ARTICLE TITLE: Cancer Screening in the United States, 2013: A Review of Current American Cancer Society Guidelines, Current Issues in Cancer Screening, and New Guidance on Cervical Cancer Screening and Lung Cancer Screening

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1. Identify patients at average, increased, and high risk of various cancers, and provide them with guidance regarding appropriate early detection options.
2. Answer questions from patients regarding emerging cancer detection technologies.
3. Summarize recent trends in the prevalence of cancer screening and adherence to recommended screening guidelines.

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Cancer Screening in the United States, 2013
A Review of Current American Cancer Society Guidelines, Current Issues in Cancer Screening, and New Guidance on Cervical Cancer Screening and Lung Cancer Screening

Robert A. Smith, PhD1; Durado Brooks, MD, MPH2; Vilma Cokkinides, PhD3; Debbie Saslow, PhD4; Otis W. Brawley, MD5

Each year the American Cancer Society (ACS) publishes a summary of its recommendations for early cancer detection, a report on data and trends in cancer screening rates, and select issues related to cancer screening. In this issue of the journal, current ACS cancer screening guidelines are summarized, as are updated guidelines on cervical cancer screening and lung cancer screening with low-dose helical computed tomography. The latest data on the use of cancer screening from the National Health Interview Survey also are described, as are several issues related to screening coverage under the Patient Protection and Affordable Care Act of 2010. CA Cancer J Clin 2013;63:87–105. © 2013 American Cancer Society.

Keywords: Mass screening, neoplasms, diagnosis, prevention and control, mortality, radiography, lung cancer screening, cervical cancer screening, prostate cancer screening

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Introduction
In this yearly report, we provide a summary of the current American Cancer Society (ACS) cancer screening guidelines, a summary of guidance to health care professionals and the public related to early cancer detection tests that are not yet recommended for mass screening due to uncertainty about the balance of benefits and harms, and the most recent data on adult cancer screening rates and trends.

In order for guidelines to reflect the most current scientific evidence, the ACS monitors the medical and scientific literature on an ongoing basis, and generally guidelines have been reviewed and updated at least every 5 years, or sooner if new evidence warrants an immediate update in recommendations. An update in the ACS guidelines development process was published in 2011, and also summarized in this journal in 2012.1,2 The annual guideline reviews, as well as the more detailed cancer screening guideline updates, are published as stand-alone articles and are available online at cacancerjournal.com. Table 1 shows the recent history of guidelines updates, as well as those currently in progress.3-15

In this update of ACS cancer screening guidelines, we describe the current guidelines, an update in the guidance for lung cancer screening announced in 2011,2 and an update in cervical cancer screening guidelines.7

Screening for Breast Cancer
Breast cancer is the most common cancer and the second most common cause of death from cancer in women in the United States.16 ACS guidelines for breast cancer screening in average-risk women were last updated in 2003,3 and screening guidelines for women at very high risk were last updated in 2007 (Table 2).4

The guidelines for the early detection of breast cancer in average-risk women consist of a combination of regular clinical breast examinations (CBEs) and counseling to raise awareness of breast symptoms beginning at age 20 years, and annual mammography beginning at age 40 years.

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Between the ages of 20 years and 39 years, average-risk women should undergo CBE every 3 years, and annually after age 40 years. CBE should take place during periodic health examinations and after age 40 years, ideally prior to mammography. When CBE is performed, it is an opportunity to discuss the importance of early breast cancer detection and answer any questions a woman may have about her own risk, new technologies, or other matters related to breast disease. Clinicians should emphasize the importance of an awareness of a family history of breast and ovarian cancers in first-degree and second-degree relatives on both the maternal and paternal side of the family. An opportunity to update the family history should take place during encounters for preventive care or screening. During these discussions, clinicians should emphasize the importance of awareness and recognition of breast changes and, if changes are perceived, the importance of seeking consultation promptly. Women may choose to do breast self-examination (BSE) regularly, occasionally, or not at all. If a woman chooses to perform periodic BSE, she should receive instructions in the technique and periodically have her technique reviewed. Women should be informed about the potential benefits, limitations, and harms (principally the possibility of a false-positive result) associated with BSE.

The ACS recommends that average-risk women should begin annual mammography at the age of 40 years. Women also should be informed about the scientific evidence demonstrating the value of detecting breast cancer before symptoms develop, and that the balance of benefits to adverse outcomes associated with screening strongly supports the value of screening and the importance of adhering to a schedule of regular mammograms. The benefits of mammography include a reduction in the risk of dying from breast cancer, and if breast cancer is detected early, less aggressive surgery being performed (ie, lumpectomy vs mastectomy), less aggressive systemic therapies, and a greater range of treatment options. Women also should be told about the limitations of mammography, specifically that mammography will not detect all breast cancers, and that some breast cancers detected with mammography may still have a poor prognosis. The harms associated with breast cancer screening include the potential for false-positive results, which can result in anxiety, and when abnormal findings cannot be resolved with additional imaging, a biopsy will be required to rule out the possibility of breast cancer. Finally, some breast cancers detected by mammography may not be progressive (ie, they would not have been detected in a woman’s lifetime had she not undergone mammography screening). Estimates of the rate of overdiagnosis are highly variable, ranging from 0% to extreme estimates that exceed 30%21,22; however, the most credible estimates (ie, those that properly adjust for lead time and trends in rising breast cancer incidence due to changes in risk) indicate that the magnitude of overdiagnosis is small and mostly confined to ductal carcinoma in situ.23,24

There is no specific upper age at which mammography screening should be discontinued. Rather, the decision to stop regular mammography screening should be individualized based on the potential benefits and risks of screening within the context of overall health status and estimated longevity.25 As long as a woman is in good health and would be a candidate for breast cancer treatment, she should continue to be screened with mammography.

In 2007, the ACS issued new guidelines for women who were known or likely carriers of a *BRCA* (breast cancer gene) mutation and other rarer high-risk genetic syndromes, or who had been treated with radiation to the chest for Hodgkin disease.4 Annual screening mammography and magnetic resonance imaging (MRI) starting at age 30 years are recommended for women with a known *BRCA* mutation, women who are untested but have a first-degree relative with a *BRCA* mutation, or women with an approximately 20% to 25% or greater lifetime risk of breast cancer based upon specialized breast cancer risk estimation models capable of pedigree analysis of first- and second-degree relatives on both the maternal and paternal side. While MRI

### TABLE 1. History of Recent Updates to ACS Cancer Early Detection Guidelines

| CANCER SITE | YEAR | DESCRIPTION |
|-------------|------|-------------|
| Breast cancer | 2003, Complete update | 3 |
| | 2007, Guidelines for MRI use in high-risk women | 4 |
| | 2013, Update anticipated | |
| Cervical cancer | 2002, Complete update | 5 |
| | 2007, Guidelines for HPV vaccine use | 6 |
| | 2012, Complete update | 7 |
| Colorectal cancer | 2001, Complete update | 8 |
| | 2003, Technology update | 9 |
| | 2006, Update for postpolypectomy and postcolorectal cancer resection surveillance | 10,11 |
| | 2008, Complete update | 12 |
| Endometrial cancer | 2001, Guidance for counseling, shared decision-making, and high-risk women | 13 |
| Prostate cancer | 2001, Guidance for shared decision-making related to testing for early detection and screening recommendations for higher-risk men | 14 |
| | 2010, Complete update | 15 |
| Lung cancer | 2001, Guidance for shared decision-making | 16 |
| | 2011, Interim guidance on lung cancer screening | 17 |
| | 2013, Complete update | 18 |

