closely resemble a traffic jam. If traffic patterns are understood, most traffic jams have engineering solutions. To offer colonoscopy services with existing resources, Rex and Lieberman have several recommendations:

1. **Improve the efficiency of delivering colonoscopy.** Most endoscopy units are not efficient with regard to room scheduling and turnover. Endoscopists could develop open access systems for screening of otherwise healthy individuals, and use physician extenders to obtain consent and perform initial history and physical examinations. Support personnel could handle much of the postprocedure follow-up with patients who do not have complex pathology.

2. **Shift current colonoscopy resources:** 20–25% of colonoscopy procedures in the United States are performed for surveillance of prior adenomas (Lieberman, unpublished data from the Clinical Outcomes Research Initiative [CORI] database). Based on the VA Cooperative Study [5], more than 70% of patients found to have adenomas at screening will have only small (<1 cm) tubular adenomas. The Indiana colonoscopy study found that 65% of patients with neoplasia had only small tubular adenomas [6]. Data from the National Polyp Study [35] suggest that these patients may have a low risk of serious pathology at surveillance examinations. Extending the interval for surveillance of patients with low risk lesions could shift considerable resources towards screening. Rex [36] estimated that screening will have a greater yield than surveillance (64 colonoscopies to detect one cancer for screening average-risk male, vs. 317 colonoscopies to detect one cancer in postpolypectomy surveillance). If specialists in gastroenterology spend more time performing colonoscopy, and less with flexible sigmoidoscopy, this will allow some resource shifting. This trend is currently observed in the CORI database which shows a significant decline in sigmoidoscopy as a fraction of endoscopic practice by GI specialists (Lieberman, unpublished data).

In summary, existing resources can be provided more efficiently and selectively to increase the capacity for screening colonoscopy (or colonoscopy to evaluate other positive screening tests).

**Costs of screening for colon cancer**

Several recent analyses of colon screening costs have reached similar conclusions: screening with any of the recommended tests is cost-effective relative to other medical interventions, and could even be cost-saving if large numbers of cancers can be prevented [24–26,37–41]. The analyses show that various screening tests are quite similar in programmatic costs over life—roughly $20 000 per life-year saved. The analysis of these studies by the United States Preventive Services Task Force stated that the current evidence is insufficient to determine the most effective or cost-effective strategy for screening [32].

Important assumptions in these analyses include the rate of cancer prevention, and the cost of cancer care. The cost of care for patients with CRC in the United States probably exceeds $50 000 [42]. This cost includes diagnostic studies, cancer surgery, chemotherapy or radiation therapy, postcancer surveillance, and end-of-life care if detection is late. As the cost of cancer care increases, averting this cost by detection and removal of advanced adenomas will probably result in cost-saving. In each model, colonoscopy results in the greatest potential for cancer prevention because of the highly accurate detection and removal of adenomas.

If cost differences between the screening tests are small, why are many insurers reluctant to include colonoscopy screening as a benefit to their clients? From the standpoint of the insurer, screening is a
large investment, with potential downstream benefit. If cancers are averted, then the cost of cancer care can be reduced—but this benefit may not be realized for many years. If individuals change insurance coverage frequently, the insurer may not wish to make a large ‘up-front’ investment for a downstream benefit that may occur after the individual is no longer covered by the insurer. Among the screening test options, colonoscopy would represent the largest up-front investment. If we approach the screening from a societal point of view (a lifetime, single-payer system), an effective cancer prevention program would be a worthwhile investment.

**Screening colonoscopy: areas of uncertainty**

Colonoscopy screening has not been studied in a clinical trial. Therefore, the balance of benefits and harms remains uncertain. Although there is little doubt that colonoscopy is beneficial in the evaluation of other positive screening tests (FOBT, sigmoidoscopy, imaging), it is uncertain if whole population colonoscopy screening would necessarily confer the degree of benefit that would justify the risk and resource utilization. For colonoscopy to be effective, the examinations will need to be accurate and complete, and performed with minimal risk. The overall success rate and risk of colonoscopy in community practice is unknown, and requires study. Future advances in colonoscopy technology may improve success rates and reduce risk.

