

American Cancer Society Guidelines for the Early Detection of Cancer

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Abstract

This issue of CA inaugurates a yearly report on American Cancer Society guidelines for early detection of cancer in asymptomatic individuals.

The current recommendations, which reflect almost 20 years of updates, cover screening recommendations for breast, colorectal, prostate, and cervical cancers, as well as for other cancers, depending on patient age, history, environmental and/or occupational exposures, etc.

A key concept for both the general public and health providers is the distinction between public health recommendations regarding screening and decisions about early detection tests that might be undertaken on an individual basis.

Although it is likely that current screening protocols will be supplanted by newer technologies, such as genetic and molecular markers of risk and disease, greater utilization of the technologies at hand will improve efforts toward establishing an organized and systematic approach to early cancer detection. (CA Cancer J Clin 2000;50:34-49.)

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Introduction

In the late 1970s, the American Cancer Society (ACS) embarked upon an evidence-based assessment of tests for the early detection of cancer in asymptomatic individuals. Based on the results, *Guidelines for the Cancer-Related Checkup: Recommendations and Rationale* was published in 1980.¹ In the ensuing years, guidelines for routine screening have changed as new data have become available.

Historical Overview

It has been nearly 20 years since the ACS released a comprehensive set of guidelines to the public and health care professionals for the cancer-related checkup in asymptomatic persons.¹ The 1980 report examined the evidence on the effectiveness, risks, and costs of nine screening tests for cancers of the lung, colon and rectum, cervix, and breast, and included appendices on the methodology for the evidence-based approach that was used at that time. (The nine tests were sputum cytology, chest x-ray, digital rectal examination, sigmoidoscopy, fecal stool occult blood test, Pap test, mammography, clinical breast examination, and breast self-examination.) Other recommendations in the original guidelines addressed age and gender-specific issues for early detection of cancers of the thyroid, testicles, prostate, ovaries, lymph nodes, oral region, and skin that could be applied during routine physical examinations.

In announcing those recommendations, the 1980 report stressed that the ACS had four primary concerns regarding the use of early cancer detection tests:

First, there should be good evidence of test efficacy; second, the medical benefits must outweigh the risks; third, the cost of the test should be reasonable compared with expected benefits; and finally, testing must be practical and feasible.¹

Since these comprehensive guidelines were first released, ACS recommendations for the early detection of *specific* cancers have changed on numerous occasions as new data have become available and as screening technology has evolved.²

The 1980 guidelines report stressed that the recommendations were “*intended to help individual physicians and patients select the best detection protocol for their personal needs,*” and inasmuch, the guidelines were “not recommendations for mass screening programs at public expense.” The report also described how these recommendations might be modified in individual cases based on risk and other considerations: “When there are insufficient data to justify a broad recommendation that everyone be screened, it may still be advisable for individual physicians to recommend a protocol for individual patients that is identical to the broad recommendations...there are important features of an early detection program recommended on an individual basis that may make it acceptable when mass screening is not.”¹

There is an important distinction between a guideline designed to assist individuals and their physicians reach an informed decision and one that is intended as a recommendation for mass screening, even though the distinction may seem academic. As noted in the original 1980 report, the distinction between mass screening and screening based on face-to-face decision-making arose when evidence was limited and/or there was a potential for harm associated with screening. Today, most organizations generally would endorse informed decisions about all screening tests in the presence of information about benefits, limitations, and risks. Thus, rather than regard this distinction as a dichotomy, the interplay between the

need for screening, and evidence of benefits, limitations, and risks, can be thought of as a continuum across which different decisions could be justifiably made based on a range of individual factors.

Where evidence of benefit is strong, i.e., supported by several randomized clinical trials showing a reduction in deaths in the group invited to be screened, the goal of mass screening may be endorsed by most organizations *along* with the goal that the screening-eligible population be fully apprised of benefits, limitations, and risks. The absence of evidence from well-designed randomized trials often is a limiting factor in whether or not a guideline for mass screening can be issued by an organization or endorsed by others, even in the presence of compelling evidence from observational studies that a screening test is effective. Even if a trial is underway, but especially if one is neither planned or not yet underway, end results may not be available to guide policy for a decade or more.

It is understandable that physicians and at-risk individuals would consider testing based on less rigorous, but seemingly persuasive evidence of test effectiveness. On the assumption that there is no solid clinical evidence to the contrary, individuals and their physicians might reasonably decide to undergo testing that is not recommended due to the lack of a solid research base, begin testing earlier, or engage in more or less frequent testing. It is also the case that decisions to engage in testing that has not yet been endorsed may be without merit, wasteful, and harmful. However, if, as was noted in the 1980 report, screening is widely embraced before it has been evaluated in a manner supported by consensus among policy makers, “what happens to each individual will add up to what happens to the population as a whole.”¹ In other words, not only can screening rates begin to approximate what one would expect after a recommendation for population-based screening, but the potential to evaluate the effectiveness of

the screening test to reduce morbidity and mortality will diminish.