ACS indicates American Cancer Society; MRI, magnetic resonance imaging; HPV, human papillomavirus.
Table 2. ACS Recommendations for the Early Detection of Cancer in Average-Risk, Asymptomatic Individuals

| CANCER SITE | POPULATION | TEST OR PROCEDURE | FREQUENCY |
|-------------|------------|-------------------|-----------|
| Breast      | Women, aged ≥20 y | BSE | It is acceptable for women to choose not to do BSE or to do BSE regularly (monthly) or irregularly. Beginning in their early 20s, women should be told about the benefits and limitations of BSE. Whether a woman ever performs BSE, the importance of prompt reporting of any new breast symptoms to a health professional should be emphasized. Women who choose to do BSE should receive instruction and have their technique reviewed on the occasion of a periodic health examination. |
|             |            | CBE | For women in their 20s and 30s, it is recommended that CBE be part of a periodic health examination, preferably at least every 3 y. Asymptomatic women aged ≥40 y should continue to receive a CBE as part of a periodic health examination, preferably annually. |
|             |            | Mammography | Begin annual mammography at age 40 y.* |
| Cervix      | Women, aged 21-65 y | Pap test and HPV DNA test | Cervical cancer screening should begin at age 21 y. For women aged 21-29 y, screening should be done every 3 y with conventional or liquid-based Pap tests. For women aged 30-65 y, screening should be done every 5 y with both the HPV test and the Pap test (preferred) or every 3 y with the Pap test alone (acceptable). Women aged ≥65 y who have had ≥3 consecutive negative Pap tests or ≥2 consecutive negative HPV and Pap tests within the last 10 y, with the most recent test occurring within the last 5 y, and women who have had a total hysterectomy should stop cervical cancer screening. Women at any age should not be screened annually by any screening method. |
| Colorectal  | Men and women, aged ≥50 y | FOBT with at least 50% test sensitivity for cancer, or FIT with at least 50% test sensitivity for cancer, or Stool DNA test, or FSIG, or DCBE, or Colonoscopy | Annual, starting at age 50 y. Testing at home with adherence to manufacturer’s recommendation for collection techniques and number of samples is recommended. FOBT with the single stool sample collected on the clinician’s fingertip during a DRE in the health care setting is not recommended. Guaiac-based toilet bowl FOBT tests also are not recommended. In comparison with guaiac-based tests for the detection of occult blood, immunochemical tests are more patient-friendly, and are likely to be equal or better in sensitivity and specificity. There is no justification for repeating FOBT in response to an initial positive finding. |
|             |            | FOBT | Interval uncertain, starting at age 50 y. |
|             |            | FSIG | Every 5 y, starting at age 50 y. FSIG can be performed alone, or consideration can be given to combining FSIG performed every 5 y with a highly sensitive guaiac-based FOBT or FIT performed annually. |
|             |            | DCBE | Every 5 y, starting at age 50 y. |
|             |            | Colonoscopy | Every 10 y, starting at age 50 y. |
|             |            | CT colonography | Every 5 y, starting at age 50 y. |
| Endometrial | Women, at menopause | | At the time of menopause, women at average risk should be informed about the risks and symptoms of endometrial cancer and strongly encouraged to report any unexpected bleeding or spotting to their physicians. |
| Lung        | Current or former smokers aged 55-74 y in good health with at least a 30 pack-year history | LDCT | Clinicians with access to high-volume, high-quality lung cancer screening and treatment centers should initiate a discussion about lung cancer screening with apparently healthy patients aged 55-74 y who have at least a 30 pack-y smoking history, and who currently smoke or have quit within the past 15 y. A process of informed and shared decision-making with a clinician related to the potential benefits, limitations, and harms associated with screening for lung cancer with LDCT should occur before any decision is made to initiate lung cancer screening. Smoking cessation counseling remains a high priority for clinical attention in discussions with current smokers, who should be informed of their continuing risk of lung cancer. Screening should not be viewed as an alternative to smoking cessation. |
| Prostate    | Men, aged ≥50 y | DRE and PSA | Men who have at least a 10-y life expectancy should have an opportunity to make an informed decision with their health care provider about whether to be screened for prostate cancer, after receiving information about the potential benefits, risks, and uncertainties associated with prostate cancer screening. Prostate cancer screening should not occur without an informed decision-making process. |
| Cancer-related checkup | Men and women, aged ≥20 y | | On the occasion of a periodic health examination, the cancer-related checkup 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. |

ACS indicates American Cancer Society; BSE, breast self-examination; CBE, clinical breast examination; Pap, Papanicolaou; HPV, human papillomavirus; FOBT, fecal occult blood test; FIT, fecal immunochemical test; DRE, digital rectal examination; FSIG, flexible sigmoidoscopy; DCBE, double-contrast barium enema; CT, computed tomography; LDCT, low-dose helical CT; PSA, prostate-specific antigen.

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

**The stool DNA test approved for colorectal cancer screening in 2008 is no longer commercially available. New stool DNA tests are presently undergoing evaluation and may become available at some future time.
may eventually prove to be cost-effective and advantageous for women at elevated risk due to other combinations of risk factors, at this time recommendations for annual screening mammography and MRI are based strictly on known or estimated high-risk mutation carrier status or a history of high-dose radiation therapy at a young age.

To estimate the risk of breast cancer in women with a significant family history who have not undergone genetic testing and do not have an affected relative who has tested positive, health professionals should use specialized software that can address family history in first- and second-degree relatives on both the maternal and paternal side. There are several models that can estimate risk based on complex family histories and assist clinicians in estimating breast cancer risk or the likelihood that a BRCA mutation is present, including the Claus model,26 Tyrer-Cuzick model,27 BRCAPRO model,28 and the Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm (BOADICEA)29 model.30 While the Breast Cancer Risk Assessment Tool (ie, the Gail model) provides a good, generalized measure of short- and long-term risk based on a woman’s age, ethnicity, history of breast biopsy and breast cancer, age at menarche, parity, and age at first live birth, it does not have the capacity to analyze detailed family histories including first- and second-degree relatives on both the maternal and paternal side.31 A link to supplemental material related to these models is included in the online publication (onlinelibrary.wiley.com/doi/10.3322/canjclin.57.2.75/full).4

Almost since the inception of mammography screening, there have been disagreements over programmatic decisions about the age at which to begin and end screening, the screening protocol, and the assessment of the balance of benefits and harms. Two recent assessments of the current evidence for the effectiveness of mammography screening were conducted in the United Kingdom (UK) and Europe.

In response to ongoing debates in the published literature over the balance of benefits and harms associated with breast cancer screening, an independent panel was commissioned by the UK’s National Cancer Director and Cancer Research UK to review the evidence for the benefits and harms of mammography screening in the UK.32 While acknowledging the growing volume of observational studies of mammography in the medical literature, the panel principally focused only on the randomized controlled trials (RCTs) of breast cancer screening and applied that evidence to estimate the benefits and harms within the context of the UK screening program, which invites women aged 50 years to 70 years to screening every 3 years. The assessment of benefit focused on the reduction in breast cancer mortality, while harms were limited to overdiagnosis and overtreatment. The panel’s meta-analysis of all 11 RCTs resulted in a relative risk of 0.80 (95% confidence interval, 0.73–0.89), suggesting a 20% mortality reduction associated with an invitation to mammography screening, which also is consistent with other meta-analyses performed thus far. To estimate the rate of overdiagnosis, the panel also examined 3 breast cancer screening RCTs in which the control group was not invited to screening at the end of the trial. Based on the results of their analysis, they estimated an overdiagnosis rate ranging from 11% to 19%.32 This estimate needs to be interpreted with caution for several reasons, but principally because the short duration of follow-up in the 2 Canadian studies results in the estimate being biased upward by lead time.24 Overall, the panel concluded that for every 10,000 women in the UK aged 50 years who were invited to screening for the next 20 years, 43 deaths from breast cancer would be prevented and 129 cases of noninvasive and invasive cancer would be diagnosed, or approximately 3 cases of overdiagnosis for every breast cancer death prevented. Put another way, 180 women aged 50 years to 70 years is the number needed to screen (NNS) every 3 years for 20 years to prevent 1 death from breast cancer, and among the 307,000 women aged 50 years to 52 years who are invited to begin screening every year, just over 1% will be diagnosed with a nonprogressive cancer in the next 20 years.32 The panel’s conclusion was that breast cancer screening saves lives, and while there are adverse events associated with screening, benefits exceed harms and on that basis the UK breast cancer screening program should continue.

