Colon Cancer Screening in 2005: Status and Challenges

DAVID F. RANSOHOFF
Departments of Medicine and Epidemiology, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina

The field of colon cancer screening has evolved dramatically in the last 15 years regarding evidence, guidelines, and practice. In 1990, no evidence from a randomized controlled clinical trial (RCT) existed to show that colorectal cancer (CRC) screening was effective in reducing CRC mortality. In 1990, although some guidelines endorsed screening, there was disagreement among recommending organizations about which tests to recommend or whether to recommend any screening tests at all. The US Preventive Services Task Force (USPSTF), arguably the most influential of the recommending organizations and the most rigorously evidence based, said that evidence was insufficient to recommend either for or against CRC screening.1 In this environment, CRC screening was not widely practiced, much less reimbursed by payers. If screening was performed at all, fecal occult blood testing (FOBT) was the most common test. Sigmoidoscopy was performed less frequently, and colonoscopy, rarely performed for screening, was used mainly for workup of a positive FOBT or sigmoidoscopy and for postpolypectomy surveillance. The primary questions facing academics, recommending organizations, and practicing clinicians in 1990 were (1) does CRC screening—of any kind—work to reduce CRC mortality, and (2) should it be implemented and reimbursed?

In 2005, the situation is dramatically different. We now know that CRC screening works, and it is now being implemented and reimbursed. Colonoscopy has become popular as a primary screening test, and new tests, such as virtual colonoscopy, are being developed. The purpose of this article is to identify current challenges in light of the evolution of evidence, guidelines, and practice and to anticipate the next phase of development and implementation.

Screening Average-Risk Persons: 1990–2005

1990–2000: Evidence and Guidelines Evolve to Support Colorectal Cancer Screening

In 1990, no strong evidence existed from an RCT showing that screening reduces CRC mortality. Some recommending organizations had supported it, but screening was not reimbursed or widely practiced. However, after 3 RCTs in the mid 1990s provided evidence of efficacy, a broad consensus developed among recommending organizations about performing screening and about which testing programs to recommend.2–4 Particularly important were the USPSTF's decision in 1996 to endorse screening2 and Medicare's decision in 2001 to reimburse for it.

Evidence about sigmoidoscopy. The first strong evidence that screening reduces CRC mortality came not from an RCT but from an unusually well done case-control study about sigmoidoscopy. Published in the New England Journal of Medicine in 1992, this study showed that CRC mortality was reduced by approximately 60% for lesions within reach of the instrument among persons who had had screening sigmoidoscopy.5 Although case-control studies are generally regarded as providing weak evidence about efficacy because bias is so hard to account for compared with RCTs, this study used an unusual kind of “control group”6 that, along with results from another study,7 provided the rationale for the USPSTF to modify its recommendations in 1996 to include sigmoidoscopy.2

Evidence about fecal occult blood testing. In 1993 and 1996, 3 landmark RCTs provided evidence that FOBT screening reduces CRC mortality. Mortality reduction was 33% among subjects who had every-year rehydrated FOBT in the US trial8 and was approximately 15% in 2 European studies for every-other-year nonrehydrated FOBT.9,10

Evidence about colonoscopy. Although by 1996 no study had assessed the efficacy of colonoscopy screening in reducing CRC mortality (and none has now), support for colonoscopy evolved on the basis of evidence from studies about FOBT and sigmoidoscopy. One line of reasoning is that, because colonoscopy is the means by
which FOBT or sigmoidoscopy screening reduces mortality (because colonoscopy is performed to work up a positive primary screening test), then colonoscopy is the mechanism by which CRC mortality is reduced and should plausibly be effective as a primary screening test. A second line of reasoning is that if endoscopic screening works in the sigmoid colon, it should also work for the rest of the colon; this argument might be incorrect if the right colon behaves differently, biologically, compared with the left. Overall these arguments have been taken to indicate that colonoscopy works. Further consideration must be given to how well it works in comparison to other tests and programs, as will be discussed below.