For these reasons, it is not only important that the evaluation of promising new screening technology proceeds rapidly, but that individuals and health professionals are fully informed about benefits and limitations. Moreover, with the growing emphasis on informed decision-making, the distinction between recommendations for populations versus individuals is becoming ever more important. Even when the benefits of a screening test are well established, those benefits are not certain in any individual case, nor are screening tests or subsequent follow-up tests without risks. There is a growing appreciation that individuals can be encouraged to undergo screening, but also should be informed about the benefits and limitations of screening, and specifically what to expect from the experience.³

Yearly Updates

In this issue of *CA*, we are inaugurating a yearly report on ACS guidelines, emerging data, and issues that may lead to a reconsideration of one or more specific guidelines in the coming year, as well as relevant issues related to participation in early detection programs, including a summary of the most recent data on adult screening rates. It is our hope that this yearly update will enhance knowledge of ACS guidelines, improve communication and informed decision-making with patients, and focus attention on the unmet potential for early detection programs to reduce mortality from cancer.

Process for the Development of Early Cancer Detection Guidelines

In 1997, the ACS revisited the process for revising existing guidelines and establishing new guidelines for the early detection of cancer in asymptomatic persons. ACS guidelines were conceptualized as a dynamic process involving three stages: De-

velopment, implementation, and evaluation. The second and third stages are key to the integrity of recommendations to the public and health care professionals, as the establishment of guidelines is an empty exercise if they are poorly communicated to the public and provider communities. Moreover, guidelines must be revised in a timely manner when omissions, new technology, or disease-related evidence warrant modifications in existing recommendations.

A set of “guidelines for guideline development”—consisting of nine steps—was formally established to document the specific methodology of scientific and expert judgment as the underpinnings of specific statements and recommendations from the ACS (Table 1). Whereas prior ACS guidelines were based on a similar process of considering scientific evidence and clinical opinion, the establishment of a formal nine-step methodology provides a more deliberate step-wise process to insure that all ACS recommendations have the same methodological and evidence-based process at their core. This process also employs a system for rating strength and consistency of evidence that is similar to that used by the Agency for Health Care Policy and Research’s (AHCPR) US Preventive Services Task Force. It combines the type of evidence and a rating of the quality of the evidence, with greater value placed on data from randomized controlled trials, followed by various observational designs, and expert opinion.

It should be emphasized that there are few instances where gold standard data are available to provide a clear and unambiguous, let alone unassailable, basis for public health policy. Thus, different organizations may evaluate the same data and reach different conclusions. Guideline differences may also be due, simply, to organizations having different periodicity for guideline review. The ACS has determined, for example, that an annual assessment of relevant data will be part of its ongoing guidelines process.

Table 1
American Cancer Society Protocol For Guidelines Development

When developing or revising guidelines, the following nine steps should be followed:

- STEP ONE:** Selection of Guidelines Development Panel—Members to oversee guideline development; multidisciplinary representation
- STEP TWO:** Define Objectives—Define the topic precisely; how will guidelines be used; who are the target groups
- STEP THREE:** Develop an Outcome Model—Describe how guidelines will influence outcomes; define how the evidence is to be assimilated and judged
- STEP FOUR:** Establish Procedures for Documentation—Record-keeping procedures for documenting rationale for each decision
- STEP FIVE:** Define Admissible Evidence—Specify the types of evidence to be considered
- STEP SIX:** Review of Scientific Evidence—Bring together all relevant data for evaluating the benefits and risks of interventions in question; develop draft guidelines
- STEP SEVEN:** Peer Review—Draft Guidelines reviewed by experts as well as members of intended user groups
- STEP EIGHT:** Evaluate Comments and Revise Draft—Evaluate comments from the peer review, based on established criteria, and develop final guideline document
- STEP NINE:** Guideline Evaluation and Revision—Evaluate the impact and acceptability of guidelines with results informing the ongoing guideline review process

Early Detection of Breast Cancer

Since 1977, ACS guidelines for the early detection of breast cancer have been updated five times, most recently in 1992⁴ and 1997.^{4,6} The genesis of the 1997 update was increasing evidence in the literature that the detectable preclinical phase (i.e., the sojourn time) for breast cancer had a shorter duration in premenopausal women compared with postmenopausal women. Data from the Two-County study estimated mean sojourn times for women between the ages of 40 and 49 at 1.7 years, compared with more than 3.3 years for women older than age 50.^{7,8} These findings, coupled with accumulating data on the value of screening for premenopausal women, indicated that the recommendation originally made in 1983, namely that women ages 40 to 49 undergo mammography every one to two years, should be reconsidered, as it was not consistent with accumulating evidence on tumor growth rates in premenopausal women.

