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American Cancer Society Guidelines for the Early Detection of Cancer: Update of Early Detection Guidelines for Prostate, Colorectal, and Endometrial Cancers

ALSO: Update 2001—Testing for Early Lung Cancer Detection

Robert A. Smith, PhD; Andrew C. von Eschenbach, MD; Richard Wender, MD (for the ACS Prostate Cancer Advisory Committee); Bernard Levin, MD; Tim Byers, MD; David Rothenberger, MD; Donato Brooks, MD (for the ACS Colorectal Cancer Advisory Committee); William Creasman, MD; Carmel Cohen, MD; Carolyn Runowicz, MD; Debbie Saslow, PhD (for the ACS Endometrial Cancer Advisory Committee); Vilma Cokkinides, PhD; Harmon Eyre, MD

ABSTRACT

Updates to the American Cancer Society (ACS) guidelines regarding screening for the early detection of prostate, colorectal, and endometrial cancers, based on the recommendations of recent ACS workshops, are presented. Additionally, the authors review the “cancer-related check-up,” clinical encounters that provide case-finding and health counseling opportunities. Finally, the ACS is issuing an updated narrative related to testing for early lung cancer detection for clinicians and individuals at high risk of lung cancer in light of emerging data on new imaging technologies.

Although it is likely that current screening protocols will be supplanted in the future by newer, more effective technologies, the establishment of an organized and systematic approach to early cancer detection would lead to greater utilization of existing technology and greater progress in cancer control. (CA Cancer J Clin 2001;51:38-75.)

INTRODUCTION

Last year, the American Cancer Society (ACS) announced that it was inaugurating a yearly report on its cancer detection guidelines. The annual report would be a single summary source on current ACS guidelines for the early detection of cancer, including background and rationale for guidelines that had been updated in the prior year, announcements of upcoming guideline reviews, and a summary of the most recent data on adult cancer screening rates.

During 2000, the ACS reviewed and revised early detection guidelines for prostate cancer, colorectal cancer, and endometrial cancer, and updated the narrative related
to the use of early detection tests for lung cancer. This report includes the recommendations and rationale for the updated guidelines, as well as a summary table of all ACS early cancer detection guidelines (Table 1).

The rationales for guidelines not updated in this report are available in the most recent updates for cervical cancer, colorectal cancer, and breast cancer, and also are included in the recent first summary report of the ACS early detection guidelines, available at www.cancer.org. That report also included a description of the ACS process for the development or update of a cancer screening guideline.

Recommendations from the American Cancer Society Workshop on Early Prostate Cancer Detection, May 4-6, 2000

Background

In 2001, approximately 198,100 men will be diagnosed with prostate cancer, and 31,500 will die from this disease. Among men prostate cancer is the most common cancer diagnosed, and the second leading cause of death from cancer. Incidence and mortality rates are considerably higher among African Americans compared with Caucasians, Asians, and Native Americans.

The recent trend in prostate cancer incidence is marked by a dramatic increase in incidence rates beginning in the mid-1980s and peaking in 1993, mostly due to the introduction of prostate specific antigen (PSA) testing for early prostate cancer detection. During that period, prostate cancer incidence rates increased 108%. Incidence rates declined just as dramatically between 1992 and 1995, with an estimated annual percentage drop of 4.2%, and since 1995, rates have been relatively stable. Overall, prostate cancer mortality rates declined between 1994 and 1997 at an annual average rate of 4.4%, with death rates declining in white men at an average annual rate of 4.5%, and in black men at a average annual rate of 2.3%.

Prostate cancer five-year survival is nearly 100% when the disease is diagnosed at a local or regional stage, but poor when diagnosed with distant metastases (32.6%). Most men with prostate cancer are diagnosed with local or regional disease (80%), but overall, both stage distribution and survival is poorer in African-American men compared with white men.

Survival is strongly influenced by the histologic grade of tumors, with five-year survival nearly 100% among men with well-differentiated disease at the time of diagnosis compared with 73.5% for men with poorly-differentiated disease. Five-year survival tends to be poorer in men younger than 50 probably because the disease tends to be more advanced at the time of diagnosis.

Guidelines Development

In 1992, the ACS issued a guideline for average-risk men, recommending annual screening for prostate cancer with digital rectal examination (DRE) and serum PSA measurement beginning at age 50. In 1997, the ACS convened a workshop to review the recommendations for testing for early prostate cancer detection, and, based on the review of...
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### Guidelines for the Early Detection of Cancer

* Beginning at age 40, annual clinical breast examination should be performed prior to mammography.
† Flexible sigmoidoscopy together with FOBT is preferred compared with FOBT or flexible sigmoidoscopy alone.
‡ Information should be provided to men about the benefits and limitations of testing.

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

<table>
<thead>
<tr>
<th>Cancer Site</th>
<th>Population</th>
<th>Test or Procedure</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast</td>
<td>Women, age 20+</td>
<td>Breast self-examination</td>
<td>Monthly, starting at age 20</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Clinical breast examination</td>
<td>Every 3 years, ages 20-39</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mammography</td>
<td>Annual, starting at age 40*</td>
</tr>
<tr>
<td>Colorectal</td>
<td>Men &amp; women, age 50+</td>
<td>Fecal occult blood test (FOBT) &amp; flexible sigmoidoscopy†</td>
<td>Annual FOBT and flexible sigmoidoscopy every 5 years, starting at age 50</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Flexible sigmoidoscopy</td>
<td>Every 5 years, starting at age 50</td>
</tr>
<tr>
<td></td>
<td></td>
<td>FOBT</td>
<td>Annual, starting at age 50</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Colonoscopy</td>
<td>Colonoscopy every 10 years, starting at age 50</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Double contrast barium enema (DCBE)†</td>
<td>DCBE every 5 years, starting at age 50</td>
</tr>
<tr>
<td>Prostate</td>
<td>Men, age 50+</td>
<td>Digital rectal examination &amp; prostate specific antigen test</td>
<td>The PSA test and the DRE should be offered annually, starting at age 50, for men who have a life expectancy of at least 10 years.‡</td>
</tr>
<tr>
<td>Cervix</td>
<td>Women, age 18+</td>
<td>Pap test and pelvic examination</td>
<td>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 3 or more consecutive satisfactory normal annual examinations, the Pap test may be performed less frequently at the discretion of the physician.</td>
</tr>
<tr>
<td>Cancer-related check-up</td>
<td>Men &amp; women, age 20+</td>
<td>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.</td>
<td></td>
</tr>
</tbody>
</table>
RECENT DATA ON PROSTATE CANCER TESTING FOR EARLY DETECTION

International data were presented that are consistent with an association between prostate cancer testing and reduced prostate cancer mortality. Although randomized trial data confirming a reduction in mortality as a result of testing are not yet available, the consensus of the workshop participants was that evidence indicating a benefit from testing is significantly stronger today than it was in 1997.

In 1993, PSA testing was made available to men ages 45 to 75 in Tyrol, Austria (population: 331,410). Some testing with DRE and PSA had already taken place between 1990 and 1993. Of 65,123 men in the county ages 45 to 75, 32.3% were tested in the first year, and 62% of men were tested at least once during the first four years of the study. Registry data from Tyrol indicate a significant shift towards more favorable stage at diagnosis, and an increase in the proportion of cases with organ-confined disease. In Tyrol, mortality remained constant between 1970 and 1993, but has declined 42% since 1994 (most recent update is 1998). In other parts of Austria, prostate cancer mortality rates are unchanged. The decrease in observed versus expected mortality is statistically significant.

Recent analysis of the National Cancer Institute’s (NCI) Surveillance Epidemiology, and End Results (SEER) data shows that prostate cancer mortality in white men younger than age 85 has declined to levels below those that existed prior to the PSA era, which began about 1986. In fact, for men ages 60 to 79, mortality rates in 1997 were lower than in any year since 1950.

In the absence of evidence of mortality reduction from a prospective randomized trial [the Prostate Lung Colorectal and Ovary (PLCO) trial is still in progress], Gann...
proposed that a reduction in prostate cancer mortality below that which existed prior to the introduction of PSA testing would be compelling evidence of the efficacy of the screening test.14 Following Gann’s lead, Tarone, Chu, and Brawley evaluated recent age-specific trends in stage-specific survival rates among white men from the SEER database. Since it is distant-stage disease that is significantly more likely to be fatal in the near term compared with regional disease, the observation that incidence rates of distant disease were declining while local and regional disease incidence rates were increasing is highly suggestive of a screening effect. They observed that the recent decline in mortality is associated with a decline in the incidence rate of advanced disease, and especially with an increase in the detection of organ-confined (i.e., non-metastatic), high-grade disease.12

Trend data from Olmsted County, MN, suggest a testing effect on mortality trends. Mortality rates increased from 1980 to 1992, and subsequently have declined 22% between 1992 and 1997. The decline in mortality was preceded by a decline in the incidence rate of advanced disease.15 Additional data supporting an effect of PSA testing on reducing prostate cancer mortality from a Department of Defense prospective population study (2,042 prostate cancer patients registered at the Center for Prostate Cancer Research, Walter Reed Army Medical Center) showed a decline in the rate of advanced disease and a corresponding improvement in disease-specific survival.16

While organizations differ in their recommendations about testing for early prostate cancer detection, there is greater agreement that physicians should be prepared to identify men who potentially would benefit from testing and provide information about prostate cancer risk, benefits, limitations, and potential harms associated with testing.17 However, evidence suggests that there are differences among physicians in what information is regarded as important for making informed decisions, and differences between what physicians and patients regard as important information for making informed decisions.18 Wolf et al have shown that patients differ in their decisions about testing, as well as individual circumstances (age, socioeconomic status, perceived risk, family history, etc.).19,20 To the extent that many men are uninformed about prostate cancer in general, and more specifically about testing for early prostate cancer detection, evidence suggests that recommendations for informed decision-making require supportive strategies for men and their health care providers.21
begin testing at age 45. Information should be provided to patients about benefits and limitations of testing. Specifically, prior to testing, men should have an opportunity to learn about the benefits and limitations of testing for early prostate cancer detection and treatment. Men who ask the clinician to make the testing decision on their behalf should be tested. A clinical policy of not offering testing, or discouraging testing in men who request early prostate cancer detection tests, is inappropriate.

High-risk groups include men of African descent (specifically, sub-Saharan African descent) and men with a first-degree relative diagnosed at a young age.\(^{2,3}\) Risk increases with the number of first-degree relatives affected by prostate cancer. The workgroup recommended that these men begin testing for early prostate cancer detection at age 45. Among men of African descent, age-specific risk increases steadily beginning at age 45. Men at appreciably higher risk of prostate cancer due to multiple first-degree relatives who were diagnosed with prostate cancer at an early age could begin testing at age 40. However, if PSA is less than 1.0 ng/dl, no additional testing is needed until age 45. If PSA is greater than 1.0 ng/dl but less than 2.5 ng/dl, annual testing is recommended. If PSA is 2.5 ng/dl or greater, further evaluation with biopsy should be considered. Men at high risk also should be informed about the benefits, limitations, and uncertainties associated with testing for early prostate cancer detection.