A separate independent review of breast cancer screening in Europe was conducted by the European Screening Network (EUROSCREEN) group, an organization of scientists and professionals with experience in implementing and evaluating screening. In contrast to the UK Independent Review Panel’s focus on only the RCTs of breast cancer screening, the EUROSCREEN group focused on data from screening programs that have been introduced in the European Union. Applying methodologic standards for the evaluation of population-based screening, the group developed pooled estimates of the benefits and harms of breast cancer screening as it presently is conducted in the European Union. The EUROSCREEN group’s report consists of 8 original reports organized in a supplement to the Journal of Medical Screening that focus on the strengths and limitations of the evidence from non-RCT study designs (observational, trend, and incidence-based mortality studies), an evaluation of the methodology for measuring harms and the occurrence of adverse events with particular emphasis on overdiagnosis, and a conclusion expressed as a balance sheet of the benefits and harms of screening.20,24,33–38 In contrast with the Independent UK Panel on Breast Cancer Screening, the EUROSCREEN group’s estimate of the balance of benefits and harms derived from the European
population-based screening programs is more favorable. For example, the pooled estimates of the mortality reduction associated with an invitation to screening were 25% in the incidence-based mortality studies and 31% in case-control studies, and 38% and 48%, respectively, among women who attended screening. For every 1000 women aged 50 years to 51 years screened biennially until age 69 years and followed until age 79 years, the NNS to diagnose one breast cancer is 14, and the NNS to prevent one breast cancer death is 111 to 143; a total of 7 to 9 breast cancer deaths will be prevented (among 30 expected in the absence of screening), and 4 cases will be overdiagnosed (in addition to 67 expected). In contrast to the Independent UK Panel on Breast Cancer Screening’s findings of an excess ratio of overdiagnosed cases to lives saved, the EUROSCREEN group estimated that approximately twice as many lives are saved compared with cases overdiagnosed.20

Each group concluded that the benefits of screening significantly outweigh the harms, and a review of each group’s report demonstrates the methodological complexity of measuring benefits and harms with the existing data. RCTs provide a clear measure of the efficacy of an invitation to screening, but the RCTs have variable numbers of screening rounds and variable rates of compliance and contamination, and not all have adequate follow-up. This is especially evident when comparing the steadily declining estimate of the NNS to save one life from 10 years of follow-up (922) to 29 years of follow-up (414) in the Swedish Two-County Trial.19 Thus, the RCTs have clear limitations as a source of data to measure the effectiveness of modern mammography. In contrast, the evaluation of incidence-based mortality provides an opportunity to measure the effect of screening based on exposure to screening and age at diagnosis (vs age at randomization) in a screened group versus an unscreened group. Although each of these expert panels focused on different data sources and reached somewhat different conclusions about the magnitude of benefits and harms, it is important to note in a period when some individual investigators have questioned the value of mammography, each of these reports affirms the importance of mammography in preventing deaths from breast cancer.

Screening for Cervical Cancer

The ACS estimates that 12,170 women will be diagnosed with invasive cervical cancer, and 4220 women will die from the disease in 2012.16 Cervical cancer incidence and mortality rates have declined since the introduction of the Papanicolaou (Pap) test in the mid-20th century, and rates continue to decline to this day. Since 2004, cervical cancer incidence rates have decreased by 2.1% per year in women aged younger than 50 years, and by 3.1% per year in women aged 50 years and older. Since 2004, mortality rates have been stable in white women, but have declined by 2.6% per year in African American women.39

In 2012, the ACS, the American Society for Colposcopy and Cervical Pathology, and the American Society for Clinical Pathology (ASCP) issued joint guidelines for cervical cancer screening based on a systematic evidence review and using a collaborative process that included 25 organizations (Table 2).7 Similar recommendations were released in 2012 by the U.S. Preventive Services Task Force (USPSTF).40 Recommendations for the use of prophylactic human papillomavirus (HPV) vaccines, including policy and implementation issues, were published in January 2007.6

The screening guidelines recommend different surveillance strategies and options based on a woman’s age, her screening history, other risk factors, and the choice of screening tests. Specifically:

- Screening for cervical cancer should begin at age 21 years. Women aged 21 to 29 years should receive cytology screening (with either conventional cervical cytology smears or liquid-based cytology) every 3 years. HPV testing should not be used for women in this age group. Women aged younger than 21 years should not be screened, regardless of their age of sexual initiation.
- For women aged 30 to 65 years, the preferred approach is to be screened every 5 years with the combination of HPV testing and cytology (“cotesting”). It is also acceptable for women to continue to be screened every 3 years with cytology alone.
- Women should discontinue screening after age 65 years if they have had 3 consecutive negative cytology tests or 2 consecutive negative cotest results within the 10-year period prior to ceasing screening, with the most recent test occurring within the last 5 years.
- Women at any age should NOT be screened annually by any screening method.

Special Considerations

These recommendations were developed for women at average risk and do not apply to women with a history of cervical cancer; women who were exposed in utero to diethylstilbestrol; women who are immunocompromised by organ transplantation, chemotherapy, or chronic corticosteroid treatment; or women who are positive for the human immunodeficiency virus (HIV).

Specifically:

- Cervical cancer screening is not indicated for women who have undergone removal of the cervix or the entire uterus and who do not have a history of cervical
intraepithelial neoplasia 2 (CIN2) or a more severe diagnosis. Women who have undergone a subtotal (supracervical) hysterectomy should be screened following the recommendations for average-risk women who have not undergone a hysterectomy.

- Women with a history of CIN2 or a more severe diagnosis should continue to follow routine screening recommendations for at least 20 years, even if screening extends beyond age 65 years.
- Women who are immunocompromised by organ transplantation, chemotherapy, or chronic corticosteroid treatment or those who are HIV positive should be tested twice during the first year after diagnosis/treatment and annually thereafter, according to guidelines from the U.S. Public Health Service and Infectious Disease Society of America.
- There is no specific age at which to stop screening for women with a history of cervical cancer or in utero exposure to diethylstilbestrol, and women who are immunocompromised (including those who are HIV positive). While the update in the guideline did not address immunocompromised women, earlier ACS guidelines relied on the joint recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. Women in these risk groups should undergo annual cervical cancer screening for as long as they are in reasonably good health and would benefit from early detection and treatment.
- Recommended screening practices should not change on the basis of HPV vaccination status.

Vaccination Against HPV

The ACS recommends routine HPV vaccination principally for females aged 11 to 12 years, but also for females aged 13 to 18 years to “catch up” those who missed the opportunity to be vaccinated or who need to complete the vaccination series. The guidelines state that there are insufficient data to recommend for or against the universal vaccination of females aged 19 to 26 years. Women in this age group who are interested in undergoing vaccination should talk with a health care professional about their risk of previous HPV exposure and the potential benefit of vaccination. Screening for CIN and cancer should continue in both vaccinated and unvaccinated women according to current ACS early detection guidelines for cervical cancer. According to the 2011 National Immunization Survey of Teens (NIS-Teen), 53% of US female adolescents aged 13 years to 17 years initiated the HPV vaccination series with either the quadrivalent or bivalent vaccine (ie, had at least one of 3 shots as recommended for the HPV vaccine), and 34.8% had completed 3 doses.

Screening and Surveillance for the Early Detection of Adenomatous Polyps and Colorectal Cancer

In 2012, the ACS estimates that 143,460 new cases of colorectal cancer (CRC) will be diagnosed in women and men, and 51,690 women and men will die from this disease. CRC incidence and mortality rates have been declining for the past 2 decades, which is largely attributable to the contribution of screening to prevention and early detection. Guidelines for screening and surveillance for the early detection of adenomatous polyps and CRC in average-risk adults were updated in 2008 in an evidence-based consensus process that included the ACS, the U.S. Multi-Society Task Force on Colorectal Cancer (USMSTF, which represents the American College of Gastroenterology, American Gastroenterological Association, and American Society for Gastrointestinal Endoscopy), and the American College of Radiology (Table 2). Recommendations for adults at increased and high risk were last updated in 2001, and in 2006 the ACS and the USMSTF issued a joint guideline update for postpolypectomy and post-CRC resection surveillance.

Recommended CRC screening tests are grouped into 2 categories: 1) tests that primarily detect cancer, which include both the guaiac-based fecal occult blood test (gFOBT) and immunochemical fecal occult blood test (FIT)s and testing stool for exfoliated DNA; and 2) tests that can detect cancer and advanced lesions, which include the endoscopic examinations and radiological examinations (ie, flexible sigmoidoscopy [FSIG], colonoscopy, double-contrast barium enema, and computed tomography colonography [CT colonography or virtual colonoscopy]). This distinction is intended to help primary care physicians support informed decision-making and to contribute to public understanding of the features, advantages, and disadvantages that distinguish these 2 groups of screening tests. Furthermore, the guidelines state that while all recommended tests are acceptable options, the prevention of CRC is the greater priority in screening.

