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2. Provide patients with guidance regarding appropriate early detection options.
3. Answer questions from patients regarding emerging cancer detection technologies.

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Cancer Screening in the United States, 2016: A Review of Current American Cancer Society Guidelines and Current Issues in Cancer Screening

Robert A. Smith, PhD[1]; Kimberly Andrews[2]; Durado Brooks, MD, MPH[3]; Carol E. DeSantis, MPH[4]; Stacey A. Fedewa, MPH[5]; Joannie Lortet-Tieulent, MSc[6]; Deana Manassaram-Baptiste, PhD, MPH[7]; Otis W. Brawley, MD[8]; Richard C. Wender, MD[9]

Each year the American Cancer Society (ACS) publishes a summary of its guidelines for early cancer detection, data and trends in cancer screening rates, and select issues related to cancer screening. In this issue of the journal, we summarize current ACS cancer screening guidelines, including the update of the breast cancer screening guideline, discuss quality issues in colorectal cancer screening and new developments in lung cancer screening, and provide the latest data on utilization of cancer screening from the National Health Interview Survey. **CA Cancer J Clin 2016;66:95-114. © 2016 American Cancer Society.**

Keywords: breast neoplasms, cervical neoplasms, colon and rectum neoplasms, lung neoplasms, screening, early detection

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Introduction

Each year, the American Cancer Society (ACS) provides an annual report for health care professionals and the public that summarizes the current ACS cancer screening guidelines and guidance related to early cancer detection, including updates in the guidelines, data on cancer screening rates, and a discussion of timely issues related to early cancer detection.

As part of the ongoing guideline development process, the ACS monitors the medical and scientific literature for new evidence that may support a change in current guidelines or development of a new guideline and new information about screening that should be conveyed to clinicians and target populations.[1,2] These annual guideline reviews, as well as the more detailed individual cancer screening guideline updates, are published as stand-alone articles and are available online at no cost. Table 1 shows the recent history of guideline updates as well as those in progress.[3-17]

In this update of ACS cancer screening guidelines, we describe the current guidelines (Table 2); an update of our breast cancer screening guideline; current issues that shape screening for breast, colorectal, and lung cancer; and the most recent data on cancer screening from the National Health Interview Survey (NHIS).

Screening for Breast Cancer

Among US women, breast cancer is the most common cancer, the second most common cause of death from cancer, and a leading cause of premature mortality from cancer in women as measured by average and total years of life lost.[18] The ACS estimates that there will be 246,660 cases of invasive breast cancer diagnosed in US women and 40,450 deaths during 2016.[19] After a period of declining age-adjusted breast cancer incidence rates (1999-2004), overall breast cancer incidence rates have been stable (2004-2012).[18] Age-adjusted breast cancer mortality rates have declined since 1989 and declined by about 1.9% per year over the period from 1998 to 2012.[18]

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TABLE 1. History of Recent Updates to American Cancer Society Cancer Early Detection Guidelines

CANCER SITE	YEAR (REFERENCE)
Breast cancer	2003: Complete update (Smith 2003[3])
	2007: Guidelines for MRI use in high risk women (Saslow 2007[4])
	2015: Complete update (Oeffinger 2015[5])
	2016: Update for women at increased and high risk initiated
Cervical cancer	2002: Complete update (Saslow 2002[6])
	2007: Guideline for HPV vaccine use (Saslow 2007[7])
	2012: Complete update (Saslow 2012[8])
	2015: Update related to follow-up of HPV negative ASC-US (Smith 2015[9])
Colorectal cancer	2001: Complete update (Smith 2001[10])
	2003: Technology update (Levin 2003[11])
	2006: Update for postpolypectomy and postcolorectal cancer resection surveillance (Rex 2006,[12] Winawer 2006[13])
	2008: Complete update (Levin 2008[14])
	2016: Update initiated
Endometrial cancer	2001: Guidance for counseling, shared decision making, and high risk women (Smith 2001[10])
Prostate cancer	2001: Guidance for shared decision making related to testing for early detection, and screening recommendations for higher risk men (Smith 2001[10])
	2010: Complete update (Woolf 2010[15])
	2017: Update planned
Lung cancer	2001: Guidance for shared decision making (Smith 2001[10])
	2011: Interim guidance on lung cancer screening (ACS Lung Cancer Guidance Workgroup 2011[16])
	2013: Complete update (Wender 2013[17])

ACS, American Cancer Society; ASC-US, atypical squamous cells of undetermined significance; HPV, human papillomavirus; MRI, magnetic resonance imaging.

The ACS guideline for breast cancer screening in average-risk women was updated in 2015[5] and represents the first guideline to follow the new process for ACS guideline development and update established in 2011.[1,2] The ACS organized an interdisciplinary Guideline Development Group (GDG) consisting of nonspecialist experts to consider the evidence and develop or update its screening guidelines. The last previous update of the ACS guideline for breast cancer screening in average-risk women was in 2003,[3] and the screening guideline for women at very high risk was last updated in 2007 (Table 2).[4] For this update, ACS chose to focus on a broad definition of average-risk women, which the GDG considered to be those women without a personal history of breast cancer, a confirmed or suspected genetic mutation known to increase risk of breast cancer (eg, *BRCA1* or *2* etc), or a history of previous radiotherapy to the chest at a young age. An update of the ACS breast cancer screening guideline for women at higher than average risk will be undertaken in 2016.

Process

The GDG applied the PICOTS approach of specifying **P**opulations, **I**nterventions, **C**omparisons, **O**utcomes, **T**iming of outcomes, and **S**ettings to develop key questions for the systematic evidence review of the literature on breast cancer screening for women at average risk of breast cancer.[5,20] The Duke University Evidence Synthesis Group was commissioned to conduct the systematic evidence review of the breast cancer screening literature.[21] Supplementary analyses to update previously published studies related to the screening interval and outcomes were obtained from the Breast Cancer Surveillance Consortium (BCSC),[22] and supplementary data and analyses on disease burden using data from the Surveillance, Epidemiology, and End Results (SEER) Program[18] were obtained from the ACS Surveillance and Health Services Research Program.

The GDG instructed the Duke University Evidence Synthesis Group to focus on both the randomized controlled trials (RCTs) of breast cancer screening and observational studies, including evaluations of population-based, organized screening programs, trend studies, and case-control studies. Historically, the main evidence used to develop guidelines for breast cancer screening predominately has derived from meta-analyses of the RCTs, which measure the efficacy of an invitation to breast cancer screening. These meta-analyses combine some or all RCTs and compare breast cancer mortality rates in the study arms invited to screening with those in the study arms not invited to screening. The advantage of an RCT is that the study design measures the efficacy of mammography, holding known and unknown biases in check, and also measures the effect of screening under ideal conditions. However, the true potential efficacy and effectiveness may not be completely measured for two reasons. First, high rates of nonadherence to the randomization assignment may affect death rates in each arm due to nonadherence beyond the true influence of selection bias in the invited group and contamination in the control group. Second, the mammography RCTs vary considerably according to whether and how much the invited group experienced a reduction in the rate of advanced disease associated with an invitation to screening, which is strongly associated with the observed

reductions in the risk of dying from breast cancer in the RCTs.[23] In addition to not measuring the effectiveness of screening only among women who are exposed to screening, the breast cancer screening RCTs used older technologies and protocols that are not reflective of modern breast cancer screening. More recently, guideline developers have relied on modeling studies and observational studies to supplement the data from the RCTs. The GDG regarded RCT results as providing good evidence of the efficacy of screening, while the results of contemporary observational studies were informative in important ways about the effectiveness of modern mammography screening among women who actually attend screening. The observational studies also have advantages for measuring age-specific benefits of mammography screening, because they can measure the effects of screening based on age at exposure, while the RCTs measure outcomes based on age at randomization.

In this update, the "Grades of Recommendation, Assessment, Development, and Evaluation" (GRADE) system was used to grade the quality of the evidence and the strength of recommendations.[24,25] In deliberating about the evidence on the key questions and formulating the recommendations, the GDG adhered to the GRADE domains, ie, confidence in the magnitude of the effects on outcomes, the balance between desirable and undesirable outcomes, and the diversity of women's values and preferences.[26,27] Consistent with the new guideline development process, the GDG sought the input of a group of expert advisors in their consideration of the evidence and subsequently to review the draft guideline recommendation statements. The draft guideline also was submitted to 26 relevant outside organizations for external review before being finalized.

