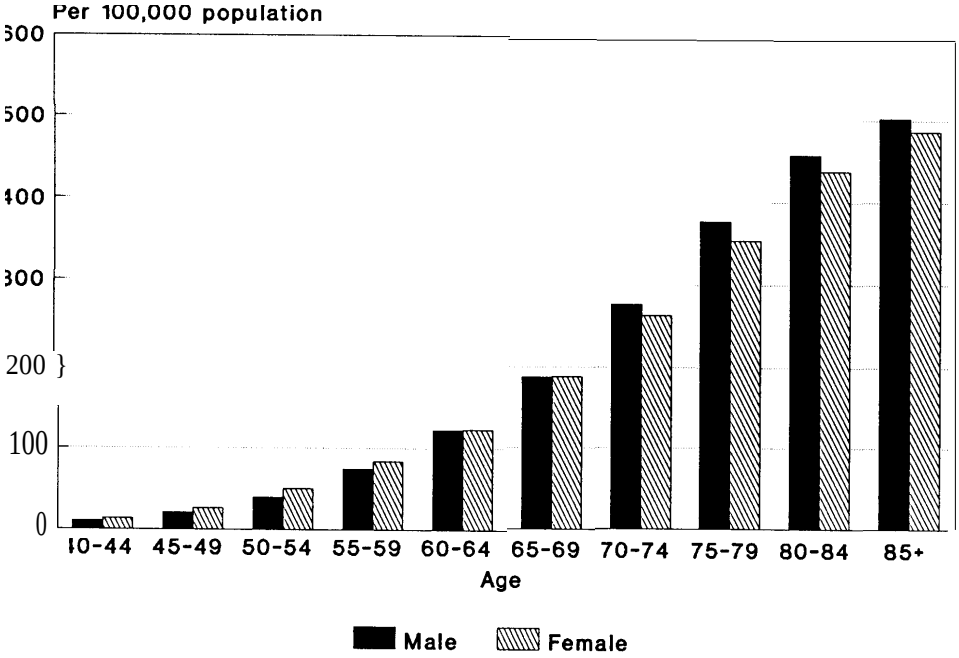
Cancer of the colon or rectum -- commonly referred to together as colorectal cancer (CRC)[1] -- is primarily a disease of the elderly. Every year, about 110,000 people 65 years of age and older are diagnosed with CRC. Almost three out of every four new cases of CRC occur in people 65 years of age and older. In 1989, about 61,500 people died from the disease. A 65-year-old man without previously diagnosed CRC has about 6 chances in 100 of ultimately developing CRC, and about 3 chances out of 100 of eventually dying from the disease (134). As a person ages, the risks of CRC increase dramatically. At 50 years of age, the incidence of CRC in men is 57 per 100,000; by 65 years of age, it has risen to 244 in 100,000; and by 75 years of age it is 411 in 100,000. Though women have a lower overall incidence rate for CRC, it still rises dramatically with age, from 46 per 100,000 at 50-54 years of age to 156 per 100,000 at 65-69 years of age (chart 1).

Although environmental factors, particularly diet, appear to play a role in the development of CRC, little is known today about how to prevent CRC through dietary or environmental interventions. Promising new approaches to cancer therapy appear to offer significantly better prognosis for people with moderately advanced colon cancer, but these improvements are likely to have only modest impacts on overall survival rates for late stage CRCs. Thus, clinicians and researchers have sought ways to reduce the burden of illness and death associated with CRC by detecting more cancers in early and still curable stages, before they progress to more advanced stages.

[1]**Colorectal cancer is also referred to as cancer of the large bowel, the portion of the alimentary canal that begins at the cecum, the juncture between the small intestine and the large intestine, and ends at the anus.**

Chart l--Annual Colorectal Cancer Incidence Rates, United States



SOURCE: U.S. Department of Health and Human Services, National Cancer Institute, *Cancer Statistics Review 1973-1986* (Bethesda, MD: May 1989)

If early detection of CRC can interrupt or delay the natural course of the disease, then detection and removal of the suspected precursors to cancer -- adenomatous polyps (benign growths in the colon or rectum) -- might actually prevent the onset of cancer itself and lower its incidence. Thus, the notion of CRC screening has come to encompass a search not only for early cancers, but also for the benign adenomatous polyps out of which most CRCs are suspected to arise.