Screening options may be chosen based on individual risk, personal preference, and access. Average-risk adults should begin CRC screening at age 50 years with one of the following options: 1) annual high-sensitivity gFOBT or FIT, following the manufacturer’s recommendations for specimen collection; 2) FSIG every 5 years; 3) colonoscopy every 10 years; 4) double-contrast barium enema every 5 years; or 5) CT colonography every 5 years. Stool DNA testing, which also was recommended in the 2008 update, is no longer commercially available for screening. Single-panel gFOBT in the medical office using a stool sample collected during a digital rectal examination is not a recommended option for CRC screening due to its very
low sensitivity for advanced adenomas and cancer. For similar reasons, the guideline recommends discontinuing the use of older, lower-sensitivity versions of the guaiac test in favor of newer, high-sensitivity gFOBT or FIT. An additional option for regular screening is annual stool blood testing (gFOBT or FIT) with FSIG performed every 5 years. Health professionals should provide guidance to adults about the benefits, limitations, and potential harms associated with screening for CRC, including information on test characteristics and requirements for successful testing. For example, when advising patients about gFOBT or FIT, it is important to stress that unless there is a commitment to annual at-home testing with adherence to the manufacturer’s instructions, the limited sensitivity observed with one-time testing would make stool testing a poor choice. In contrast, evidence from randomized clinical trials and modeling have shown that a commitment to annual testing with high sensitivity can result in a reduced risk of developing CRC and a reduced risk of dying from CRC that rivals colonoscopy.

The ACS and other organizations recommend more intensive surveillance for individuals at higher risk for CRC. Individuals at higher risk include: 1) individuals with a history of adenomatous polyps; 2) individuals with a personal history of curative-intent resection of CRC; 3) individuals with a family history of either CRC or colorectal adenomas diagnosed in a first-degree relative, with differing recommendations based on the relative’s age at diagnosis; 4) individuals at significantly higher risk due to a history of inflammatory bowel disease of significant duration; or 5) individuals at significantly higher risk due to the known or suspected presence of one of 2 hereditary syndromes, specifically hereditary nonpolyposis colon cancer (HNPCC) or familial adenomatous polyposis. For these individuals, increased surveillance generally means a specific recommendation for colonoscopy if available, and may include more frequent examinations and examinations beginning at an earlier age. As noted above, an update in recommendations for follow-up colonoscopy for individuals with a history of adenomatous polyps or a personal history of curative-intent resection of CRC was issued in 2006 jointly by the ACS and the USMSTF. The USMSTF has since updated its recommendations for colonoscopy surveillance after screening and polypectomy.

In 2012, findings from 2 long-anticipated studies related to CRC screening were published. Schoen et al reported results from the FSIG study in the National Cancer Institute’s (NCI) Prostate, Lung, Colorectal and Ovarian (PLCO) cancer screening trial. In 1995, PLCO randomized 154,900 men and women aged 55 years to 74 years to undergo a baseline FSIG and a second FSIG at 3 or 5 years. After median follow-up of 11.9 years, the investigators observed a 21% reduction in CRC incidence, and a 26% reduction in CRC mortality compared with the usual-care group. Mortality from CRC in the distal colon was reduced by 50% compared with the group that received usual care, while no reduction in deaths from proximal CRCs was observed. These outcomes are similar to those observed in the UK Flexible Sigmoidoscopy Trial, which observed a 23% reduction in incidence and a 31% reduction in mortality after a median of 11.2 years of follow-up.

In 1993, Winawer et al published initial findings from the National Polyp Study, which demonstrated a substantial reduction in CRC incidence associated with prior colonoscopy. Nearly 20 years later, the same team of researchers published long-term follow-up data on the association between colonoscopic polypectomy and the risk of CRC mortality among the 2602 patients who had adenomatous polyps removed during the study. With a median of 15.8 years of follow-up, 12 patients had died of CRC, whereas 25.4 deaths were expected based on general population rates, indicating 53% fewer deaths from CRC and providing support for the hypothesis that the removal of adenomatous polyps during endoscopy is associated with a reduced risk of dying from CRC.

While the findings from these 2 trials add further evidence supporting the efficacy of endoscopy for reducing incidence and mortality from CRC, and for FSIG principally in the distal colon, there still is ongoing debate over the high rate of screening colonoscopy compared with the use of alternative, less expensive, and less complex screening tests. Modeling data suggest that each of the individual tests is a good value (especially when FSIG is combined with high-sensitivity FOBT) and will result in similar mortality reductions and cost-effectiveness over a lifetime of screening. However, models are sensitive to assumptions, among which the most important is the adherence rate. The use of FSIG in the United States has steadily declined from 9.4% in 2000 to 2% in 2010. Use of a take-home FOBT test within the past year also has been declining, from less than 20% in 2000 to 8.8% in 2010, although the decline in stool testing primarily has been in middle and upper socioeconomic groups. As Byers notes, while annual testing with highly sensitive FIT is an appealing alternative to colonoscopy every 10 years, the evidence supporting the potential to achieve high rates of annual testing outside of highly organized systems, let alone high rates of follow-up of abnormal tests, is not encouraging. Primary care physicians rejected FSIG because it was time-consuming and complex and had low reimbursement, and they also have gravitated toward colonoscopy referral because they regard endoscopic examinations as more effective than stool testing. Without organized programs that could rationally and effectively increase both access and regular adherence with high-sensitivity stool testing and FSIG, colonoscopy is likely to remain the dominant screening test for CRC.
Testing for Early Prostate Cancer Detection

Prostate cancer is the most common cancer, apart from skin cancer, diagnosed in men in the United States, with an estimated 241,740 new cases expected to be diagnosed in 2012. In 2010, the ACS updated its 2001 guideline for the early detection of prostate cancer. The guideline states that men who have at least a 10-year life expectancy should have an opportunity to make an informed decision with their health care provider about whether to be screened for prostate cancer with DRE and serum prostate-specific antigen (PSA), after receiving information about the benefits, risks, and uncertainties associated with prostate cancer screening (Table 3). Prostate cancer screening should not occur without an informed decision-making process. Men at average risk should receive this information beginning at age 50 years. Men at higher risk, including African American men and men with a family member (father or brother) diagnosed with prostate cancer before age 65 years, should receive this information beginning at age 45 years. Men at appreciably higher risk (multiple family members diagnosed with prostate cancer before age 65 years) should receive this information beginning at age 40 years. Men should either receive this information directly from their health care providers or be referred to reliable and culturally appropriate sources. Patient decision aids are helpful in preparing men to make a decision regarding whether to be tested. For men who are unable to decide, the screening decision can be left to the discretion of the health care provider, who should factor into the decision his or her knowledge of the patient’s general health preferences and values. Asymptomatic men who have less than a 10-year life expectancy based on age and health status should not be offered prostate cancer screening. For men who choose to be screened for prostate cancer after a process of shared or informed decision-making: 1) screening is recommended with the serum PSA with or without DRE (DRE is recommended along with PSA for men with hypogonadism, due to the reduced sensitivity of PSA); 2) for men whose PSA is less than 2.5 ng/mL, screening intervals can be extended to every 2 years (screening should be conducted yearly for men whose PSA level is 2.5 ng/mL or higher); and 3) a PSA level of 4.0 ng/mL or higher has historically been used to recommend referral for further evaluation or biopsy, which remains a reasonable approach for men at average risk of prostate cancer. For PSA levels between 2.5 ng/mL and 4.0 ng/mL, health care providers should consider an individualized risk assessment that incorporates other risk factors for prostate cancer, particularly for high-grade cancer, which may be used for a referral recommendation. Factors that increase the risk of prostate cancer include African American race, family history of prostate cancer, increasing age, and abnormal DRE findings. A prior negative biopsy lowers risk. Methods are available that merge this information to achieve an estimate of a man’s overall risk of prostate cancer and, more specifically, of his risk of high-grade prostate cancer.