**Prostate Cancer Early Detection Tests**

Measurement of serum PSA level is the most accurate method for the detection of prostate cancer and is superior to DRE. Nevertheless, DRE should be included in testing whenever appropriate. The positive predictive value of an abnormal DRE in patients with low PSA levels (i.e., 1.0 ng/dl) is very low and does not warrant further evaluation. In men for whom DRE is an obstacle to testing, PSA alone is an acceptable alternative.

Since PSA is prostate-tissue specific and not prostate-cancer specific, there is no absolute value that is applicable to all men. The range of “normal” PSA levels has conventionally been considered to be between zero and 4.0 ng/dl. A lower cut-off value of 2.5 ng/dl has been shown to improve the early detection of organ-confined prostate cancers; however, this also increases the number of men undergoing biopsy in whom no cancer is detected.

Age-specific reference ranges and PSA density (amount/volume) have been employed to improve specificity. Because PSA is prostate-tissue specific and not prostate-cancer specific, elevations of PSA into the “abnormal” range may occur due to benign prostatic hyperplasia or prostatitis. Benign prostate tissue produces a higher percentage of free PSA than does cancerous tissue. This biologic observation can be used to improve the predictive value of the test in men with elevated total PSA levels. For men with PSA results between 4.0 and 10.0 ng/dl, restricting transrectal ultrasound-guided biopsy to men with less than 20% free-PSA improves testing accuracy. Applying this strategy to men with PSA levels between 2.5 and 10.0 ng/dl may lead to detection of early disease in a larger number of men.
and may result in a lower biopsy rate compared with older strategies.

**Conclusion**

The new guideline represents a stronger recommendation than was issued in the 1997 update. Because the potential benefits of early detection must be balanced against potential risks, the new guideline is consistent with the 1997 guideline insofar as it is not a recommendation for mass screening for prostate cancer in average-risk men. Rather, it is an endorsement that men should have an opportunity to be tested and should actively participate in the testing decision. Following a discussion of benefits and limitations of prostate cancer testing, some men may choose not to be tested at that time. However, by including “should” in the recommendation, the ACS is more clearly stating that asymptomatic men age 50 and older ought to have an annual opportunity to make an informed decision about testing for early prostate cancer detection. For this reason, the Advisory Group felt that it is improper to discourage testing, or not to offer testing.

The advisory group recommends that clinicians devote adequate time to inform patients about the potential benefits and risks of testing for early prostate cancer detection. Utilizing educational tools as a way to efficiently inform patients is encouraged. Asking questions to assess the patient’s beliefs about prostate cancer and the treatments for this disease may help the patient to arrive at a clear preference.

Despite ideal efforts to share the decision-making process with patients, some individuals will be unable or unwilling to state a clear preference and will prefer to follow the clinician’s advice to be tested or to forgo testing. For these individuals, the advisory group believes that the potential to prevent a premature prostate cancer death is high enough to justify testing this informed individual. This wording has been added to the new guideline.

The new guideline continues to emphasize the importance of informed decision-making as opposed to screening individuals without the opportunity to participate in the decision-making process. Meeting this standard will usually require that testing take place within the context of the clinician-patient relationship with the opportunity to discuss potential benefits and limitations of testing. Screening individuals outside of the clinical arena, for example, in community settings or health fairs, is only warranted if patients have the opportunity to participate in an educational process and to discuss their decision with a clinician. The advisory group believes that individuals are more likely to discuss these issues freely with their own clinicians and recommends that testing for early prostate cancer detection should occur within the context of the patient’s usual clinical care.

**American Cancer Society Guidelines on Screening and Surveillance for the Early Detection of Adenomatous Polyps and Cancer—Update 2001**

**Background**

In 2001, an estimated 138,900 Americans will be diagnosed with colorectal cancer and about 57,100 will die from this disease. Colorectal cancer is second only to lung cancer as a cause of cancer death in the US. Among US adults, colorectal cancer incidence and mortality rates have declined between 1985 and 1997 at an average annual rate of 1.6% and 1.8%, respectively. However, these encouraging national trends are more evident in
whites than in blacks, and small incremental declines in disease burden presently are overshadowed by both the sizeable public health costs from colorectal cancer and the unrealized potential for prevention.

Without preventive interventions, about 5.6% of Americans will develop colorectal cancer at some point during their lives. When colorectal cancer is diagnosed at an early, localized stage, five-year survival is 90%, yet only 37% of incident cases are diagnosed while still localized. The same methods used to detect colorectal cancers at early, curable stages can also identify and remove adenomas, which give rise to colorectal cancer. Methods for early detection can therefore actually prevent colorectal cancer.

**Guidelines Development**

Since 1980, the ACS has recommended screening for colorectal cancer, and guidelines for colorectal cancer screening were last updated in 1997. Late in 2000, the ACS Colorectal Cancer Advisory Committee convened a workshop in Atlanta to review recent scientific evidence for colorectal cancer screening. The workshop re-visited the historical evidence, but focused especially on research findings from the past five years and studies now underway.

During the current guideline review, published articles related to colorectal cancer, screening, risk, and risk factors were identified using MEDLINE (National Library of Medicine) for the years 1995 through 2000, bibliographies of identified articles, and through the personal files of the advisory group and expert panel members. Key reports were distributed to workshop attendees prior to the October 2000 meeting. Following the workshop, ACS Colorectal Cancer Advisory Group members discussed new evidence and deliberated over guidelines modifications, which were then decided by consensus. Each advisory group member and workshop attendee reviewed the draft of this manuscript.

**DEFINITIONS: EARLY DETECTION METHODS**

**Fecal Occult Blood Test**

Fecal occult blood testing (FOBT) refers to the implementation of the protocol for collecting and testing six samples from three consecutive stools at home. Prior to testing with a guaiac-based test, individuals are instructed to avoid non-steroidal anti-inflammatory drugs such as ibuprofen, naproxen, or aspirin (more than one adult aspirin per day) for seven days prior to testing; to avoid vitamin C in excess of 250 mg from either supplements or citrus fruits and juices for three days before testing; and to avoid red meats for three days before testing.

A single test of a stool sample in the clinical setting (as, for instance, is often done with the stool sample collected on the fingertip during a DRE) is not an adequate substitute for the recommended procedure of collecting two samples from three consecutive specimens. This is because colonic neoplasms often bleed intermittently and/or because blood is often not present throughout the entire stool. Further, several studies have shown that the yield of the three-sample protocol is higher than that for the first sample.
The most commonly used FOBTs are guaiac-based tests, such as Hemoccult II® and Hemo-
cuccilSENSA® (Smith, Kline, and French, Sunnyvale, CA), which are uncomplicated and can be pro-
cessed in the physician’s office. There are immunochemical-based FOBTs that may be processed in a
laboratory, or in a doctor’s office, but they are much less commonly used.29

Flexible Sigmoidoscopy

Flexible sigmoidoscopy refers to a procedure that allows direct
visual examination of the distal portion of the colorectum by a
trained examiner using a flexible 60-cm endoscope following a
satisfactory cleansing of the descending and sigmoid colon and
rectum. Even though flexible sigmoidoscopy visualizes only the
distal portion of the colorectum, when the scope reaches the
splenic flexure, it can nonetheless identify approximately 80% of
those individuals with a significant neoplasm anywhere in the
colorectum.30 This is because people often have more than one
adenoma within the colorectum, and adenomas in the distal
colorectum can be a marker of risk for lesions in the proximal colorectum.

Colonoscopy

Colonoscopy refers to a procedure that allows direct visual examination of the entire
colorectum using a colonoscope. Ideally, the colonoscopic examination should be extended
to the cecum. Even though some benign and
malignant neoplasms can be missed by colonoscopy, it is considered the most sensitive
of the screening methods. Thus, most other detection methods have been compared with
colonoscopy, which is considered the standard.31

Double Contrast Barium Enema

Double contrast barium enema (DCBE) refers to a procedure that allows radiologic
examination of the entire colorectum by instilling both barium and air to define the contours of the colorectal mucosa.32
DCBE is less sensitive than colonoscopy for
visualizing smaller neoplasms, especially ade-
nomas smaller than 1 cm.25

Digital Rectal Examination

DRE refers to the palpation of the anus and
lower rectum by the practitioner using a gloved
finger. Although DRE is a useful method for
identifying masses in the anal canal or lower rectum, it has very poor sensitivity for detecting
colorectal cancer due to limited reach. While
DRE is often included as part of a routine
physical examination, it is not recommended as a
stand-alone screening test for colorectal
cancer. However, DRE should be performed
prior to insertion of a sigmoidoscope or
colonoscope.

New Screening Methods

Several new methods being developed may
be clinically useful for colorectal screening
in the future. Computed tomography
colonography (CT colonography, also
sometimes called virtual colonoscopy) is a
procedure that allows imaging the colorectum
by CT radiographs.33 Molecular screening
refers to a method of detecting mutations
associated with colorectal neoplasia in the
DNA of stool samples. This methodology is
now being evaluated as a potential screening
Neither of these methods is currently ready for widespread clinical application outside the context of controlled clinical trials.

The specific genetic events leading to the development of colorectal cancer are rapidly being elucidated.\(^{36}\) Colorectal adenomas, which are normally polypoid, but can sometimes be flat, are clearly the precursor lesions for almost all colorectal cancers, and adenomas usually are present for several years before they evolve to cancer.\(^{37}\) Ideally, screening the colorectum should first find and remove colorectal adenomas, thus preventing colorectal cancer, and second, detect early colorectal cancer. Not all or even most adenomas will become malignant, but insofar as there is no way to determine which will progress and which will not, the best strategy is to remove them.

The ACS guidelines for the early detection of colorectal adenomas and colorectal cancer are summarized in Tables 2 and 3. These guidelines offer a set of screening choices for different levels of colorectal cancer risk. Each of the choices has inherent characteristics related to accuracy, prevention potential, costs, and risks. Following is an explanation of the main features of these updated ACS recommendations.

**Recommendations for Individuals at Average Risk**

Approximately 70% to 80% of all colorectal cancers occur among people at "average risk."\(^{26}\) Average risk is defined by exclusion of anyone who is not otherwise defined as being at increased risk or very high risk (see below). There are no factors yet identified that would place a person at lower-than-average risk with respect to an initial recommendation for screening.

Adults at average risk should begin colorectal cancer screening by age 50. Although the incidence of invasive disease is low at age 50, about 25% of adults at age 50 will have adenomatous polyps.\(^{36}\) Thus, the underlying logic for beginning screening at age 50 is related more to the potential to detect and remove precursor lesions than to the potential for detection of invasive disease.