The detection of neoplasms (cancers and adenomatous polyps) in the colon or rectum involves either direct inspection of the colon and rectum or indirect measurement of biochemical markers for the presence of cancer or polyps. Today, the most common screening technologies are the fecal occult blood test (FOBT), which analyzes samples of stool for the presence of blood, and flexible fiberoptic sigmoidoscopy (FSIG), a flexible tube with a light and mirror at the end inserted into the colon through the anus to examine the dista1[2] end of the large bowel.

The full impact of screening does not end with these tests. Over the course of his or her remaining life, an elderly person would not only undergo repeated CRC screening tests but also followup diagnostic testing when the screening tests are positive, polyp removal (polypectomy) when polyps are found as part of the screening ***or*** followup tests, and periodic surveillance with colonoscopy after polypectomy to screen for new polyps. In addition, when cancers are found, patients undergo evaluation and treatment for the cancer based on the stage at detection.

Numerous expert groups in the United States and other industrialized countries have made recommendations "about the frequency with which elderly people should receive particular colorectal screening tests. Although the American Cancer Society and the National Cancer Institute both recommend periodic screening for CRC with an annual FOBT and FSIG every 3 to 5 years for all Americans beginning at age 50, the U.S. Preventive Services Task Force, an expert group sponsored by the U.S. Department of Health and Human Services, declined to recommend either for or against periodic screening with either FOBT or sigmoidoscopy in average risk individuals.

The differences in recommendations regarding CRC screening for average-risk older people reflect two facts. First, the evidence on the effectiveness of specific CRC technologies is inadequate; and second, the criteria (either implicit or explicit) for judging the evidence that does exist differ among the expert groups. At issue is whether a screening test for CRC must be shown to reduce CRC incidence or mortality in order to be considered effective, or whether demonstrating a shift in the distribution of detected cancers to earlier stages is sufficient for considering a screening regimen effective. Those who require direct evidence that CRC screening will reduce the incidence of or mortality from CRC have found the existing evidence inadequate to recommend embarking on a screening strategy for CRC. The critics also point out that screening and diagnostic follow-up have medical risks and costs. Advocates focus on the heavy burden of illness and death brought about by CRC and conclude that even indirect evidence that screening may alter the course of a substantial proportion of such cases cannot be ignored.

EVIDENCE ON EFFECTIVENESS

Although a large literature exists on the use of the FOBT as a strategy for CRC screening, only six controlled studies of FOBT screening in asymptomatic individuals have been reported, and four of these are still underway. All but one of the studies are large randomized clinical trials conducted in older average-risk individuals, beginning at ages 45 to 60-years-old. The exception is a study of volunteers

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2. Distal" refers to the parts of the large bowel closest to the anus. "Proximal" is the term for the part-of the large bowel that is closest to the cecum, the point of juncture between the small intestine and the large intestine.

over 40 years old attending a cancer prevention clinic in New York City who were assigned to the experimental or control group according to the month in which they presented at the clinic.

Despite imperfect compliance, rates of detection of CRC are consistently higher in the intervention groups than in the control groups, and a higher proportion of those found are early cancers. Only one of the trials has reported on mortality differences between intervention and control groups. A large trial of biannual FOBT screening of 45- to 70-year-olds in Denmark found a 27 percent lower CRC mortality rate in the group offered screening after about 3 years of study, but the number of deaths ***in*** the study so far is very small and the difference is not statistically significant by conventional standards.

To summarize, the six controlled studies of FOBT screening suggest that in an ongoing screening program, FOBT screening improves the stage distribution of cancers detected, which may translate into decreases in cancer mortality. However, even in very large trials, no such mortality effect has been identified to date.