While there had been compelling evidence over the years for the value of screening women between 40 and 49 years of age for breast cancer, it was more inferential compared with the evidence of benefit among women between 50 and 69 years of age. Prior to 1997, no single trial had shown a statistically significant reduction in breast cancer deaths among women between 40 and 49, whereas two trials had shown a statistically significant benefit for women aged 50 and older. Between 1995 and 1997, however, new analyses of Swedish clinical trial data and meta-analyses taking advantage of longer periods of follow-up showed increasing benefits for women in their 40s, some of whom were randomized to receive an invitation for breast cancer screening.

Meta-analyses of all trial data, with average follow-up of 12.7 years, resulted in a relative risk (RR) of 0.82 (18% fewer breast cancer deaths in the study group), and a RR of 0.71 (29% fewer deaths in

the study group) for all five Swedish randomized controlled trials.⁹ Each point estimate was statistically significant at the 95% confidence level, although the all-trial meta-analysis had the lowest RR for breast cancer mortality due to the excess rate of breast cancer deaths among control group women in the Canadian National Breast Screening Study.

The meta-analysis of Swedish trials was undertaken because those studies were both contemporary and homogeneous. In addition, each meta-analysis included two second-generation trials, i.e., Gothenburg and Malmö, which applied more advanced screening protocols and observed 44% and 36% fewer breast cancer deaths, respectively, in the invited groups compared with the control groups. At this time, both meta-analyses and two individual trials have shown a statistically significant reduction in breast cancer mortality for women who were between 40 and 49 years old at randomization.

The consistency of results in the other meta-analyses and the recent results from Gothenburg and Malmö, indicate that the potential benefit of screening for pre- versus postmenopausal women is more similar than different. Further, more recent analyses of trial data have provided important insights about screening in different age groups of women and have shown that the wide screening interval used to screen all women was less effective for those younger than 50 years of age.¹⁰⁻¹²

ACS RECOMMENDATIONS

The ACS currently recommends that women begin monthly breast self-examination (BSE) at age 20. Between ages 20 and 39, women should have a clinical breast examination (CBE) every three years, and beginning at age 40, women should have an annual mammogram and CBE (Table 2). (The ACS withdrew its recommendation for a baseline examination between the ages of 35 and 40 at the time of the previous guidelines update.⁵) The ACS also stressed in the updated

guidelines that CBE should take place prior to mammography and, ideally, there should be a short interval between the timing of the two examinations. CBE should be performed prior to mammography because if a mass is identified, it can be brought to the attention of the radiologist. Conversely, if CBE follows mammography and a mass is detected that was not seen on the mammogram, then the patient would need to return for additional directed imaging. There is also the risk that the recent mammogram may offer some false sense of reassurance that a subsequent palpable mass is not worrisome if it wasn't seen on the mammogram.¹³

There is no upper age limit on the ACS breast cancer screening guidelines as long as a woman is in good health. Women at significantly higher risk for breast cancer should talk with their health care providers about initiating screening earlier. Recommendations were recently developed by the Cancer Genetics Studies Consortium¹⁴ for women at higher risk for breast cancer due to significant family history.

Early Detection of Cervical Cancer

The ACS supported the first interdisciplinary conference on cervical cancer screening in 1948 and endorsed annual screening with the Papanicolaou smear (Pap test) in 1957.¹⁵ During the past 40 years, the ACS and other organizations have strongly advocated routine screening for cervical cancer with the Pap test.

It is generally accepted that screening for cancer of the cervix, specifically precancerous lesions, is effective in reducing both the incidence and mortality from cervical cancer. While there has never been a randomized trial of the efficacy of screening for cancer of the cervix, cytologic screening was an accepted part of medical care by both women and providers before the randomized trial with a mortality endpoint had become the standard evaluation methodology.¹⁶ Even so, the logic of cytologic screening has always

Table 2
American Cancer Society Recommendations for the Early Detection of Cancer in Average Risk, Asymptomatic People

Cancer Site	Population	Test or Procedure	Frequency
Breast	Women, age 20+	Breast self-examination Clinical breast examination Mammography	Monthly, starting at age 20 Every 3 years, ages 20-39 Annual, starting at age 40* Annual, starting at age 40
Colorectal	Men & women age 50+	Fecal occult blood test & flexible sigmoidoscopy† -or- Double contrast barium enema† -or- Colonoscopy†	Annual fecal occult blood test and flexible sigmoidoscopy every 5 years starting at age 50 Double contrast barium enema every 5-10 years starting at age 50 Colonoscopy every 10 years starting at age 50
Prostate	Men age 50+	Digital rectal examination & prostate specific antigen test	Annual digital rectal examination and prostate specific antigen test should be offered to men starting at age 50.
Cervix	Women, age 18+	Pap test and pelvic examination	All women who are, or have been, sexually active, or have reached age 18 should have an annual Pap test and pelvic examination. After a woman has had more than 3 consecutive satisfactory normal annual examinations, the Pap test may be performed less frequently at the discretion of the physician.
Cancer-related check-up	Men & women age 20+	Examinations every 3 years from ages 20 to 39 years and annually after age 40. The cancer-related check-up should include: Examination for cancers of the thyroid, testicles, ovaries, lymph nodes, oral cavity, and skin, as well as health counseling about tobacco, sun exposure, diet and nutrition, risk factors, sexual practices, and environmental and occupational exposures.	