The 2001 guideline provides five options for screening of average-risk individuals as summarized in Table 2. The screening options are:

1. FOBT annually
2. Flexible sigmoidoscopy every five years
3. Annual FOBT plus flexible sigmoidoscopy every five years
4. DCBE every five years
5. Colonoscopy every 10 years

Annual FOBT alone has been shown to reduce risk of death from colorectal cancer by about one third when repeated annually.\(^{38}\) A positive FOBT should be followed by a colonoscopy because of the possibility that an important lesion can be visualized and biopsied during the examination. If a clinically relevant source of bleeding is not identified, then a source outside the large bowel should be investigated. An alternative to colonoscopy is DCBE, or flexible sigmoidoscopy followed by DCBE. The addition of flexible sigmoidoscopy to the DCBE is based on the likely greater sensitivity of endoscopy for smaller lesions,
although the incremental benefit of flexible sigmoidoscopy when added to the DCBE has not been well evaluated. Because of the importance of accuracy in a diagnostic workup, these examinations should be performed by experienced practitioners or centers.

Flexible sigmoidoscopy every five years also is regarded as an effective screening test. Evidence from case control studies has shown significant mortality reductions from cancers within reach of the sigmoidoscope, as well as a lower incidence of colorectal cancer associated with a prior history of screening with sigmoidoscopy. The periodicity for regular screening with flexible sigmoidoscopy is more frequent than for colonoscopy because of a range of factors that may affect the overall sensitivity of flexible sigmoidoscopy: (1) flexible sigmoidoscopy generally is not done by specialists and thus the range of practitioner experience and expertise is variable; (2) bowel preparation usually is less complete than for colonoscopy, meaning that important lesions may be obscured by stool; and (3) as no sedation is given with flexible sigmoidoscopy, patient discomfort or spasm may interfere...
with the completeness of the test. Two randomized, controlled trials are now underway to measure the benefits of sigmoidoscopic screening, but results will not be known for several years.43, 44

Because combining flexible sigmoidoscopy with FOBT can increase the benefits of either test alone, the ACS regards annual FOBT accompanied by flexible sigmoidoscopy every five years as a better choice than either FOBT or flexible sigmoidoscopy alone.39,40,42 FOBT offers the potential to detect occult blood from a lesion anywhere in the colorectum, while flexible sigmoidoscopy is superior at detecting distal polyps as well as non-bleeding advanced neoplasias. Both direct and indirect evidence suggest combined testing with FOBT and flexible sigmoidoscopy offers advantages over either FOBT or flexible sigmoidoscopy alone.26,45

Examining the entire colorectum, either by colonoscopy every 10 years30 or by DCBE every five years,32 is also a good choice. A supplementary DCBE may be needed if a colonoscopic exam fails to reach the cecum, and a supplementary colonoscopy may be needed if a DCBE identifies a possible lesion, or does not adequately visualize the entire colorectum. DCBE is usually less expensive than colonoscopy, but colonoscopy appears to have greater sensitivity and provides direct visualization of lesions, which can be biopsied or excised during the procedure.

The choice of colonoscopy or DCBE for screening can be made on an individual basis, depending on factors such as personal preference, cost, feasibility, tolerance of potential complications, and the local availability of trained clinicians able to offer a high-quality examination. For those who elect either colonoscopy or DCBE for screening, there is no need for annual FOBT.

Recommendations for Individuals at Increased risk

Approximately 15% to 20% of colorectal cancers occur among people at “increased risk” (approximately twice average risk).26 People who have been diagnosed as having adenomatous polyps should have a colonoscopy to remove all polyps from the colorectum, after which a colonoscopic exam should be repeated at an interval to be determined on the basis of the size, multiplicity, and histologic appearance of the adenoma(s) (Table 3).26 If a colonoscopic examination is not available, not feasible, or not desired by the patient, a DCBE, or flexible sigmoidoscopy followed by a DCBE can be used for surveillance. A similar recommendation applies to individuals with a personal history of curative-intent resection of colorectal cancer (Table 2).

A family history of either colorectal cancer or colorectal adenomas increases one’s risk of developing colorectal cancer.46,47 Risk is increased for individuals with a family history involving first-degree relatives, and is even higher if a first-degree relative (parent, sibling, or offspring) has had a colorectal cancer or an adenomatous polyp diagnosed before age 60 years, and/or if more than one first-degree relative has been affected at any age. On the other hand, individuals with a single first-degree relative diagnosed with colorectal cancer or an adenomatous polyp after age 60, or with affected relatives who are more distant than first degree, can be considered to be at “average risk.”

People with a family history of either colorectal cancer or colorectal adenomas that occurred in a first-degree relative before age
Guidelines for the Early Detection of Cancer

### TABLE 3

<table>
<thead>
<tr>
<th>Risk Category</th>
<th>Age to Begin</th>
<th>Recommendation</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>INCREASED RISK</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>People with a single, small (&lt; 1 cm) adenoma</td>
<td>3-6 years after the initial polypectomy</td>
<td>Colonoscopy&lt;sup&gt;1&lt;/sup&gt;</td>
<td>If the exam is normal, the patient can thereafter be screened as per average risk guidelines.</td>
</tr>
<tr>
<td>People with a large (&gt;1 cm) adenoma, multiple adenomas, or adenomas with high-grade dysplasia or villous change</td>
<td>Within 3 years after the initial polypectomy</td>
<td>Colonoscopy&lt;sup&gt;1&lt;/sup&gt;</td>
<td>If normal, repeat examination in 3 years; If normal then, the patient can thereafter be screened as per average risk guidelines.</td>
</tr>
<tr>
<td>Personal history of curative-intent resection of colorectal cancer</td>
<td>Within 1 year after cancer resection</td>
<td>Colonoscopy&lt;sup&gt;1&lt;/sup&gt;</td>
<td>If normal, repeat examination in 3 years; If normal then, repeat examination every 5 years.</td>
</tr>
<tr>
<td>Either colorectal cancer or adenomatous polyps, in any first-degree relative before age 60, or in two or more first-degree relatives at any age (if not a hereditary syndrome)</td>
<td>Age 40, or 10 years before the youngest case in the immediate family</td>
<td>Colonoscopy&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Every 5-10 years. Colorectal cancer in relatives more distant than first-degree does not increase risk substantially above the average risk group.</td>
</tr>
<tr>
<td><strong>HIGH RISK</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Family history of familial adenomatous polyposis (FAP)</td>
<td>Puberty</td>
<td>Early surveillance with endoscopy and counseling to consider genetic testing</td>
<td>If the genetic test is positive, colectomy is indicated. These patients are best referred to a center with experience in the management of FAP.</td>
</tr>
<tr>
<td>Family history of hereditary non-polyposis colon cancer (HNPCC)</td>
<td>Age 21</td>
<td>Colonoscopy and counseling to consider genetic testing</td>
<td>If the genetic test is positive or if the patient has not had genetic testing, every 1-2 years until age 40, then annually. These patients are best referred to a center with experience in the management of HNPCC.</td>
</tr>
<tr>
<td>Inflammatory bowel disease</td>
<td>Cancer risk begins to be significant 8 years after the onset of pancolitis, or 12-15 years after the onset of left-sided colitis</td>
<td>Colonoscopy with biopsies for dysplasia</td>
<td>Every 1-2 years. These patients are best referred to a center with experience in the surveillance and management of inflammatory bowel disease.</td>
</tr>
</tbody>
</table>

Colonoscopy is unavailable, not feasible, or not desired by the patient, double contrast barium enema alone, or the combination of flexible sigmoidoscopy and double contrast barium enema are acceptable alternatives. Adding flexible sigmoidoscopy to DCBE may provide a more comprehensive diagnostic evaluation than DCBE alone in finding significant lesions. A supplementary DCBE may be needed if a colonoscopic exam fails to reach the cecum, and a supplementary colonoscopy may be needed if a DCBE identifies a possible lesion, or does not adequately visualize the entire colorectum.
60, or in multiple first-degree relatives of any age (if not a hereditary syndrome), should have a colonoscopy, which should be repeated at intervals to be determined on the basis of the initial examination (Table 3). If a colonoscopy is not available, not feasible, or not desired by the patient, a DCBE, or flexible sigmoidoscopy followed by a DCBE can be used.

Recommendations for Individuals at High Risk

Approximately 5% to 10% of all colorectal cancers occur among people at “high risk,” defined as much greater than twice average risk.26 Along a continuum of “high risk” are those individuals with inflammatory bowel disease and those individuals with one of two hereditary syndromes that place them at very high risk for colorectal cancer.

When either ulcerative colitis or Crohn’s disease affects a significant extent of the colorectum, the risk of colorectal cancer is greatly increased beginning eight years after the onset of colorectal symptoms.48 Individuals with extensive inflammatory bowel disease affecting the colon should begin endoscopic surveillance with biopsy for dysplasia every one to two years after eight years of symptoms. Prophylactic colectomy should be considered in the presence of persistent dysplasia.

Familial adenomatous polyposis syndrome (FAP) is a genetic condition affecting one in 10,000 people that is caused by a mutation in the APC gene on chromosome 5.47 People with FAP develop hundreds of colorectal polyps and will almost certainly develop colorectal cancer unless the colon is removed.

Hereditary non-polyposis colorectal cancer (HNPCC) syndrome is an inherited genetic condition that can also cause colorectal cancer among many people in a family, even though multiple polyps are not present. HNPCC is caused by mutations in mismatch repair genes located on chromosomes 2, 3, or 7.47 HNPCC has been classically defined as colorectal cancer in three or more family members, two of whom are first-degree relatives of the third, involving people in at least two generations, and with at least one person diagnosed with colorectal cancer under age 50. However, other variants of this classic syndrome exist.

As genetic tests are now available to detect the mutations that lead to FAP and HNPCC, genetic counseling should be offered to individuals with family histories suggestive of these hereditary syndromes (Table 3).

CHANGES FROM THE 1997 RECOMMENDATION

These updated ACS guidelines for colorectal cancer screening remain comparable to guidelines issued in 1996 by the US Preventive Services Task Force (USPSTF)49 and a 1997 interdisciplinary task force convened by the Agency for Health Care Policy Research (AHCPR).26 Each of those guidelines called for screening to begin at age 50 in average-risk adults and each endorsed annual FOBT, flexible sigmoidoscopy every five years, or combined testing with FOBT and flexible sigmoidoscopy. While the USPSTF endorsed annual FOBT, endorsements for flexible sigmoidoscopy or combined annual FOBT and flexible sigmoidoscopy were made without a recommendation for periodicity due to lack of evidence.49

The interdisciplinary task force was more specific, recommending either annual FOBT, flexible sigmoidoscopy every five years, or combined FOBT and flexible sigmoidoscopy beginning at age 50 and repeated at intervals recommended for each test.26 The ACS recommended, at a minimum, annual FOBT
and flexible sigmoidoscopy every five years. The USPSTF did not recommend DCBE or colonoscopy for colorectal cancer screening, whereas both the interdisciplinary task force and the ACS endorsed these two tests as reasonable options.