Guidelines. Guidelines followed evidence. In 1990, some guidelines had recommended screening, although, as noted, the USPSTF did not. In 1992, the US Congress decided not to reimburse for CRC screening for Medicare patients, declining to follow recommendations based on the cost-effectiveness analysis that Congress had commissioned from the Office of Technology Assessment. That analysis concluded, on the basis of available evidence before RCTs, that CRC screening was cost-effective compared with other medical and screening practices. However, lacking both RCT evidence and popular support for what would be a costly (even if cost-effective) program, Congress declined to support screening. By 1996, however, evidence from 3 RCTs and the case-control study dramatically changed guidelines when the USPSTF decided to endorse CRC screening. That evolution of evidence and recommendations set the stage for the events of the year 2000, when CRC screening became popular.

2000: Colorectal Cancer Screening Becomes Popular and Reimbursed

By 2000, evidence about efficacy was already several years old, as was the 1996 USPSTF endorsement. However, screening was not widely practiced, and importantly—Medicare had not decided to fully reimburse it. The events of 2000 changed the situation and provided lessons about how public policy gets made.

March 2000 became the nation’s first colon cancer awareness month when Katie Couric, host of NBC’s Today Show, promoted CRC screening after her husband’s death from CRC. Couric was featured in a cover story in Time Magazine and produced a 5-part series on the Today Show, including a broadcast of her own screening colonoscopy. These events affected practice in the United States.

In July 2000, two reports in the New England Journal of Medicine—and their interpretation in an accompanying editorial and the media—dramatically affected the popularity and practice of CRC screening, particularly colonoscopy. The studies were the first reports of the yield of screening colonoscopy in an asymptomatic average-risk population. Before this time, information about the prevalence of colonic neoplasms (ie, cancer and adenomas) had come from autopsy studies. Although knowing the prevalence, or yield, of screening for such lesions is related only indirectly to the outcome of CRC mortality reduction, such lesions may be considered strong surrogate outcomes because of other evidence about CRC, for example, from the RCTs of FOBT. One goal of the studies was to compare sigmoidoscopy with colonoscopy by assessing how many lesions would be missed by sigmoidoscopy. Because the expected prevalence of CRC, the most important outcome, would be too low to provide a useful comparison even in groups involving several thousand subjects, the studies also assessed (as had some previous studies) a lesion that would be more common: advanced adenomas generally defined as a tubular adenoma ≥1 cm, with villous histology, or with advanced histology. They were included as outcomes not because their natural history is known to be ominous (ie, how often and how rapidly they become incurable cancer); their natural history is unknown. Rather, they were included as possibly useful surrogates that would provide a bigger sample size for research studies to measure. Advanced adenomas have taken on a kind of life of their own in terms of becoming important targets for CRC screening.

The studies found, as was widely expected, that sigmoidoscopy, which examines approximately half of the colon, misses roughly half of the lesions in the colon. Sigmoidoscopy detects a few right-sided lesions indirectly when it discovers a lesion in the left colon considered to be a sentinel lesion that provokes a full colonoscopy. The number of right-sided lesions detected in this manner depends on what is considered a sentinel lesion, whether it is a large or advanced adenoma, an adenoma of any size, or a hyperplastic polyyp. Because small adenomas and hyperplastic polyps are so common, the decision about what is a sentinel lesion has substantial implications for workup at sigmoidoscopy screening. The 2 New England Journal of Medicine studies found that many right-sided CRCs and advanced adenomas were not accompanied by sentinel lesions and would be missed by sigmoidoscopy.

This finding was not a surprise to clinicians or policy makers in the field. Sigmoidoscopy had been recommended by the USPSTF in 1996 and by other recommending organizations despite this deficiency, and it was to be recommended again in 2002, after these articles. However, in 2000, the finding was considered important.
“news” when an accompanying editorial, entitled “Going the distance—the case for true colorectal-cancer screening,”20 said that performing sigmoidoscopy screening was like performing mammography screening of only one breast—ie, unsatisfactory. A report on the front page of the New York Times said that “The test most commonly recommended to screen healthy adults for colorectal cancer misses too many precancerous growths and should be replaced by a more extensive procedure that examines the entire colon, doctors are reporting today.”21 The news article went on to say that sigmoidoscopy had “been used for screening on the optimistic theory that if no abnormalities were seen in the lower colon, none were likely to be found higher up.”21

The problem with the news report, based on the editorial, was that recommending organizations had not relied on an optimistic theory that right-sided lesions would be found. To recommend sigmoidoscopy, guidelines organizations had used other considerations, such as effectiveness, cost-effectiveness, and availability, whereas the editorial considered mainly the thoroughness of a test at one examination. Although colonoscopy may be the best test at any one application, that does not necessarily translate to the best test in a program of repeated applications of tests over time, as will be discussed below.