* Beginning at age 40, annual CBE should be performed prior to mammography.

† DRE should be performed at the time of sigmoidoscopy, barium enema, and colonoscopy.

measured up well against criteria applied to determine the value of a screening test.

Screening with the Pap smear is comparatively inexpensive and is widely accepted by both the public and providers. Cervical cancer is characterized by a long lead time, with potentially cancerous lesions progressing through a succession of identifiable stages prior to invasive disease. If detected prior to the point of progression to invasive disease, a variety of treatment options are available and the disease is almost certainly curable.

Because of the strong association between infection with particular subtypes of human papilloma virus (HPV) and cervical cancer, HPV testing has been proposed as a strategy for screening, for the triage of mildly abnormal Pap smears, or for risk assignment to identify high-risk groups for more aggressive surveillance.¹⁷⁻²² Current testing for HPV DNA uses the Hybrid Capture test, which is the only test that has been approved by the US Food and Drug Administration for commercial use.²³ The Hybrid Capture test, however, only determines the presence of HPV and not the specific subtype of HPV infection. Polymerase chain reaction, on the other hand, can identify the specific subtype of HPV infection, but there is no commercially approved test at this time.

The potential for HPV testing rests on the assumption that infection with particular subtypes of HPV, in particular HPV type 16 and 18, is a necessary, not just sufficient, etiologic factor in cervical neoplasia.²⁴ HPV infection appears to be an important co-factor in nearly all cervical cancers—as demonstrated by a 99.7% prevalence of HPV DNA in a review of 1,000 cervical cancer specimens.²⁵

At this time, HPV testing does appear to have value for triage of women with atypical squamous cells of undetermined significance and atypical glandular cells of undetermined significance, specifically with regard to greater cost effectiveness in the management of the patient with a mildly abnormal Pap smear, al-

though formal recommendations will await the completion of ongoing studies. On the other hand, routine HPV testing as a basis for selecting a high-risk group would be problematic for several reasons beyond the lack of complete certainty of its status as a necessary precursor to cervical cancer.

First, HPV infection may be active, latent, or transient, and thus the potential for misclassification at testing is high. Second, and even more problematic for a program of risk assessment with cross-population screening, is the fact that exposure opportunities vary in individuals over time. Apart from the fact that a woman may test negative because the infection is latent or the viral load low, she may also become infected in the period after testing.²⁵ Third, as HPV infection is common in adults who have had more than one sexual partner, and as most individuals with HPV infection do not develop cervical cancer, public health education would face an enormous challenge to avoid stigma associated with testing positive for a sexually acquired infection. Finally, HPV testing as a primary screening test, or as an adjunct to the Pap test, would need to meet similar, basic performance criteria required for any screening test. While these caveats do not entirely rule out the potential role of HPV testing, at this time, additional epidemiological and clinical research is needed before HPV infection status is likely to play a key role in secondary prevention strategies for cervical cancer.

There is broad, general consensus on screening recommendations for cervical cancer.²⁶⁻³⁰ Most organizations link the beginning of testing to either the onset of sexual activity, or age 18 if the sexual history is believed to be unreliable. Overall, these guidelines reflect the strong evidence that the underlying etiology of cervical cancer is associated with sexually acquired viral infections, and that the disease has a long latency period.^{28,31-34}

The ACS recommends that women should begin annual screening at the age

of 18, or after the onset of sexual activity, whichever comes first. After three consecutively negative Pap tests, screening may be performed less frequently at the discretion of the physician (Table 2).²⁷ Again, the ACS does not set an upper age limit for screening.

Early Detection of Prostate Cancer

Following widespread implementation of prostate specific antigen (PSA) testing in the late 1980s and early 1990s, prostate cancer incidence in the US increased significantly, consistent with the pattern expected after introduction of a sensitive screening test.³⁵ At the same time, the mean age at diagnosis of prostate cancer was lowered by two years, from 70.7 to 68.8 years.³⁶ Numerous cancer registries reported the shift toward diagnosis at earlier stage of disease than was predicted by the early cohort studies. This increase in the number of prostate cancers detected at early stages also significantly impacted the numbers of patients treated with curative intent. Between 1974 and 1993, the proportion of men diagnosed with prostate cancer treated by radical prostatectomy tripled, from 9.2% to 29.2%.³⁷

PSA was characterized in 1979³⁸ and was first used to monitor patients after prostate cancer treatment as a measure of disease recurrence and/or progression. Strong evidence of its value in detecting early prostate cancer in men with no symptoms or signs of prostate disease was reported, beginning in 1989.^{39,40} In the ensuing years, large numbers of men in the US and elsewhere obtained this test and, as expected with an effective test, the annual incidence rate of prostate cancer increased markedly, peaking prior to the first recommendation for routine testing issued by the ACS.