The 1997 ACS recommendation for annual FOBT and flexible sigmoidoscopy every five years at a minimum represents an important difference between the Society’s guidelines and those of the USPSTF and the AHCPR Task Force. The ACS made this recommendation on the basis of three data sets that showed: the benefits of FOBT; substantial risk reduction from sigmoidoscopic exams, and the safety, reasonable cost, and frequent availability of flexible sigmoidoscopy in many clinical systems.

Guidelines for average-risk individuals have been modified since the 1997 ACS recommendation to allow for greater flexibility in achieving screening goals, due to evidence showing little progress in colorectal screening rates. Based on data from the Behavioral Risk Factor Surveillance System (BRFSS), for example, fewer than one in five adults reported having had an FOBT in the previous year, and only 9.5% of adults reported having had both an FOBT test and flexible sigmoidoscopy during an interval recommended by the ACS.

Additional evidence gathered from focus groups with primary care providers and medical directors of managed care organizations indicates an overall lack of preparedness to offer FOBT and flexible sigmoidoscopy in the primary care setting. Moreover, a recent report indicated that medical directors were more likely to regard flexible sigmoidoscopy as an unreasonable expectation in a capitated plan compared with other screening tests (i.e., mammography, Pap testing, etc.). At this time, therefore, economic and health care system disincentives to screening are impinging on the choices available to physicians and patients. For these reasons, the ACS Colorectal Cancer Advisory Committee determined that FOBT or flexible sigmoidoscopy alone could be reasonable choices for routine colorectal cancer screening.

Either test alone is better than no screening at all, although both annual FOBT and flexible sigmoidoscopy every five years are preferred compared with either test alone. Nevertheless, the Advisory Committee strongly asserts that if FOBT alone is chosen, individuals should be tested annually using the recommended take-home multiple sample method. It is important to realize that it is the repeated use of this screening method in a properly implemented screening program that has proven effectiveness.

Annual screening is better than biennial screening, and all positive tests must be properly followed up with a complete examination of the colon. Specifically, there is no justification for repeating FOBT after an initial positive finding. Providers who are not yet prepared to offer tests other than FOBT in their clinics or by referral should immediately begin to find ways to make these tests available for their patients. Finally, the ACS asserts that third-party payers and health plans should not limit reimbursement for colorectal screening to FOBT alone, nor should providers suffer any economic disincentive to offering screening tests in addition to FOBT.

Recently, there has been increased attention to colonoscopy in the media and by some professional groups as the preferred method of screening for colorectal cancer. The inclusion of colonoscopy as a primary screening option has been an important feature of the ACS guidelines since 1997. Colonoscopy can
directly examine the entire colorectum, while flexible sigmoidoscopy can examine only the distal portion of the colon. Nevertheless, because adenomas are often multiple, flexible sigmoidoscopy can often identify about 80% of people who have a significant neoplasm anywhere in their colorectum.30

Randomized trials of colonoscopic screening are just now getting underway, so the effectiveness of this method will not be precisely known for several years. However, the ACS Colorectal Cancer Advisory Committee believes that there is sufficient indirect evidence of benefit from colonoscopy to justify an individual’s selection of this test for colorectal cancer screening, provided the individual understands the potential risks associated with the procedure. The cost-effectiveness of colonoscopy will likely improve with declining procedure costs, increasing availability, and targeted age/risk algorithms. Nevertheless, the Advisory Committee concluded that there are remaining questions about the efficacy and effectiveness of colonoscopy, as well as practical issues related to cost, access, and availability that need to be answered before colonoscopy is likely to be widely available as a screening test for average-risk adults.

An alternative to colonoscopy for visualization of the colorectum is a DCBE, which, when performed by an experienced radiologist, can be a cost-effective method for finding larger lesions.26,32 However, because DCBE may be less sensitive for detecting smaller neoplasms,60 it probably should be repeated more frequently (every five years) than colonoscopy.

A potential advantage of presenting a menu of appropriate screening options is that it makes it possible for any clinician to screen all of his or her eligible patients. Rather than recommending a specific option for everyone, the ACS suggests that, whenever possible, patients participate in a shared decision-making process. In this model, patients are presented with information about each of the screening options, such as accuracy, cost, potential for prevention, discomfort, and risk. Individuals then select the option that reflects their personal values and preferences.

An additional issue that is beginning to gain attention is when to stop screening. Although it is clear that individuals with significant co-morbidity that would preclude treatment should not be screened, there is little evidence or experience regarding an age at which screening should be discontinued. At this time, as long as an individual is in good health, he or she will likely benefit from screening.

Unfortunately, there are several obstacles to this shared decision-making approach. Logistic barriers, availability of well trained personnel, the time it takes to explain options to patients, cost, and insurance coverage frequently restrict options. Because of these circumstances, clinicians may be able to successfully implement only one or two of the screening modalities, limiting options for patients. As familiarity and screening skills grow in the broader medical community, and as insurance and cost obstacles are removed, a greater range of options will be available for more patients. Pignone and colleagues, for example, have shown that decision aids consisting of educational videos, brochures, and chart markers increased the ordering and performance of colorectal cancer screening tests.60a

Of primary importance at this time is that clinicians recommend at least one of the appropriate screening options for all of their eligible patients. Evidence demonstrates that when a screening recommendation comes directly from the clinician, compliance with colorectal cancer screening can be quite high.61 The ACS and other organizations are preparing
materials to assist clinicians in informing patients about colorectal cancer screening options, and detailed information about the characteristics of colorectal cancer screening tests—and testing in the primary care setting—will be published in CA later this year.

Future developments will expand the methods now available for the early detection of colorectal neoplasia. Lower dose, higher-resolution CT imaging of the bowel, for instance, is continuing in development. Genetic testing for mutations present in neoplastic cells excreted in feces is now also being studied as a screening method. Although these newer methods hold promise, it will likely be several years before there is adequate accumulation of evidence to determine their clinical effectiveness. Thus, although we anticipate the introduction of new screening modalities, it is not advisable to postpone screening using currently available methods.

We hope that these new ACS guidelines on screening and surveillance for the early detection of colorectal adenomas and cancer—which will be updated in the future, as new scientific data become available—will be useful for both clinicians and the general public.

Although we do not yet have randomized, controlled trial data to precisely compare the costs, risks, and benefits of the various methods for screening, a growing consensus indicates that there is a compelling case for screening using any of several methods or combinations of methods now available. By applying the knowledge we already have, it is likely that the majority of deaths from colorectal cancer in the US can be prevented.

**American Cancer Society Guidelines on Testing for Early Endometrial Cancer Detection—Update 2001**

**Background**

Endometrial cancer is the most common gynecologic malignancy among women in the US. In 2001, the ACS estimates there will be 38,300 newly diagnosed cases of endometrial cancer, and 6,600 deaths. Incidence rates for women age 50 and older declined from 116 per 100,000 in 1975 to 76 per 100,000 in 1986, but have remained stable since then. Among women 50 years of age and older, mortality rates have declined from 17.4 per 100,000 in 1973 to approximately 13 per 100,000 in 1997.

Endometrial cancer is uncommon before age 40; the incidence increases with increasing age, peaking between ages 75 and 79, with a median age at diagnosis of 66. When endometrial cancer is diagnosed while still localized, five-year survival is 96%, compared with 77% for regional disease, and 44% for disease with distant metastasis. A majority of cases (77%) are diagnosed while still localized.

**Guidelines Development**

The ACS guidelines for the early detection of endometrial cancer were last reviewed in October 1992, and recommended revisions were approved by the ACS Board of Directors in November 1992. At that time, it was recommended that all women at increased risk for endometrial cancer consider tissue sampling of the endometrium, beginning at menopause. Factors associated with increased endometrial
cancer risk included infertility, failure to ovulate, obesity, abnormal uterine bleeding, unopposed estrogen therapy, and tamoxifen therapy. Endometrial tissue sampling at various intervals after menopause was indicated depending on the degree of risk and other factors as determined by the physician.

In 2000, the ACS convened an expert panel to review the existing guideline for the early detection of endometrial cancer in asymptomatic women in the context of evidence that has accumulated since the last revision.

During the current guideline review, published articles related to endometrial cancer screening, risk, and risk factors were identified using MEDLINE (National Library of Medicine) for the years 1991 through 2000, bibliographies of identified articles, and from the personal files of the panel members. The database was searched using key words including neoplasia, endometrium, early detection, as well as words related to each of the individual risk factors. Panel members reviewed the papers related to one or more assigned risk factors based on their area of expertise. Members met via conference call from May through October 2000 to discuss the data and recommendations. Each member reviewed the draft manuscript and provided suggestions for revisions.

Definitions: Early Detection Methods

Endometrial cancer may be detected through a variety of means. While screening for endometrial cancer has been evaluated in prospective studies, the efficacy of endometrial screening has never been evaluated in a large prospective randomized controlled trial.

Today, the endometrial biopsy is the most common technique used to obtain endometrial tissue, and evaluation of endometrial histology has been the gold standard for determining the status of the endometrium.66 Cooper and colleagues have argued that hysteroscopy-directed biopsy is superior to endometrial biopsy in the collection of endometrial tissue samples, but for individuals not trained or without access to equipment, in-office endometrial biopsy without visual control is regarded as a reasonable approach for diagnostic sampling.67 Endometrial biopsy is easily performed as an office procedure and has good sensitivity, with the small number of false negatives most likely a result of sampling error. The observation that the positive predictive value of endometrial biopsy in average-risk women and in asymptomatic women is low, while higher yields are seen in women in specific risk groups, has led to the suggestion that screening may be a reasonable strategy in women at increased risk.68 More recently, transvaginal ultrasound (TVU) has been used as a noninvasive screening test to evaluate the endometrium. However, as yet, there is no agreed-upon criterion for endometrial thickness that has both a high sensitivity and specificity; a high rate of false-positive results is also a limiting factor.69 Endometrial thickness can vary depending upon whether the woman is pre- or postmenopausal, is on replacement therapy (estrogen replacement therapy versus hormone replacement therapy), or is taking tamoxifen. TVU may be too non-specific to be an effective screening tool.70-72 Two recent studies reported disappointing
results for endometrial cancer screening with endometrial biopsy and TVU for asymptomatic women on tamoxifen therapy, and each commented on the harms associated with diagnostic assessments, including unnecessary biopsies and, in some cases, uterine perforations. In an accompanying editorial, Runowicz concluded that the current data do not warrant routine screening for endometrial cancer in asymptomatic women on tamoxifen therapy.

Historically, the Pap test has led to the early diagnosis of some endometrial cancers, although detection is primarily incidental. Evaluations of the potential of the Pap test to be a test for both cervical cancer and endometrial cancer have shown both sensitivity and positive predictive value to be too low for the Pap test to be a practical screening test for endometrial cancer. However, abnormal endometrial cells on the Pap test may be markers for increased risk, especially when they are present in the secretory phase of the menstrual period, or when the patient is postmenopausal.