These more complicated considerations22 were lost in the attention given to the thoroughness of the examination and what was missed. The interpretation of these 2 studies, along with other events in 2000, had a dramatic effect on CRC screening in general and on colonoscopy in particular. By the end of 2000, Medicare had decided to reimburse for colonoscopy screening, and colonoscopy as the best primary screening test began to be discussed and to be advocated by some gastroenterology organizations.


Since 2000, evidence and guidelines have not substantially evolved regarding tests recommended as options for average-risk persons, but practice has evolved. Medicare’s decision to reimburse for screening colonoscopy has had a ripple effect among other payers. Now that guidelines are generally supportive and make little preference among available tests, the field has moved into a kind of “postguideline” environment that involves other forces beyond guidelines, as will be discussed below.

Evidence. Evidence about screening efficacy has not evolved substantially since 2000. Two important RCTs about sigmoidoscopy screening, initiated in the 1990s, will provide results about CRC incidence and mortality.18,23 These studies are expected to provide critical data that will likely have implications also for colonoscopy. Because such RCTs are so costly and time consuming, even for a cancer as common as CRC, these may well be the last RCTs to include CRC incidence and mortality as an outcome.

Guidelines. Guidelines since 2000 have also been basically stable regarding average-risk persons. Any of several CRC screening programs is recommended, including FOBT alone, sigmoidoscopy alone, a combination of FOBT and sigmoidoscopy, and colonoscopy.24,25 With several choices recommended and none preferred (with one exception, as discussed below), other events and forces in the postguideline environment are becoming important. The current broad consensus has been achieved in part because of a deliberate effort on the part of major guidelines organizations to coordinate recommendations. Guidelines have discussed but not made recommendations about newer technologies such as virtual colonoscopy or stool DNA testing, in part because of the need to accumulate sufficient evidence and because of the time lag after publication of evidence; such new modalities will likely be considered in detail over time.

Practice. Practice has evolved, although details of how it is evolving are not clear. Gastroenterologists now report, at least anecdotally, performing many more colonoscopies than before. Some spend up to 50% or even 80% of their practice time simply performing colonoscopy; this is a dramatic increase from 5 years ago. In the United States, there is no ongoing systematic approach to describe practice patterns over time, although useful snapshots are available.26–30

Lessons From Evolution

One lesson from this evolution is that implementation of CRC screening has required not only evidence, but also strong popular support. On the one hand, this should not be unexpected. Widespread implementation of breast cancer screening was achieved long after evidence was available from RCTs, boosted by endorsement of public figures such as Happy Rockefeller and Betty Ford. Prostate cancer screening has become widely practiced on the basis of popular support, along with some guidelines organizations’ endorsement, even without evidence from an RCT of mortality reduction. Public perception and support, a necessary ingredient for any degree of implementation, may also take on a kind of life of its own, as discussed below. Such issues need to be considered in anticipating and planning for the future.
Screening: Challenges in 2005
Implementation of Any Kind of Colorectal Cancer Screening

Achieving implementation of any kind of CRC screening is a major challenge in 2005. The reasons that screening rates are low compared with those for breast cancer or cervical cancer screening are critical to understand and address, and they are receiving detailed attention from the research and policy communities; they are not discussed further here.\textsuperscript{28,31–38} It seems likely that the current low rates will improve over time,\textsuperscript{27} building in part on lessons learned from implementation of mammography screening.

Role of Fecal Occult Blood Testing

FOBT and sigmoidoscopy, historically the primary screening tests, are still recommended as mainstream tests and may improve individually or in combinations that may make them more attractive, as discussed below. FOBT, specifically Hemoccult II (Beckman Coulter, Inc, Fullerton, CA), has been the most widely used test in practice and has potential for future improvement. Use of a program of FOBT screening (in which screening is performed yearly or every other year) may result in a cumulative sensitivity of the program that is competitive with a program of a more sensitive test (such as colonoscopy) performed less frequently. Specifically, a combined program of FOBT plus sigmoidoscopy may be as effective as or more effective than a program of colonoscopy screening every 10 years, as discussed below. For this reason, and because improved FOBT tests such as that based on immunohybrid of human hemoglobin may be more sensitive than the widely used Hemoccult II based on the peroxidase-like activity of hemoglobin, FOBT screening should not be excluded from consideration by physicians, patients, and policy makers.