The principal strengths of the PSA test are its superior sensitivity, reasonable cost, and high patient acceptance. The principal drawback of the test is its imperfect specificity owing to the fact that com-

mon conditions, such as benign prostatic hyperplasia and prostatitis, can cause borderline or even markedly abnormal test results. These false positive results can lead to expensive diagnostic evaluation and unwarranted patient anxiety. At the other extreme, the high sensitivity of the test can result in overdiagnosis, i.e., the chance that small, indolent tumors (which might require no treatment and which may never have surfaced clinically) would be gathered in the same net as aggressive, potentially life-threatening cancers.

The impact of PSA and related testing on mortality was not immediately apparent from early studies. No randomized controlled trials of PSA-based prostate cancer screening had been performed before it became a widespread practice. The observed increase in detection and the stage shift at diagnosis—without eventual impact on mortality—would be evidence that prostate cancer screening was actually ineffective. However, evidence is now accruing that mortality has, in fact, been reduced. Between 1990 and 1995, the prostate cancer death rate in the US for white men younger than 75 years of age fell more than 14%.⁴¹ This may be coincidental to the preceding increase in PSA use, but there are few other changes in treatment or diagnosis that would account for the decline in death rates.

Evidence supporting the effectiveness of PSA alone, or in combination with digital rectal examination (DRE) and transrectal ultrasonography (TRUS), is available from several sources. Early comparative studies showed that prostate cancer detection in asymptomatic men could be increased by PSA and related testing. In addition, it was demonstrated that the stage distribution of screening-detected cancers was much more favorable than that of the general, unscreened population. The ACS National Prostate Cancer Detection Project showed that after five years of annual testing by PSA, DRE, and TRUS, 91.7% of cancers detected were localized to the prostate com-

pared with 66.0% in a contemporaneous national database covering men in the same age groups.⁴²

There remain many uncertainties surrounding the early detection of prostate cancer. From some perspectives, the lack of randomized controlled trial data is sufficient reason to limit introduction of PSA testing, but for most, the key issue relates to problems of potential overdiagnosis.⁴³⁻⁴⁵

Unlike many other tumors, prostate cancers generally develop and progress slowly. Given that the disease typically occurs late in life, some screening-detected cancers are unlikely to be life-threatening. Autopsy studies have shown many men to have clinically occult prostate cancers at the time of their deaths from other causes. To have detected and treated these cancers is unlikely to have yielded benefit. In addition, observation alone is an accepted treatment option for some early prostate cancers, especially in older men. If the patient is only to be watched for progression to more advanced cancer, there is less reason to strive for early detection. Future research may yield prostate cancer screening tools that have greater specificity, detecting tumors that clearly warrant immediate intervention.

ACS RECOMMENDATIONS

In 1992, the ACS published a recommendation that men over 50 years of age be tested annually by DRE and PSA.⁴⁶ The American Urological Association made a similar recommendation. The ACS recommendation was reviewed in 1997, and the most recent guideline is that both the PSA blood test and DRE be offered annually, beginning at age 50, to men who have at least a 10-year life expectancy, as well as to younger men who are at high risk (Table 2).⁴⁷

The ACS also recommends that information be given to patients regarding potential risks and benefits of early detection and treatment to aid informed decisions about testing. Men in high-risk groups, such as those with two or more

affected first-degree relatives (i.e., father and a brother, or two brothers) or African Americans may consider screening at a younger age, perhaps 45.⁴⁷

The American College of Physicians has issued a guideline that is similar to the ACS recommendations, i.e., that physicians should be prepared to discuss the benefits and known harms of screening, diagnosis, and treatment, and then assist men in making individual decisions.⁴⁸

Early Detection of Colorectal Cancer

The goal of screening for colorectal cancer is both the detection of early-stage adenocarcinomas and the detection and removal of adenomatous polyps, for which there is general acceptance of their precursor role in the development of colorectal cancer. Screening reduces colorectal morbidity and mortality by both diagnosing occult disease at a more favorable stage and preventing disease by removing precursor lesions..

There are three common screening tests for colorectal cancer that may be used alone or in combination. These modalities vary according to the degree of underlying evidence supporting their use, potential efficacy, cost-effectiveness, and acceptability among patients. Nevertheless, any of these tests applied in a program of regular surveillance has the potential to reduce deaths from colorectal cancer.