The importance of informed and shared decision-making has been a central element of ACS recommendations on prostate cancer screening since 1997 and especially since 2001. In fact, the importance of making an informed decision about screening for early cancer detection before testing takes place is a cross-cutting theme in most guidelines. However, studies have shown that informed and shared decision-making measures are inconsistently used and that, when such discussions do take place, the content is

| TABLE 3. Core Elements of the Information to Be Provided to Men to Assist With Their Decision About Prostate Cancer Screening* |
|---------------------------------------------------------------|
| Prostate cancer is an important health concern for men:       |
| • Screening with the PSA blood test alone or with both the PSA and DRE detects cancer at an earlier stage than if no screening is performed. |
| • Prostate cancer screening may be associated with a reduction in the risk of dying from prostate cancer. However, evidence is conflicting and experts disagree about the value of screening. |
| • For men whose prostate cancer is detected by screening, it is currently not possible to predict which men are likely to benefit from treatment. Some men who are treated may avoid death and disability from prostate cancer. Others who are treated would have died of unrelated causes before their cancer became serious enough to affect their health or shorten their lives. |
| • Depending on the treatment selected, the treatment of prostate cancer can lead to urinary, bowel, sexual, and other health problems. These problems may be significant or minimal, permanent or temporary. |
| • The PSA and DRE may have false-positive or false-negative results, meaning men without cancer may have abnormal results and undergo unnecessary additional testing, and clinically significant cancers may be missed. False-positive results can lead to sustained anxiety about prostate cancer risk. |
| • Abnormal results from screening with the PSA or DRE require prostate biopsies to determine whether the abnormal findings are cancer. Biopsies can be painful, may lead to complications such as infection or bleeding, and can miss clinically significant cancer. |
| • Not all men whose prostate cancer is detected through screening require immediate treatment, but they may require periodic blood tests and prostate biopsies to determine the need for future treatment. |
| • In helping men to reach a screening decision based on their personal values, once they understand the uncertainties, risks, and potential benefits, it can be helpful to provide reasons why some men decide for or against undergoing screening. For example: |
| • A man who chooses to be screened might place a higher value on finding cancer early; might be willing to be treated without a definite expectation of benefit; and might be willing to risk injury to urinary, sexual, and/or bowel function. |
| • A man who chooses not to be screened might place a higher value on avoiding the potential harms of screening and treatment, such as anxiety or risk of injury to urinary, sexual, or bowel function. |

PSA indicates prostate-specific antigen; DRE, digital rectal examination.
highly variable, incomplete, and falls short of accepted standards. Moreover, compared with clinicians in academic settings, community-based clinicians are more likely to endorse annual PSA testing as a standard of care. In an effort to address these shortcomings, the 2010 ACS guideline provides detailed recommendations on the core information related to screening and treatment that should be shared with men to enable them to make a truly informed decision.13

The ACS published these recommendations in 2010 following an extensive review of the evidence related to screening, including 2 recently published, long-term, multicenter RCTs of screening with PSA and DRE: the European Randomized Study of Screening for Prostate Cancer (ERSPC) and the PLCO cancer screening trial.67,68 Based on evidence from these RCTs and other studies, the ACS determined that the balance of benefits and harms related to the use of PSA for the early detection of prostate cancer still was uncertain and the existing evidence was insufficient to support a recommendation for or against the routine use of PSA screening.13 In 2012, the USPSTF released new recommendations on screening for prostate cancer. In 2008, the USPSTF recommended against prostate cancer screening in men aged 75 years and older, but concluded that there was insufficient evidence to recommend for or against prostate cancer screening for men aged 50 years to 74 years (C rating).69 In 2012, having evaluated largely the same evidence considered in the ACS review, the USPSTF concluded with moderate certainty that the harms of PSA testing outweigh the benefits and on that basis recommended against PSA-based screening for all men.70

The basis for the USPSTF’s new recommendation was “convincing evidence” from the multicenter trials that the number of men who avoid dying from prostate cancer due to screening is, at best, very small, while the harms related to the treatment of screen-detected cancers were judged to be at least moderate. These estimated harms included incontinence and erectile dysfunction in 200 to 300 of 1000 men treated with surgery or radiotherapy, and death in 5 of 1000 men within one month of prostate cancer surgery. The USPSTF made no distinction in their recommendations between men at average risk for prostate cancer and men known to be at an increased risk of developing and dying from prostate cancer (African Americans and men with a family history of prostate cancer). While the USPSTF acknowledged that African American men and men with a family history of the disease are at an increased risk of developing and dying from prostate cancer, they noted that the gaps in the evidence regarding the potential benefits of screening also apply to these men.

The differences between the ACS and USPSTF recommendations can be attributed in large part to differences in how each organization evaluated the recent evidence from the RCTs. The ACS judged the initial interim analyses from the ERSPC and PLCO as informative but not definitive. In contrast, the USPSTF has been criticized for reaching a definitive conclusion based on incomplete data.71

While there are clear differences in each organization’s recommendations, the ACS and USPSTF also share a number of similarities. Both recognize the fact that many men are harmed by undergoing screening that leads to the detection and treatment of prostate cancers that would never have become clinically apparent (overdiagnosis and overtreatment), or are so slow-growing that death from another cause is a higher probability. Although recommending against PSA screening, the USPSTF acknowledges that some men will continue to request screening and some physicians will continue to offer it. Like the ACS, they state that screening under such circumstances should respect patient preferences. There is also agreement that screening for prostate cancer in the absence of discussion and shared decision-making is not consistent with the evidence and should not take place. In their critique of the USPSTF’s recommendation against PSA testing, Carlsson et al endorsed 3 principles to measurably improve PSA screening outcomes in the United States.71 First, avoid PSA screening in men with a limited life expectancy. The ACS recommends that a man have at least 10 years of projected longevity or PSA testing is not appropriate.13 Second, avoid treatment in men who do not need treatment. This is a more challenging issue, and more research is needed to distinguish with confidence low-risk prostate cancers from those that truly need curative therapy. However, new data from the PIVOT (Prostate Intervention Versus Observation Trial) trial and other prospective studies comparing long-term outcomes may prove to be informative about choosing between curative therapy versus active surveillance.73 Third, men who need treatment should be referred to high-volume centers so that the risk of treatment-related complications is reduced.

Screening for Endometrial Cancer

In 2001, the ACS concluded that there was insufficient evidence to recommend screening for endometrial cancer in women at average risk, or those at increased risk due to a history of unopposed estrogen therapy, tamoxifen therapy, late menopause, nulliparity, infertility or failure to ovulate, obesity, diabetes, or hypertension.8 The ACS recommends that women at average and increased risk should be informed about the risks and symptoms (in particular, unexpected bleeding and spotting) of endometrial cancer at the onset of menopause, and should be strongly encouraged to immediately report these symptoms to their physicians (Table 2). Women at very high risk of endometrial cancer due to: 1) known hereditary HNPCC genetic mutation carrier status; 2) a substantial likelihood of being a mutation carrier (ie, a mutation is known to be present in the family);
or 3) the absence of genetic testing results in families with a suspected autosomal dominant predisposition to colon cancer should consider beginning annual testing for the early detection of endometrial cancer at age 35 years. The evaluation of endometrial histology with the endometrial biopsy is still the standard for determining the status of the endometrium. Women at high risk should be informed that the recommendation for screening is based on expert opinion, and they also should be informed about the potential benefits, risks, and limitations of testing for early endometrial cancer detection.

Screening for Lung Cancer

Lung cancer is the most common cause of death from cancer in men and women, accounting for approximately 28% of all cancer deaths in the United States and nearly 2.4 million years of life lost in 2009. Historically, there has been a concerted effort to reduce the burden of disease by preventing the uptake of cigarette smoking, promoting smoking cessation, and the investigation of various approaches to detecting lung cancer early in its natural history, including screening for lung cancer with chest x-ray (CXR) or sputum cytology. Studies of CXR screening have produced disappointing results, in part due to study design limitations, but also as a result of the inherent limitations of CXR to detect small lesions in the lung. In contrast, early investigations of screening for lung cancer with low-dose helical computed tomography (LDCT) demonstrated considerably greater sensitivity for the detection of small pulmonary nodules, leading to the initiation of RCTs in the United States and Europe.

In the United States, the National Lung Screening Trial (NLST) was launched in 2002, randomizing 53,454 adults aged 55 years to 74 years who were at high risk of lung cancer into 2 arms: one that would be invited to 3 rounds of annual LDCT screening and one that would be invited to 3 rounds of annual CXR. Participants were current or former smokers (quitting within the past 15 years) who were in reasonably good health and had at least a 30 pack-year history of smoking. In 2010, the NCI announced that the study had observed 20% fewer lung cancer deaths in the LDCT arm compared with the CXR arm, and that there was no evidence that adverse events associated with lung cancer screening were sufficiently common to question the balance of benefits and harms.

