**Improving the Cost-Effectiveness of Colorectal Cancer Screening**

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From several perspectives, prevention of colorectal cancer by adenoma detection is gaining acceptance as a more desirable goal for screening than detection of asymptomatic, early-stage cancer. While clinical trials of fecal occult blood (FOB) screening (1–4) have shown substantial reductions in colorectal cancer mortality, incidence rates appear to remain unaffected. This finding suggests that, while some adenomas certainly bleed and are detectable by the FOB test, the main yields from FOB screening are early-stage asymptomatic cancers that have superior prognoses to clinically detected cancers. To detect adenomas in quantity, endoscopy is currently the most sensitive method available.

The results of an economic analysis by Loeve et al. (5) in this issue of the Journal show that flexible sigmoidoscopy (FS) screening not only can be cost-effective but, under certain assumptions, also might actually be cost-reducing. Colorectal cancer is an expensive disease to treat and, by preventing its development, the avoided costs of treatment can be offset against the costs of a screening program. In contrast, the detection of colorectal cancers, even those at an early stage, appears to have little effect on morbidity and treatment costs (6–8). In the randomized trials of FOB screening, surgery was avoided in only 10% of the patients with screen-detected cancers (6). Although localized cancers are cheaper to treat than disseminated disease, their treatment is comparable in cost to very late-stage disease, which results in early death. Thus, the shift to detection of earlier stage disease by screening does not reduce the average costs of treating colorectal cancer to a meaningful degree (6–8). In fact, since screening typically detects cancer earlier than through symptomatic detection, the discounted costs are higher under the screening scenario.

Screening oriented toward adenoma detection is not without its problems, however. While adenomas are present in the colons of at least 30% of the population by age 60 years (9,10), most remain benign until death or become malignant only very slowly. A strategy that aims to prevent cancer through adenoma detection is, therefore, bound to generate overtreatment in those who have developed an adenoma but who are destined to die of other causes before the adenoma has become malignant. A great deal more needs to be understood about this important false-positive group, if only because adenoma detection still typically leads to colonoscopic surveillance indefinitely. A less aggressive surveillance strategy has been recently widely endorsed (11), in which colonoscopic surveillance is recommended only at the discretion of the physician in those with a single, small, tubular adenoma in whom the risk of developing metachronous adenomas or cancers is deemed low (12,13). Ransohoff et al. (14) have estimated that, in this low-risk group, the prevention of a single death from colorectal cancer might require 1000 colonoscopies, thereby incurring two perforations and 0.2 procedure-related deaths.

The costs of repeated colonoscopic surveillance dominate the costs of any screening program involving either FOB or endoscopic surveillance (7,14,15). Marshall et al. (15) have demonstrated that the total burden of costs of colonoscopic surveillance depends on 1) the interval between screens in those with negative examinations and 2) the interval between colonoscopic surveillance examinations in those found to have adenomas. Increasing the screening interval decreases not only the costs of the screening procedure itself but also the proportion of people who become positive and enter colonoscopic surveillance. If adenomas are detected in 10% of the people at each screen then, by the fifth successive screen, one third will have shifted to colonoscopy surveillance. In the Office of Technology of the U.S. Congress assessment (7), compliance with annual FOB testing over 20 years would result in nearly half of all subjects undergoing surveillance.

The recommended interval between FS screens has recently lengthened from 3 years (16) to 5 years (11), although others have recommend a 10-year interval (17) or even a one-time examination (18). Unfortunately, there are few studies on which to base recommendations on the duration of effect, and most studies are either small or retrospective. In one study (10), of the 259 average-risk individuals (aged 50 years) who underwent a second screening FS an average of 3.4 years after a negative screen, none were found to have a large adenoma or cancer. The duration of protection associated with a single sigmoidoscopy was at least 10 years in one case–control study (19), while another found that efficacy decreased after 7 years (20). Marshall et al. (15) showed that the likely costs of a screening program would be halved if the screening interval were to be increased from 3 to 5 years, and they would fall 10-fold if the interval increased from 5 to 10 years.

In the U.K. and in Italy, the efficacy and duration of effect of one-time FS screening at age around 60 years are being evaluated prospectively in a randomized, controlled trial (21,22). The case for one-time FS screening rests on the observation that most distal adenomas arise in the sixth decade and then slowly become malignant only over the next 10–20 years (18). An equivalent case can be made for one-time colonoscopy with respect to proximal cancers, most of which occur in the absence of a distal marker (23). However, proximal adenomas tend to develop at an older age than distal adenomas (24), suggesting that the optimum ages for examining the different parts of the bowel might themselves be different.

The analysis published in this issue of the Journal by Loeve et al. (5) is the first, to our knowledge, to suggest that preventing cancer through endoscopic screening can, in the long term, be cost-saving. As the authors point out, however, this conclusion rests crucially on a specific set of assumptions and cost defini-
tions. The assumptions were derived by discussion within a specific panel of experts, as opposed to experimental observations, and sensitivity analysis of variations in assumptions suggests that net savings can easily be turned into net costs. Even in the most favorable scenario, the break-even point appears not to occur until the fifth decade of an ongoing program. Unfortunately, health planners tend not to be so farsighted, and it is difficult to envisage that the technologies for treating and screening for colorectal cancer will remain unchanged for that length of time. Hopefully, before then, there will be alternatives to inserting tubes into the colon to search for polyps and more accurate markers for predicting which of these polyps require removal. Possibly, by then, a safe dietary supplement or a pharmacologic agent may have abolished the adenoma entirely, confining it to the pathology museum. In the meantime, we should pursue the goal of colorectal cancer prevention by constructing a solid foundation of clinical evidence as the basis of selecting, for example, the appropriate screening method, the screening interval, and surveillance strategy. It is practical considerations such as these that alter, by many millions of dollars either way, the ultimate costs of a screening program.

REFERENCES