FECAL OCCULT BLOOD TEST

The fecal occult blood test (FOBT) aims to discover the presence of blood in stool, which may derive from colorectal cancer or more commonly from large (greater than 2 cm) polyps. As small polyps do not tend to bleed, and bleeding from cancers or large polyps is intermittent, annual testing, as well as serial specimens during the annual test, are needed.⁴⁹ A positive FOBT test is the trigger for a diagnostic workup to examine the entire colon, either with a double contrast barium enema (DCBE) or colonoscopy, to identify

the source of bleeding. Specimens should be collected from successive bowel movements over a three-day period, following a preparatory diet, with two samples placed on each test card. (Red meats, poultry, fish, and raw vegetables, as well as medications including vitamin C and iron, should not be consumed in the period prior to testing. Nonsteroidal anti-inflammatory drugs and aspirin should be avoided unless the individual is taking low doses of aspirin for vascular disease.) Once three samples have been collected, FOBT cards should be returned according to the provider's instructions. A single sample FOBT with stool collected by DRE during an office visit is not recommended. While convenient, this particular protocol has very poor sensitivity, and false positives may result from DRE-related trauma.⁵⁰

FLEXIBLE SIGMOIDOSCOPY

The advantage of flexible sigmoidoscopy (FSIG) over FOBT is that it allows the examiner to visualize the distal bowel directly, and it has higher sensitivity and specificity for both adenocarcinomas and polyps. The disadvantage of FSIG is that the length of the scope only permits visualization of less than half of the bowel. The combination of annual FOBT and FSIG every five years is superior to either FOBT or FSIG alone, insofar as the two exams together constitute a quasi-total colon exam. FOBT provides for some surveillance in the proximal colon (outside of the reach of FSIG), and FSIG in the distal colon has higher sensitivity and specificity than FOBT and provides an opportunity to visualize cancer and polyps.

RADIOGRAPHIC STUDIES

Radiographic screening for colorectal cancer can be performed with contrast studies using barium alone (single contrast), or barium and air (double contrast). The DCBE is more commonly used as a screening test because of its superiority at detecting smaller lesions and polyps. How-

ever, because the addition of air into the colon can cause some discomfort, the single contrast study may be used for patients who might not tolerate the DCBE well.

COLONOSCOPY

Colonoscopy has a unique advantage among all screening tests for colorectal cancer in that the entire bowel can be visualized, and clinically significant adenomas can be identified and removed. Evidence for the effectiveness of colonoscopy is indirect, in that no large trials with mortality endpoints have been conducted to evaluate the efficacy of screening for colorectal cancer with colonoscopy. However, as is the case with DCBE, the high sensitivity of the test to detect cancer at a more favorable stage and to identify and remove adenomatous polyps has been regarded as sufficient for colonoscopy to be included among recommended screening tests.

A study of the cost-effectiveness of colorectal screening by the Office of Technology Assessment that was subsequently refined by the Agency for Health Care Policy and Research (AHCPR) panel concluded that each of the various alternatives for colorectal cancer screening fell below the \$40,000 *marginal cost per year of life saved* dollar benchmark.^{51,52} However, while each modality is "cost-effective," and will save lives, the screening strategies were not considered equal in their potential to reduce morbidity and mortality. FSIG alone, for example, has the poorest performance as a screening test. Under various assumptions of polyp dwell time, combination screening using annual FOBT and either FSIG or DCBE every 10 years is similarly cost-effective to more frequent schedules. However, if most colorectal cancers develop from adenomas, and if the dwell time is 10 years or longer, the AHCPR panel concluded that screening with colonoscopy had the greatest potential—if the unit cost could be reduced to \$300 or less.⁵¹

A unique issue with colorectal cancer screening, however, is that the higher pro-

gram costs associated with false positives can be viewed as an investment against future screening costs among those individuals with false positive exams. Because screening intervals are wider for DCBE (five to 10 years) and colonoscopy (10 years), an individual with a false positive on FOBT followed by a total colon exam judged to be normal may not require re-screening for five to 10 years.^{50,52,53}

ACS RECOMMENDATIONS

The ACS recommends three options for regular colorectal surveillance beginning at age 50: FOBT and FSIG, with FOBT repeated annually and FSIG repeated every five years after initial screening; total colon exam (TCE) with DCBE every five to 10 years; or TCE with colonoscopy every 10 years. Annual DRE is no longer recommended, due to low sensitivity, but DRE should be performed prior to FSIG, DCBE, or colonoscopy.

A multidisciplinary expert panel convened by the AHCPR issued similar guidelines in 1997, with two additional alternatives for routine screening: Annual FOBT alone (without periodic FSIG) or FSIG alone every five years (without annual FOBT) were considered acceptable based on the panel's judgment that the scientific evidence was sufficiently persuasive of their independent efficacies.

These guidelines have been endorsed by the American College of Gastroenterology, the American Gastroenterological Association, the American Society of Colon and Rectal Surgeons, the American Society for Gastrointestinal Endoscopy, Crohn's and Colitis Foundation of America, the Oncology Nursing Society, and the Society of American Gastrointestinal Endoscopic Surgeons.⁵² The ACS has also endorsed the expert panel's guidelines, but does not recommend periodic FSIG without annual FOBT, or FOBT alone unless no FSIG is available in the community, as each examination alone is less sensitive than the two combined.⁵³ Similar guidelines for higher

risk individuals were also issued by the ACS and the AHCPR panel.^{52,53}

Lung Cancer

At this time, no organization recommends routine screening for lung cancer either among the general adult population or in individuals who are at higher risk due to tobacco or occupational exposures.^{26,54-56}

Lung cancer is unique among the cancers discussed here because the need for a secondary prevention strategy to reduce deaths is due to largely preventable behavior, i.e., cigarette smoking. However, the current public health challenge involves changing behaviors in current and former smokers who began smoking before the health hazards were widely understood, as well as in those who subsequently adopted cigarette smoking despite warnings about the health hazards.