Findings from the NLST established that lung cancer mortality in specific high-risk groups can be reduced by annual screening with LDCT. However, although the evidence is convincing, it needs to be appreciated that organizations issuing new lung cancer screening guidelines are doing so with limited information from the NLST and ongoing RCTs in Europe and elsewhere. Furthermore, there is uncertainty about capacity; expertise; and the prevalence of expert, multispecialty groups in the United States to provide lung cancer screening and follow-up, and to do so with a high level of quality. Because cancer screening tests commonly are associated with both benefits and adverse events, and because the NLST results would likely stimulate great interest in lung cancer screening, the ACS issued interim guidance on lung cancer screening in 2011, stating that “adults between the ages of 55-74 who meet the eligibility criteria of the NLST and are concerned about their risk of lung cancer may consider screening for early lung cancer detection.” Rather than a direct recommendation for screening, the guidance emphasizes shared decision-making prior to making a decision about lung cancer screening.

Following the announcement of the NLST results in late 2010, the ACS joined with the American College of Chest Physicians, the American Society of Clinical Oncology, and the National Comprehensive Cancer Network to produce a systematic review of the evidence related to lung cancer screening with LDCT. Both RCTs and observational studies were included in the review, which focused on literature published from January 1996 through April 2012. The systematic review focused on evidence related to the benefits and harms associated with LDCT screening for lung cancer, groups likely to benefit from screening, and settings in which screening was most likely to be effective. In developing this guideline, which is an update of the interim guidance, particular weight was given to the NLST based on its larger study size, and the fact that it has shown a statistically significant difference of 20% fewer lung cancer deaths in a group invited to screening with LDCT versus CXR. Greater detail related to the evidence underlying the updated recommendations is available in the systematic evidence review and the updated guidelines.

The updated recommendations emphasize that clinicians with access to high-volume, high-quality lung cancer screening and treatment centers should ascertain the smoking status and smoking history of their patients aged 55 years to 74 years (Table 4), and should initiate a discussion about lung cancer screening with those who have at least a 30 pack-year smoking history, currently smoke, or have quit within the past 15 years, and who are in relatively good health. Core elements of this discussion should include the benefits, uncertainties, and harms associated with screening for lung cancer with LDCT (Table 5). Adults who choose to be screened should follow the NLST protocol of annual LDCT screening until they reach age 74 years. CXR should not be used for cancer screening.

When possible, adults who choose to be screened should enter an organized screening program at an institution with expertise in LDCT screening, with access to a multidisciplinary team skilled in the evaluation, diagnosis,
and treatment of abnormal lung lesions. If an organized, experienced screening program is not accessible but the patient strongly wishes to be screened, they should be referred to a center that performs a reasonably high volume of lung CT scans, diagnostic tests, and lung cancer surgeries. If such a setting is not available and the patient is not willing or able to travel, the risk of harms associated with lung cancer screening may be substantially higher than the observed risks associated with screening in the NLST, and therefore screening is not recommended. Referring physicians should help their patients identify appropriate settings with this expertise.

At this time, very few government or private insurance programs provide coverage for the initial LDCT preformed for lung cancer screening. Clinicians who decide to offer screening bear the responsibility of assisting patients determine whether they will have to pay for the initial test themselves and, if so, how much they will have to pay. In light of the firm evidence that screening high-risk individuals can substantially reduce death rates from lung cancer, both private and public health care insurers should expand coverage to include the cost of annual LDCT screening for lung cancer in appropriate high-risk individuals.

Smoking cessation counseling constitutes a high priority for clinical attention in patients who are currently smoking. Current smokers should be informed of their continuing risk of lung cancer, and referred to smoking cessation programs. Screening should not be viewed as an alternative to smoking cessation.

Clinicians should not discuss lung cancer screening with LDCT with patients who do not meet the recommended criteria (Table 4). If lung cancer screening is requested, these patients should be informed that at this time, there is too much uncertainty regarding the balance of benefits and harms for individuals at younger or older ages and/or with less lifetime exposure to tobacco smoke and/or with sufficiently severe lung damage to require oxygen (or other health-related NLST exclusion criteria), and therefore screening is not recommended.

### Testing for Early Ovarian Cancer Detection

Although the annual incidence of ovarian cancer is low compared with breast cancer and precursor lesions of the cervix, it is the most lethal of the gynecologic cancers. Fewer than one-half of women diagnosed with ovarian cancer survive longer than 5 years, and although 5-year survival of localized ovarian cancer is greater than 90%, only 15% of all patients are diagnosed with localized disease.

Screening and diagnostic methods for ovarian cancer include pelvic examination, CA 125 antigen as a tumor marker, transvaginal ultrasound (TVU), and, potentially, multimarker panels and bioinformatic analysis of proteomic patterns. The sensitivity and specificity of pelvic examination for the detection of symptomatic ovarian cancer are poor and do not support physical examination as a screening method. CA 125 has limited sensitivity and specificity (ie, while CA 125 levels are increased in many women with ovarian cancer, only one-half of early ovarian cancers produce enough CA 125 to cause a positive test, and noncancerous diseases of the ovaries, other cancers, and other noncancerous influences also can increase the blood levels of CA 125). TVU is capable of detecting small

### TABLE 4. Eligibility Criteria for the National Lung Screening Trial

| Age | Ages 55-74 y, with no signs or symptoms of lung cancer. |
|-----|--------------------------------------------------------|
| Smoking history | Active or former smoker with a 30-pack-y history (a pack-y is the equivalent of 1 pack of cigarettes per d per y. One pack per d for 30 y or 2 packs per d for 15 y would both be 30 pack-y). |
| Active smoker | If active smoker, should also be vigorously urged to enter a smoking cessation program. |
| Former smoker | If former smoker, must have quit within the past 15 y. |
| General health exclusions | Life-limiting comorbid conditions. Metallic implants or devices in the chest or back. Requirement for home oxygen supplementation. |

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ovarian masses and may distinguish some benign masses from some malignant adnexal masses, although it still only poorly predicts which masses are cancers and which are due to benign disease. As an independent test, ultrasound has shown poor performance in the detection of ovarian cancer in women at average or high risk.83 There are ongoing attempts to develop a blood test for ovarian cancer based on measuring genes, proteins, or multiple marker assays that may be present in higher or lower amounts in women with ovarian cancer compared with women who do not have ovarian cancer, but this work is still experimental and, however promising, prospective validation studies still will be required.84,85 At this time, the lack of supporting evidence indicating that any one or combination of these strategies is efficacious has prevented organizations from issuing recommendations for ovarian cancer screening.

Two large prospective randomized trials, one in the United States and the other in the United Kingdom, have been studying screening average-risk women with a combination of CA 125 and TVU. The US trial, the PLCO cancer screening trial,86 reported results in 2011.87 In the PLCO trial, 78,216 women aged 55 years to 74 years were randomized to a group offered 6 annual rounds of screening with CA 125 and TVU for 4 years (n=39,105) or a group that received usual care (n=39,111). Participants were followed for a maximum of 13 years, with mortality from ovarian cancer as the main study outcome. At the conclusion of the study, the number of deaths from ovarian cancer was similar in each group (ie, there were 3.1 ovarian cancer deaths per 10,000 women-years in the group invited to screening vs 2.6 deaths per 10,000 women-years in the control group [relative risk, 1.18; 95% confidence interval, 0.82–1.71]). The authors concluded that simultaneous screening with CA 125 and TVU was not associated with a reduction in ovarian cancer mortality compared with usual care.87 However, the authors also noted that the absence of a stage shift in the group invited to screening compared with the control group suggests that the screening protocol in the PLCO trial may not have been sensitive enough to diagnose ovarian cancer sufficiently early to alter its natural history. However, for each of the 2 tests under evaluation, lower cutoff values would result in higher false-positive rates. An alternative approach, which is currently under evaluation in the UK Collaborative Trial of Ovarian Cancer Screening, is assessing the efficacy of multimodal screening including annual CA 125 screening with a risk of ovarian cancer algorithm (ROCA) and TVU as a second-line test versus annual screening with TVU only.88 The ROCA measures changes in CA 125 over time rather than with a single cutoff point, and is believed to improve sensitivity for smaller tumors without measurably increasing the false-positive rate. PLCO investigators retrospectively evaluated CA 125 screening values in the PLCO study group to determine if calculating ROCA scores rather than using a fixed CA 125 cutoff would have more favorably affected the trial’s outcome. While the use of ROCA scores in the simulation was associated with fewer deaths in the intervention arm, the difference between deaths in the intervention group and control group still was not statistically significant. The authors caution that this simulation does not rule out the possibility of observing a benefit from using ROCA scores in the ongoing UK Collaborative Trial of Ovarian Cancer Screening.89

Currently, no organization recommends screening average-risk women for ovarian cancer. Based principally on the results of the PLCO trial, in 2012 the USPSTF recommended against screening for ovarian cancer (D recommendation), concluding that there was adequate evidence that annual screening with TVU and CA 125 does not reduce ovarian cancer mortality, and that likewise there was adequate evidence that screening for ovarian cancer can lead to important harms, mainly surgical interventions in women without ovarian cancer.90

In 1994, a National Institutes of Health Consensus Panel concluded that women with 2 or more first-degree relatives diagnosed with ovarian cancer should be offered counseling about their ovarian cancer risk by a gynecologic oncologist (or other specialist qualified to evaluate family history and discuss hereditary cancer risks) since these women have a 3% chance of being positive for an ovarian cancer hereditary syndrome.91 The panel further advised that women with a known hereditary ovarian cancer syndrome, such as mutations on BRCA1 and BRCA2, including breast-ovarian cancer syndrome, site-specific ovarian cancer syndrome, and HNPCC, should receive annual rectovaginal pelvic examinations, CA 125 determinations, and TVU until childbearing is completed or at least until age 35 years, at which time prophylactic bilateral oophorectomy is recommended. Although women with these hereditary syndromes are estimated to represent only 0.05% of the female population, they have a 40% estimated lifetime risk of ovarian cancer.