It must be remembered that screening refers to the evaluation of the asymptomatic patient. When bleeding occurs, evaluation becomes diagnostic rather than screening. A history of bleeding or demonstrated radiographic evidence of endometrial pathology removes a patient from the realm of screening and demands investigation, i.e., an endometrial biopsy.

Risk Factors

The expert panel reviewed the factors generally believed to place women at increased risk of endometrial cancer: Increasing age, unopposed estrogen therapy, late menopause, tamoxifen therapy, nulliparity, infertility or failure to ovulate, obesity, hypertension, diabetes, and HNPCC. In addition, the potential benefit of screening average-risk women for endometrial cancer was examined.

Hormone Replacement Therapy

Unopposed estrogen therapy in women with an intact uterus increases the risk of endometrial cancer two- to 10-fold, with an average relative risk of 4 to 5, and risk increases with duration of use. Unopposed estrogen therapy is not recommended for women with an intact uterus for this reason. The addition of progestin to estrogen, either cyclic or continuous, reduces the risk of endometrial cancer to either the expected risk of women not taking HRT, or in some studies, to lower than expected. The length of cyclic progestin therapy appears important, with at least 10 days (preferably 14 days) necessary to decrease the risk associated with unopposed estrogen therapy. Cyclic therapy promotes regular withdrawal bleeding much like a menstrual period. Any other bleeding should be considered abnormal and evaluated accordingly. Continuous estrogen and progestin therapy should lead to amenorrhea in most women.

Late Menopause

Late menopause, defined as menopause occurring after age 55, increases risk of endometrial cancer two-fold. Of greater concern is that peri- or post-menopausal women may report as menses what is actually abnormal bleeding. Bleeding after age 55 should be treated as symptomatic bleeding and not as menstruation.

Tamoxifen Therapy

In various studies, the relative risk of endometrial cancer in women taking tamoxifen ranged from 1.0 to 7.5.
Although some case control studies have not noted an effect on risk, prospective data have shown an elevated risk for endometrial cancer in women who had or who were at high risk for breast cancer and were taking tamoxifen, with annual risk increasing by two in 1,000.

**Nulliparity & Infertility**

Overall, nulliparity appears to confer an approximately two-fold risk of developing endometrial cancer compared with parity of one or more. Several studies have shown a marked decrease in risk associated with a greater number of full-term pregnancies. The literature does not support a significant risk of endometrial cancer associated with infertility, although some studies have shown an elevated risk.

**Polycystic Ovary Syndrome**

Only 5% of endometrial cancers are diagnosed in women younger than age 40. Case reports have suggested that polycystic ovary syndrome (PCOS), which affects approximately 5% of reproductive aged women, may be a risk factor for endometrial cancer in younger women. Coulam et al observed a three-fold relative risk of developing endometrial cancer after a diagnosis of chronic anovulation. However, according to Dahlgren et al, patients with PCOS are also more likely to have other risk factors for endometrial cancer, such as histories of nulliparity, than population-based controls. Although the data suggest that young patients with a history of PCOS may be at increased risk for endometrial cancer, the existing evidence is limited and is poorly controlled for known confounding risk factors.

**Obesity & Hypertension**

Studies show that very obese women have a two-to-four-fold relative risk of endometrial cancer. Obesity is defined as body weight over 200 pounds or a body mass index exceeding 27. Hypertension has not been shown to be a risk factor independent of obesity.

**Diabetes**

Diabetes is an independent risk factor for endometrial cancer and confers about a two-fold relative risk after adjusting for obesity. No data were found on the relationship between the type or duration of diabetes and endometrial cancer risk.

**HNPCC**

Women with HNPCC account for only 2% to 10% of all female cases of colon cancer; however, about 5% of all endometrial cancers occur in women with this risk factor. These women have a 22% to 50% lifetime risk of developing endometrial cancer according to various studies, and the disease tends to occur at a younger age, i.e., about 15 years younger than in women without the HNPCC-associated mutation. The greatest risk of developing endometrial cancer in HNPCC carriers occurs between ages 40 and 60 years, at which time the absolute risk is greater than 1% per year.
screening for endometrial cancer is warranted for women who have no identified risk factors.\textsuperscript{126-131} There have been no large prospective randomized controlled scientific studies designed to measure the effectiveness of screening, probably because most endometrial cancer (77\%) is diagnosed at an early, favorable stage. Early diagnosis usually results from the presence of alerting symptoms, specifically bleeding. Therefore it is recommended that, at the time of menopause, women at average risk should be informed about risks and symptoms of endometrial cancer, and strongly encouraged to report any unexpected bleeding or spotting to their physicians.

Recommendations for Women at Increased Risk

Based on a thorough review of the literature, there is no indication that screening for endometrial cancer should be recommended for women at increased risk for endometrial cancer because of history of unopposed estrogen therapy, late menopause, tamoxifen therapy, nulliparity, infertility or failure to ovulate, obesity, diabetes, or hypertension. As is the case with average-risk women, individuals at increased risk who develop endometrial cancer tend to present with symptoms at an early, favorable stage.\textsuperscript{131}

As with average-risk women, at the time of menopause, those at increased risk based on the risk factors identified above, should be informed about the risks and symptoms of endometrial cancer, and strongly encouraged to report any unexpected bleeding or spotting to their physicians. Asymptomatic women at increased risk should also be informed about the potential benefits, risks, and limitations of testing for early endometrial cancer detection, to ensure informed decisions about testing.

Recommendations for Women at High Risk

The expert review panel concluded that new data warranted the following recommendation: The American Cancer Society recommends that annual screening for endometrial cancer with endometrial biopsy should be offered by age 35 for women with or at risk for hereditary nonpolyposis colorectal cancer (HNPCC). Women in this high-risk group should be informed about the risks and symptoms of endometrial cancer, and should be informed about potential benefits, risks, and limitations of testing for early endometrial cancer detection.

The population defined as at high risk for endometrial cancer includes women known to carry HNPCC-associated mutations, women who have a substantial likelihood of being a mutation carrier (i.e., a mutation is known to be present in the family), and women from families with an autosomal dominant predisposition to colon cancer in the absence of genetic testing results, in accordance with the criteria of the Cancer Genetics Studies Consortium Task Force on HNPCC.\textsuperscript{132}

The accepted definition of HNPCC, based on a 1991 meeting of the International Collaborative Group, includes: (1) At least three relatives with histologically verified colorectal cancer, with one a first-degree relative of the other two; the diagnosis of familial adenomatous polyposis should be excluded. (2) At least two successive generations should be affected. (3) At least one case of colorectal cancer should be diagnosed before age 50 years. Meetings in 1996 added to this definition: (4) Pedigrees with a colon cancer case before the age of 40 years, and (5) pedigrees with a higher incidence of tumors associated with HNPCC.\textsuperscript{133}

At the present time, there are no data
indicating that annual screening of women with HNPCC does or does not detect endometrial cancers at a sufficiently early stage to improve survival compared with diagnosis when symptoms are present. However, because of the high risk of endometrial cancer in this group and because of the potentially life-threatening nature of this disease, screening is recommended.

The best age to begin screening women with the HNPCC risk factor is not known. Others have proposed that annual screening be initiated at age 25 or between ages 25 and 35. This panel recommends screening begin by age 35. Women with an HNPCC-associated mutation or with a substantial likelihood of having an HNPCC-associated mutation should be informed that this recommendation is based on expert opinion in the absence of scientific evidence.

Further, health professionals should counsel women with or at risk for HNPCC about preventive measures. Women who are no longer considering child-bearing and who are undergoing surgery for colorectal cancer should be offered the option of having a prophylactic hysterectomy at the same time, which may reduce the risk of endometrial cancer. Prophylactic oophorectomy to reduce the risk of ovarian cancer should also be offered.

The expert panel’s recommendations were based predominantly on the risk of endometrial cancer posed by each risk factor and the presumed benefit of early detection in defined populations. The consensus identified HNPCC as the only association with sufficient risk to warrant routine screening. Women with or at risk for HNPCC should be offered screening annually by age 35. Because this recommendation is based on expert opinion in the absence of scientific studies, informed decision-making following a discussion of options, including benefits, risks, and limitations of testing, is appropriate.

It is important to note that this screening guideline is directed at asymptomatic women only. Any woman experiencing unexpected bleeding or spotting should undergo an endometrial biopsy and/or other diagnostic tests as appropriate. Such a biopsy, however, is considered a diagnostic procedure rather than a screening test.

Testing for Early Lung Cancer Detection

Background

In the US, lung cancer is the second most common cancer diagnosed in men and women, and the leading cause of cancer mortality. The American Cancer Society estimates there will be 169,500 new cases of lung cancer diagnosed in 2001 (90,700 new cases in males and 78,800 new cases in females), and 157,400 deaths. Overall, the five-year survival rate for lung cancer is poor (15.8%), due mostly to the fact that the majority of new cases are diagnosed at a regional or distant stage, in which case survival is especially poor. Approximately 50% of patients survive five years if the disease is...
diagnosed while still localized, and among patients with stage 1 disease, survival is better among patients with T1 tumors (< 3 cm) compared with T2 tumors (≥ 3 cm). Survival appears to be further improved among patients with smaller T1 lesions. Martini et al observed significantly better survival among those with T1 lesions smaller than 10 mm compared with individuals with larger T1 lesions, and data from the NCI’s SEER program (1988-1992) show progressively better five-year survival among patients with smaller T1 lesions. In contrast, Patz et al observed no survival advantage by tumor size among 500 patients with tumors smaller than 30 mm. Nevertheless, only 16% of new diagnoses are classified as localized stage, and fewer than 25% of patients are asymptomatic at the time of diagnosis.

From a public health standpoint, lung cancer is unique among leading cancers because the underlying causal factor responsible for approximately 87% of cases, i.e., exposure to tobacco smoke, is obvious and for the most part avoidable. Despite this commonly known association, nearly half of US adults are current or former smokers; currently, about one in four adults still smokes cigarettes, and a significant percentage of children still take up smoking.

Although the risk of lung cancer declines significantly over time after cessation of smoking, especially the earlier cessation occurs, risk of lung cancer still persists and remains appreciably elevated for former smokers who have accumulated a high pack-year exposure history.

At this time and for the foreseeable future, millions of individuals who are current and former smokers will have elevated lung cancer risk, and thousands of young people join those ranks each day. Given the high lung cancer incidence and mortality rates cited above, and the large number of current and former smokers at risk for lung cancer, there has been a persistent, ongoing debate concerning the need for and usefulness of screening for lung cancer.

**Evidence of Effectiveness of Early Lung Cancer Detection**

To date, prospective studies of lung cancer screening have not demonstrated persuasively that screening for lung cancer with chest radiography alone or in combination with sputum cytology saves lives. While the results of prospective trials have been disappointing, particularly in view of such significant disease burden, these trials also were methodologically limited at inception in their ability to demonstrate a benefit from screening. 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 is underway now, i.e., the multicenter PLCO sponsored by the NCI.