Studies of the impact of sigmoidoscopic screening on cancer incidence or mortality are even fewer than for FOBT. Only three studies of outcomes of screening programs using sigmoidoscopy have been reported. Two of these were long-term observational studies of screened subjects without comparison groups. The third was a randomized clinical trial of rigid sigmoidoscopy as part of a program of periodic preventive health services offered to non-elderly enrollees in an Hospital Maintenance Organization (HMO).

These studies have universally shown dramatic shifts of detected cancers to early stages. Although two of the three studies reported declines in the incidence or mortality of cancers, critics have concluded that attribution of such changes to screening is not possible given the studies' methods.

Taken as a whole, the evidence on FOBT and sigmoidoscopy suggests a major shift in the stage at which CRCs are detected but inadequate evidence that this stage shift actually reduces death rates from cancer over time. How can these two seemingly contradictory findings be reconciled? One possible explanation is that there are biases in the detection of cancers in these studies. The stage shift may reflect earlier diagnosis, not improved outcomes. This greater "lead time" between diagnosis and death would improve the stage distribution of cancers detected without affecting mortality in randomized trials. There is also a real possibility that "length bias" -- the higher rate of detection of the slowest growing tumors which by definition are less lethal than faster growing tumors -- may account for the inconsistency. Those who believe that length bias can be a powerful influence on outcomes are likely to discount the evidence on stage shift as inadequate, whereas those who see the dramatic shifts in stage at detection as unlikely to be caused simply by lead time or length bias accept this evidence as sufficient to justify periodic CRC screening with sigmoidoscopy or FOBT.

POTENTIAL COST-EFFECTIVENESS OF CRC SCREENING IN THE ELDERLY

Cost-effectiveness analysis is a process of comparing the net health care costs brought about by a screening strategy with the health effects achieved as a result. Estimating the cost-effectiveness of CRC screening in the elderly is a difficult undertaking because of the uncertainty about whether CRC screening is effective at all in preventing CRC or reducing its lethality. If CRC screening is not effective in reducing CRC incidence or mortality in the elderly, then it is clearly not cost-effective. It is only costly. It may even be both costly and risky, because the screening and followup procedures associated with CRC screening strategy carry their own medical risks.

Whether CRC screening can extend the lives of elderly people through prevention or earlier detection of CRCs is simply unknown at present. Indirect evidence does exist, however, about the natural course of the disease, the accuracy of the various screening tests in detecting polyps and CRC, rates of medical complications associated with the various tests and cancer treatment, and the life

expectancy of people with CRC at various stages. Though this evidence is imperfect and has some important gaps, if used judiciously it is possible to explore the potential impact of CRC screening on the health of elderly people. These potential net health impacts can then be compared with the net health care costs associated with screening in elderly people.

To resolve the dilemma posed by uncertainty about net effects, the Office of Technology Assessment (OTA) estimated the net health care cost per additional year of life gained from CRC screening using data and assumptions that were in every case unfavorable toward screening. OTA examined the existing evidence on screening test accuracy, the natural course of the disease in the elderly, medical risks, and costs with the objective of deliberately underestimating the effectiveness and overestimating the costs associated with screening. If the resulting conservative estimate of cost-effectiveness of CRC screening compares favorably with other preventive interventions for the elderly, particularly those that have already been included as Medicare benefits, then confidence that CRC screening is at least as cost-effective as these other services would be high.