Disease Burden

The age to begin mammography screening and the screening interval have been persistent objects of debate, with some organizations recommending beginning annual mammography screening at age 40 years[3,28] and others recommending biennial mammography screening beginning at age 50 years, with shared decision making between ages 40 and 49 years.[29] Because the underlying risk of disease is a factor in considering the value of inviting a target group to screening, the GDG approached the first of these questions by examining data on the burden of breast cancer by age in smaller age ranges (1-year and 5-year age groups) compared with the more common presentation of data by 10-year age groups (ie, ages 40-49 years, 50-59 years, etc) or comparing women in their 40s with women ages 50 years and older.

The risk of developing breast cancer increases with advancing age. Of particular relevance to the age at which to begin screening is the similarity of the different indicators of disease burden among women ages 45 to 49 years and 50 to 54 years. The 5-year risk among women ages 45 to 49 years (0.9%) and women ages 50 to 54 years (1.1%) is similar, as is the proportion of all incident cases (10% and 12%, respectively) (Fig. 1A), and the proportion of deaths due to diagnoses in these age groups, i.e., incidence-based mortality (10% and 11%, respectively) (Fig. 1B). In addition, the age-specific proportion of all incidence-based person-years of life lost is the same for women ages 45 to 49 years and 50 to 54 years based on age at diagnosis (approximately 15% each) (Fig. 1C), and these age groups together account for 30% of all person-years of life lost at 20 years of follow-up. This examination of the burden of disease within 5-year age groups indicates that traditional comparisons of women in their 40s with women in their 50s, or with women ages 50 years and older, obscure similarities among women ages 45 to 54 years. Indeed, these similarities would make it difficult to justify beginning screening at age 50 years, and not at age 45 years. In contrast, for each of these indicators, the burden of disease is lower among women ages 40 to 44 years, especially in the earliest years, which are more similar to the last few years of the decade of the 30s. Also noteworthy is the burden of disease in women ages 70 years and older. More than a third of all breast cancer deaths are attributable to women diagnosed after age 70 years (Fig. 1B). Given that a majority of women between ages 70 and 80 years are in good health and can expect to live 10 years or longer, the data suggest important opportunities to avoid morbidity and mortality from breast cancer in older women.

Benefits of Screening

In the systematic review conducted for the update of the ACS breast cancer screening guideline, the strength of the evidence was judged to be high across all study designs that invitation or exposure to mammography screening compared with usual care was associated with reduced breast cancer mortality overall, as well as in age-specific subgroups.[21] The magnitude of the observed mortality reductions varied across the different study designs, from 15% to 54% fewer deaths associated with mammography screening, depending on the study design and whether the mortality reduction was associated with invitation versus exposure to screening. As would be expected, both case-control studies and incidence-based mortality studies based on exposure to screening demonstrated the greatest overall mortality reductions, in large part because deaths from breast cancer only in women exposed to screening are included in the analysis. A similar pattern was observed for age-specific mortality reductions associated with mammography screening.

Harms Associated With Screening

In addition to consideration of the burden of disease and the benefit of breast cancer screening in terms of mortality

TABLE 2. American Cancer Society Recommendations for the Early Detection of Cancer in Average-Risk, Asymptomatic People[a]

CANCER SITE	POPULATION	TEST OR PROCEDURE	RECOMMENDATION
Breast	Women ages 40-54 y	Mammography	Women should undergo regular screening mammography starting at age 45 y; women ages 45-54 y should be screened annually; women should have the opportunity to begin annual screening between ages 40 and 44 y
	Women ages ≥55 y	Mammography	Women aged ≥55 y should transition to biennial screening or have the opportunity to continue screening annually; women should continue screening mammography as long as their overall health is good and they have a life expectancy ≥10 y
Cervix	Women ages 21-29 y	Pap test	Cervical cancer screening should begin at age 21 y; for women ages 21-29 y, screening should be done every 3 y with conventional or liquid-based Pap tests
	Women, ages 30-64 y	Pap test & HPV DNA test	For women ages 30-64 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 ages ≥65 y	Pap test & HPV DNA test	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 in the last 5 y, should stop cervical cancer screening
	Women who have had a total hysterectomy	—	Women who have had a total hysterectomy should stop cervical cancer screening
Colorectal	Men and women ages ≥50 y, for all tests listed	Guaiac-based fecal occult blood test (gFOBT)[b] with at least 50% test sensitivity for cancer, or fecal immunochemical test (FIT)[b] with at least 50% test sensitivity for cancer, or	Annual; testing stool sampled from regular bowel movements with adherence to manufacturer's recommendation for collection techniques and number of samples is recommended; FOBT with the single stool sample collected during a digital rectal examination is not recommended; "Throw in the toilet bowl" FOBTs also are not recommended; compared 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; patients should be referred to colonoscopy
		Multitarget stool DNA test,[b] (mtsDNA) or	Every 3 y, per manufacturer's recommendation
		Flexible sigmoidoscopy,[b] (FSIG) or	Every 5 y, FSIG can be performed alone, or consideration can be given to combining FSIG performed every 5 y with a highly sensitive gFOBT or FIT performed annually
		Double contrast barium enema,[b] or	Every 5 y
		Colonoscopy	Every 10 y
		CT colonography[b]	Every 5 y
Endometrial	Women at menopause	—	At the time of menopause, women should be informed about risks and symptoms of endometrial cancer and strongly encouraged to report any unexpected bleeding or spotting to their physicians
Lung	Current or former smokers ages 55-74 y in good health with at least a 30 pack-year smoking history	Low-dose helical CT (LDCT)	Clinicians with access to high-volume, high-quality lung cancer screening and treatment centers should initiate a discussion about annual lung cancer screening with apparently healthy patients ages 55-74 y who have at least a 30 pack-year 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 ages ≥50 y	Prostate-specific antigen test with or without digital rectal examination	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

CT, computed tomography; FSIG, flexible sigmoidoscopy; HPV, human papillomavirus; Pap, Papanicolaou. [a]All individuals should become familiar with the potential benefits, limitations, and harms associated with cancer screening. [b]All positive tests must be followed up with colonoscopy.

reduction and lives saved, guideline developers now must also devote more attention to the experiences collectively described as harms, which include being recalled for an abnormality that is later determined to be a false-positive, undergoing biopsy because of a false-positive finding that could not be resolved with additional imaging, the anxiety that may be associated with each, and overdiagnosis and overtreatment. These differ quantitatively, from recall for additional imaging, to biopsy, to overtreatment, and they differ qualitatively in terms of their effects and the value different women are likely to place upon them. For some women, being recalled has little or no lasting adverse effects, while other women will experience greater and sometimes persistent adverse effects. The GDG judged women's values and preferences as having a more important role in decisions during periods when the balance of absolute benefits based on disease burden and harms associated with regular screening is less clear.

The Screening Interval

Recommended breast cancer screening intervals principally are based on average tumor growth rates to ensure that, among women attending regular screening, the majority of breast cancers will be detected by screening before symptoms develop. These estimates have been an indirect method for determining the appropriate screening interval, because no RCTs have compared outcomes based on annual versus biennial screening. The estimated period of time that a clinically asymptomatic breast tumor is detectable by mammography is known as the sojourn time, and evaluations of RCT data have estimated that sojourn times were shorter among women in their 40s (1.7 years) compared with women ages 50 to 59 years (3.3 years) and women ages 60 to 69 years (3.8 years).[30] For women ages 40 to 54 years (1.73 years) versus women ages 55 69 years (3.51 years), a similar pattern has been observed.[31] More recently, data from the US BCSC have been used to compare screening outcomes among women undergoing annual versus biennial screening by age and other factors.[32-35] However, the screening intervals representing annual and biennial screening were wide (9-18 months and 19-33 months, respectively), and the GDG chose to assess the effect on tumor characteristics by age with screening intervals that more closely approximated 12 months versus 24 months. In the commissioned analysis, Miglioretti and colleagues compared outcomes associated with annual (11-14 months) versus biennial (23-26 months) screening among 15,440 women with breast cancer. Among premenopausal women, those who were screened biennially had statistically higher risks of being diagnosed with an advanced cancer; specifically, they had a 28% higher risk of being diagnosed with tumors that were stage IIB or higher, a 21% higher risk of being diagnosed with a tumor greater than 15 mm in size, and an 11% chance of being diagnosed with any less favorable prognostic tumor characteristic compared with women undergoing annual screening. Among postmenopausal women, there was no clear advantage of annual screening compared with biennial screening.[22]