EVIDENCE OF SCREENING EFFECTIVENESS

To date, prospective studies of lung cancer screening have not demonstrated persuasively that screening with chest radiography alone or in combination with sputum cytology saves lives.⁵⁷ While the results of prospective trials have been disappointing in the presence of such significant disease burden, these trials also were methodologically limited at inception in their ability to demonstrate a benefit from screening.^{58,59} Although none of the studies showed fewer deaths in the experimental group compared with the control group, none of the studies compared disease outcome in a group offered screening with a group strictly not invited to, or encouraged to, have screening. Such a study, the multicenter Prostate, Lung, Colorectal, and Ovarian Trial sponsored by the NCI, is now underway.⁶⁰

Low-Dose Computed Tomography

Newer technology appears to be more promising than conventional chest x-rays for the early detection of lung cancer. The Early Lung Cancer Action Project

(ELCAP) was designed to evaluate screening with low-radiation dose computed tomography (CT).⁶¹ In a report on the baseline experience with 1,000 volunteers aged 60 and older with smoking histories of at least 10 pack-years who would be acceptable candidates for thoracic surgery, low-dose CT significantly outperformed conventional chest x-ray in the detection of small pulmonary nodules. Low-dose CT identified 233 participants with non-calcified nodules, and 27 malignancies, of which 26 were resectable and 23 were stage I disease.

In contrast, conventional chest x-ray identified 68 non-calcified nodules, of which seven were malignant, and four were stage I. Workup of positive CT results was based on the size of the nodule and change observed on repeat screening. Based on the average tumor size in the ELCAP study, the authors project five-year survival of 80% for cases diagnosed with low-dose CT.⁶¹ Other promising methods for the early detection of lung cancer include fluorescence bronchoscopy and molecular screening for transformation of bronchial epithelial cells.

In spite of the limitations of existing data, it is generally accepted that lung cancer screening is not effective, whereas it would be more appropriate to regard the current evidence-based situation as one in which there are insufficient data to recommend for or against lung cancer screening. An International Conference on Prevention and Early Diagnosis of Lung Cancer held in Verase, Italy in December 1998, reviewed historical data, as well as information on new technologies for the early detection of lung cancer. At the conclusion of the meeting, conference participants endorsed a statement that there were insufficient data to recommend for or against screening, and that individuals at risk for lung cancer should be informed about the differences in results from trials and case-finding series, so that with aid of their physicians, they would be able to make informed decisions about screening.

Others have also concluded that case-finding is a reasonable approach for individuals at high risk.⁶²

ACS RECOMMENDATIONS

At this time, the ACS does not recommend routine screening for lung cancer among the general adult population or in individuals who are at higher risk due to tobacco or occupational exposures.²⁶ However, the recommendations from the Verase meeting have prompted the ACS to initiate a process for reconsidering the current advice, potentially stressing both the limits of existing data, as well as the paradoxical findings of trial results versus case-finding series.

The Cancer Related Check-up

Apart from participating in screening that has been recommended as part of a population-based initiative, an individual's periodic encounters with clinicians are viewed by the ACS as having potential for health counseling and a cancer-related check-up. Health counseling may include guidance about smoking cessation, diet, physical activity, and the benefits and risks of undergoing various screening tests. These encounters may include case-finding examinations of the thyroid, testicles, ovaries, lymph nodes, oral region, and skin. Also, self-examination of the skin and breasts can be encouraged, as can the importance of awareness of symptoms of testicular cancer in young men. The ACS recommends a cancer-related check-up every three years for asymptomatic individuals between the ages of 20 and 39, and annually for asymptomatic men and women ages 40 and older.

Cancer Screening in the US

Participation in screening depends on acceptance of its value by providers and the public. Low participation in cancer screening programs by both providers and the public can be due to low prioritization,

low awareness, low perceptions of cancer risk, relative inaccessibility of test facilities, costs, and aversion to the test itself, or to test results. However, most studies have shown that each of these barriers can be largely overcome. What is clear is that high levels of participation in a screening program depend on key interactions between providers and individuals.