One important problem is that proper testing with FOBT using Hemoccult II involves examining 3 different bowel movements. Physicians in practice often use a 1-card (in-office) test,\textsuperscript{30} perhaps in part because of the difficulty of arranging office logistics and systems to keep track of home-based collection. The single-card approach is considered inadequate because of low sensitivity and specificity.\textsuperscript{39} Furthermore, positive results often are not worked up by a whole-colon examination, as recommended.\textsuperscript{40} Part of the problem may be that FOBT screening involves a system that is complicated (and is not reimbursed) and that, if not fully implemented, can cause substantially reduced effectiveness of screening compared with that obtained in clinical trials.

Role of Sigmoidoscopy

Sigmoidoscopy, the other historical or traditional test, is supported by all recommending organizations as an acceptable option and may be particularly effective when combined with FOBT, as noted previously. One practical problem in implementation is that many primary care physicians, who have traditionally performed the test in screening, have never received the hands-on supervised training required to gain proficiency.\textsuperscript{41} From a practical standpoint, the procedure may be reimbursed at a rate that is too low to justify the required equipment, staff time, and dedicated space.\textsuperscript{32,43} Although sigmoidoscopy screening is not particularly popular in the United States,\textsuperscript{28} the fact that it is being studied in the United Kingdom as a possible once-in-a-lifetime test\textsuperscript{18} suggests that it should at least remain as a consideration.

Role of Colonoscopy

Before 2000, colonoscopy was seldom used as a primary screening test. Since 2000, colonoscopy has become a popular primary screening test, and questions are being discussed about whether there is sufficient capacity to satisfy demand\textsuperscript{44–47} and about whether colonoscopy should be considered the best test. Although a front-page story in the New York Times\textsuperscript{44} in 2003 described long waits for colonoscopy and suggested great demand, the long-term role of colonoscopy—and the demand for it—is in great flux, with major implications for how gastroenterologists practice medicine and for making plans about resources and training.\textsuperscript{48,49}

Is colonoscopy the best test? Guidelines are almost unanimous in saying, at least on paper, that colonoscopy is simply one of several options. Only the American College of Gastroenterology has used the phrase “preferred strategy,” and it qualified the recommendation by saying “whenever resources and appropriately trained experts are adequate to supply it and reimbursement is available.”\textsuperscript{50}

The USPSTF in 2002 published a detailed analysis of the question about whether colonoscopy is best. The results of this assessment may seem surprising but, with reflection, are readily understandable. The Task Force wrote, “Some groups believe that recent evidence showing the superior single-test accuracy of colonoscopy proves its broader superiority and have recommended it as the procedure of choice for screening. However, these analyses have not always considered differences in yield over time, complications, and real-world performance, which may not always favor colonoscopy.”\textsuperscript{51} In a detailed and revealing assessment of cost-effectiveness analyses
Comparing different tests and programs, the Task Force concluded, “The most effective strategy tended to be colonoscopy every 10 years or the combination of annual fecal occult blood testing and sigmoidoscopy every 5 years.” The report also said, “Whether one method of colorectal cancer screening is superior to other methods is not clear from these analyses. Many observers have interpreted recent studies documenting the relative greater single-test accuracy of colonoscopy compared with sigmoidoscopy, fecal occult blood testing, or double-contrast barium enema for detection of colorectal cancer or adenomas as proof that colonoscopy should be the screening method of choice for colorectal cancer. The five multiple-strategy analyses that we identified, however, did not uniformly find that colonoscopic screening was the most effective or cost-effective strategy.”