Cancer Screening and Primary Care

Periodic encounters with clinicians, either for acute care or for checkups, offer the potential for health counseling, cancer screening, and case finding.92,93 However, when individuals see a clinician for a preventive health examination, there is an opportunity for more comprehensive counseling and testing and indeed, it has been consistently observed that individuals who have had a recent preventive health examination are more likely to have undergone cancer screening.94 A preventive health examination is an opportunity to provide a referral for screening or, if appropriate, to perform the test in the office, and it is an opportunity for case-finding...
surveillance of cancer screening: colorectal, breast, cervical, and prostate cancers

In a previous report, we detailed national trends in cancer screening for the period between 1987 and 2005 based on the National Health Interview Survey (NHIS). In 2012, we provided updated national cancer screening estimates based on the 2010 NHIS, showing the extent of change (percentage increases or decreases) in cancer screening prevalence for 2 time periods (2005-2008 and 2008-2010). Using the most recent survey data (2010), we describe differences in cancer screening by race and ethnicity and 2 socioeconomic indicators (having health insurance and educational attainment) strongly associated with access to and use of medical/preventive services (Table 6). Since there are no updated survey results since 2010, we are reproducing the most recent data for the convenience of the reader (Table 6).

Discussion

ACS guidelines for average-risk adults endorse screening for breast cancer, cervical cancer, and CRC based on clear evidence that screening reduces morbidity and mortality. At this time, informed and/or shared decision-making is recommended for adults considering prostate cancer screening based on the uncertainty of the balance of benefits and harms. New lung cancer screening guidelines also stress shared decision-making, but emphasize that primary care physicians should assess the current and former smoking status of their patients aged 55 years to 74 years and, if they meet general health and smoking history criteria that would have made them eligible for the NLST, a discussion about lung cancer screening should then be initiated. A direct recommendation for lung cancer screening is not endorsed at this time by the ACS or any other organization because of the need for discussions about the potential benefits and harms, and also because of the need to identify and refer to high-quality local services.

Each of these screening recommendations has different age, gender, risk, and testing interval requirements. Screening adults at high risk of these cancers requires both the proper identification of high-risk status based on a detailed assessment of family history or other considerations, and application of a protocol that commonly involves beginning screening earlier and with different protocols than those recommend for average-risk adults.

Achieving high rates of cancer screening is a persistent challenge in both organized and nonorganized (ie, opportunistic) systems. In the United States, where opportunistic screening predominates, fulfilling the cancer screening needs of average- and high-risk adults requires a multifactorial combination of infrastructure, incentives, and systems to identify, contact, and follow the target population. Furthermore, health professionals must be aware of the screening recommendations for adults at average and high risk; the underlying evidence and logic for including and excluding individuals from invitations to screening; and the benefits, limitations, and harms associated with screening. Adults also need to have a basic awareness of what they can and cannot expect from screening. Finally, there should be no financial or other access barriers to screening and follow-up care.

Anhang Price et al summarized the literature on the association between organizational factors and cancer screening rates, and observed that screening rates were highest when strategies were in place that: 1) promoted recruitment, referral, and appointment scheduling; 2) reduced the number of organizational interfaces required to complete screening; and 3) promoted continuous patient care (ie, continuity in patient information, management, and therapy). Some aspects of health care reform in the Patient Protection and Affordable Care Act (ACA) of 2010 are designed to support the implementation of practice system changes that facilitate these strategies, and new models of primary care delivery, in particular the medical home, also include organizational features that enable these strategies and are associated with higher rates of preventive care. This type of practice enhancement is sorely needed since the NCI-led National Survey of Primary Care Physicians’ Recommendations and Practice for Breast, Cervical, Colorectal, and Lung Cancer Screening has revealed that during 2006 to 2007, fewer than one-half of primary care practices had a reminder system to alert patients that they are due for breast or cervical cancer screening. What also has been clear for some time is that these system features enhance and...
further enable the more fundamental factors that are associated with recent and regular cancer screening (ie, access to care as measured by a source of usual care and health insurance, tailored interventions, and a recommendation for screening from a health care provider).102,103 While these systems improve adherence to cancer screening, they are only one part of the comprehensive system of technical aids, staff engagement, and tailoring that are needed to achieve the highest rates of regular cancer screening. For example, Sarfaty et al recently

| TABLE 6. Prevalence (%) of Recent Cancer Screening Examinations Among US Adults by Race and Ethnicity, Health Insurance Coverage, and Educational Level, NHIS, 2010 |
|-----------------------------------------------|
| US ADULTS | RACE AND ETHNICITY |
| YEAR 2005a | YEAR 2008a | ABSOLUTE % CHANGE (2008-2005) |
| % | SE | % | SE | % | SE | % | SE | % | SE | % | SE |
| Colorectal cancer (adults aged ≥50 y) | | | | | | | | | | | |
| Either a FSIG or colonoscopyb | 64.8 | 0.6 | 53.2 | 0.6 | -6.4 | 59.1 | 0.6 | 5.9 | 61.5 | 0.7 | 55.5 | 1.7 | 17.0 | 1.8 | 14.9 | 2.3 |
| FOBT home kitc | 12.1 | 0.4 | 10.0 | 0.4 | -2.1 | 8.8 | 0.3 | -1.2 | 9.2 | 0.4 | 8.4 | 0.9 | 0.8 | 0.7 | 7.0 | 1.4 |
| FOBT or endoscopyd | 43.1 | 0.6 | 50.2 | 0.6 | -7.1 | 56.4 | 0.6 | 6.2 | 58.5 | 0.7 | 53.0 | 1.6 | 15.3 | 1.8 | 14.5 | 2.2 |
| Breast cancer (women aged ≥40 y) | | | | | | | | | | | |
| Mammograme | 51.2 | 0.6 | 53.0 | 0.7 | 1.8 | 51.0 | 0.7 | -2.0 | 51.5 | 0.9 | 50.6 | 1.6 | 46.5 | 1.7 | 47.7 | 2.8 |
| Cervical cancer (women aged ≥18 y) | | | | | | | | | | | |
| Pap testf | 79.6 | 0.4 | 78.3 | 0.5 | 1.3 | 76.4 | 0.5 | -1.9 | 77.7 | 0.6 | 77.8 | 1.1 | 73.4 | 1.1 | 66.1 | 2.0 |
| Prostate cancer (men aged ≥50 y) | | | | | | | | | | | |
| PSAg | 40.7 | 0.9 | 44.1 | 1.0 | 3.4 | 41.3 | 0.9 | -2.8 | 44.4 | 1.0 | 35.2 | 2.4 | 24.3 | 2.3 | 34.4 | 4.7 |