Studies have consistently shown that the single most important factor in whether or not an individual has ever had a screening test, or has been recently screened, is a recommendation from his or her health care provider.⁶³⁻⁶⁷ Since the average physician/patient encounter is short and typically for acute care, the situational context of the visit is generally not conducive to cancer screening or to discussions about cancer screening or preventive health counseling.⁶⁸ In addition, other factors such as physician/patient ratios, the organization of the practice, lack of preventive health orientation and reminder tools (flowsheets, patient data systems, etc.), neglect, physician specialty, etc., all have been identified as "structural" barriers to screening.^{64,69}

These factors combined lead to a situation where screening commonly occurs opportunistically rather than regularly, and are reflected in less than optimal screening rates among US adults. Although significant progress has been made in screening for some cancers, considerable progress in compliance remains to be made. Clinical practice tools that have been shown to enhance screening include flowsheets, chart reminders, computerized tracking and reminder systems, and group practices.⁷⁰⁻⁷⁵

The data on screening in the US (Table 3) are from the Behavioral Risk Factor Surveillance System (BRFSS) for 1995 to 1997. The BRFSS is an ongoing system of surveys conducted by state health departments in cooperation with the Centers for Disease Control and Prevention. Comparable methods are used from state to state and from year to year.

All 50 states and the District of Columbia each year randomly select a sample of the population of non-institutionalized adults 18 and older who have telephones. Interviews are conducted by telephone and cover selected risk factors and preventive health measures.

The data in Table 3 provide the most recent estimates of screening behaviors among US adults, although the median state value is used as a proxy for a true national estimate. The National Health Interview Survey (NHIS), conducted by the National Center for Health Statistics, is designed to provide better national estimates of screening behaviors. However, when this manuscript was being developed, the most recently published NHIS data were from 1994 for mammography and the Pap test, and from 1992 for colorectal cancer screening. To the authors' knowledge, there were no ongoing, systematic state or national surveillance estimates of prostate cancer screening among men aged 50 and older at the time this article was written.

Reasonably precise estimates of screening behaviors among specific racial and ethnic groups are also scarce. Aggregating several years of data is one way to improve the stability of an estimate for a smaller group, but this assumes that questions were asked the same way for multiple years. This becomes a challenge for colorectal cancer screening behaviors, where the BRFSS questionnaire changed its wording from "proctoscopic exam" in 1995 to "sigmoidoscopy or proctoscopy" in 1997, and to "sigmoidoscopy or colonoscopy" in 1999.

Conclusions

At this time, the early detection of cancer and precursor lesions represents a largely unmet potential to reduce morbidity and mortality from malignancies. Presently, screening in the US is opportunistic, and thus the absence of a systematic approach to screening and follow-up means a high

Table 3
Prevalence (%) of Cancer Screening Among US Adults
(BRFSS, 1995-1997)

	Age	Males	Females	Total
Colorectal Cancer				
FISG*	50+	Median: 45.3 Range: (19.0 - 58.1)	Median: 37.7 Range: (24.6 - 49.0)	Median: 40.8 Range: (22.3 - 51.6)
FOBT†	50+	Median: 24.3 Range: (7.9 - 33.2)	Median: 28.7 Range: (15.6 - 42.4)	Median: 26.0 Range: (13.5 - 37.8)
DRE‡	40+	Median: 41.5 Range: (23.4 - 56.6)	Median: 41.4 Range: (27.2 - 52.1)	Median: 40.7 Range: (27.3 - 52.8)
Prostate Cancer				
PSA blood test and DRE§	50+	NA	—	—
Breast Cancer				
Recent mammogram¶	40-49	—	Median 65.4 Range: (50.2-74.4)	—
	50+	—	Median: 57.0 Range: (41.8-70.1)	—
	65+	—	Median: 54.1 Range: (38.3-67.7)	—
Cervical Cancer				
Recent Pap test**	18-44	—	Median: 84.6 Range: (79.0-92.5)	—
	45+	—	Median: 73.4 Range: (60.1-86.8)	—

Key: Flexible sigmoidoscopy = FISG; fecal occult blood test = FOBT; digital rectal examination = DRE; prostate specific antigen = PSA; Papanicolaou = Pap
 NA = data not available
 * Ever had a sigmoidoscopy. Source: BRFSS, 1997.
 † Had blood stool test in the past 2 years. Source: BRFSS, 1997.
 ‡ Rectal exam within the past year. Source: BRFSS, 1995.
 § Both a PSA blood test and DRE within the past year.
 ¶ Women (40-49) who had mammography within last 2 years; women (50+) who had mammography within the last year. Source: BRFSS, 1996.
 ** Within past 2 years (women with a uterine cervix). Source: BRFSS, 1996.

proportion of incident cases have less than optimal prognoses. Improvements in screening quality control and quality assurance can lead to gains in both sensitivity and specificity, thus improving performance and reducing avoidable costs.

It is likely that the current screening protocols will be eventually left behind to be replaced by genetic and molecular markers of risk and disease, as well as newer screening technologies that achieve gains in mean sojourn time,

sensitivity, and specificity. Ultimately, screening failures will be measured not by death from cancer, but by the development of invasive disease. As we anticipate these exciting new developments, we must be reminded of the value of the technology at hand and its current underutilization. There is great potential within our reach if our health care system will dedicate itself to achieving an organized and systematic approach to early cancer detection. **CA**

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