The conclusion that colonoscopy is not the best test is not based on the cost of colonoscopy or on some public health consideration. The Task Force concluded that colonoscopy was not necessarily the most effective at any cost. The explanation is in part the “assumptions each model makes about the biological behavior of colon cancer”: assumptions about the biology of how cancers develop and grow. Although colonoscopy may be the best test at any one application, such thoroughness does not make colonoscopy the most effective (ie, most sensitive) at reducing CRC mortality in a program of repeated testing over time. The biological reason is that, first, a less sensitive test such as FOBT applied repeatedly could have multiple chances to detect an existing lesion, thus leading to a very high program sensitivity. Second, a test applied frequently (eg, more frequently than the 10-year interval recommended for colonoscopy) could find new lesions that had not existed at the time of an earlier examination. If cancers most likely to be fatal are those that develop and grow rapidly, this second feature is a critical advantage of a more-frequently-applied test, because fast-growing cancers would be systematically missed by a test performed infrequently. Increasing the frequency of colonoscopy would incur an increased rate of complications, as discussed below. The Task Force’s analysis shows how comparisons must be made between programs of screening and not between individual tests.

### Complication rates of repeated colonoscopy.

Although the risk of complications from any one colonoscopy may be very small, the cumulative risk from repeated colonoscopies performed over time may become quantitatively important. Cumulative risk can be roughly estimated in the following way. A large study in the United States that carefully checked for postcolonoscopy complications found that one colonoscopy incurs a roughly 0.3% risk of serious complication, such as blood loss requiring transfusion, myocardial infarction, or stroke (there were no perforations in this study). In a long-term comprehensive study of colonoscopy in a Swedish county, the complication rate was 0.2% for bleeding and 0.1% for perforation, with no colonoscopy-related deaths. A study in the United Kingdom’s National Health Service found, in 9223 colonoscopies, rectal bleeding requiring hospitalization in just less than 0.1% (6 instances) and a perforation rate of just more than 0.1% (1 per 769), and it found that colonoscopy was a possible factor in the death of 6 persons (just less than 0.1%). On the basis of these figures, Table 1 shows a cumulative risk of serious complications and death for a person receiving various numbers of colonoscopies from age 50 to 80 years; the numbers can be adjusted to reflect different complication rates. The table does not try to describe which kinds of patients might be receiving frequent colonoscopy or the degree of possible benefit; it is intended primarily to show a way to estimate complication rates incurred by varying numbers of colonoscopic examinations as one step in an effort to estimate and compare risks and benefits. The main point is that although the risk of complications from any single examination may be small, the cumulative rate may, with repeated examinations over time, become an important consideration (Table 1).

The cumulative risk from repeated colonoscopy can then be compared with the benefit of screening, ie, the reduction of CRC mortality. For an average-risk person, the overall risk of mortality from CRC is roughly 2% from age 50 to 80 years. The degree to which colonoscopy screening reduces that mortality is not known but would be roughly 60% on the basis of the degree of reduction found in case-control studies about lesions within reach of the sigmoidoscope. The degree of reduction of cancer incidence by colonoscopy screening, estimated from the National Polyp Study (NPS), has been considered to be 76% to 90%; however, the

### Table 1. Estimating the Cumulative Rate of Serious Complications and Death From Colonoscopy Performed From Age 50 to 80 Years

<table>
<thead>
<tr>
<th>Number of colonoscopies, age 50 to 80 y (interval)</th>
<th>Cumulative risk</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Serious complication</td>
</tr>
<tr>
<td>3 (every 10 y)</td>
<td>1%</td>
</tr>
<tr>
<td>6 (every 5 y)</td>
<td>2%</td>
</tr>
<tr>
<td>10 (every 3 y)</td>
<td>3%</td>
</tr>
</tbody>
</table>

Risks of complications can be compared with benefit of CRC mortality reduction; for details, see text.
NPS did not provide a direct concurrent comparison, as did the case-control studies, with persons not having colonoscopy. If screening colonoscopy reduces CRC mortality by 60% (so that a 2% absolute risk is reduced by 1.2%, to 0.8%), then that absolute risk reduction of 1.2% could be compared with the cumulative risk of the procedure, as shown in Table 1. Using, instead, a 90% incidence reduction, based on the upper limit of mortality reduction estimated in the NPS, then the absolute CRC mortality reduction would be 1.8%. An additional consideration regarding the risks from a screening procedure is that, whatever the mortality reduction in screening programs, the risk of complications is incurred by all persons having screening, including those who would never develop CRC and so would not benefit from screening. It is not known in advance who is at risk to develop CRC; the point is that the degree of risk from complications of screening is relatively high for otherwise healthy persons to incur. Although these calculations provide only rough estimates, they provide a framework to consider the balance between benefits and risks, and they illustrate the importance of considering how the risk of complications may accumulate over time in a program of screening.