**Detection Technologies**

Current technologies for detecting early lung cancer include imaging modalities and cytological and molecular evaluations of lung sputum.

**Chest x-ray**

Chest x-ray may have some, although limited, potential as a screening tool, especially...
in comparison with new imaging technologies that achieve higher resolution. With a chest x-ray, for example, normally two images are taken—a posterior/anterior view and a lateral view. The sensitivity of chest x-rays for lung cancer detection, therefore, is dependent on the size and location of the lesion, quality assurance factors related to image quality, and the skill of the interpreting physician. Failure to detect lesions at a favorable size, or even larger, can occur because the mediastinum and other aspects of chest structure may obstruct them. Errors in perception on the part of the interpreter are also common.

Low-Radiation-Dose Computed Tomography

Low-radiation-dose computed tomography (CT) (i.e., spiral or helical CT) produces multiple images of the lung conventionally in 5-mm multiplanar slices. Low-dose CT is more sensitive than chest x-ray in the detection of small pulmonary nodules, which poses challenges to establishment of protocols for triaging cases with clear malignant potential. However, this newer imaging technology for the early detection of lung cancer appears to be more promising than conventional chest x-rays.

The Early Lung Cancer Action Project (ELCAP) is a non-randomized trial designed to evaluate screening with low-radiation dose CT. In a report of the baseline experience with 1,000 volunteers aged 60 years and older with a smoking history 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, 26 of which were resectable and 23 were stage 1 disease. In contrast, conventional chest x-ray identified 68 non-calcified nodules, seven of which were malignant, and four were stage 1. Work-up of positive CT results was based on the size of the nodule and any changes observed on repeat screening. The ELCAP trial is ongoing and is continuing both recruitment of new participants as well as main-taining follow-up on all enrollees.

Other studies of low-dose CT in the US are underway or being planned. A prospective, randomized trial planned by the American College of Radiology Imaging Network should soon begin recruiting individuals to participate in a study designed to test the efficacy of low-dose screening CT. In addition, the NCI is evaluating the feasibility of a prospective trial of screening for lung cancer with low-dose CT.

Sputum Cytology

Sputum cytology was believed to have potential for the early detection of lung cancer, but showed little added advantage over chest x-ray in the NCI cooperative trials, and was not associated with any reduction in deaths from lung cancer. In those trials, approximately one in four cancers was detected by sputum cytology alone, and the majority of these were squamous cell carcinomas diagnosed at a favorable stage. Attempts to refine the use of sputum cytology, however, are continuing. One disadvantage of sputum cytology is that

Nearly half of US adults are current or former smokers; currently, about one in four adults still smokes cigarettes, and a significant percentage of children still take up smoking.
other methods must be applied to identify the location of the cancer.

**Molecular Screening**

Other promising methods for the early detection of lung cancer include fluorescence bronchoscopy and molecular screening for mutations associated with transformation of bronchial epithelial cells. Attempts to identify a subgroup of individuals at appreciable risk for lung cancer beyond smoking history have focused on molecular risk assessment in current and former smokers. Evaluation of lung epithelium for evidence of accumulated genetic damage through polymerase chain reaction techniques is another new area of investigation.\(^{149}\)

**Guidance About Early Lung Cancer Detection**

Lung cancer is unique among the cancers discussed in this article because the need for a secondary prevention strategy to reduce deaths is due largely to a preventable behavior, i.e., cigarette smoking. However, the current public health challenge for reducing lung cancer mortality applies also to all individuals at elevated risk of lung cancer, which includes both current and former smokers. At this time, no organization recommends routine screening for lung cancer among the general adult population, or for individuals who are at higher risk due to tobacco or occupational exposures.\(^{49,155–152}\)

In December 1998, the International Conference on Prevention and Early Diagnosis of Lung Cancer was held in Varese, Italy, to review the historical data on lung cancer screening as well as information on new technologies for the early detection of lung cancer.\(^{153}\) At the conclusion of the meeting, conference participants endorsed a statement noting that the current evidence about the efficacy of lung cancer screening was an imperfect basis for public health policy, and in fact, results of the trials and case-finding series were paradoxical.

While these data did not provide a sufficient basis to endorse lung cancer screening, neither were they persuasive that lung cancer screening is ineffective. Based on promising results from investigations with spiral CT and other evolving early detection tests, conference attendees strongly encouraged “national governments and public health organizations involved in cancer prevention and control to more aggressively address tobacco control and to urgently consider the issues surrounding the early detection of lung cancer.”\(^{154}\) The consensus statement also indicated that there should be an accelerated program to determine the efficacy and effectiveness of these new technologies for early lung cancer detection. Finally, the consensus statement concluded that individuals at risk for lung cancer should be informed about the evidence from trials and case-finding series with conventional and new technology, as well as potential benefits and risks associated with testing for early lung cancer detection, so that they may make informed decisions.

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**INFORMED DECISION-MAKING ABOUT TESTING FOR EARLY LUNG CANCER DETECTION**

The ACS does not recommend lung cancer screening for asymptomatic individuals at risk for lung cancer. However, historically the ACS has distinguished recommendations for mass
screening from those decisions that may be made by individuals. When the ACS withdrew its previous recommendation for lung cancer screening in 1980, the statement asserted that the new recommendation was not intended to discourage individuals from having early detection tests, and that “individual physicians and patients may decide that the evidence is sufficient to warrant the use of these screening tests on an individual basis.”

In the past few years, however, results from screening studies using spiral CT have been regarded as sufficiently encouraging to lead a growing number of institutions and facilities to promote CT screening to asymptomatic individuals at risk for lung cancer, with such promotion likely to increase. Since both media reports and local advertising may stimulate interest in spiral CT testing among health care providers and individuals at higher risk, the ACS has determined that updated guidance about early lung cancer detection is appropriate. Further, given the high rate of positive results that occur with CT screening for lung cancer and the complexity of the algorithm for working up small nodules, there is reason to be concerned about broad dissemination of lung screening outside of experienced, multi-specialty settings and prior to validation of this new technology.

For this reason, it is critically important during this period of evolving investigations into the efficacy of spiral CT and other modalities that appropriate and influential professional organizations provide a foundation for best practices based upon the current state-of-the-art, and also promote informed decision-making for patients about possible benefits, risks, and limitations of testing for early lung cancer detection. Individuals interested in early detection also should be encouraged to participate in trials.

The ACS recommends that, to the extent possible, individuals at risk for lung cancer due to current or prior smoking history, history of significant exposure to second-hand smoke, or occupational history, be aware of their continuing lung cancer risk. Those who seek testing for early lung cancer detection should be informed about what is currently known about the benefits, limitations, and risks associated with conventional and emerging early detection technologies, as well as the associated diagnostic procedures and treatment.

Given the complexity of diagnostic and follow-up algorithms associated with early lung cancer testing, the ACS discourages testing in a setting that is not linked to multi-disciplinary specialty groups for diagnosis and follow-up. Individuals who choose to undergo testing should have access to testing and follow-up that meet state-of-the-art standards, with informed decision-making at every step of an ongoing process. According to recommendations made by Weed, “individuals should understand what they are agreeing to do, what will happen to them, and what may happen to them or not, as a result of their participation.”

Ideally, the route to testing should be through an individual's primary care physician, who should be prepared to help patients understand their risks and reach informed decisions about testing, and to provide support if early detection tests are positive. Absence of a referral from a primary care physician due to lack of provider endorsement of testing, or not having a primary care provider, should not be a barrier to testing. However, if an individual seeks testing and does not have a referral from a primary care provider, the radiologist who provides testing is obliged to provide...
information about benefits, risks and limitations of testing as described above, and must become the individual’s physician of record until proper alternative care arrangements can be made.

At this time, there is an urgent need for rapid resolution of the underlying evidence-based questions about the benefit of spiral CT for early lung cancer detection. Lung cancer is the leading cause of cancer mortality in the US, and the world. If this technology is effective at identifying early, resectable lung cancers, the public health impact could be substantial. Present and future disease burden, rapid diffusion of this technology into the community, and rapid evolution of imaging technologies place high demands on the need for evidence-based guidance for policy. In the meantime, because of increasing availability and promotion of testing, it is critically important that individuals who are interested in testing understand both the limits of our knowledge about the potential benefits of screening with low-dose CT, as well as potential harms associated with diagnostic procedures and treatment.

Individuals who are current smokers also should be informed that the more immediate preventive health priority is the elimination of tobacco use altogether, since smoking cessation offers the surest route at this time to reducing the risk of premature mortality from lung cancer.143

The Cancer Related Check-up

Apart from participation in screening that can be recommended as part of a population-based initiative, the ACS has viewed periodic encounters with clinicians 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 ages 20 to 39, and annually for asymptomatic men and women ages 40 and older.

CANCER SCREENING IN THE US

Recognizing that cancer screening can impact important population measures (i.e., cancer-specific mortality and incidence), existing public health surveillance provides valuable information for monitoring population-based prevalence of cancer screening utilization in the US. This section will present estimates of screening test utilization in the general population for cervical, breast, and colorectal cancers. Due to lack of consensus among the agencies and organizations that develop screening guidelines, nationwide surveillance mechanisms have not been established to assess the extent of PSA testing among men in the US. However, public health officials in New York have ranked prostate cancer as a priority public health problem, particularly for African-American male residents, and statewide data have been available on PSA screening. Lastly, this section will present and highlight recent data on race-ethnic disparities in cancer screening in the US.
# TABLE 4

Prevalence (%) of Cancer Screening Among US Adults (BRFSS, 1999)

<table>
<thead>
<tr>
<th>Age</th>
<th>Males</th>
<th>Females</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Median (Range)</td>
<td>Median (Range)</td>
<td>Median (Range)</td>
</tr>
<tr>
<td><strong>Colorectal Cancer</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Either a Flexible Sigmoidoscopy or Colonoscopy*</td>
<td>50+ 34.2 (25.7 – 49.0)</td>
<td>30.3 (21.1 – 37.0)</td>
<td>32.3 (22.6 – 46.2)</td>
</tr>
<tr>
<td>Fecal Occult Blood Testing (home-kit)†</td>
<td>50+ 17.1 (9.8 – 35.6)</td>
<td>21.3 (13.1 – 37.2)</td>
<td>19.0 (11.6 – 35.8)</td>
</tr>
<tr>
<td><strong>Prostate Cancer</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prostate Specific Antigen Blood Test</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NY State‡1</td>
<td>50+ 64 — — — — — —</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NY African-American Survey‡2</td>
<td>60 — — — — — —</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Breast Cancer</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mammogram1</td>
<td>40-64 — —</td>
<td>58.6 (45.8 – 71.5) — —</td>
<td></td>
</tr>
<tr>
<td></td>
<td>-50+ — —</td>
<td>63.5 (51.8 – 76.3) — —</td>
<td></td>
</tr>
<tr>
<td></td>
<td>-65+ — —</td>
<td>60.8 (50.3 – 79.5) — —</td>
<td></td>
</tr>
<tr>
<td>Mammogram and Clinical Breast Exam2</td>
<td>40-64 — —</td>
<td>53.4 (42.0 – 65.5) — —</td>
<td></td>
</tr>
<tr>
<td></td>
<td>50+ 57.2 (43.7 – 69.2) — —</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>65+ 52.4 (41.7 – 72.4) — —</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Cervical Cancer</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pap test£</td>
<td>18-44 — —</td>
<td>88.3 (79.6 – 95.0) — —</td>
<td></td>
</tr>
<tr>
<td></td>
<td>45+ — —</td>
<td>81.0 (72.4 – 87.6) — —</td>
<td></td>
</tr>
</tbody>
</table>