2015 Breast Cancer Screening Recommendations

The updated ACS guideline (Table 3) affirms that screening mammography is the most effective way for a woman to reduce her likelihood of dying prematurely from breast cancer. The guideline provides women at average risk both guidance and flexibility to choose the age at which to begin screening and the screening interval. After careful examination of the evidence of benefit and the burden of disease among women ages 40 to 54 years, the GDG made a strong recommendation that women should undergo mammography screening starting at age 45 years. A strong recommendation is an indication of consensus that the benefits of the intervention outweigh undesirable effects and an expectation that most individuals would choose to be screened.[26,27]

The lesser, but not insignificant, burden of disease for women ages 40 to 44 years and the higher cumulative risk of adverse outcomes associated with beginning screening earlier supported a qualified recommendation that women ages 40 to 44 years have an opportunity to begin screening before age 45 years. A qualified recommendation indicates consensus that there is evidence of benefit but less certainty about either the balance of benefits and harms or about patients' values and preferences.[26,27] Although it is likely that a majority of women ages 40 to 44 years will choose to begin screening at age 40 years or within this period, many may not. Some women will value the potential benefits of beginning screening earlier and will be willing to accept the increased odds of additional testing. Others may choose to defer beginning screening until age 45 years, based on the relatively lower risk of breast cancer in the early 40s.

Because annual mammography screening provides additional benefit over biennial screening in younger women, we recommend that women who are ages 45 to 54 years and women ages 40 to 44 years who choose to begin screening before age 45 years, should be screened annually. These are qualified recommendations. Women age 55 years and older should transition to biennial screening or have the opportunity to continue annual screening (also a qualified recommendation), because breast cancer tends to grow more slowly after menopause; is easier to detect due to decreasing breast density; and, importantly, the updated BCSC analysis did not show a prognostic advantage from annual versus biennial screening in postmenopausal women.[22] Age 55 years

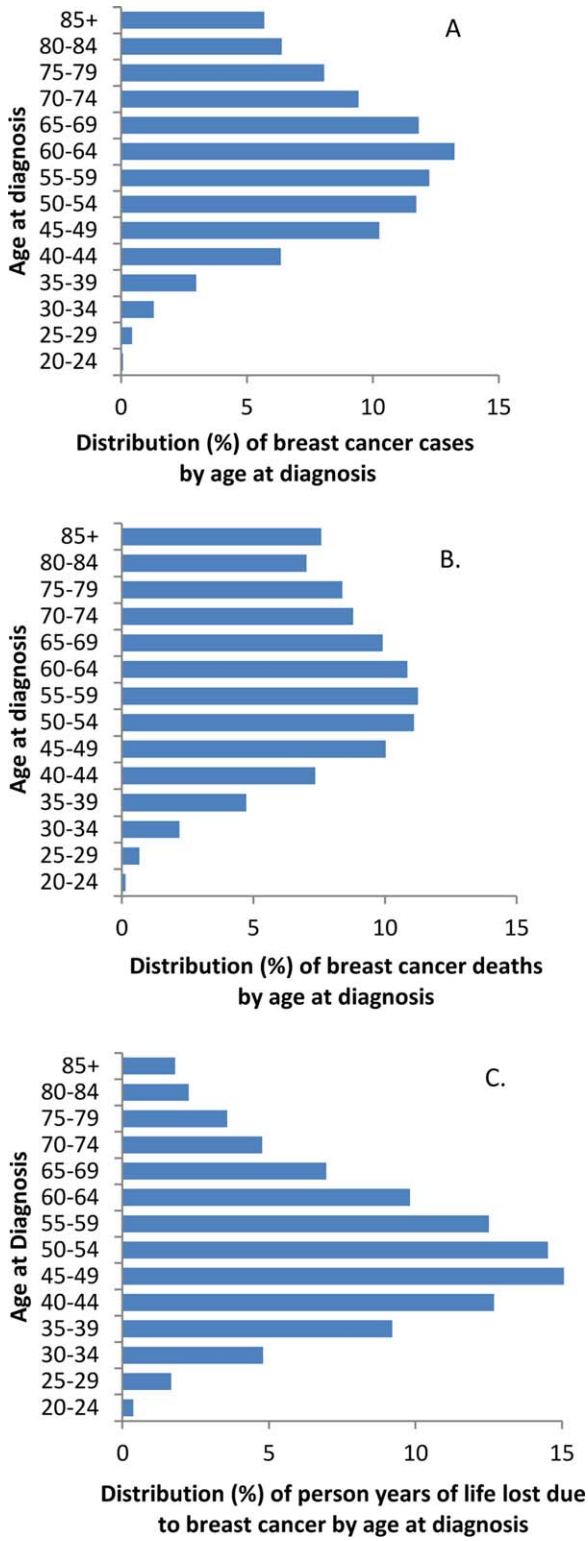

FIGURE 1. Breast Cancer Burden by Age at Diagnosis, 2007 to 2011. (A) Age distribution of invasive female breast cancer cases (n = 292,369) from 2007 to 2011 is illustrated. Source: National Cancer Institute Surveillance, Epidemiology, and End Results (SEER) 18 registries. (B) The distribution of breast cancer deaths from 2007 to 2011 is illustrated by age at diagnosis (n = 16,789) among patients who were followed for 20 years after diagnosis. (C) The distribution of person-years of life lost because of breast cancer from 2007 to 2011 is illustrated by age at diagnosis (total = 326,560) among patients who were followed for 20 years after diagnosis. Source: National Cancer Institute, SEER 9 registries. The years of potential life lost are based on the National Center for Health Statistics 2011 US female life table. Adapted from Reference 5.

represents the age by which most American women have reached menopause.[36]

The new guideline recognizes the potential benefit of continuing screening for women in good health at older ages but also the importance of identifying those women with life-limiting comorbidity who are unlikely to benefit from screening. Women should continue screening mammography as long as their overall health is good and they have a life expectancy of 10 years or longer (qualified recommendation). In applying clinical judgement about longevity, clinicians should use mortality indices that incorporate age, comorbidities, and functional status.[37] In addition, women should be provided opportunities for individualized decision making considering potential benefits and harms and incorporating health priorities and patient preferences.[38]

Historically, the ACS had recommended periodic clinical breast examination (CBE) for women younger than 40 years and annual CBE for women age 40 years and older. In this update, the absence of clear evidence that CBE contributes significantly to early breast cancer detection before or after age 40 years or to mortality reductions[21] led the GDG to conclude that it could no longer be recommended

TABLE 3. American Cancer Society Guideline for Breast Cancer Screening, 2015[a]

THE ACS RECOMMENDS THAT ALL WOMEN SHOULD BECOME FAMILIAR WITH THE POTENTIAL BENEFITS, LIMITATIONS, AND HARMS ASSOCIATED WITH BREAST CANCER SCREENING
Recommendations[b]
1. Women with an average risk of breast cancer should undergo regular screening mammography starting at age 45 y (*strong recommendation*)
1a. Women ages 45-54 y should be screened annually *(qualified recommendation)*
1b. Women aged ≥55 y should transition to biennial screening or have the opportunity to continue screening annually *(qualified recommendation)*
1c. Women should have the opportunity to begin annual screening between ages 40 and 44 y *(qualified recommendation)*
2. Women should continue screening mammography as long as their overall health is good and they have a life expectancy ≥10 y *(qualified recommendation)*
3. The ACS does not recommend clinical breast examination for breast cancer screening among average-risk women at any age *(qualified recommendation)*

ACS, American Cancer Society. [a]These recommendations represent guidance from the American Cancer Society for women at average risk of breast cancer: women without a personal history of breast cancer, a suspected or confirmed genetic mutation known to increase risk of breast cancer (eg, *BRCA*), or a history of previous radiotherapy to the chest at a young age. [b]A strong recommendation conveys the consensus that the benefits of adherence to that intervention outweigh the undesirable effects that may result from screening. Qualified recommendations indicate there is clear evidence of benefit of screening but less certainty about the balance of benefits and harms, or about patients' values and references, which could lead to different decisions about screening.[26,27]

for average-risk women at any age (qualified recommendation). This new recommendation should not be interpreted as discounting the potential value of CBE in low-resource and medium-resource settings where mammography screening may not be feasible.[39] CBE also may have a role in some groups of women at very high risk, but this question will be addressed in the update of recommendations for high-risk women.