**New Tests**

New tests, in various stages of development and implementation, may become attractive options in the future, depending on research results and on how those results are viewed by recommending organizations.

**Virtual colonoscopy.** Virtual colonoscopy, under development for more than a decade, is now showing results that may make it a mainstream screening test. The approach involves performing an abdominal computerized tomographic examination that is analyzed by computer to render an image resembling that seen at optical colonoscopy. Recently the approach has been shown to achieve a sensitivity (94%) and specificity (96%) for large polyps ≥1 cm that is high enough, for the first time, to compete with optical colonoscopy. Indeed, virtual colonoscopy may detect lesions that optical colonoscopy misses. It is yet unclear, however, whether such high levels of performance may routinely be obtained in practice but the fact that such results have been achieved in any setting constitutes an important advance for the technology. If it is possible to perform computerized tomographic examination without laxative preparation, then virtual colonoscopy will have a competitive advantage because laxatives are a disliked feature of both virtual colonoscopy and optical colonoscopy. Other issues affecting use of virtual colonoscopy include decisions about what threshold lesion size should prompt workup with optical colonoscopy. If that size is small (eg, <1 cm), then the number of workups incurred to investigate small polyps (or stool that looks like small polyps) will make virtual colonoscopy cumbersome and expensive. Despite such challenges, the overall trajectory of development of virtual colonoscopy is quite positive, thus suggesting that it is likely to become a contender as a mainstream CRC screening test.

**Fecal DNA testing.** Fecal DNA testing is based on the idea that, because cancer is a disease of mutations that occur as tissue evolves from normal to adenoma to cancer, those mutations should be detectable in stool. Preliminary reports that persons with advanced cancer have detectable DNA mutations in stool provided the basis for a large study, using a panel of 21 mutations, in more than 4000 asymptomatic persons who received screening colonoscopy, fecal DNA testing, and FOBT with Hemoccult II. The DNA marker panel, including mutations in APC, K-ras, and p53, showed a sensitivity of 52% for CRC and a specificity of 94%. Although fecal DNA testing may not be widely adopted in its current form and cost, the future for such an approach would seem promising if sensitivity could be increased by additional markers such as methylation and if cost could be reduced (disclosure: the author was chair of the scientific advisory board of Exact Sciences until 2002; since then, he has had no financial relationship with Exact).

**Beyond Guidelines: Forces Affecting Decision Making in the Larger Environment**

After guidelines have recommended screening and reimbursement has begun, other forces become prominent in a postguideline environment of decision making. In this environment, decisions are driven by considerations different from those assessed in the idealized and evidence-based process that recommending organizations use to develop guidelines.

Each of the 3 decision makers in clinical care—professional policy-making organizations, physicians, and patients—uses different sources of evidence, different values about that evidence, and different processes of decision making. Policy-making organizations strive to use a process that is explicit, quantitative, and transparent. In contrast, patients use a process that may depend heavily on rules of thumb, anecdotal experience, and strong personal preference. These differences help account for a disconnect that occurs when screening practice is more aggressive than policy makers would seem to suggest, as has happened for breast cancer screening for
persons younger than 50 years and for much prostate cancer screening.75,76

A physician’s perspective is somewhere in between that of policy-making organizations and patients; additionally, physicians have their own set of interests that do not necessarily overlap with either.74 Physicians have a critical role in decision making because they present much of the information that patients receive and because physicians may be directly involved in making decisions. Physicians want what is best for their patients, but they can experience pressures that conflict with those interests. The situation can be illustrated by looking at how a physician may see the decision to order prostate-specific antigen (PSA) testing to screen for prostate cancer. This example is particularly instructive because many physicians believe that prostate cancer screening is, overall, harmful to patients and not in their patients’ interest (because the known and commonly occurring harms from impotence and incontinence may outweigh a still-uncertain benefit76), but physicians nonetheless may feel compelled to encourage screening—a situation that may occur in other decisions, such as those about colon cancer screening and surveillance.