*Recent sigmoidoscopy or colonoscopy test within the preceding five years. Source: BRFSS 1999.
† Recent fecal occult blood test using a home kit test performed within the preceding year. BRFSS 1999.
‡1 Men 50 and older who had heard of a PSA test and had ever had a PSA blood test done. Source New York BRFSS 1994-1995, conducted by the NY Department of Health.
‡2 Men 50 and older who had heard of a PSA test and had ever had a PSA blood test done. Data Source: New York African American Men survey, 1995, conducted by the NY Department of Health.
1 Women 40 and older who had a mammogram in the last year. BRFSS 1999.
2 Women 40 and older who had a mammogram in the last year and a clinical breast exam. BRFSS 1999.
£ Women who had a Pap test within the preceding three years. BRFSS 1999.
Guidelines for the Early Detection of Cancer

TABLE 5
Prevalence (%) of Cancer Screening in US Adults: Five Racial and Ethnic Groups (BRFSS, 1997)

<table>
<thead>
<tr>
<th>Type of Cancer Screening Test</th>
<th>White</th>
<th>Black</th>
<th>Hispanic</th>
<th>American Indian/Alaska Native</th>
<th>Asian/Pacific Islander</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flexible sigmoidoscopy or proctoscopy within the past five years</td>
<td>30.4</td>
<td>28.2</td>
<td>22.4</td>
<td>27.6</td>
<td>—</td>
</tr>
<tr>
<td>California*</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>24.3</td>
</tr>
<tr>
<td>Hawaii*</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>40.7</td>
</tr>
<tr>
<td>Fecal Occult Blood Test – home kit</td>
<td>18.2</td>
<td>20.3</td>
<td>14.2</td>
<td>12.3</td>
<td>—</td>
</tr>
<tr>
<td>California*</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Hawaii*</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Mammogram within the past two years</td>
<td>73.7</td>
<td>76.1</td>
<td>63.5</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Alaska*</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>93.5</td>
<td>—</td>
</tr>
<tr>
<td>Hawaii*</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>23.8</td>
<td>—</td>
</tr>
<tr>
<td>A Pap test within the past three years and women with intact uterine cervix</td>
<td>84.7</td>
<td>91.1</td>
<td>80.9</td>
<td>95.5</td>
<td>—</td>
</tr>
<tr>
<td>Hawaii*</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>84.2</td>
</tr>
<tr>
<td>New York*</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>75.9</td>
</tr>
<tr>
<td>Washington*</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>84.1</td>
</tr>
</tbody>
</table>

* Indicates state-specific prevalence estimates available for the corresponding race-ethnic group; in contrast, all other data estimates are median values for all participating states.


Cancer Screening: Colorectal, Breast, and Cervical Cancers

Data Sources

The estimated proportion of the US adult population that undergoes specific tests for early cancer detection in the US is presented in Table 4. These data are from the CDC’s BRFSS for 1998 and 1999. While there are other sources of surveillance data for cancer screening (i.e., the periodic cancer supplement to the National Health Interview Survey), the BRFSS provides an annual update of national estimates by conducting a statewide telephone survey of civilian, non-institutionalized adults (i.e., persons 18 years of age or older).

The BRFSS is conducted annually by state health departments in collaboration with the CDC in all 50 states, the District of Columbia, and Puerto Rico. The BRFSS survey methodology includes standardized core-questionnaires, complex multi-stage cluster sampling designs, and random-digit dialing methods to select households with telephones. Data are weighted to provide prevalence estimates representative of the state’s adult population. From its inception, the focus of
the BRFSS has been to establish a surveillance system for the collection of population-based health behaviors, sociodemographics, and related health care factors (i.e., access to health care) known to affect chronic diseases (i.e., including cancer) and the health status of the general population.

Colorectal Cancer Screening

Colorectal cancer screening utilization among adults 50 and older is low. Men were slightly more likely than women to have received an endoscopic exam (flexible sigmoidoscopy or colonoscopy) within the preceding five years (34.2% versus 30.3%). On the other hand, women were slightly more likely than men to have conducted an FOBT using the home kit within the previous year (21.3% versus 17.1%) (Table 4).

Several factors have been associated with a lower prevalence of colorectal cancer screening: Lack of health insurance coverage; lack of provider referral, ages 50 to 59, and 80 and older; lower income and educational attainment; and race and ethnicity (blacks, individuals of Hispanic origin, American Indians/Alaskan Natives, and Asians/Pacific Islanders all report lower colorectal cancer screening rates compared with non-Hispanic whites).55,61,160

Breast Cancer Screening

The proportion of women reporting a mammogram in the last year was 58.6% among those 40 to 64 years of age, and 60.8% among those aged 65 and older. The pattern of screening with mammography and clinical breast exam in the previous year was similar to that for mammography alone but the median percentages for each of the respective age groupings were no greater than 60% (Table 4).

Cervical Cancer Screening

Women in the 18-to-44-year-old age group were more likely to have had a Pap test in the preceding three years compared with women 45 and older (88.3% versus 81.0%) (Table 3). High rates of participation in cervical cancer screening reflect high acceptance of the Pap test among women and their providers as well as the convenience of testing during routine gynecologic examinations.

With respect to screening for both breast and cervical cancer, there still are missed opportunities for screening among older women, and screening rates, in particular, are lower among women of low income, those with less education, and those lacking health

Cancer Screening Reminders

We need to develop systems that help health care providers identify men and women for whom cancer screening is appropriate, and also to remind them at appropriate regular intervals when screening tests are due.

Promoting the Benefits of Cancer Screening

The benefits of cancer screening must be promoted in the community by health care providers and cancer control professionals. Various approaches to communication and the implementation of systems should be expanded to reach the public and thus generate demand. All men and women should be provided with information about tests for the early detection of specific cancers.
For instance, a recent study reported that a combination of patient, provider practice, and access barriers accounted for primary care providers not screening their asymptomatic older women patients.

Another important aspect of missed opportunities in breast and cervical cancer screening is regular participation. A recent report indicated that for both mammography and Pap testing, there was a substantial gap in the proportion of women who were ever screened and the proportion who were ever screened within a recommended interval. This distinction may indicate that some women who participate in initial screening do not continue to be screened at regular intervals.

**PSA Testing: New York Data**

In New York, more than half of adult men 50 years of age and older had heard of the PSA test (58%); of these men, two-thirds reported receiving physician advice to get the test and 64% reported ever having had a PSA test. In addition, the 1995 NY Department of Health conducted a telephone-based survey of African-American men 50 and older to assess knowledge, attitudes, and practices regarding prostate cancer and screening participation. Among NY African-American men 50 and older, 43% had heard of the PSA test. Among these men, 51% said that they had received advice from a physician to get a PSA test, and 60% of those reported that they had received the test (Table 4).

Further analysis of these data found that physician advice was the strongest independent predictor of whether or not a man had received a PSA test after accounting for other socio-demographic differences. Unfortunately, the lack of data on DREs precluded the assessment of the proportion of men who have been screened with combined DRE and PSA.

**Cancer Screening: Racial and Ethnic Patterns**

Disparities in risks for cancer exist among racial and ethnic groups in the US. Recently, the CDC reported the most comprehensive compilation of cancer screening utilization data across five racial and ethnic groups—whites, blacks, Hispanics, American Indian or Alaska Natives, and Asian/Pacific Islanders. These data are summarized for cancer screening utilization during 1997 for colorectal, cervical, and breast cancers (Table 5).

In the 1997 BRFSS, whites comprised 75.4% of the respondent group. Blacks represented 9.7% of the cohort, Hispanics represented 11.1%, American Indians or Alaska Natives accounted for 1.0%, and Asians or Pacific Islanders accounted for 2.8%. Although racial and ethnic minority groups account for increasingly larger proportions of the US population, information is limited about the health behaviors and preventive health care services utilization of individuals in minority groups, especially at the state and local levels. Nevertheless, the data presented here clearly identify some disparities among racial and ethnic groups, and also highlight, that in some instances, comparisons by race and ethnicity do not reveal disparities that might be expected.

Compared with Caucasian women, African-American women were equally likely to have received a mammogram and a Pap test. In part, the improving rates of screening utilization among black women (and in particular, those who are medically underserved and uninsured) may be a reflection of the increased access and coverage for breast and cervical cancer.
screening through CDC’s National Breast and Cervical Cancer Early Detection Program.\textsuperscript{165} Between July 1991 and September 1995, the program provided 327,017 mammograms and 472,188 Pap tests; 46.7% of the mammograms and 46.5% of the Pap test were provided to women of racial and ethnic minorities.\textsuperscript{166}

Hispanic women aged 50 and older have the lowest mammography utilization rates within the past two years (63.5%) and Hispanic women aged 18 and older have the lowest Pap test utilization rates within the last three years (80.9%) compared with other racial and ethnic groups.

The following subgroups showed the lowest utilization rates for colorectal cancer screening: 22.4% of Hispanics aged 50 and older report having had a flexible sigmoidoscopy test or proctoscopy test done within the last five years while 14.2% of Hispanics and 12.3% of American Indian/Alaska Natives report having done a FOBT with a home kit.

Differences in median percentages for screening participation between racial and ethnic groups, as well as state differences within each racial and ethnic group, are likely mediated by various factors, including socioeconomic and cultural factors,\textsuperscript{167} lifestyle behaviors (e.g., lack of physical activity, alcohol intake, and cigarette smoking), aspects of the social environment, (e.g., educational and economic opportunities, neighborhood and work conditions), aspects of the affecting health care environment (e.g., access to health care, physician recommendation), and migration trends.\textsuperscript{168,169}

**PARTICIPATION IN SCREENING—SUMMARY POINTS**

Overall, US national screening rates for cancer show that there is considerable room for improvement, especially in achieving higher rates of regular screening and in reducing disparities among the medically underserved. The medical community, in partnership with cancer control professionals, is in a unique position to play the key role of recommending cancer screening to patients, for which the benefit of their endorsement has been consistently demonstrated. By taking action on several fronts, their efforts can help realize improvements in screening and early cancer detection in the population as a whole.