| HEALTH INSURANCE | EDUCATIONAL LEVEL (NO. OF YEARS OF EDUCATION) |
|-------------------|-----------------------------------------------|
| HAVE HEALTH INSURANCE | NO HEALTH INSURANCE | <11 YEARS | 12 YEARS | 13 TO 15 YEARS | >16 YEARS |
| % | SE | % | SE | % | SE | % | SE | % | SE | % | SE |
| Colorectal cancer (adults aged ≥50 y) | | | | | | | | | | | |
| Either a FSIG or colonoscopyb | 62.2 | 0.6 | 18.8 | 2.5 | 43.9 | 1.3 | 54.2 | 1.0 | 63.1 | 1.1 | 69.2 | 1.0 |
| FOBT home kitc | 9.2 | 0.4 | 1.6 | 0.3 | 5.8 | 0.6 | 6.8 | 0.5 | 11.0 | 0.7 | 10.4 | 0.7 |
| FOBT or endoscopyd | 59.4 | 0.6 | 17.8 | 2.5 | 42.1 | 1.3 | 51.9 | 1.0 | 59.5 | 1.1 | 66.7 | 1.0 |
| Breast cancer (women aged ≥40 y) | | | | | | | | | | | |
| Mammograme | 55.0 | 0.8 | 16.9 | 2.4 | 37.7 | 1.7 | 48.5 | 1.3 | 53.3 | 1.3 | 57.0 | 1.5 |
| Cervical cancer (women aged ≥18 y) | | | | | | | | | | | |
| Pap testf | 80.0 | 0.5 | 55.8 | 2.2 | 62.5 | 1.6 | 71.6 | 1.1 | 81.0 | 0.9 | 85.5 | 0.8 |
| Prostate cancer (men aged ≥50 y) | | | | | | | | | | | |
| PSAg | 49.5 | 1.0 | 13.9 | 3.6 | 26.2 | 1.9 | 34.8 | 1.6 | 43.0 | 1.8 | 53.9 | 1.7 |

NHIS indicates National Health Interview Survey; SE, standard error; FSIG, flexible sigmoidoscopy; FOBT, fecal occult blood test; Pap, Papanicolaou; PSA, prostate-specific antigen.
aPrevalence estimates for 2005 and 2008 are shown here to describe differences in the absolute percentage change in cancer screening use with respect to most recent data for 2010. Prevalence is weighted and age adjusted using the 2000 Census.
bRecent sigmoidoscopy within the preceding 5 y or colonoscopy within the preceding 10 y.
cRecent FOBT using a home test kit performed within the preceding y.
dRecent FOBT using a home test kit performed within the preceding y OR recent sigmoidoscopy or colonoscopy within the preceding 10 y.
eWomen aged ≥40 y who had a mammogram within the last y.
fWomen who had a Pap test within the preceding 3 y with intact uteri.
gA PSA test within the past y for men who had not been told they had prostate cancer. Source: National Health Interview Survey 2005, 2008, and 2010 (National Center for Health Statistics, Centers for Disease Control and Prevention, Atlanta, GA).
surveyed clinical and nonclinical staff in 15 primary care practices to measure adherence rates to the 4 steps associated with referral to and completion of screening colonoscopy (order the test, schedule the test, contact no-shows, reschedule no-shows) and the 7 steps associated with referral to and completion of FOBT or FIT (distribute cards, contact nonresponders, communicate test results, refer patients with positive findings for colonoscopy, schedule colonoscopy, contact no-shows, reschedule no-shows). While respondents reported high rates of adherence with step 1 for both colonoscopy and stool testing (ordering the test or distributing cards), fewer than one-half of practices contacted no-shows (step 3 and step 2, respectively), and more than one-third of practices reported not contacting patients with positive stool tests who did not show up for colonoscopy, thereby missing an opportunity to both increase screening rates and, for patients with positive findings, to avoid further disease progression in those patients who truly had cancer. While the transition to medical homes should provide structural and staffing resources to achieve high rates of cancer screening and follow-up by implementing the steps outlined by Sarfaty et al, it will be important to ensure that payment models are in place to support the additional staffing and infrastructure costs, and also that old practice patterns do not migrate into the new setting.

The ACA includes provisions for coverage of 16 adult preventive services, including breast, colorectal, and cervical cancer screening without any patient cost-sharing (i.e., no copay or requirement to meet a deductible) for individuals with new health insurance plans or policies beginning on or after September 23, 2010. This common feature of plans should contribute to increased rates of screening since out-of-pocket costs have been shown to be a significant deterrent to the use of preventive services.

However, there have been reports that some patients undergoing screening for breast cancer and CRC are being charged for screening examinations that they expected would be covered under the ACA’s provision against cost-sharing for preventive services that had received an A or B rating from the USPSTF. In 2012, the Henry J. Kaiser Family Foundation, the ACS, and the National Colorectal Cancer Roundtable published a report, Coverage of Colonoscopies Under the Affordable Care Act Prevention Benefit, that summarized findings from interviews with state health insurance regulators, state consumer assistance program directors, medical directors of major insurance companies, medical experts, insurance billing experts, and patients related to copays that were applied to procedures that were initiated as screening examinations. The investigators found that patients can encounter unanticipated cost-sharing for CRC screening when: 1) polypectomy is performed during a screening colonoscopy; 2) a colonoscopy is performed as part of a 2-step screening process following a positive stool blood test; and 3) an asymptomatic individual is defined as being at higher risk of CRC and is undergoing earlier or more frequent screening compared with average-risk adults. Under these 3 scenarios, there was significant variation in whether insurers regarded the examination as “screening,” and therefore covered it with no additional out-of-pocket costs. Under scenarios 1 and 2, these differences arose because some insurers regarded a screening examination that resulted in polypectomy as “diagnostic,” and a colonoscopy for a positive FOBT as diagnostic as well, rather than a continuation of the screening process that began with FOBT. Under scenario 3, these earlier or more frequent examinations may be regarded as “surveillance screening,” and thus coded as diagnostic examinations even though the patient is asymptomatic. Some state regulators reported that unexpected cost-sharing for screening examinations was the common source of complaints related to the implementation of the ACA. The investigators found that differences in the use and meaning of medical terminology (screening vs diagnostic vs surveillance), differences in the use and application of procedure codes, and inconsistent guidance from the federal government and state regulators had led to inconsistent procedure coding and thus variable interpretation of when cost-sharing should be waived. The report concluded that without additional federal guidance, there likely would continue to be inconsistent interpretation of when cost-sharing for screening examinations should be waived.

Increased insurance coverage for millions of Americans also is a feature of the ACA. Under the ACA, increased insurance coverage will be made available in 2014 through the expansion of Medicaid for nonelderly adults with an income less than 133% of the federal poverty level and through tax credits for lower-income adults that can be used to purchase coverage through health insurance exchanges. Regulatory changes requiring complete coverage for breast and cervical cancer screening (described above) mean that women with health insurance will have access to these screening tests without the barrier of cost-sharing, an important feature in the new legislation because women without insurance have roughly one-half the rate of recent screening compared with women with insurance, and also have worse outcomes. Levy et al sought to estimate the number of women in the United States who would gain health insurance after passage of the ACA and, likewise, the number of women who likely would remain uninsured and would need to access screening through the Centers for Disease Control and Prevention’s National Breast and Cervical Cancer Early Detection Program (NBCCEDP). Their underlying methodology assumed that the impact of the ACA would be similar to the effect the 2006 Massachusetts health care insurance reform law had on expanding coverage, and that uptake of newly available cancer screening services would be similar to that observed in the Oregon Medicaid randomized experiment. Thus, according to their estimates, mammography use would increase by 39% and Pap testing by 55% compared with the uninsured group over 2-year and 3-year intervals as per existing USPSTF guidelines.
Levy et al estimated that approximately 6.8 million low-income women aged 18 years to 64 years (the authors used the current eligibility age for Pap testing under the NBCCEDP) would gain health insurance under the ACA, 2.8 million of whom would be aged 40 years to 64 years. In contrast, 4.5 million low-income women would remain uninsured, of whom 1.7 million are aged 40 years to 64 years. Based on the Oregon experience and distributing uptake over the screening interval (every 2 years for mammography and every 3 years for Pap testing), Levy et al estimate an increase in the demand for mammography of approximately 1,000,000 additional examinations over a 2-year period, and 3.8 million additional Pap tests over a 3-year period. With respect to the ability of the NBCCEDP to meet the needs of women who still will not have health insurance after 2014, based on use between 2007 and 2009, the report estimates that the need for services will still be 3 times to 5 times higher than the numbers presently served. However, these estimates were made before the Supreme Court gave states the option of not expanding Medicaid, which means at this time they are optimistic and likely underestimate the number of low-income women who will have access to breast and cervical cancer screening under the ACA.

In conclusion, the ACA should be seen as a work in progress, and in the near term coverage that provides expanded access to screening without cost-sharing should contribute to higher screening rates, but will also add new pressures on the multistep processes needed to assure screening uptake and follow-up. To the degree that it is possible, attempts to organize screening could rationalize this process to improve the efficiency of delivering these services.

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