The problem occurs when “External pressures related to physicians’ self-interest may create tension with the idealized quantitative prescriptive decision-making approach used by professional organizations. The dynamics are, on the one hand, hard to measure, but on the other hand, are totally obvious to anyone familiar with the practice of medicine. This dynamic might be considered ‘economic,’ even if its features are not all monetary.”74

For example, in deciding about whether to be aggressive and to order a PSA test for prostate cancer screening or to order frequent colonoscopy for CRC screening or surveillance, a physician can consider the test’s ability to detect curable cancer or precancerous lesions balanced against how often a complication might occur from that testing, in a manner similar to that used by policy-making organizations.74 At the same time, “There is an entirely different perspective or dynamic in which a physician faces a tempting ‘no-lose’ situation by ordering PSA testing [or intensive CRC screening or surveillance], because a physician will be positively reinforced for recommending PSA screening regardless of the test’s result. A negative result makes a patient grateful for reassurance, while a positive result makes a patient grateful for early detection.”76 In the same vein a physician may worry about personal legal liability if a test is not ordered and cancer is later detected, even if the physician has repeatedly counseled the patient.77 In this situation, considerations of quantitative diagnostic discrimination and harms and benefits to patients may give way to an entirely different set of dynamics. A colleague was only partly exaggerating to make the point when he said he decides about ordering a diagnostic procedure that he performs by asking himself, “Will I get paid if I do it? Will I get sued if I don’t do it? Will the patient be happy if I do it?” Although professional decision making is more complicated than this exaggerated example suggests, the example illustrates real-world factors that are generally underappreciated, understudied, and must be accounted for.”74

CRC screening differs from prostate cancer screening in several important ways. The evidence of efficacy for CRC screening makes any harms from screening more acceptable; furthermore, the potential harms of CRC screening and treatment are much less than those involved in screening for and treating prostate cancer. However, the prostate cancer example illustrates the powerful forces at work that tend to make the risk from intensive screening or surveillance acceptable to patients and physicians; these forces can be independent of evidence of efficacy. For prostate cancer screening, even in the face of evidence of a high rate of harms from screening and treatment and in the absence of any strong evidence of efficacy, powerful forces nevertheless tend to cause physicians to see a benefit, to themselves, of being aggressive about ordering tests and treatment; the same forces tend to make patients happy with the result of screening and treatment, even if they are harmed.76 Such forces also operate in situations where there is evidence of efficacy, such as CRC screening (and for other cancers and diseases).76 The point is that, to the extent that strong forces, to be aggressive, can operate independently in the absence of evidence of efficacy,76 those forces must be recognized and managed so that they do not unreasonably drive medical practice.76

Even beyond these forces that make screening and surveillance aggressive are more purely economic forces. Such economic concerns are reflected in a recent article focusing on how implementation of virtual colonoscopy would affect the demand for colonoscopy.48 On the one hand, it is perfectly reasonable for policy makers and clinicians to try to plan for future manpower and resource needs. On the other hand, if the field of gastroenterology becomes overly dependent on one technology—and anecdotal reports suggest that some gastroenterologists are now spending up to 50% and even 80% of their time simply performing colonoscopies—then the profession risks becoming, like Seattle in the 1970s, a one-industry town
that is extremely vulnerable to a market downturn. Such a situation risks causing distorted decision making at both policy and practice levels.

**Other Challenges**

**Postpolypectomy Surveillance**

Surveillance is a separate topic whose importance will increase as screening is increasingly performed, because so many persons screened will be found to have adenomas and thus will be potentially eligible for postpolypectomy surveillance. Surveillance is the follow-up of persons thought to have an increased risk of subsequent CRC. Because 30%–50% of Americans older than 50 years have one or more adenomatous polyps, surveillance could become the most common reason for colonoscopy, involving a large proportion of the American population. In the early 1990s, it was believed that virtually all polyp formers (persons with any adenomatous polyp) had a high risk of subsequent CRC that warranted intensive surveillance. Indeed, the original purpose of the NPS was to compare a less intensive strategy of colonoscopy at 3 years after initial polypectomy vs a more intensive

---

### Table 2. Guidelines for Screening Persons With Positive Family History

|----------|-----------------------------|-------------------------------------------|-------------------------------|---------------|