The GDG did not address breast self-examination, which the ACS did not recommend in 2003;[40] thus there is no change from the 2003 guideline. Although the ACS breast cancer screening guideline does not recommend routine breast self-examination, some women may choose to examine their breasts regularly or occasionally. Because not endorsing BSE may seem counterintuitive to patients, health care professionals should explain that there is very limited evidence supporting the value of routine BSE for the early detection of breast cancer over a woman's own awareness of her breast changes. Familiarity with how her breasts normally look and feel and prompt reporting of breast changes that are associated with signs and symptoms of breast cancer should be emphasized.[41]

Information, Assessment, and Decision Making

The ACS recommends that women should be informed about the benefits, limitations, and harms associated with breast cancer screening. During encounters, health care professionals can identify women who may be at increased or very high risk of breast cancer, answer questions she may have about her own risk, address risk reduction and healthy behaviors, and answer questions related to conventional or new imaging technologies. With respect to risk, it is important that clinicians establish and routinely update the patient's family history of breast and ovarian cancers in first-degree and second-degree relatives, including age at diagnosis, on both the maternal and paternal sides of the family. Clinicians should describe the effect of family history on breast cancer risk and emphasize the importance of the patient's role in helping keep the family history up to date if there has been a change. Attention to family history beginning in the 20s and afterward not only is an opportunity to identify a patient who may benefit from genetic counseling and pedigree assessment but also to counsel women who may underestimate or overestimate the contribution of family history to their own risk.[42]

Women should be informed that early breast cancer detection with mammography is associated with a significantly reduced risk of being diagnosed with an advanced breast cancer and of dying from breast cancer.[23] Detection of breast cancer while it is still localized to the breast also provides women with an opportunity for less aggressive treatment, which may include the option to undergo breast-conserving therapy, avoid extensive lymph node dissections that increase the risk of lymphedema, and/or avoid chemotherapy.[43,44] Women should also be informed of the importance of adhering to a schedule of regular screening to ensure the greatest likelihood of having a growing breast cancer detected while it is still small and localized to the breast and about the limitations and harms associated with breast cancer screening.[45] Mammography will not detect all breast cancers, and 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 mostly will result only in short-term anxiety.[46] When abnormal findings cannot be resolved with additional imaging, a biopsy will be required to rule out the possibility of breast cancer; the majority of these are benign. Finally, some invasive 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, and the likelihood of nonprogression is higher in women diagnosed with ductal carcinoma in situ (DCIS). The chances that a woman undergoing regular screening will be diagnosed with an overdiagnosed breast cancer is uncertain but has been estimated by Marmot et al[47] to be slightly greater than 1% over a lifetime of screening. Given the uncertainty over the magnitude of overdiagnosis[21,47] and the fact that most women will not be diagnosed with breast cancer in their lifetime, it may be that the most useful way to convey the chances of being diagnosed with a cancer that would never cause a problem is the lifetime risk versus expressing the risk of overdiagnosis as a fraction of all breast cancers diagnosed. This preference was expressed by a citizens' jury of 25 women assembled in the United Kingdom to consider how information about breast cancer screening should be presented to women invited for screening.[48]

Screening for Breast Cancer in Women at Increased and High Risk

In 2007, the ACS issued a guideline for women who were known or likely carriers of a *BRCA* 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 is 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-degree and second-degree relatives on both the maternal and paternal sides. While MRI may eventually prove to be advantageous for women at elevated risk because of

other combinations of risk factors, at this time, recommendations for annual screening mammography and MRI are limited to the risk criteria described above.

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-degree and second-degree relatives on both the maternal and paternal sides.[49-51] There are several models that can estimate risk based on complex family histories and assist clinicians to estimate breast cancer risk or the likelihood that a *BRCA* mutation is present, including the Claus model,[52] International Breast Cancer Intervention Study (IBIS) (the Tyrer-Cuzick model),[53] the BRCAPRO model,[54,55] and the Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm (BOADICEA)[56] model.[49] Although the Breast Cancer Risk Assessment Tool (BCRAT), or Gail model,[57] provides a good, generalized measure of short-term 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 that include first-degree and second-degree relatives on both the maternal and paternal sides, and it does not perform as well across the spectrum of risk compared with the more complex risk calculators cited above. As noted in the original article[4] and highlighted in a more recent investigation,[58] each of these models is unique and will identify some women at higher risk who will not be identified by the other models. Thus, as noted previously,[4] there may be value to considering the unique features of each model and using more than one for risk estimation in the clinical setting. However, it also is important to identify which subgroups of women may be better served by one model versus another, and it also is a high priority to further refine these models to improve their predictive value.

Although most clinicians do not routinely use risk calculators, every clinician needs to have at least a basic awareness of indications for referral to a genetic counselor. A family history of multiple relatives with breast or ovarian cancer and/or a relative with breast or ovarian cancer diagnosed under age 50 years, on either the paternal or maternal side, should prompt consideration of referral to a genetic counselor.

As noted above, the ACS will initiate the update of the breast cancer screening recommendations for women at increased and high risk in 2016.

Screening for Cervical Cancer

The ACS estimates that 12,990 women will be diagnosed with invasive cervical cancer and that 4120 women will die from the disease in 2016.[19] Cervical cancer incidence and mortality rates have declined since the introduction of the Papanicolaou (Pap) smear in the mid-20th century, and rates continue to decline.[18] For the period from 2003 to 2012, delay-adjusted cervical cancer incidence rates have decreased at an average annual percentage rate of 2.4% per year, and, over the same period, cervical cancer mortality rates have declined at an average annual rate of 0.9%.[18]

In 2012, the ACS, the American Society for Colposcopy and Cervical Pathology, and the American Society for Clinical Pathology issued a joint guideline for cervical cancer screening based on a systematic evidence review and using a collaborative process that included 25 organizations (Table 2).[8] Similar recommendations were released in 2012 by the US Preventive Services Task Force (USPSTF).[59] This screening guideline recommends surveillance strategies and options based on a woman's age, screening history, and her choice of screening tests. Women younger than 21 years should not be screened regardless of their age of sexual initiation, and women at any age should not be screened annually by any screening method. Specifically:

- Screening for cervical cancer should begin at age 21 years. Women ages 21 to 29 years should receive cytology screening every 3 years with either conventional cervical cytology smears or liquid-based cytology. Human papillomavirus (HPV) testing should not be used for screening women in this age group (although it can be used as a reflex test for women diagnosed with atypical squamous cells of undetermined significance [ASC-US]).
- For women ages 30 to 65 years, the preferred approach is cotesting every 5 years with cytology and HPV testing. 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 before ceasing screening, with the most recent test occurring within the last 5 years. Consistent with the 2012 guideline, an HPV-negative ASC-US result should be regarded as negative for the purpose of discontinuing screening.[9]
- The ACS recommends that women with an HPV-negative ASC-US result should return for screening in 3 years rather than 5 years, consistent with the American Society for Colposcopy and Cervical Pathology recommendation.[9]
- Recommended screening practices should not change on the basis of a woman's HPV vaccination status.

In 2014, the US Food and Drug Administration approved one HPV DNA test for primary cervical cancer screening, ie, as a stand-alone test without concomitant cytology testing. Interim clinical guidance has been developed for providers interested in primary HPV testing as a screening approach.[60] The ACS continues to monitor

emerging data and experience as well as the resolution of remaining questions about this screening strategy.

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. In addition, women who have had their cervix removed should not be screened unless they 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 women ages 30 to 65 years for at least 20 years, even if screening extends beyond age 65 years.