**Reducing overall mortality?**

The ‘holy grail’ of screening is mortality reduction. Some may argue that if all-cause mortality is not reduced by colon cancer screening, then the benefit may not offset harm. For example, let us assume that a hypothetical individual would have died from consequences of CRC at age 80. If his colon cancer is prevented by screening, but he has a myocardial infarction and dies at age 80, is there a benefit? Although society is spared the cost of caring for a patient with cancer, would the resources spent for screening, have been better spent on some other form of health care? These are difficult questions to answer in clinical trials. The modelling analyses are helpful because they account for all causes of death, and consistently show that there is a benefit from screening. A clinical trial to resolve this issue would require 10–20 years, large numbers of patients, and an enormous budget. As in other areas of medicine, we may lack precise information for medical decision making. As new information becomes available from the VA Study follow-up and the CONCeRN trial in women, this can be incorporated into the models, and reduce areas of uncertainty.

**Timing of colonoscopy screening**

The appropriate timing for screening colonoscopy is uncertain, and has implications for cost, resource utilization, and benefit. Imperiale *et al.* [44] found that detection of serious pathology is uncommon in asymptomatic persons age 40–49 years, who had screening colonoscopy. Ness *et al.* [39] found that screening colonoscopy at age 50–54 years would be cost-effective, in comparison to no screening. The VA Cooperative Study data showed that the prevalence of any advanced pathology in men, age 50–59, was 5.7%, and few had cancer. Only 2% had advanced proximal neoplasia, and most of these patients would have been detected with sigmoidoscopy [5]. In contrast, 4.9% of patients age 60–69 years, and 5.9% of patients age 70–74 years had advanced proximal neoplasia. Less than one half of these patients would have been detected with sigmoidoscopy. Therefore, a strategy of screening sigmoidoscopy during the 6th decade, followed by complete colonoscopy at age 60 years might be a cost-effective screening strategy in men.
When to repeat screening? ▲▼

Expert groups have recommended that colonoscopy screening be performed at 10-year intervals, based largely on the expected natural history of progression of colonic neoplasia. There has not been a study evaluating a 10-year interval. Rex et al. [45] performed follow-up colonoscopy at 5.5 years in 154 average-risk persons who had a negative baseline colonoscopy—only one patient had an adenoma greater than 1 cm. These data suggest that a 6-years interval is quite safe. Would a negative screening colonoscopy at age 60 years identify a low-risk person who does not need further screening? These data are crucial to decision-making about when to stop screening. The VA Cooperative Study will follow its population for 10 years, which will provide some prognostic information in men who have had a baseline screening colonoscopy. For now, there is some uncertainty about the appropriate screening interval.

Will screening colonoscopy be superseded? ▲▼

Will screening colonoscopy be replaced by new methods of screening? This is an important question because of resource utilization. If society determines that screening colonoscopy should be offered to everyone, significant resources will need to be dedicated to provide endoscopy services, and train endoscopists. If colonoscopy is subsequently replaced, then there will be issues of excess capacity, and wasted resources. The ideal screening test of the future will target colonoscopy precisely at those patients most likely to develop cancer. If a genetic or biologic marker could successfully risk-stratify patients, colonoscopy may only need to be offered to 10–20% of the population who develop high-risk lesions. For patients with sporadic colorectal cancer, this ideal test remains in the distant future. In the best case scenario, once a marker was identified, years of testing would likely precede widespread acceptance. Imaging studies are not likely to provide precise targeting because they will identify patients with advanced and nonadvanced lesions. Unless clinicians are willing to ignore small polyps found on imaging studies, these tests are not likely to reduce the need for colonoscopy services. Therefore, for the next generation, colonoscopy will be the most accurate test for assessing risk and enhancing prevention.

=top Conclusion ▲▼

Colorectal cancer screening in average-risk populations with colonoscopy could have a significant impact on colorectal cancer incidence and mortality [32]. Advantages over other forms of screening include the ability to examine the entire colon, and remove pathology during the exam. Uncertainties exist about the application of the procedure in practice—would completion rates and complication rates be similar to those reported from clinical trials? Further study is needed in community practice. Would one or two exams during a lifetime be sufficient if they are negative? Are there sufficient resources to provide colonoscopy to large populations? Despite these questions, there is little doubt that colonoscopy screening would have a large impact on colorectal cancer incidence and mortality. Until selective screening can be targeted at those individuals most likely to develop colorectal cancer, colonoscopy screening may offer the most effective means to reduce mortality.

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