**Value of Screening**

Participation in screening depends on the acceptance of the value of screening by providers and the public. Low participation in cancer screening among both providers and the public can be due to low prioritization, low awareness, low perceptions of risk, low access, costs, and aversion to the test itself, or to test results. However, most investigations 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 compliance with screening recommendations by both 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.\textsuperscript{61,170-173} 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 discussions about cancer screening or preventive health counseling.\textsuperscript{174} 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. These factors combined lead to a situation where screening commonly occurs opportunistically rather than regularly, and these current circumstances 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 with recommended screening intervals remains to be made. When screening is organized, however, individuals have a greater likelihood of receiving routine screening. Tools that have been shown to enhance screening include flowsheets, chart reminders, computerized tracking and reminder systems, and group practices.

CONCLUSION

At this time, the early detection of cancer and precursor lesions offers 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 proportion of incident cases have less than optimal prognosis. There remains considerable room for improvement in the quality assurance of screening. Improvements in screening quality control and quality assurance can lead to gains in both sensitivity and specificity, thus improving performance and reducing avoidable costs. New screening technologies focused not only on solid tumors, but also on genetic and molecular markers of risk and disease, are under development and eventually will replace the existing screening modalities. Ultimately, screening failures will be measured not by death from cancer, but by the development of invasive disease. Nevertheless, it must be emphasized that there is an unmet potential of a greater benefit from cancer screening that is achievable today. As we anticipate these exciting new developments, we must be reminded of the value of the technologies at hand, and their 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.

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LONG-TERM ESTROGEN REPLACEMENT THERAPY MAY INCREASE OVARIAN CANCER RISK

Women who have used older estrogen replacement therapy (ERT) regimens for 10 years or more may have a significantly higher risk of dying from ovarian cancer than do those who never used ERT, according to a report by American Cancer Society epidemiologists in the *Journal of the American Medical Association* (2001;285:1460-1465).

“Our study suggests that long-term use of estrogen replacement therapy, often without accompanying use of progesterone in the past, may increase risk of ovarian cancer death and that the increased risk remains a long time after cessation,” says lead author Carmen Rodriguez, MD, MPH, senior epidemiologist in the department of epidemiology and surveillance research at the ACS.

Questions About Long-Term ERT Use

Earlier studies had suggested that ERT increases the risk of ovarian cancer but were too small or too short to determine whether risk increased with long-term use. To answer the long-term risk question with more certainty, Rodriguez and her colleagues analyzed data from more than 211,000 postmenopausal women who completed an extensive health questionnaire as part of the ACS’ Cancer Prevention Study II (CPS II) in 1982. The women included in the ERT study had no history of cancer, hysterectomy, or ovarian surgery at the time the study began.

The researchers looked at causes of death for women who died between the beginning of CPS II in 1982 and 1996, whether they had ever used ERT, and if so, when and for how long. A total of 944 ovarian cancer deaths occurred among the women in the study between 1982 and 1996.

Long-term ERT use was linked to an increased risk of ovarian cancer death, which remained elevated for up to 29 years after therapy was discontinued. After that, the risk slowly decreased over time.

Women using ERT at the beginning of the study and who had been using it for 10 years or longer at the time were 2.2 times more likely to die of ovarian cancer during the next 14 years than those who had never used ERT. Those
who had used ERT for 10 years or more and quit fewer than 15 years before the study began were at double the risk of those who had never used ERT. Those who used ERT for 10 years or more but had quit more than 15 years before the study began were at 1.3 times the risk of those who had never used it. Overall, when all women who had ever used ERT were considered together, regardless of the length of use or when they had quit, average risk of dying from ovarian cancer was 1.23 times that of those women who had never used it.

No Data on Combination HRT

The ACS epidemiologists noted that their findings may or may not apply to combined hormone replacement therapy (HRT), explaining that there is no clear consensus among previously published studies as to whether the addition of progesterone to estrogen protects against ovarian cancer, raises the risk, or has no effect at all.

Data relevant to that issue were recently presented at the 2001 annual meeting of the American Association for Cancer Research by James Lacey, MPH, PhD, and colleagues from the National Cancer Institute. They reported on follow-up of 40,762 women who enrolled in the Breast Cancer Detection Demonstration Project between 1979 and 1981. In this cohort, use of ERT alone doubled a woman’s risk of developing ovarian cancer whereas use of estrogen plus progesterone was associated with a 30% increase that was not statistically significant.

The balance of risks and benefits with hormone replacement therapy is different for each woman.

Heart Disease More Common than Cancer

“There is continuing debate about the overall impact of ERT on life expectancy,” said Michael Thun, MD, Vice President of epidemiology and surveillance research at the ACS and a co-author of the JAMA article. “This is largely because the reduction in heart attacks seen in many epidemiological studies has not yet been replicated in clinical trials. But death from heart disease is still more common than death from breast and ovarian cancers combined,” he says. “If ERT does in fact lower cardiovascular disease risk, this benefit could outweigh the increased cancer risk.”

Data from the NCI study reported by Lacey et al. are reassuring in that they suggest that estrogen taken in combination with progesterone may not increase the risk of ovarian cancer. Such combination regimens have become the standard for hormone replacement in women with intact uteri.

Thun stressed that the balance of risks and benefits with hormone replacement therapy is different for each woman, and depends on variables such as age, body mass, whether and when she has had children or has had a hysterectomy, whether she has a personal or family history of cancer, as well as other factors.

RISK OF ERECTILE DYSFUNCTION SIMILAR FOR DIFFERENT PROSTATE CANCER TREATMENTS

More than 80% of prostate cancer patients develop erectile dysfunction (ED) as a result of treatment, regardless of whether they have surgery or external beam radiation therapy, according to a study published in the Journal of Urology (2001;165:430-435).

Previous studies of ED among prostate cancer survivors have reported a wide range
of prevalence rates, from about 20% to 88%. To help further clarify this issue, Timothy Siegel, MD, and colleagues from the Center for Prostate Disease Research, Rockville, MD, compared erectile function in patients receiving radical prostatectomy, external beam radiation, or watchful waiting.

Siegel et al. used data on more than 800 prostate cancer patients that had been collected prospectively as part of the Department of Defense Center for Prostate Disease research program. Prior to treatment, 69% of the men reported normal erectile function. At an average of 53 months after treatment, 10% of men who had undergone radical prostatectomy and 15% of those treated with external beam radiation had intact erectile function.

In contrast, 38% of the men who chose watchful waiting had adequate erections after six months. Overall, more than 80% of the men who were treated by prostatectomy or external beam radiotherapy developed ED during the study, regardless of age.

ED Should Be Expected with Active Treatment

"Patients who elect non-nerve sparing radical prostatectomy or external beam radiation therapy should expect a high incidence (greater than 85%) of erectile dysfunction after therapy," the authors wrote. "In our experience, erectile dysfunction did not develop based on the type of therapy received, but only whether a patient received active therapy for prostate cancer."

In an accompanying editorial, Ian Thompson, Jr., MD, University of Texas Health Sciences Center at San Antonio, commented that, "These sobering results disagree with the common perception that erectile dysfunction is nonexistent with surveillance, and is infrequent after radiation and slightly greater with surgery."

In a second editorial, Irwin Goldstein, MD, Boston University School of Medicine, focused on the importance of outcomes studies in urological oncology that use well-validated survey instruments for assessing sexual function, and of collecting and analyzing data on physiological and psychological variables relevant to sexual function.

SMOKERS AT HIGHER RISK OF COMPLICATIONS FROM BREAST RECONSTRUCTION SURGERY

Women who quit smoking for at least three weeks prior to breast reconstruction surgery after a mastectomy may significantly reduce their risk of complications, according to a report in Plastic and Reconstructive Surgery (2001;107:342-349). In many cases, the risk can be reduced to that of nonsmokers, according to the study.

The study is based on records of more than 700 women who had undergone breast reconstruction surgery with either an implant or a TRAM (transverse rectus abdominis musculocutaneous) flap.

Of the participants, 155 were current smokers at the time of the procedure, 76 were ex-smokers, and 517 were nonsmokers. Women who had quit as recently as three weeks prior to undergoing either type of surgical procedure were classified as ex-smokers.

The fact that the former smokers’ overall complication risk was similar to that of nonsmokers surprised investigators, said Randall Yetman, MD, co-author and plastic surgeon at the Cleveland Clinic. Almost 40% of the smokers experienced complications, such as

“I routinely tell my breast cancer patients that smoking might increase their risk of complications and that most of these complications detract from the appearance and feel of the reconstructed breast.”
mastectomy flap necrosis, fat necrosis, abdominal wall necrosis, seroma, wound dehiscence, and infection, compared with about 25% of nonsmokers and ex-smokers.

**Smoking Impairs Wound Healing**

During the surgery, blood supply to the tissue at the reconstruction site is reduced. Smoking causes constriction in blood vessels that impairs wound healing and reduces oxygen delivery to the tissues. Therefore, women who smoke are even more vulnerable to tissue necrosis and other complications in the area of the reconstruction. Wound dehiscence, fat necrosis, and lumpiness of the reconstructed breast, for example, were all about three times more common among smokers than among nonsmokers.

Jeanne A. Petrek, MD, director of the surgical program at the Evelyn H. Lauder Breast Center at Memorial Sloan-Kettering Cancer Center, New York City, notes that although the results of a single study cannot be considered definitive, “It is intuitive that because smoking decreases blood supply and can lead to surgical complications at other sites, it would be expected to increase the risk of the complications noted in this study.

Based on these considerations, I routinely tell my breast cancer patients that smoking might increase their risk of complications and that most of these complications detract from the appearance and feel of the reconstructed breast. And, I offer appropriate pharmacological agents and counseling to help these women stop smoking for as long as possible before surgery.”

Debbie Saslow, PhD, director of breast and cervical cancer at the American Cancer Society, agrees that, “although there are limited data, women could be told that one study indicates that complications might be increased if they continue to smoke, but that if they stop smoking for three weeks before the surgery, it could make a big difference in their results. However, many women in this situation are already experiencing tremendous fear and stress, so we should make sure that the issue is approached in a supportive and sensitive way.”

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**Erratum**

In the January/February 2001 issue, in the article, “American Cancer Society Guidelines for the Early Detection of Cancer: Update of Early Detection Guidelines for Prostate, Colorectal, and Endometrial Cancers” (Smith RA, von Eschenbach AC, Wender R, et al. *CA Cancer J Clin* 2001;51:38-75), an error occurred in the text on page 43. The PSA and PSA-free levels are given in nanograms per deciliter (ng/dl), but should be given in nanograms per milliliter (ng/ml). We apologize for the error and any confusion this may have caused.
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In the January/February 2001 issue, in the article “Cancer Statistics, 2001” (Greenlee RT, Hill-Harmon MB, Murray T, Thun M. CA Cancer J Clin 2001;51:15-36), an error occurred in Figure 10 (page 34). The colors indicating distant stage statistics for melanoma of the skin (black and white), oral cavity & pharynx (white), ovary (white), and prostate (black) were printed incorrectly; however, the numerical data listed was correct.

Figure 10 is reproduced here and reflects the correct color for distant stage statistics according to the key. We apologize for the error and any confusion this may have caused.

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