Vaccination Against HPV

The ACS currently is updating its HPV vaccine use guideline based on recommendations developed by the Advisory Committee on Immunization Practices (ACIP), a federal advisory committee chartered to provide advice and guidance to the Director of the Centers for Disease Control and Prevention (CDC). ACIP recommendations for the routine use of vaccines are harmonized to the greatest extent possible with recommendations made by national primary care and pediatric professional organizations. The ACIP recommends that routine HPV vaccination be initiated at age 11 or 12 years. The vaccination series can be started beginning at age 9 years. Vaccination is also recommended for females ages 13 through 26 years and for males ages 13 through 21 years who have not been vaccinated previously or who have not completed the 3-dose series. Males ages 22 through 26 years may be vaccinated. The ACIP recommends vaccination of men who have sex with men and immunocompromised persons through age 26 years if not vaccinated previously. HPV vaccination of females is recommended with bivalent vaccine (2vHPV), quadrivalent vaccine (4vHPV) (as long as this formulation is available), or 9-valent vaccine (9vHPV). Vaccination of males is recommended with 4vHPV (as long as this formulation is available) or 9vHPV.[61] The CDC report notes that vaccine effectiveness would decrease with older age and likelihood of previous HPV exposure,[62] and the 2007 ACS guideline concluded that there were insufficient data to recommend for or against universal vaccination beyond the age of 18 years and suggested individualized decision making.[7]

According to the 2014 National Immunization Survey of Teens (NIS-Teen), 60% of US female adolescents ages 13 to 17 years had initiated the HPV vaccination series (ie, had at least one of three shots as recommended for the HPV vaccine), and 39.7% had completed three doses, representing a small increase in each category since 2013.[63] In 2012, the CDC estimated that 84% of unvaccinated girls had missed at least one opportunity to receive the HPV vaccine during a health care encounter. The CDC report notes that, if the HPV vaccine had been administered during health care visits when another vaccine had been received, coverage rates for receiving more than one dose (three doses are recommended) would have reached 92.6%.[64] As the authors noted in the report, both failure to administer the vaccine during health care encounters and failure to address parental misperceptions about the value and need for the HPV vaccine represent missed opportunities for clinicians to educate parents and increase vaccine coverage.

The ACS has partnered with the CDC on two initiatives aimed at increasing HPV vaccination rates and ultimately reducing the incidence of and mortality from HPV-associated cancers and precancerous lesions. The National HPV Vaccination Roundtable is a national coalition of organizations working together to prevent HPV-associated cancers and precancers by increasing and sustaining US HPV vaccination. The HPV VACs (Vaccinate Adolescents Against Cancers) Project focuses on expanding current cancer prevention and early detection interventions in federally qualified health care centers to increase HPV vaccination through improved provider awareness and education and improved system-wide processes. In addition, the ACS is partnering with state health departments and other state-based entities to facilitate system changes that increase the availability and utilization of the HPV vaccine.

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

The ACS estimates that 134,490 new cases of colorectal cancer (CRC) will be diagnosed in women and men and that 49,190 women and men will die from this disease during 2016.[19] CRC incidence and mortality rates have been declining for the past 2 decades, largely attributable to the contribution of screening to prevention and early detection.[65] The guideline for screening and surveillance for the early detection of adenomatous polyps and CRC in average-risk adults was updated in 2008 in an evidence-based consensus process that included the ACS; the US Multi-Society Task Force on Colorectal Cancer (USMSTF), which represents the American College of Gastroenterology, the American Gastroenterological Association, and the American Society for Gastrointestinal Endoscopy; and the American

College of Radiology (Table 2).[14] Recommendations for adults at increased and high risk were last updated in 2001[10]; and, in 2006, the ACS and the USMSTF issued a joint guideline update for postpolypectomy and post-CRC resection surveillance.[12,13] Those guidelines have since been updated by the USMSTF.[66]

In the last update of the guideline, recommended CRC screening tests were grouped into two categories, ie, 1) tests that *primarily* detect cancer, which include the guaiac-based fecal occult blood tests (gFOBT) and the fecal immunochemical tests (FIT)-based fecal occult blood tests (FOBTs) and testing stool for exfoliated DNA (sDNA); and 2) tests that can detect cancer and advanced precursor lesions, which include the endoscopic and radiologic examinations, ie, flexible sigmoidoscopy, colonoscopy, double-contrast barium enema, and computed tomography (CT) colonography (or virtual colonoscopy). This distinction was intended to help primary care physicians support informed decision making and to contribute to public understanding of the features, advantages, limitations, and disadvantages that distinguish these screening tests from one another. Furthermore, the guideline states that, while all recommended tests are acceptable options, prevention of CRC is the greater priority of 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) multitarget stool DNA (mtsDNA) test every 3 years; 3) flexible sigmoidoscopy every 5 years; 4) colonoscopy every 10 years; 5) double-contrast barium enema every 5 years; or 6) CT colonography every 5 years. Single-panel gFOBT in the medical office using a stool sample collected during a digital rectal examination (DRE) is not a recommended option for CRC screening because of its very low sensitivity for advanced adenomas and cancer.[67] For similar reasons, the guideline recommends discontinuing the use of older, lower sensitivity versions of the guaiac test (such as Hemoccult II; Beckman Coulter, Inc, Brea, Calif) in favor of newer, high-sensitivity gFOBT (such as Hemoccult SENSA; Beckman Coulter, Inc), FIT, or the multitarget sDNA test. 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 there must be a commitment to annual at-home testing with adherence to the manufacturer's instructions, or the limited sensitivity observed with one-time testing would make stool testing an inferior choice. In contrast, evidence from RCTs and modeling has shown that a commitment to annual testing with high-sensitivity stool tests can result in a reduced risk of developing CRC and a reduced risk of dying from CRC that is similar to the benefit attained with colonoscopy.[68,69]

The ACS and other organizations recommend more intensive surveillance for individuals at higher risk for CRC.[10,12,13,66,70] Individuals at higher risk for CRC include: 1) individuals with a personal 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, or 4) individuals at significantly higher risk because of a history of inflammatory bowel disease of significant duration, or 5) individuals at significantly higher risk because of a known or suspected presence of one of two hereditary syndromes, specifically Lynch syndrome (hereditary nonpolyposis colon cancer) 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 beginning examinations at an earlier age. The USMSTF also has issued new recommendations for the genetic evaluation and management of Lynch syndrome.[71]

Quality Issues in Screening With Colonoscopy

Nearly 90% of CRC screening in the United States occurs via colonoscopy. Variation in the quality of colonoscopy performance between endoscopists has been described for several years.[72,73] Although collection and reporting on a range of colonoscopy quality indicators has been encouraged by gastroenterology and public health organizations for nearly a decade, thus far, endoscopy practices have been slow to adopt these measures.[74,75]

Factors that are widely accepted as indicators of the quality of colonoscopy include adequacy of the bowel preparation to allow good visualization of the colon lumen and wall; the endoscopic withdrawal time; the cecal intubation rate; and, arguably most important, the adenoma detection rate (ADR). The ADR is defined as the proportion of patients undergoing screening colonoscopy who had one or more adenomas detected. Early iterations of quality standards indicated that endoscopists should identify one or more adenomas in at least 25% of men and 15% of women aged 50 years and older undergoing screening colonoscopy. As data on the actual prevalence of adenomas have accumulated, these standards have been revised; a recent update by gastroenterology organizations recommends a target composite ADR of $\geq$25% (for men, $\geq$30%; for women, $\geq$20%).[76]

Interval cancers are cancers that are diagnosed between the time of a negative screening colonoscopy and the

scheduled time for the next screening colonoscopy; a significant proportion of these cancers arise from lesions that were missed at the time of the index, ie, most recent, colonoscopy.[77,78] Several studies have demonstrated a strong correlation between the average ADR recorded for an individual endoscopist and the likelihood of interval cancers among the patients served by that endoscopist.[77,79,80] Despite the clinical importance of this measure, wide variations in the ADR between individual endoscopists persist.[72]

The first large study to directly correlate CRC outcomes with the ADR examined data on 45,026 screening colonoscopies performed by 186 endoscopists. Forty-two cases of interval CRC were diagnosed in this group. The hazard ratio for an interval CRC was more than 10-fold greater among patients treated by the endoscopists who had the lowest ADRs (<11%) compared with those who had the highest ADRs (>20%). These finding were interpreted as showing that an endoscopist's rate of adenoma detection was an independent predictor of the risk of interval cancer.[80] Results from a second study were even more compelling. Data were analyzed on colonoscopies performed in a large US integrated health delivery organization over a 12-year period (January 1, 1998 through December 31, 2010).[79] The investigators assessed the associations between the ADR and the risks of CRC diagnosed 6 months to 10 years after the index colonoscopy and CRC-related death. They evaluated 314,872 colonoscopies performed by 136 gastroenterologists, whose ADRs ranged from 7.4% to 52.5%, and identified 712 interval colorectal adenocarcinomas and 147 deaths associated with interval CRC. When the gastroenterologists were placed into quintiles based on their ADRs (from the lowest quintile [ADR $\leq$19.06%] to the highest quintile [ADR $\geq$33.51%]), patients who were examined by gastroenterologists in the lowest ADR quintile had nearly twice the risk of being diagnosed with an interval cancer compared with patients who were examined by gastroenterologists in the highest ADR quintile group. In addition, the risk of a fatal interval CRC was 62% lower among patients whose colonoscopy was performed by gastroenterologists in the highest quintile. Each 1% increase in the ADR was associated with a 5% decrease in the risk of a fatal interval CRC.[79]