Some experts argue that such an analysis is inappropriate at this time (20). Because there is no direct evidence of effectiveness for either FOBT or FSIG, critics argue that an analysis that predicts any positive health effects is not truly pessimistic; a truly pessimistic analysis would posit no health effects. Moreover, evidence on FOBT may become available within the next two to five years as the five ongoing or completed clinical trials report their results. A large National Cancer Instutitue (NCI)-sponsored trial of FSIG screening in older people is also in planning and will probably provide information on that screening procedure within the next 15 years. In the absence of the direct evidence that can come only from these trials, critics argue, an assessment of the medical benefits and potential cost savings associated with screening would entail too many unproven assumptions. Given the high costs and potential medical complications of screening in the elderly, the most prudent strategy is to wait a few years for the results of such studies before deciding whether to take any action, such as providing a Medicare CRC screening benefit, that would encourage screening in the elderly.

The proponents of this view reject the value of the substantial body of indirect evidence that does exist on the accuracy of the screening tests, the natural course of the disease in the elderly, and the effectiveness and cost of treating CRC. It is also not clear that the existing FOBT trials, even when they are reported, will settle the question of FOBT screening effectiveness once and for all. If results differ across trials, for example, the reasons for such discrepancies could be debated for years. Most important, a decision to wait must be recognized as carrying its own implicit value judgment that the potential lives saved from CRC screening are not as important as the potential medical risks and costs of undertaking screening. OTA's analysis is intended to explore just how great the potential gains from screening might be using what information is available now.

OTA constructed a model of the cost-effectiveness of periodic CRC screening in a population at age 65 and continuing until they die or reach the age of 85. OTA made pessimistic assumptions (i.e., biased against finding in favor of screening) about the accuracy of the screening tests, the speed of progression of polyps to cancer and cancers from early to late stages, the proportion of cancers that arise out of polyps, the stages at which cancers would be found in an unscreened elderly population, and the impact of early detection of CRC on life expectancy.

OTA found that a CRC screening regimen consisting of an annual FOBT beginning at age 65 would prevent approximately 23,000 cases of CRC in the 2.1 million people who were 65 years of age in 1989 and would provide almost 45,000 added years of life to that population.[3] These benefits would come at a net discounted cost of roughly $1.5 billion over the remaining lives of the people in the cohort. This net lifetime expenditure amounts to about $737-$1,263

[3]Both added yearn of life and costs are discounted at 5 percent per year.

for every person who complies with screening, diagnostic protocols and surveillance guidelines. The net cost per added year of life is about $35,000. Screening strategies that combine annual FOBT with sigmoidoscopy prevent more cancers and add more years of life but are also more expensive; consequently, the net discounted health care cost per added year of life ranges from approximately $42,000 to $47,000 depending on the frequeney with which sigmoidoscopy is included in the screening program.

Studies of other preventive services legislated as covered services under Medicare in the past (pneumococcal pneumonia vaccine, cervical cancer screening, and breast cancer screening[4]) have reported lower costs for each additional year of life gained from screening. However, when both costs and years of life gained were discounted to their present value at an annual rate of 5 percent, as they were in this study, breast cancer screening in elderly women was estimated to cost about $34,000 per year of life gained. This is approximately equal to the cost per year of life gained from annual FOBT screening in the elderly under the pessimistic set of assumptions.

OTA attempted to submit CRC screening to a stringent test of cost-effectiveness by making assumptions that were uniformly unfavorable to screening. For most of the assumptions, we are reasonably confident that the true value is more favorable to screening than the value assumed in the analysis. By combining so many unfavorable assumptions together, the analysis represents a reasonable upper bound on the potential costs per year of life gained from each screening regimen. Data were sparse to support several assumptions, however. A test of how sensitive the results of the study are to changes in the assumed costs of treating cancer determined that even if such costs are as low as $5,000 per case for both early and late cancer, the discounted net cost per year of life gained from annual FOBT screening is still under $40,000. The results of the analysis were more sensitive to a change in assumptions about the speed with which colorectal polyps become cancers. If a very rapid rate of progression is assumed, the cost per additional year of life gained by an annual FOBT could be as high as $50,000. The ability of the FOBT to detect early cancers (FOBT sensitivity rate) also has a major influence on the outcome of the analysis. If FOBT is a very poor detector of early cancer, the cost per year of life gained from annual FOBT testing in the elderly could be as high as $47,000.