**If affected relative with CRC is older**

- **Increased risk is indicated by**
  - If single FDR, it is not clear that the modest increase in risk justifies routine use of colonoscopy over other screening methods
  - If close relative with CRC

- **What action**
  - Routine screening as for average risk
  - Routine screening as for average risk; start age 40 y

**If affected relative with CRC is younger**

- **Increased risk is indicated by**
  - When affected relatives are younger may justify beginning screening before age 50 y
  - If relative had CRC before 55 y or adenomatous polyp before age 60 y

- **What action**
  - Make special efforts to ensure that screening takes place
  - Start age 40 y or 10 y younger; colonoscopy every 3–5 y

**If relative has adenomatous polyps**

- **What action**
  - Same as for CRC
  - Issue has not been studied adequately

---

NOTE. Recommendations for screening based on family history vary substantially at several levels. One difference concerns the type of family history that indicates increased risk. Is 1 FDR sufficient or 2? Other differences concern how the age of the relative may affect risk. Lastly, if risks are increased, there are differences regarding what kinds of tests should be performed (regular screening tests such as FOBT and sigmoidoscopy or more aggressive tests such as colonoscopy), at what age, and how often. All these distinctions have substantial implications for the numbers of persons getting screened and for the amount of resources that would be involved.

FDR, first-degree relative.
strategy of colonoscopy at 1 year, because in that era the risk of subsequent CRC was thought to be so high. We now know, because of evidence from the NPS and other sources, that the natural history after polypectomy is much less ominous than initially thought during the planning of the NPS. This new knowledge has led to a relaxing of recommendations about postpolypectomy surveillance. Still at issue in 2005 is what the surveillance interval should be. How these questions are answered will have substantial implications for manpower, resources, and patient care.

Family History

Family history will also become increasingly important as screening is increasingly performed. Furthermore, if a family history of adenoma is considered an important risk factor, then the numbers of potentially affected relatives become much larger. In the face of this potentially large use, current guidelines are characterized by being both highly intensive and highly variable (Table 2). Most suggest intense management of some kind (such as more extensive testing or an earlier age to start examinations). However, there is substantial variability about key issues, and this variability may leave clinicians and patients uncertain about what to do. As shown in Table 2, the features that vary include (1) what constitutes a positive family history (eg, 1 first-degree relative or 2 and what age of the relative), (2) what tests should be performed when the family history is positive and starting at what age, and, (3) regarding adenomas, whether family history should be treated the same way as for relatives with CRC (Table 2).

Such variability in recommendations may simply reflect genuine uncertainty about what the currently available data mean, but clinicians will nevertheless need to figure out what to do in the face of such variability. Perhaps clinicians will conclude that any of several recommendations (either more aggressive or less aggressive) is acceptable; or, perhaps, in a litigation-prone environment, the heart may beat to the fastest pacemaker, so the more aggressive recommendation will be preferred. In any case, if we plan to get serious about family history, and especially if having a relative with any adenoma makes the family history positive, then we have a lot of work ahead. One challenge is that few people know accurate details even about their own personal history of polyps (eg, histology and size), much less about the history of their relatives’ polyps.

Conclusions

Fifteen years ago, the primary unanswered question in this field concerned whether CRC screening was effective in reducing CRC mortality and whether screening should be implemented and reimbursed. Because that question has been answered and because guidelines and reimbursement are leading to implementation, the next set of challenges is emerging. These challenges concern making choices among different screening tests and strategies and concern details of decisions about postpolypectomy surveillance and family history. Strong forces in the larger environment of decision making tend to make decisions aggressive for both screening and for follow-up, potentially involving inefficient use of resources and, in some cases, net harm to patients. Making sensible policy and clinical decisions will require not only considering traditional kinds of evidence about biology and effectiveness, but also understanding and acting on the strong forces of public perception, economics, and the sometimes-conflicting motivations of the 3 actors who together make decisions about screening: policy makers, physicians, and patients.

References

11. US Congress Office of Technology Assessment. Costs and effectiveness of colorectal cancer screening in the elderly—back-


81. Sandler RS. First-degree relatives of patients with adenomas had an increased risk for colorectal cancer. ACP J Club 1998;129:75.