These and other studies clearly delineate the impact of variations in colonoscopy performance on CRC detection and mortality and reinforce the need for fully implemented colonoscopy quality-assurance programs in all screening environments. It is incumbent on endoscopy centers and individual endoscopists to track these measures, to ensure that feedback and corrective action take place if necessary, and to make data on practice performance available to prospective patients and to referring physicians. A standardized colonoscopy reporting and data system has been published to assist continuous quality-improvement initiatives within and across practices that use colonoscopy.[75] Similarly, primary care clinicians should ask their consulting endoscopists to provide information on colonoscopy quality, or these data should be made available to primary care referral networks, to make evidence-based recommendations about choice of endoscopists. Recommendations on the role that primary care practices can play in contributing to the quality of colonoscopy received by their patients are available.[81]

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 180,890 new cases and 26,120 deaths expected in 2016.[19] Prostate cancer incidence and mortality rates have been declining in both black and white men since the 1990s.[18]

The current ACS guideline for the early detection of prostate cancer was published in 2010[15] and 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 a serum prostate-specific antigen (PSA) test, with or without DRE, after receiving information about the benefits, risks, and uncertainties associated with prostate cancer screening (see Table 4).

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 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 PSA test with or without the DRE (DRE is recommended along with PSA for men with hypogonadism because of 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, and screening should be conducted yearly for men whose PSA

TABLE 4. Core Elements of the Information to Be Provided to Men to Assist With Their Decision About Prostate Cancer Screening (Wolf, 2010[15])

PROSTATE CANCER IS AN IMPORTANT HEALTH CONCERN FOR MEN
• Screening with the prostate-specific antigen (PSA) blood test alone or with both PSA test and digital rectal examination (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, 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 test and DRE may have false-positive or false-negative results, meaning that men without cancer may have abnormal results and get 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 test or DRE require prostate biopsies to determine whether or not the abnormal findings are cancer; biopsies can be painful, may lead to complications like 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 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

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 for prostate cancer. For those with PSA levels between 2.5 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.[15] Factors that increase the risk of prostate cancer include African American race, family history of prostate cancer, increasing age, and abnormal DRE. 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, his risk of high-grade prostate cancer.

Screening for Endometrial Cancer

The ACS estimates that, during 2016, 60,050 women will be diagnosed with endometrial cancer, and 10,470 women will die from this disease.[19] In 2001, the ACS concluded that there was insufficient evidence to recommend screening for endometrial cancer in women at average risk or at increased risk because of a history of unopposed estrogen therapy, tamoxifen therapy, late menopause, nulliparity, infertility or failure to ovulate, obesity, diabetes, or hypertension.[10] 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 for endometrial cancer because of 1) known Lynch syndrome genetic mutation carrier status, 2) substantial likelihood of being a mutation carrier (ie, a mutation is known to be present in the family), or 3) absence of genetic testing results in families with suspected autosomal dominant predisposition to colon cancer should consider beginning annual testing for early endometrial cancer detection at age 35 years. The evaluation of endometrial histology with an endometrial biopsy is still the standard for determining the status of the endometrium.[82] 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, harms, and limitations of testing for early endometrial cancer detection.

Screening for Lung Cancer

Lung cancer is the most common cancer affecting both men and women and will account for an estimated 224,390 new cases in 2016.[19] Lung cancer also is the leading cause of death from cancer in men and women and will account for an estimated 158,080 deaths in 2016, which is approximately 27% of all cancer deaths in the United States.[19]

On the basis of results from the National Lung Screening Trial (NLST)[83] and a systematic evidence review,[84] the ACS issued a new lung cancer screening guideline in 2013.[17] The ACS lung cancer screening guideline emphasizes 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 ages 55 to 74 years (Table 5) and should initiate a discussion about lung cancer screening with those patients who have at least a 30 pack-year smoking history, currently smoke, or have quit within the past 15 years, and are in relatively good health. Core elements of this discussion should include the benefits, uncertainties, and harms associated with screening for lung cancer with low-dose CT (LDCT) (see Table 6). Adults who choose to be screened should

TABLE 5. Eligibility Criteria for the National Lung Screening Trial

Age	55-74 y, with no signs of symptoms of lung cancer
Smoking history	Active or former smoker with a 30 pack-year history (a pack-year is the equivalent of 1 pack of cigarettes per d per y; 1 pack per d for 30 y or 2 packs per d for 15 y would both be 30 pack-years)
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 15 y
General health exclusions	Metallic implants or devices in the chest or back; requirement for home oxygen supplementation; prior history of lung cancer or other lung cancer symptoms

follow the NLST protocol of annual LDCT screening until they reach age 74 years. Chest x-ray 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 and 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, then 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 to such a setting, then the risk of harms associated with lung cancer screening may be substantially higher than the observed risks associated with screening in the NLST, and screening is not recommended. Referring physicians should help their patients identify appropriate settings with this expertise.

Smoking-cessation counseling constitutes a high priority for clinical attention for 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 LDCT lung cancer screening with patients who do not meet the recommended criteria (Table 5). If lung cancer screening is requested, then 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. Where risk seems to approximate or exceed the NLST eligibility criteria in one category but not another, clinicians will need to use their best judgment in deciding whether to engage the patient in a discussion about screening.

The USPSTF's "B" rating of their recommendation for lung cancer screening in 2014 led to coverage for lung cancer screening under the Affordable Care Act; and, in early 2015, the Center for Medicare and Medicaid Services (CMS) determined that the evidence was sufficient to "add a lung cancer screening counseling and shared decision-making visit and, for appropriate beneficiaries, annual screening for lung cancer with LDCT, as an additional preventive service benefit under the Medicare program," contingent on meeting specific coverage criteria, which are extensive and intended to ensure that LDCT lung cancer screening achieves high quality at each of several critical steps. Coverage for Medicare beneficiaries is consistent with the ACS guideline[17] and the USPSTF recommendation,[85] with the exception that coverage extends to age 77 years.[86]

A beneficiary must receive a written order for LDCT lung cancer screening during a lung cancer screening counseling and shared decision-making visit, which must be provided by a physician or qualified nonphysician practitioner. The counseling and shared decision-making visit must include the following elements, which also must be documented in the patient's medical record: 1) determination of

TABLE 6. Key Discussion Points for the Process of Shared Decision Making Related to Screening for Early Lung Cancer Detection With Low-Dose Helical Computed Tomography

• Benefit: Screening with LDCT has been shown to substantially reduce the risk of dying from lung cancer
• Limitations: LDCT will not detect all lung cancers or all cancers early, and not all patients who have a lung cancer detected by LDCT will avoid death from lung cancer
• Harms: There is a significant chance of a false-positive result, which will require additional periodic testing, and, in some instances, an invasive procedure to determine whether or not an abnormality is lung cancer or some nonlung-related, incidental finding; less than 1 in 1000 patients with a false-positive result experience a major complication resulting from a diagnostic workup; death within 60 d of a diagnostic evaluation has been documented but is rare and most often occurs in patients with lung cancer
• Helping individuals clarify their personal values can facilitate effective decision making:
○ Individuals who value the opportunity to reduce their risk of dying from lung cancer and who are willing to accept the risks and costs associated with having a LDCT and the relatively high likelihood of the need for further tests, even tests that have the rare but real risk of complications and death, may opt to be screened with LDCT every year
○ Individuals who place greater value on avoiding testing that carries a high risk of false-positives and a small risk of complications, and who understand and accept that they are at a much higher risk for death from lung cancer than from screening complications, may opt not to be screened with LDCT

LDCT, low-dose helical computed tomography.

eligibility; 2) shared decision making using one or more decision aids that describe benefits and harms of screening, follow-up diagnostic testing, over-diagnosis, false-positive rate, and total radiation exposure; 3) the importance of annual screening, impact of comorbidities, and the ability or willingness to undergo diagnostic tests and therapy; and 4) the importance of smoking cessation or maintaining smoking cessation if the patient already has quit. Current smokers should receive information about tobacco-cessation interventions.[86]