To summarize, the net health care costs of any CRC screening strategy are high. The present value of the lifetime health care costs of an annual FOBT screen for the 2.1 million people who were 65 years old in 1989 may be as high as $1.5 billion, but these high costs have the potential for adding 45,000 years to these people's lives, and the net costs per added year of life are within a range that has been judged reasonable for one other screening examination (mammography) that had been legislated as a Medicare benefit.

The lifetime health care costs of screening strategies that include FSIG as well as FOBT are even higher than those for FOBT alone ($2.4 billion to $2.6 billion, depending on the frequency of FSIG screening), and the added health benefits associated with FSIG over and above FOBT may be quite low. Thus, the additional cost per added year of life gained for FSIG screening over and above FOBT screening may be much higher than those of other preventive services that have been legislated as Medicare benefits.

IMPLICATIONS FOR MEDICARE

If CRC screening were a covered Medicare benefit, Medicare's share of the net cost of screening would be high. Even today, Medicare covers a large but unknown proportion of the total net costs of such a screening strategy, because all diagnostic, followup, and surveillance procedures are covered Medicare services. The costs of the screening tests themselves,

[4]Mammography was briefly legislated as a covered benefit under Medicare, but the provision was repealed when the Medicare Catastrophic Health Act of 1988 was repealed late in 1989.

particularly the FOBT, are very low compared to the costs of followup, treatment, and surveillance. Medicare's average allowed charge for the FOBT when it is ordered for diagnostic reasons is under $4 and for FSIG is about $100.

The national cost estimates above are based on the assumption that all elderly Medicare beneficiaries will follow the screening regimen outlined in the model. In reality, the use of CRC screening examinations in the elderly is quite low, and it is unknown how much it will increase by making FOBT alone or in combination with FSIG a covered Medicare benefit. In 1987, for example, only 34 percent of people 60 years of age or over reported ever having undergone a screening FOBT test and 7.4 percent reported ***ever*** being screened with proctoscopy (rigid sigmoidoscopy) Thus, the net additional health care cost of a Medicare CRC screening benefit may be much lower than the estimates given here. On the other hand, if screening is differentially used by those at low risk of CRC, then the medical benefits projected in the cost-effectiveness analysis would be reduced, and the cost per year of life added would be higher.

The total costs of CRC screening to Medicare and beneficiaries also depend on the amount that Medicare pays for screening, followup and surveillance examinations. In the estimates of screening costs, OTA used Medicare's average allowed charges in 1988 for procedures conducted in physicians' offices. To the extent that FOBT and endoscopy procedures are billed at rates above these amounts and physicians do not accept assignment of the Medicare allowed amount as reasonable, these allowed charges underestimate total health care costs. In addition, when followup and surveillance colonoscopies are performed in hospital outpatient departments, Medicare also pays the hospital for the technical costs of the procedure. If Medicare cannot limit the payment rates for surveillance colonoscopies to the average amounts allowed in physicians' offices, the actual outlays could be higher than the estimates given in this paper.

Finally, the net costs of the strategy are very sensitive to the frequency with which CRC screening results in followup or surveillance colonoscopy. If physicians recommend and patients who have had adenomatous polyps removed comply with a frequent schedule of surveillance with colonoscopy (every two years instead of every four), the costs of the strategy could be much higher than estimated in this paper. The extra costs could amount to almost $1 billion over the lifetime of the 1989 65-year-old population if all members of the population fully comply with the protocol.

This analysis highlights the substantial net costs that can be associated with a preventive service, even one that offers a high potential for major health benefits. CRC screening in the elderly will NOT reduce total health care costs. Depending on which tests are employed and how widely they are used, screening may raise the total lifetime health care cost for a 65-year-old person who undergoes screening as a result of a Medicare benefit by as much as $1,300. That expenditure, which will be borne in large part by Medicare, offers a good chance, but not a certainty, of providing elderly people with substantial gains in health.