Patients who are appropriate candidates for LDCT lung cancer screening should receive a written order for lung cancer screening with LDCT. For subsequent screening examinations, the written order for LDCT lung cancer screening may be furnished during any appropriate visit with a physician or qualified nonphysician practitioner without repeating the shared decision-making process. Written orders must contain the following information: 1) date of birth; 2) actual pack-year smoking history (number of pack-years); 3) current smoking status, and for former smokers, the number of years since quitting smoking; 4) statement that the beneficiary is asymptomatic (no signs or symptoms of lung cancer); and 5) National Provider Identifier of the ordering practitioner.[86]

Imaging facilities and radiologists also must meet criteria linked to reimbursement. Radiologist qualifications include: 1) board certification or board eligibility with the American Board of Radiology or equivalent organization, 2) documented training in diagnostic radiology and radiation safety, 3) involvement in the supervision and interpretation of at least 300 chest CT acquisitions in the past 3 years, and 4) documented participation in continuing medical education in accordance with current American College of Radiology standards. Radiology imaging facilities that provide LDCT lung cancer screening will need to: 1) meet dose and technical standards related to the LDCT examination; 2) use a standardized lung nodule identification, classification and reporting system; 3) make smoking-cessation interventions available to current smokers; and 4) collect and submit data to a CMS-approved registry for each LDCT lung cancer screening performed. CMS has specified minimum data elements that will be collected to measure adherence to quality-assurance standards and for program evaluation.[86]

Testing for Early Ovarian Cancer Detection

Although the annual incidence of ovarian cancer is low compared with that for breast cancer and precursor lesions of the cervix, it is the most lethal of the gynecologic cancers.[18] Approximately 22,280 women will be diagnosed with ovarian cancer in 2016, and 14,240 will die from the disease.[19] Fewer than half of women diagnosed with ovarian cancer survive longer than 5 years; and, although the 5-year survival of localized ovarian cancer is greater than 90%, only 15% of all cases are diagnosed with localized disease.[18]

Diagnostic methods for ovarian cancer that have been considered as potential screening tests include pelvic examination, cancer antigen 125 (CA 125) antigen as a tumor marker, transvaginal ultrasound (TVU), and, potentially, multimarker panels and bioinformatic analysis of proteomic patterns. However, thus far, the performance of these tests, alone or in combination, for the early detection of ovarian cancer has been poor. The sensitivity and specificity of pelvic examination for the detection of asymptomatic ovarian cancer are poor and do not support a recommendation for physical examination as a screening method. CA 125 has limited sensitivity and specificity; ie, although CA 125 levels are increased in many women with ovarian cancer, only 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.[87-89] TVU is capable of detecting small ovarian masses and may distinguish some benign masses from some malignant adnexal masses, although it still poorly predicts which masses are cancers and which are because of benign disease. As an independent test, ultrasound has shown poor performance in the detection of ovarian cancer in average-risk or high-risk women.[90] 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 who have ovarian cancer compared with women who do not have ovarian cancer, but this work is still experimental, and, however promising, prospective validation studies will be required.[91,92]

Currently, no organization recommends screening average-risk women for ovarian cancer. Based principally on results from the Prostate, Lung, Colorectal, and Ovarian Cancer (PLCO) study, 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.[93]

The UK Collaborative Trial of Ovarian Cancer Screening (UKCTOCS) was launched in 2001 to assess the efficacy of a multimodal screening strategy (MMS) for ovarian cancer screening that included annual CA 125 screening using a risk of ovarian cancer algorithm (ROCA) with TVU as a second-line test versus annual screening with TVU only, and a third group that received usual care.[94] The ROCA measures changes in CA 125 over time rather

TABLE 7. Prevalence (%) of Recent Cancer Screening Examinations Among US Adults: National Health Interview Survey, 2013[a]

	2005[a]		2008[a]		2010[a]		2013		ABSOLUTE % CHANGE		
CANCER SCREENING	%	SE	%	SE	%	SE	%	SE	2013-2005	2013-2008	2013-2010
Colorectal cancer (adults aged ≥50 y)											
Endoscopy[b]	46.8	0.6	53.2	0.6	56.4	0.6	55.9	0.5	9.1	2.7	−0.5
FOBT home kit[c]	12.1	0.4	10.0	0.4	8.8	0.3	7.8	0.3	−4.3	−2.2	−1.0
FOBT or endoscopy[d]	43.1	0.6	50.2	0.6	59.1	0.6	58.6	0.5	15.5	8.4	−0.5
Breast cancer (women aged ≥40 y)											
Mammogram[e]	51.2	0.6	53.0	0.7	50.8	0.7	51.3	0.7	0.1	−1.7	0.5
Cervical cancer (women 21-65 y)											
Pap test[f]	85.2	0.4	84.4	0.5	83.0	0.5	80.8	0.5	−4.4	−3.6	−2.2
Prostate cancer (men aged ≥50 y)											
PSA[g]	40.7	0.9	44.1	1.0	41.3	0.9	34.5	0.8	−6.2	−9.6	−6.8

FOBT, fecal occult blood test; Pap, Papanicolaou; PSA, prostate-specific antigen; SE, standard error. [a]Prevalence estimates for 2005, 2008, and 2010 are shown here to describe differences in the absolute percentage change in cancer screening use with respect to most recent data for 2013. Prevalence is weighted and age-adjusted using the 2000 Census. [b]Endoscopy includes recent sigmoidoscopy within the preceding 5 years or colonoscopy within the preceding 10 years. [c]This includes recent FOBT using a home test kit performed within the preceding year. [d]This includes recent FOBT using a home test kit performed within the preceding year OR sigmoidoscopy within the preceding 5 years or colonoscopy within the preceding 10 years. [e]These are women aged ≥40 years who had a mammogram within the preceding year. [f]These are women with intact uteri who had a Pap test within the preceding 3 years. Estimates by education are among women ages 25 to 65 years. [g]This includes PSA tests within the past year for men who had not been told they had prostate cancer. Source: National Health Interview Survey 2005, 2008, 2010, and 2013 (National Center for Health Statistics, Centers for Disease Control and Prevention, Atlanta, GA).

than with a single cutoff point and has shown improved sensitivity for smaller tumors without measurably increasing the false positive rate. In 2015, long-awaited results of the UKCTOCS were published. The primary analysis showed a non-statistically significant 15% ovarian cancer mortality reduction in the MMS group and 11% in the TVU group compared with the usual care group; however, a pre-specified analysis comparing the MMS group with the usual care group eliminating the prevalent cases (i.e., women diagnosed with ovarian cancer at the time of the first screening exam) showed a statistically significant 20% ovarian cancer mortality reduction. Jacobs, et al. caution that the study requires further followup, but noted that these results may hold promise for an effective ovarian cancer screening strategy that overcomes some of the downsides of previous approaches.[95] In an earlier publication, Menon and colleagues reported interim results comparing the performance of a single biomarker threshold with the ROCA. In the UKCTOCS, women were triaged based on CA 125 results interpreted through the ROCA: normal-risk women were returned to annual screening; intermediate-risk women underwent repeat CA 125; and women at elevated risk underwent repeat CA 125 and TVU. Women with persistently elevated ROCA scores underwent clinical evaluation. On the basis of 296,911 women-years of annual screening, 640 women had undergone surgery, and 133 (21%) had been diagnosed with primary, invasive epithelial ovarian or tubal cancers. The sensitivity and specificity of the MMS for detection of ovarian cancer were 85.8% and 99.8%, respectively, while single CA 125 threshold approaches of >35, >30, and >22 U/mL would have had sensitivity of 41.3%, 48.4%, and 66.5%, respectively. Compared with the fixed cutoff strategies, the MMS based on the ROCA doubled the number of screen-detected ovarian cancers. Determination of the efficacy of the use of an MMS strategy to screen for ovarian cancer awaits additional publications from UKCTOCS.

In 1994, a National Institutes of Health Consensus Panel concluded that women who had 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), because these women have a 3% chance of being positive for an ovarian cancer hereditary syndrome.[96] The panel further advised that women with a known hereditary ovarian cancer syndrome, such as breast-ovarian cancer syndrome or site-specific ovarian cancer syndrome associated with mutations on *BRCA1* and *BRCA2*, or hereditary nonpolyposis colon cancer Lynch II syndrome 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

TABLE 8. Prevalence (%) of Recent Cancer Screening Examinations Among US Adults by Race and Ethnicity, Health Insurance Coverage, and Education Level: National Health Insurance Survey, 2013[a]

	RACE AND ETHNICITY								HEALTH INSURANCE				EDUCATIONAL LEVEL							
	WHITE, NON-HISPANIC		BLACK, NON-HISPANIC		HISPANIC		ASIAN		YES		NO		SOME HIGH SCHOOL OR LESS		HIGH SCHOOL DIPLOMA OR GED		SOME COLLEGE/ ASSOC DEGREE		COLLEGE GRADUATE	
CANCER SCREENING	%	SE	%	SE	%	SE	%	SE	%	SE	%	SE	%	SE	%	SE	%	SE	%	SE
Colorectal cancer (adults aged ≥50 y)																				
Endoscopy[b]	58.0	0.6	56.5	1.4	41.5	1.4	48.6	2.3	58.8	0.6	20.3	2.6	40.0	1.2	52.6	0.9	58.0	1.0	65.4	0.9
FOBT home kit[c]	7.4	0.3	8.5	0.6	8.4	0.8	10.9	1.3	8.1	0.3	2.2	0.4	6.8	0.7	7.3	0.6	8.6	0.6	7.9	0.5
FOBT or endoscopy[d]	60.5	0.6	59.4	1.4	44.9	1.4	53.2	2.5	61.6	0.6	21.9	2.7	43.1	1.3	55.2	0.9	60.7	1.0	68.0	0.9
Breast cancer (women aged ≥40 y)																				
Mammogram[e]	52.1	0.8	52.6	1.8	45.9	1.7	50.3	2.5	54.8	0.7	22.3	2.3	38.7	1.7	47.7	1.3	51.9	1.2	59.5	1.2
Cervical cancer (women 21-65 y)																				
Pap test[f]	82.8	0.6	82.3	1.1	77.1	1.1	70.6	2.0	85.2	0.5	60.6	1.3	68.5	1.6	75.7	1.1	83.4	0.9	87.3	0.8
Prostate cancer (men aged ≥50 y)																				
PSA[g]	36.5	0.9	32.9	2.2	24.3	2.5	26.3	3.7	36.2	0.8	20.2	5.8	23.7	1.9	28.6	1.4	35.7	1.5	43.1	1.5

Assoc, associate; FOBT, fecal occult blood test; GED, general educational development; Pap, Papanicolaou; PSA, prostate-specific antigen; SE, standard error. [a]Prevalence is weighted and age-adjusted using the 2000 Census. [b]Endoscopy includes sigmoidoscopy within the preceding 5 years or colonoscopy within the preceding 10 years. [c]This includes recent FOBT using a home test kit performed within the preceding year. [d]This includes recent FOBT using a home test kit performed within the preceding year OR sigmoidoscopy within the preceding 5 years or colonoscopy within the preceding 10 years. [e]These are women aged ≥40 years who had a mammogram within the preceding year. [f]These are women with intact uteri who had a Pap test within the preceding 3 years. Estimates by education are among women ages 25 to 65 years. [g]This includes PSA tests within the past year for men who had not been told they had prostate cancer. Source: National Health Interview Survey 2005, 2008, 2010, and 2013 (National Center for Health Statistics, Centers for Disease Control and Prevention, Atlanta, GA).

these hereditary syndromes are estimated to represent only 0.05% of the female population, they have a 40% estimated lifetime risk of ovarian cancer. The National Comprehensive Cancer Network's latest statement on genetic/familial high-risk assessment for breast and ovarian cancer states that, although there "may be circumstances where clinicians find screening helpful, data do not support routine ovarian screening." With these caveats in mind, the National Comprehensive Cancer Network notes that TVU and CA 125 may be considered at the discretion of the physician for women starting at ages 30 to 35 years for women at high risk.[97]

Surveillance of Cancer Screening Rates: Colorectal, Breast, Cervical, and Prostate Cancers

In this update, we provide the most recent national screening data from the NHIS, a nationally representative, in-person, household survey that includes questions regarding cancer screening every 2 to 3 years. The most recent data available are from the 2013 NHIS and were previously presented in our 2015 review, but they are included here as a convenience to the reader. Table 7 displays cancer screening prevalence in 3 time periods (2005-2013, 2008-2013, and 2010-2013) and the extent of change, as expressed as the percentage of increase or decrease, between these time periods. Between 2005 and 2013, CRC screening increased by 15.5%, whereas cervical and prostate cancer screening declined by 4.4% and 6.2%, respectively. There has been little change in breast cancer screening since 2005. Given recent changes in the ACS breast cancer screening guideline,[5] we also estimated breast cancer screening rates by age group in our current review. In 2013, receipt of mammography increased with age: 43.1%, 50.1%, 56%, and 53.5% of women ages 40 to 44, 45 to 49, 50 to 54, and ≥55 years, respectively, had (or reported having) received a mammogram in the past year; and 68.9% of women aged ≥55 years received a mammogram in the past 2 years. Furthermore, despite the lack of recommendation for breast cancer screening or baseline mammography before women turn 40, approximately 14.5% of women ages 35 to 39 years reported receiving a mammogram in the past year, and nearly a third (31.5%) reported ever having received a mammogram. In Table 8, we display cancer screening prevalence by race and ethnicity and 2 socioeconomic indicators (having health insurance

and educational attainment) that are strongly associated with access to and use of preventive medical services. In 2013, CRC screening rates ranged from 44.9% in Hispanics to 60.5% in non-Hispanic whites and were nearly 3 times as high among the insured (61.6%) compared with the uninsured (21.9%). The proportion of women receiving mammographic screening ranged from 45.9% in Hispanic women to 52.6% in non-Hispanic black women and was twice as high in the insured (54.8%) compared with the uninsured (22.3%). Cervical cancer screening rates ranged from 70.6% in Asian women to 82.8% in non-Hispanic white women and were 25% higher in insured women (85.6%) compared with uninsured women (60.6%). There is a paucity of data on LDCT for lung cancer screening in community practice, although a study using 2010 NHIS data estimated that 1.8% of current higher risk smokers and 4.4% of high-risk former smokers (who quit in the past 15 years) had undergone LDCT for lung cancer screening in the past year.[98,99] It is important to note that, while the NHIS is a nationally representative and useful tool for measuring progress toward cancer screening, there are several limitations to sample surveys, which include respondents' recall bias and tendency to overestimate screening practices as well as nonresponse bias, which may be partially, but not fully, accounted for in the survey weighting procedures.[100] Thus, in most instances, these data likely overestimate the rate of recent cancer screening.

Discussion

Achieving the fullest potential of cancer screening benefits enormously from the systems within which each of the key steps that need to occur is governed by rules, roles, relationships, and oversight. Without a system, screening will not be as effective as it might be. Without the assurance of standardized, timely, and routine risk assessment, we fail to identify and properly triage adults at high risk. Without reimbursement and a consistent expectation of competent discussions about risk and what to expect from screening, these conversations and, when appropriate, informed and shared decision making commonly do not occur; and, when they do occur, the content is inconsistent and incomplete. Without reminder and outreach systems, a majority of the target population is not screened according to recommendations. Without systems to ensure complete diagnostic evaluation and enrollment in treatment, many individuals with positive test results do not receive timely high-quality follow-up. Without centralized assessment of technical quality of screening (which does exist for mammography and cytology screening examinations), there is no assurance that every screening examination has a high probability of meeting a minimum standard of quality. Without registries and routine review of screening outcomes, the health professionals involved in screening have little opportunity to assess their performance; and, thus, they have neither the reinforcement that their performance meets high standards nor the motivation to seek additional training when improvement is needed. Without centralized data linking patient information, screening history, and screening outcomes, we don't have the opportunity to measure the effectiveness of screening programs and identify opportunities to improve the process and to achieve better outcomes.

If reliable, valid, comprehensive approaches to screening were in place, the CMS would not have needed to link reimbursement for lung cancer screening provided to Medicare beneficiaries to a complex process of documentation to ensure that adults referred to screening have met pre-established criteria for eligibility, have undergone a process of informed decision making, have been offered smoking cessation (if they are current smokers), and that the imaging facility and professional staff meet quality standards, participate in a data registry, and meet standards for reporting the findings of screening examinations to patients and referring physicians. While this new process is extraordinary and, at first, may seem burdensome, it imposes requirements for quality standards that would be routine practice if cancer screening were organized. These requirements undoubtedly will influence the quality of lung cancer screening for the eligible high-risk population younger than age 65 years who are covered by private health plans and may eventually stimulate similar systems-like elements for other cancer screening. ■

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